Proceedings of
The 23rd International Conference of Public Health Sciences
“Sustainable Public Health: Innovations for Global Impact”

Tuesday 3rd October 2023
Mandarin Ballroom, Mandarin Hotel, Sam Yan, Rama IV Rd., Bangkok, Thailand

Organized by:
College of Public Health Sciences, Chulalongkorn University, Thailand (Host)
United Nations Office for Project Services – Myanmar (Co-Host)
Universitas Negeri Malang – Indonesia (Co-Host)
Proceedings of
The 23rd International Conference of
Public Health Sciences

“Sustainable Public Health: Innovations for Global Impact”

October 3, 2023
A Virtual Conference
Mandarin Ballroom, Mandarin Hotel, Bangkok, Thailand

College of Public Health Sciences, Chulalongkorn University, Thailand
United Nations Office for Project Services, Myanmar
Universitas Negeri Malang, Indonesia
Chulalongkorn University aims to be a prominent national institution with global recognition. Its primary focus is on producing knowledge and innovation that are crucial for the creative and sustainable development of Thai society. To achieve this vision, the university consistently provides support to all of its faculties, institutes, colleges, and other entities in carrying out a range of academic activities, including in-class teaching, research, and conferences, such as the one we are gathered for today. With a primary focus on graduate-level teaching in the field of public health and public health sciences, the College of Public Health Sciences is a cornerstone of academia. It employs a robust mechanism that integrates research in both public health and public health sciences in response to research questions related to health and public health issues in Thailand and the broader region. Recognizing the vital role of the university in disseminating knowledge through academic services to society, the College is committed to its mission. As part of this commitment, the College annually organizes the Public Health Sciences International Conference, a platform for scholarly exchange and dissemination of cutting-edge research. Today marks the 23rd anniversary of this significant event, highlighting our dedication to advancing knowledge and fostering collaboration in the field of public health and public health sciences.
Welcome Message

Prof. Chitlada Areesantichai, Ph.D.
Chairperson, Executive Committee, 23rd ICCPHS
Dean
The College of Public Health Sciences, Chulalongkorn University, Thailand
https://www.cphs.chula.ac.th/

On behalf of College of Public Health Sciences, Chulalongkorn University, I would like to welcome you to the 23rd International Conference of Public Health Sciences for the year 2023 with the Theme “Sustainable Public Health: Innovations for Global Impact”.

In the pursuit of human betterment through knowledge and innovation, every year the College holds a Public Health Sciences academic conference. Today marks our 23rd anniversary.

The College of Public Health Sciences focuses on postgraduate education in the field of public health and public health sciences. It combines research both in public health and public health science to address research questions about health and public health issues within Thailand and the region.

For today’s conference, the College provides a range of academic activities, including:

▪ The 20th Professor Emeritus Charas Suwanwela, M.D. Lecture on “Thailand and Global Health” where the College is honored to have Dr. Nopporn Cheanklin, Former Director, Health System Research Institute, Thailand as the keynote speaker;
  ▪ A series of lectures on many issues pertaining to health;
  ▪ Presentations for research and academic work both in oral presentation and poster presentation;
  ▪ Showing of products, medical & public health sciences technology, as well as related services;
  ▪ Awards for individuals or organizations in recognition of their contribution to the field of public health sciences.

The conference is a one full – day activity:

▪ Our conference participants are policy-makers, academicians, researchers, lecturers, graduate students, and general public, totaling 284 people;
▪ The guest lecturers are from the College of Public Health Sciences, and from partner organizations: (This year Universitas Negeri Malang – Indonesia and Access to Health Fund’s Takeda Programme – United Nations Office of Project services – Myanmar)
  ▪ We have 54 oral presentations and 17 poster presentations;
  ▪ Our sponsors are organizations that support this conference’s activities.
Dr. Aye Yu Soe  
Access to Health Fund,  
United Nations Office for Project Services, Myanmar

It is my special honor to attend this conference on behalf of the Access to Health Fund managed by the United Nations Office for Project Services. First and foremost, I would like to express our sincere gratitude to the College of Public Health Sciences, Chulalongkorn University for extending an invitation to us to participate in this International Conference and for providing us with the opportunity to present our dedicated work in Myanmar over the past few years.

For us as a health fund, and for our partners who implement the health programs in remote and hard-to-reach areas of Myanmar, this conference is a great opportunity to present our work to an international audience, learn about all the innovative work of the international community and get exposure to an international audience.

When we look at Myanmar, it is clear that the past few years have presented extraordinary challenges. We have struggled to deliver quality healthcare to vulnerable populations in Myanmar, especially in hard-to-reach areas. Myanmar is a neighboring country to Thailand and is situated in South East Asia—disease epidemiology and other public health challenges are more or less the same. However, in addition to these challenges, there is active conflict in Myanmar and the situation for health professionals is very challenging.

For the Access to Health Fund, our mission is to improve health outcomes for vulnerable populations residing in Myanmar, particularly in the areas of maternal, newborn, and child health, nutrition, as well as the management of infectious diseases such as HIV, tuberculosis, and malaria. The role of community and ethnic health workers has become increasingly crucial in ensuring that quality healthcare reaches these vulnerable populations.

By bringing health services to people who may otherwise have no access to them, and by strengthening local health systems that serve these populations, we stay committed to continue our work throughout the crisis that Myanmar is currently facing. At this conference, we aim to present one of our health programs that focuses on supporting local health providers to build sustainable systems for healthcare provision, ensuring that communities continue to benefit long after the program ends.

The theme that brings us together at this conference, ‘Sustainable Public Health: Innovations for Global Impact,’ presents an opportunity for all of us to learn from each other—in our different capacities as academics, scholars, and program implementers—and we would like to exchange our knowledge and experience in the different academic sessions organized by the school today. Thank you very much again. It is an honor and pleasure to attend this special occasion.
I am Assoc. Prof. Dr. Sapto Adi represents my faculty, Faculty of Sport Science Universitas Negeri Malang, One of the Public Universities in Indonesia as one of the co-hosts of this remarkable gathering, the 23rd International Conference of Public Health Sciences. Together with my fellow co-hosts, we share the privilege and excitement of welcoming you all to this inspiring event. This is our 1st event to participate in the College of Public Health Science in International conference. Over the following year, we will explore the unique opportunity to learn and grow together, united by a common purpose.

The theme of our conference, “Sustainable Public Health: Innovations for Global Impact” encapsulates the essence of what we aim to achieve. In an increasingly interconnected world, our collective well-being is intricately linked to the health of populations across borders. It is not just a matter of local concern but a global imperative.

As we embark on this exciting journey together, please know that your active participation is the beating heart of this conference. Your inquiries, interactions, and enthusiasm will impact the discussions and outcomes of the following days.

I would like to extend our heartfelt appreciation to the individuals, organizations, and partners whose support and dedication have made this conference possible. Your faith in the power of collaboration and information sharing is genuinely commendable.

Let us seize this moment to connect, learn, and create meaningful change. Together, we can fully realize the immense potential of our combined intelligence and creativity.

Thank you, and I wish you all an enriching, productive, and memorable experience.
The 23rd International Conference of Public Health Sciences

Organizers

- College of Public Health Sciences, Chulalongkorn University, Thailand
- United Nations Office for Project Services, Myanmar
- Universitas Negeri Malang, Indonesia

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- Nuchanad Hounnaklang, Ph.D.
- Onuma Zongram, Ph.D.
- Ms. Kunyanin Sridachati
- Ms. Surada Suwannapak

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- Farah Paramita, S.Gz., M.P.H.
- Lucky Radita Alma, S.K.M. M.P.H.
Nurnaningsih Herya Ulfah, Ph.D.
Ms. Khaung Myitzu Hane

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Prepared by
Ms. Kunyanin Sridachati
Ms. Surada Suwannapak

Cover Designed by Ms. Kunyanin Sridachati
# Conference Program

**The 23rd International Conference of Public Health Sciences**  
**“Sustainable Public Health: Innovations for Global Impact”**  
**Tuesday 3rd October 2023**  
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<td>08.00 – 08.30</td>
<td>Registration</td>
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<tr>
<td>08.30 – 09.30</td>
<td>Opening Session</td>
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By **Professor Chitlada Areesantichai, Ph.D.**  
Dean, College of Public Health Sciences, Chulalongkorn University, Thailand

**Mr. Oren Ginzburg,**  
Fund Director, Access to Health Fund, United Nations Office for Project Services, Myanmar

**Sapto Adi, Ph.D.**  
Dean, Public Health Department, Faculty of Sport Science, Universitas Negeri Malang, Indonesia

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**Welcome Remarks**

By **Professor Bundhit Euarporn, Ph.D.**  
President, Chulalongkorn University

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**Opening Remarks**

By **Professor Pirom Kamolratanakul, M.D.**  
Chairperson, Chulalongkorn University Council

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**Outstanding Awards Ceremony**

**2023 Distinguished College of Public Health Sciences Researcher Award**  
under the Professor Emeritus Charas Suwanwela, M.D. Fund

Presented by **Professor Emeritus Charas Suwanwela, M.D.**

**2023 Distinguished Award for Thai Traditional Medicine**  
under the Prince Krom Luang Wongsadhirajasant Fund

Presented by **Professor Emeritus Wongkulpat Snidvongs, M.D.**

**2023 Distinguished Award for Substance Abuse, Alcohol & AIDS**  
under the Associate Professor Vichai Poshyachinda, M.D. Fund
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<td>09.30 – 10.00</td>
<td>The 20th Professor Emeritus Charas Suwanwela, M.D. Lecture: “Thailand and Global Health”</td>
<td>By Nopporn Cheanklin, Ph.D. Former Director, Health System Research Institute, Thailand</td>
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<td></td>
<td>Moderator: Professor Sathirakorn Pongpanich, Ph.D.</td>
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<td>10.00 – 10.30</td>
<td>Coffee Break</td>
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<td>10.30 – 12.00</td>
<td>Symposium: (Main Room)</td>
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<td></td>
<td>Topic I: Contextualizing Sport Psychology in South East Asia: Evidence from a Qualitative Study on Indonesian Elite Athlete Psychosocial Demands</td>
<td>By Kurniati Rahayuni, Ph.D. Universitas Negeri Malang – Indonesia</td>
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<td>Moderator: Associate Professor Wattasit Siriwong, Ph.D.</td>
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<td>Topic II: Enhancing the Capacity of Frontline Local Health Organizations to Bring Health Services to Vulnerable Populations in Shan State, Myanmar</td>
<td>By Dr. Kyaw Htin Soe Access to Health Fund’s Takeda Programme – Myanmar</td>
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<td>Moderator: Associate Professor Nutta Taneepanichskul, Ph.D.</td>
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<td>Topic III: Chula Health Street a University Treasure</td>
<td>By Professor Chitlada Areesantichai, Ph.D. College of Public Health Sciences, Chulalongkorn University</td>
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<td>Moderator: Assistant Professor Pramon Viwattanakulvanid, Ph.D.</td>
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<td>12.00 – 13.00</td>
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<td>13.00 – 14.15</td>
<td>Outstanding Award oral Presentation (Main Room)</td>
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<td>13.00 – 13.15</td>
<td>Presentation 1: Development of A Rehabilitation Treatment Model for Drug Patients with The Participation of the Prang Ku District Community, Sisaket Province</td>
<td>By Miss Panom Sriyongyod Department of Psychiatry and Drug Dependence Prangku hospital</td>
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<td>13.15 – 13.30</td>
<td>Presentation 2: Harm Reduction for People Who Use Drugs by Raks Thai Foundation</td>
<td>By Raks Thai Foundation</td>
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| 13.30 – 13.45 | Presentation 3: Conservation and Promotion of Thai Traditional Medicine Wisdom | By Mr. Sawat Jitprom  
The Club President of the Local Folk Doctors and Thai Traditional Medicine Practitioners, Phatthalung Province |
| 13.45 – 14.00 | Presentation 4: Innovation–Driven Enterprise | By Withaya Chanchai, Ph.D., CRCST  
Head of the Public Health Department in the Major of Occupational Health and Safety program, Faculty of Medicine, Siam University, and Founder of Healthmedic Co., Ltd |
| 14.00 – 14.15 | Presentation 5: Innovative Therapeutic Agents Derived from Natural Products for a Better Life | By Assistant Professor Anchalee Prasansuklab, Ph.D.  
Lecturer, College of Public Health Sciences, Chulalongkorn University  
Chairperson: Assistant Professor Montakarn Chuemchit, Ph.D.  
Co-chairperson: Associate Professor Kanchana Runghishirunrat, Ph.D. |
<p>| 14.15 – 14.30 | Coffee Break | |
| 14.30 – 16.30 | Oral and Poster Presentation (4 Breakout Room) | |
| | Breakout Room 1 (Main Room): Oral Presentation | (6 minutes presentation 2 minutes Q&amp;A) |
| Presentation 1.1 | Efficacy of Multilingual Colorectal Cancer Printable Educational Materials in a Multicultural Setting: Malaysia (OP3) | By Nariza Alysa Azryn |
| Presentation 1.2 | Projection of Diabetes Mellitus Prevalence and Mortality till 2045 in Indonesia: A Dynamic Modeling Based on Risk Factors and Prevention and Control Programs (OP15) | By Mugi Wahidin |
| Presentation 1.3 | Medication Adherence in Hypertensive Patients with Poly-Pharmacy in Malang, East Java, Indonesia (OP19) | By Nurma Afiani |
| Presentation 1.4 | Smoking Behavior of the Elderly Population: Analysis of 2020 Susenas Data (OP28) | By Margareth Maya P. Naibaho |
| Presentation 1.5 | Impact of COVID-19 Outbreak Control on Diabetes and Hypertension Screening in Thailand (OP41) | By Bumi Herman |
| Presentation 1.6 | Phenomenological Study: Breast Cancer Survivors’ Experience to Improving Quality of Life (OP46) | By Della Zulfa Rifda |
| Presentation 1.7 | Preliminary Survey on Factors Influencing Pre-Exposure Prophylaxis (PrEP) Usage among Men Who Have Sex with Men (MSM) in Yangon, Myanmar (OP49) | |</p>
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<th>Presentation 1.8</th>
<th>Ease of Cigarette Accessibility Correlates with Students’ Smoking Initiation Behavior in Kuningan Indonesia (OP50)</th>
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<td>Arkar Min Khant</td>
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<th>Presentation 1.9</th>
<th>Pentahelix Collaboration in Stunting Prevention among School-Age Children in Sumedang, West Java, Indonesia (OP1)</th>
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<td>By</td>
<td>Isti Kumalasari</td>
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<th>Presentation 1.10</th>
<th>Quality of Care for Children Under Five with Malaria Using IMCI at Public Health Center: A Systematic Review (OP53)</th>
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<th>Preliminary Survey on Knowledge, Attitudes, and Practices about Indoor Air Pollution among Myanmar Residents (OP31)</th>
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<td>Nachaphun Denijs</td>
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<th>Presentation 1.13</th>
<th>Overcoming Health System Disruption through Telemedicine: A Social Media-Based Qualitative Study of Telemedicine in Myanmar from March 2020 to December 2022 (OP34)</th>
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<td>By</td>
<td>Aye Nyein Ei</td>
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**Chairperson:** Assistant Professor Anchalee Prasansuklab, Ph.D.  
**Co-chairperson:** Nurnaningsih Herya Ulfah, Ph.D  
**Committee:** Nuchanad Hounnaklang, Ph.D.

**Breakout Room 2: Oral Presentation**  
(6 minutes presentation 2 minutes Q&A)

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<tr>
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<th>Socioeconomic Difference of Husband’s Involvement in Antenatal Care in Rural Indonesia (OP2)</th>
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<th>Antenatal CareMediates the Association Between Unintended Pregnancy and Low Birth Weight Among Millennials in Rural Indonesia: Husband Support Matters (OP5)</th>
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<th>Presentation 2.3</th>
<th>Correlates of Early Initiation of Breast Feeding and Prelacteal Feeding: A Cross-Sectional Study in Sindh Province of Pakistan (OP7)</th>
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<td>Ramesh Kumar</td>
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<th>Presentation 2.4</th>
<th>Child Marriage and Its Association with Maternal Healthcare Utilization in Indonesia (OP13)</th>
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<th>Presentation 2.5</th>
<th>Profile and Determinants of Low Birth Weight [LBW] Infants in Indonesia: An Analysis of The National Socio-economic Survey 2021 (OP17)</th>
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<td>2.6</td>
<td>Prevalence and sociodemographic correlates of intimate partner violence in East Java, Indonesia (OP24)</td>
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<td>Contraceptive Use among Older Married Women aged 36-49 years in Indonesia (OP35)</td>
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<td>Intimate Partner Violence against Myanmar Women Migrant Workers in Bangkok, Thailand (OP39)</td>
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<td>Factors Associated with Knowledge, Attitudes, and Self-efficacy of Breastfeeding among Myanmar Migrant Pregnant Mothers in Samut Sakhon Province, Thailand (OP40)</td>
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<td>2.11</td>
<td>The Influence of Client Satisfaction on Recommendations Among Abortion Seekers at PPAT, Thailand (OP52)</td>
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<td>2.12</td>
<td>A Qualitative Study on Adolescents Lifestyles Related to Stunting Prevention (OP54)</td>
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<td>2.13</td>
<td>Applying International Technical Guidance on Sexuality Education to Design Activity and Sound Book for Kindergarten Students (OP22)</td>
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**Committee:**
- Chairperson: Assistant Professor Tepanata Pumaiibool, Ph.D.
- Co-chairperson: Mika Vernicia Humairo, S.K.M., M.P.H
- Committee: Associate Professor Nutta Taneepanichskul, Ph.D.
- Committee: Onuma Zongram, Ph.D.

**Breakout Room 3: Oral Presentation**
(6 minutes presentation 2 minutes Q&A)

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<tr>
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<tr>
<td>3.1</td>
<td>Ethnomycological Survey on the Higaonon Tribe of Lugait, Misamis Oriental, Philippines (OP9)</td>
<td>Genevie P. Pinton</td>
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<td>Ethnomycological Survey of Wild Mushroom Species Utilized by The Subanen Tribe in Selected Barangays in Tangub City, Misamis Occidental, Philippines (OP10)</td>
<td>Sheila Marie Y. Plimaco</td>
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<td>3.3</td>
<td>The Association of Ambient Air Pollutants with COPD and Lung Cancer in Upper Northern Thailand during 2013-2022 (OP11)</td>
<td>Pachara Sapbamrer</td>
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<tr>
<td>Presentation</td>
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<td>3.4</td>
<td>The Occurrence and Genomic Characteristics of The BlaIMI-1 Carbapenemase-producing Enterobacter Cloacae Complex Retrieved from Natural Water Sources in Central Thailand (OP12)</td>
<td>By Wipawee Songsaeng</td>
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<td>3.5</td>
<td>Development of Aerosol Spray Against Genetic Fipronil- and Pyrethroid-resistant Aedes Aegypti Mosquitoes in Dengue-risk Areas in Thailand (OP33)</td>
<td>By Jakkrawarn Chompoosri</td>
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<td>3.6</td>
<td>Prostaglandin I2 Inhibit Platelet Activation and Preserve Ultrastructure during Platelet Isolation by Centrifugation (OP16)</td>
<td>By Paradee Unchaleevilawan</td>
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<td>3.7</td>
<td>Climate Change Anxiety: Psychological Responses to Climate Change in New Students in Universitas Negeri Malang, Indonesia (OP20)</td>
<td>By Ikhwanul Ihsan Armalid</td>
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<td>3.8</td>
<td>Laundry Waste Treatment for Decreasing BOD Levels using the Household Filtration Model in Malang City (OP21)</td>
<td>By Mika Vernicia Humairo</td>
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<td>3.9</td>
<td>The Expression of miR-30b-5p during Erythropoiesis (OP27)</td>
<td>By Sittichok Sonkamkaew</td>
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<td>3.10</td>
<td>Curcuminoid analogs as the hemoglobin F inducer (OP30)</td>
<td>By Jirarud Kenkit</td>
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<td>3.11</td>
<td>Social Relationships and Connectedness of Older Adults in Urban Aging Society: Are Community Participant and Health Condition Influence? (OP38)</td>
<td>By Resti Pujihasvuty</td>
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<td>3.12</td>
<td>Cadmium, Lead, and Mercury levels in Vivipara Angularis Muller Muscles and Sediments of Lake Mainit at Jabonga, Agusan del Norte (OP32)</td>
<td>By Ethel M. Galliguez</td>
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<td>3.13</td>
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<td>By Phiranut Saenewong Na Ayuttaya</td>
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<td>Psycholgical Well-being in Terms of Coping Strategies of Students with the Wrong Major (OP51)</td>
<td>By Andi Ardiansyah Nurdin</td>
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**Chairperson:** Assistant Professor Anuchit Phumartwiwath, Ph.D.

**Co-chairperson:** Nohan Arum Romadlona, M.K.M

**Committee:** Narumol Bhumaphan, Ph.D.

**Committee:** Mrs. Saowanee Sematong

**Breakout Room 4: Oral Presentation**

(6 minutes presentation 2 minutes Q&A)

**Presentation 4.1** Efficacy of A Pilot Training Programme for Barbershop and Beauty Salon Workers as Health Change Agents of “Beauty & Health” Programme in Malaysia (OP45)
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<td>4.2</td>
<td>Model Implementation of Halal Certification Essence for Micro, Small and Medium Business in East Java (OP4)</td>
<td>Chan Wan Thung</td>
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<td>4.3</td>
<td>Implementation of PoCQI Model to Improve Quality of Care at Time of Birth in 12 Hospitals of Pakistan: A Quality Improvement Project (OP6)</td>
<td>Rini Puji Astuti</td>
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<td>4.4</td>
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Chairperson: Vo Thi Hue Man, Ph.D.
**Co-chairperson:** Kyaw Htin Soe, Ph.D  
**Committee:** Assistant Professor Pramon Viwattanakulvanid, Ph.D.

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<th>Committee</th>
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| **14.30 – 16.30** | **Poster Presentation** | Assistant Professor Pokkate Wongsasuluk, Ph.D. | Senior Lecturers  
Nanta Auamkul, M.D, M.P.H  
Professor Ratana Somrongthong, Ph.D.  
Napaphan Viriyautsahakul, M.D.  
Associate Professor Chaweewon Boonshuyar  
Associate Professor Khemika Yamarat, Ph.D.  
Nipunporn Voramongkol, M.D, MPH.  
Kriangkrai Lerdthusnee, Ph.D. |

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<td><strong>16.30 – 17.00</strong></td>
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Dean, College of Public Health Sciences, Chulalongkorn University |

**Closing Remarks**  
**By** Professor Chitiada Areesantichai, Ph.D.

**MC:** Assistant Professor Kriawuth Kallawicha, Ph.D.  
Assistant Professor Wandee Sirichokchatchawan, Ph.D.
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Medication Adherence in Hypertensive Patients with Poly-Pharmacy in Malang, East Java, Indonesia

Nurma Afiani a, *, Ira Nurmala b, Mahmudah b, Sri Haryuni c

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c Faculty of Health Science, Universitas Kadiri, Kediri, Indonesia

Abstract

Background: Medication adherence is the main key to controlling blood pressure in people with hypertension. Medication was started for patients with a systolic blood pressure of 140 mmHg or more and/or diastolic blood pressure of 90 mmHg or more. Various kinds of antihypertensive drugs can be used as initiation or maintenance. The objective of this research was to examine the relationship between poly-pharmacy and medication adherence.

Method: In this study, we used a cross-sectional design and selected participants from primary health centers in Malang City, East Java, Indonesia through purposive sampling from July to August 2023. A total of 140 patients who met specific criteria were included in the study. We collected data using the Morisky Medication Adherence Scale (MMAS). We analyzed the data using chi-square test.

Results: Of all the participants, 104 (74.3%) consumed single antihypertensive pills, while 36 (25.7%) consumed antihypertensive combination pills. The antihypertensive types consumed included Angiotensin Converting Enzyme Inhibitors (ACEI) with 60 (42.9%) users, Beta Blockers (BB) with 20 (14.3%), Calcium Channel Blockers (CCB) with 12 (8.6%), Angiotensin Receptor Blockers (ARB) with 12 (8.6%), ACEI combined with Diuretics with 12 (8.6%), and ACEI combined with CCB with 24 (17.1%). According to the study, medication adherence has a significant relationship with the number of antihypertensive pills taken (p-value < 0.001).

Conclusion: Patients with hypertension who take more pills have lower adherence rates. A single-pill-combination can improve patients’ adherence. Taking medication as prescribed helps to maintain blood pressure and prevent cardiovascular complications.

Keywords: Adherence, Hypertension, Medication, Poly-pharmacy

1. Introduction

Hypertension is one of the most common cardiovascular diseases that can lead to complications of other cardiovascular diseases and is a major risk factor for death [1]. According to GBD (Global Burden of Disease) data, high blood pressure is the leading cause of death in the world based on risk factors. Between 1990 and 2019, elevated blood pressure caused over 10 million deaths worldwide. The GBD data for 2019 reveals that the most common cause of death among individuals aged over 50 and over 70 years in Indonesia is cardiovascular disease. This disease has resulted in 330,082 deaths in the over 70 years age group and 254,436 deaths in the over 50 years age group. Moreover, it is estimated that the number of cardiovascular disease cases will rise by 27% globally by 2030 [2]. The leading causes of death in cardiovascular disease are: ischemic heart disease (49.2%), ischemic stroke (17.7%), intra-cerebral hemorrhage (15.5%), hypertension (6.2%), and subarachnoid hemorrhage (2%) [2]. The Ministry of Health’s Basic Research program (Riskesdas) found that

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hypertension prevalence in Indonesia is 34.11%, and it is higher in East Java at 36.32% [3]. Proper management is crucial in reducing the incidence of hypertension.

In order to effectively manage chronic conditions such as hypertension, adhering to a therapy program is critical. In situations where lifestyle modifications alone prove insufficient in achieving the desired blood pressure target, medication management is an efficient and effective strategy to consider [4]. Good blood pressure control in patients with hypertension is a form of secondary prevention. Secondary prevention is an important step in the management of hypertension, given that this disease cannot be cured but can be controlled [5]. Maintaining a stable blood pressure is important for hypertensive patients as it helps to control blood pressure and prevent complications (disability limitation). If blood pressure is unstable, it can lead to various complications such as coronary disease, left ventricular hypertrophy, valvular heart disease, cardiac arrhythmias (including atrial fibrillation), cerebral stroke, and renal failure [6].

The management of hypertension in Indonesia refers to the results of a consensus conducted by the Indonesian Society of Hypertension Physicians (PERHI). Medication through the administration of antihypertensive drugs is given when lifestyle modifications are unable to lower blood pressure. Patients with grade II and grade I hypertension with comorbidities will receive single or combination antihypertensive drugs according to the indication [7]. Hypertensive patients with co-morbidities will receive even greater amounts of medication [8]. Polypharmacy is expected to be an increasingly pertinent issue in countries with ageing population [9]. Polypharmacy in this study defined as taking ≥2 medications. This study which analyzes the number, type of antihypertensive drugs and drug compliance is expected to be important information for stakeholders in Malang City, East Java, Indonesia. This study aims to identify the level of medication adherence in hypertensive patients who take more than one type of drug (poly-pharmacy) at the Malang City Health Center, East Java.

2. Methods

2.1. Design and participants

We conducted a cross-sectional study among hypertensive patients in Community Health Centers (Puskesmas) Malang city, East Java province, from July to August 2023. This study focuses on Malang city areas to examine the type of antihypertensive that consumed by hypertensive patients. The population of hypertensive aged more than forty-five years old in Malang city was 7.278 [10]. We included 140 hypertensive patients in this study. This study used non-probability sampling. The sample was chosen by purposive sampling techniques. Eligible participants were hypertensive patients who had been diagnosed with hypertension for at least six months, were taking at least one antihypertensive medication, taking more than one medications, had not experienced any emergency conditions and agreed to participate. We excluded participants who did not consume antihypertensive pill and aged less than forty-five years old. To control for confounding factors, the study utilized strict sample criteria, ensuring accurate results.

2.2. Ethical consideration

The approval of this study followed an ethical review by Malang Hospital with number 893/04/411.701/2023.

2.3. Procedure

We encountered the participants at the community health center during their regular health examinations and while collecting medication. We obtained approval from hypertensive patients after explaining the process and dangers of the research. Following that, we asked the participants to complete the MMAS survey and specify the number and type of medications they were taking. We verified the sort and quantity of medication taken by the participants by examining their medical records. Additionally, we gathered demographic information from the participants, such as their
Table 1. Characteristic of hypertensive patients (n=140)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (n=140)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46 – 55</td>
<td>12</td>
<td>8.57</td>
</tr>
<tr>
<td>56 – 65</td>
<td>64</td>
<td>45.71</td>
</tr>
<tr>
<td>≥ 66</td>
<td>64</td>
<td>45.71</td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>62</td>
<td>44.29</td>
</tr>
<tr>
<td>Female</td>
<td>78</td>
<td>55.71</td>
</tr>
<tr>
<td>Educational background</td>
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<td></td>
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<tr>
<td>Elementary</td>
<td>38</td>
<td>27.14</td>
</tr>
<tr>
<td>Junior high school</td>
<td>42</td>
<td>30.00</td>
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<tr>
<td>Senior high school</td>
<td>40</td>
<td>28.57</td>
</tr>
<tr>
<td>Bachelor</td>
<td>20</td>
<td>14.29</td>
</tr>
<tr>
<td>Salary per month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3,194,143.98 IDR</td>
<td>96</td>
<td>68.57</td>
</tr>
<tr>
<td>&gt;3,194,143.98 IDR</td>
<td>44</td>
<td>31.43</td>
</tr>
<tr>
<td>Antihypertensive types</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI</td>
<td>60</td>
<td>42.90</td>
</tr>
<tr>
<td>BB</td>
<td>20</td>
<td>14.30</td>
</tr>
<tr>
<td>CCB</td>
<td>12</td>
<td>8.60</td>
</tr>
<tr>
<td>ARB</td>
<td>12</td>
<td>8.60</td>
</tr>
<tr>
<td>Combination*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI+Diuretic</td>
<td>12</td>
<td>8.60</td>
</tr>
<tr>
<td>ACEI+CCB</td>
<td>24</td>
<td>17.10</td>
</tr>
<tr>
<td>Medication adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>66</td>
<td>47.14</td>
</tr>
<tr>
<td>Middle</td>
<td>28</td>
<td>20.00</td>
</tr>
<tr>
<td>High</td>
<td>46</td>
<td>32.86</td>
</tr>
</tbody>
</table>

* ACEI=Angiotensin Converting Enzyme Inhibitors, BB=Beta Blockers, CCB= Calcium Channel Blockers, ARB=Angiotensin Receptor Blockers.

age, gender, salary per month, and educational background.

2.4. Measures

We used MMAS-8 (Morisky Medication Adherence Scale-8) in the Indonesia language to measure participant’s adherence in consuming antihypertensive pills. We calculated Cronbach’s alpha for reliability of MMAS-8 in our previous study [11]. MMAS-8 questionnaire in Bahasa Indonesia version proved to be valid dan reliable (alpha cronbach 0.773). The MMAS-8 questionnaire consist of eight questions structured with a “yes” and “no” answer model that identified patient behavior related to medication. The questions was divided into 4 aspects, namely forgetting or not taking medicine (4 questions), stop taking medicine (2 questions), medication interference (1 question) and difficulty remembering (1 question). The MMAS-8 score range is 0-8. A score of 8 indicated that the level of adherence was high, a score of 6-7 concluded that the level of adherence was middle, and a score of <6 showed a low level of adherence. We also used other questionnaire to identify sociodemographic data, such as age, gender, salary per month, and educational background.

2.5. Statistical analyses

All data were analyzed using the IBM Statistical Package for Social Sciences (SPSS) software program, version 24.0. Characteristics were described using descriptive statistics, including percentages for categorical variables. The statistical test used in this study was chi-square.

3. Results

The characteristics of hypertensive patients were shown in Table 1. A total of 140 participants completed the questionnaire. The majority of hypertensive patients (45.71%) were 56-65 years
Fig. 1. Medication adherence in hypertensive patients

Table 2. Chi-square analysis of characteristic, antihypertensives types and medication adherence

<table>
<thead>
<tr>
<th></th>
<th>Medication adherence</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Low</td>
<td>Middle</td>
</tr>
<tr>
<td>Antihypertensives types</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Combination</td>
<td>56</td>
<td>26</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46 – 55</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>56 – 65</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>≥66</td>
<td>34</td>
<td>18</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>Educational background</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>32</td>
<td>6</td>
</tr>
<tr>
<td>Junior high school</td>
<td>18</td>
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<tr>
<td>Senior high school</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Bachelor</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Salary per month</td>
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</tr>
<tr>
<td>≤3,194,143.98 IDR</td>
<td>60</td>
<td>24</td>
</tr>
<tr>
<td>&gt;3,194,143.98 IDR</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

* p-value < 0.05, if statistically significant at α = 0.05

of age and (45.71%) were ≥66 years of age. Of the hypertensive patients who participated, 44.29% were male and 55.71% were female. Most of the participants (30%) were graduated from junior high school. The majority of participants (68.57%) had under-average income with salaries less than 3,194,143.98 IDR per month.

The majority of hypertensive patients consumed single pill (74.29%). The most commonly used agents in monotherapy were those that act on the Angiotensin Converting Enzyme Inhibitors (42.90%). The majority used agents in combination therapy were combination of Angiotensin Converting Enzyme Inhibitors and Calcium Channel Blockers (17.10%). Most of the hypertensive participants (47.14%) had low level of medication adherence. Fig. 1 shows that hypertensive patients taking monotherapy have better medication adherence. The majority of these patients had high compliance (80%). Hypertensive patients taking combination pills (polyparmacy) had lower medication adherence, with 70% showing low compliance.

The result of the statistical analysis have been shown in Table 2. Based on the analysis results, certain characteristics of the respondents has a significant relationship with medication adherence. The results showed that antihypertensives types (p-value < 0.001), age (p-value < 0.001), education background (p-value < 0.001), and salary per month (p-value < 0.001) was statistically significantly associated with medication adherence. Gender did not have a significant relationship with medication adherence (p-value = 0.896). Most respondents who consumed combination
therapy had low level of medication adherence. Based on age, most respondents aged > 65 years had a low level of adherence. Patients who consumed monotherapy and were younger were better to adhere to the therapy program. Based on educational background, most respondents graduated from elementary school and under-average salary per month had a low level of medication adherence. Hypertensive patients with higher education and income are more compliant.

4. Discussion

The present study found that there were nearly the same number of male and female hypertensive participants. However, the number of female patients was slightly higher than that of males. Hormonal factors have an impact on the rise in blood pressure, particularly in women who have gone through menopause. This is due to the decrease in estrogen production, which is a crucial factor in maintaining the elasticity of blood vessels, reducing inflammation in blood vessels, and improving lipid metabolism [12]. Most of the respondents are elderly. Older age is one of the key factors affecting the medication adherence of patients with hypertension [13]. The aging population period has led to high rates of degenerative diseases due to decreased organ function in the elderly, one of which is an increase in blood pressure. By 2030 it is predicted that globally there will be an increase of 27% in the number of cases of cardiovascular disease due to the aging population [2]. Most participants were retired with a low income or salary per month. Medication adherence was low to all of retired elderly group, except in the group of elderly with high income [14]. However, having health insurance made it easy for those with hypertension to obtain medication [15]. Most of the participants had graduated from junior high school, and educational background is often associated with the ability to seek out sources of disease-related information [16].

This study found that medication adherence had a significant correlation with the number of antihypertensive pills taken. Poly pharmacy means that the patient takes many medications. The choice of antihypertensive for each patient is based on: metabolic and subjective side effects, the presence of other diseases that may be ameliorated or worsened by antihypertensive, the presence of other drugs that may interact with other antihypertensive, and the cost of treatment [17]. In this study, most respondents received monotherapy, with the antihypertensive program adjusted to their individual condition. According to PERHI, patients with grade II hypertension should consider combination therapy using two drugs, such as thiazide diuretics and ACEI, ARB, BB, or CCB. However, only 25.71% of those participants actually received this type of therapy. This lack of combination therapy may be contributing to suboptimal treatment outcomes for patients with grade II hypertension. By using a combination of antihypertensive medications at minimal doses, patients can experience synergistic effects while minimizing potential side effects from each individual drug [18].

It is important for people with hypertension to meet their blood pressure goals, and taking medication as prescribed is necessary to achieve this. According to the 2021 Hypertension Management Consensus in Indonesia conducted by the Indonesian Society of Hypertension Physicians (PERHI), the ideal blood pressure target to be attained is <140/90 mmHg within three months [4]. To reach this target, it is recommended to use a combination of antihypertensive. Research suggests that single-pill combinations can enhance hypertension adherence [19]. Unfortunately, single-pills-combination are not widely available, so a combination pill of more than one type of antihypertensive is used. The large number and types of pills that must be taken often cause problems due to difficulty remembering the number and type, which is one of the causes of low adherence to taking medication [9]. The therapy program for hypertension are often neglected by elderly patients due to cognitive impairment, including reduced thinking ability and forgetfulness [20].

5. Conclusion

Medication adherence in hypertensive patients are influenced by number of antihypertensive pill,
age, educational background, and salary per month. Patients with hypertension who take more pills tend to have lower adherence rates. However, taking a single-pill-combination can improve patients’ adherence. Hypertension patients who adhere to their medication regimen are more likely to maintain stable blood pressure and prevent cardiovascular complications. The accuracy of the selection of antihypertensive drugs is something that must be further identified. The limitation of this research was did not conduct any examination or assessment of the accuracy of drug selection based on indications. It was important to choose appropriate drugs to avoid causing discomfort to those with hypertension, which may lead to medication non-adherence.

6. Recommendations

It is important to note that single pill antihypertensive have been shown to significantly improve medication adherence in hypertensive patients. Therefore, healthcare providers should strongly consider prescribing single pill combination as a means of improving patient outcomes.

Acknowledgements

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Conflict of Interest

The authors have no conflict of interest to declare.

References


[13] Uchmanowicz B, Chudiak A, Uchmanowicz I,


Association between Parental Knowledge, Attitude and Practices Regarding Children’s Malocclusion in Yangon, Myanmar

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College of Public Health Sciences, Chulalongkorn University, Bangkok, Thailand

Abstract

**Background:** Malocclusion, the misalignment of teeth within or between the upper and lower arches, is a significant global oral health problem among children. Children affected by malocclusion, such as dento-facial disharmonies, may experience mental distress significant enough to warrant psychological and psychiatric consultation. The knowledge, attitudes, and practices of parents play a crucial role in the early prevention and treatment of malocclusion of their children as if the children are financially and decisively dependent on their parents. This study aims to assess the association between knowledge, attitudes, and practices of parents regarding malocclusion in children residing in Yangon, Myanmar.

**Methods:** This Cross-sectional study was conducted in Yangon, Myanmar with a convenient sampling method. The research included a sample of 103 parents, encompassing both males and females aged between 20 to 50 years having children aged between 6 to 12 years.

**Results:** By linear regression analysis, we found that educational level, knowledge and attitude significantly associate parents’ practices regarding children's malocclusion. Three key factors: The higher the level of education ($\beta = 0.379$, $p < 0.01$), the more they adopted good practice. Secondly, compliance with Knowledge: Parents who possessed greater knowledge about malocclusion ($\beta = 0.747$, $p < 0.01$) were more likely to engage in practices related to their children's oral health. Lastly, Positive attitudes toward addressing malocclusion ($\beta = 0.541$, $p < 0.01$) were associated with increased engagement in practices aimed at promoting children's oral health.

**Conclusion:** This study underscores the significance of knowledge and attitude in driving parents' practices concerning children's malocclusion in Yangon, Myanmar. To enhance children’s oral health, targeted educational efforts and awareness campaigns for parents are essential. Empowering parents with knowledge and fostering positive attitudes can encourage them to take proactive steps in preventing and treating malocclusion in their children. Strengthening these initiatives is vital to improving oral health outcomes among the younger population in the region.

**Keywords:** Malocclusion, Knowledge, Attitude, Practice, Parents

1. Introduction

Malocclusion is the deviation in the alignment of the teeth within the arch or between the upper and lower arch [1]. On the global level, malocclusion is considered to be one of the most prevalent oral pathologies, secondary to dental caries and periodontal disease marking the third most prevalent among worldwide dental public health disease priorities [2]. The prevalence of malocclusion among children at a global level is 56% without relevant gender difference. One out of two children have malocclusion in which it is a highly prevalent condition in a worldwide level. When it comes to malocclusion distribution regarding continents, there were higher percentage scores, that is, 81% in Africa and 71% in Europe, and 53% in America and 48% in Asia [3].

In children especially during the mixed...
dentition, malocclusion is highly prevalent because both of the deciduous and permanent teeth are present at the same time in the upper and lower dental arches with an abundant range of deviations, such as physiologic occlusal changes at this stage usually beginning with the eruption of the first permanent molars [4].

Genetic factors are highly susceptible to malocclusion. Heritability proportions have been exhibited with many dental and facial features such as mid and lower facial parts, such as spacing, crowding and Bolton type tooth size discrepancies with the prevalence rate of more than 60% which is considered to be moderate to high [5]. Hereditary factors can come together with environmental factors such as oral bad habits, for example, thumb sucking habit, oral respiration habit and tongue thrusting habit [6]. These oral bad habits can cause certain types of malocclusion like anterior open bite, posterior cross-bite, and jaw problems, for instance, clockwise rotation of the mandible which can compromise the facial esthetics [6-8].

The children with malocclusion are being bullied because of their dento-facial appearance and these negative effects can have an impact on oral conditions on social life and a positive sense of dentofacial self-confidence. The prevalence of bullying among schoolchildren aged 11 to 12 years of age was 47%, and schoolboys are being bullied more than school girls. Among maxillofacial abnormalities, the three most bullied appearances are dental spacing or missing teeth, shape and shade of the teeth for example, teeth staining and proclined upper incisors. Therefore, dental appearances were the feature most frequently targeted for bullying, followed by strength and being obese or skinny. Orthodontic treatment has a considerable impact on children’s oral health–related quality of life (OHRQoL) because those children with malocclusion are being bullied by their unappealing dento-facial appearance [9].

Therefore, early orthodontic intervention should be considered and provided in order to prevent the development of malocclusion and to eliminate factors interfering with the regular development of the dental arches. Maxillofacial appearance has a long-lasting implication on people especially the younger generation. An unacceptable dental esthetics has often been associated with a negative effect on self-esteem, career development and peer acceptance. To protect the impact on their mental health, children having from very severe to moderate malocclusion should be accessed and corrective treatments and interventions should be instituted as soon as possible [10]. Early access to orthodontic treatment can prevent the dental traumatic injuries in patients with proclined upper teeth [11]. If malocclusion is left untreated during the mixed dentition phase, it can cause malocclusion in permanent dentition. Consequently, the negative impact of malocclusion during mixed dentition, may result deleterious effects in the emotional and social aspects of children in the early ages [12]. The knowledge, attitudes, and practices of parents play a crucial role in the early prevention and treatment of malocclusion of their children as if the children are financially and decisively dependent on their parents. On the other hand, there is a limited number of literatures available concerning with the children’s malocclusion and the knowledge, attitudes, and practices of parents regarding this dental public health problem in Myanmar. Thus, this study aims to access the level of knowledge, attitude, and practice of parents regarding malocclusion in their children and investigate the association between parents’ individual characteristics, levels of knowledge, attitude, and practice regrading malocclusion in their children.

2. Materials and Methods
2.1. Study design, setting and participants
This study is a cross-sectional survey conducted during 2023 in 10 districts of Yangon, Myanmar. The participants were parent who meet the inclusion criteria include age between 20 to 50 years, having 1 to 3 children of aged 6 to 12 years, living together with their children for at least 1 year, and live in Yangon, Myanmar at least 6 months. The exclusion criteria are those parents who are dentists, dental nurses, and dental technicians. The protocol of this study was approved by the Research Ethic Review Committee for Research Involving Human
Research Participants, Chulalongkorn University.

2.2. Questionnaire Characteristics

The structural questionnaire was developed and assessed for reliability and content validity by three experts. The values of the Item Objective Congruence (IOC) was more than 0.5 for each variable. The questionnaire comprised 4 sections, the first was socio-demographic variables of study participants, and the 2nd, 3rd and 4th sections were on knowledge, attitude and practice, respectively. The questionnaire was then, translated into the Myanmar language. In the knowledge and practice section, “yes” is always the right answer and for the attitude section, “strongly agree” and “agree” are denoted as the “positive attitude”.

2.3. Data Collection

An electronic survey was designed to assess parents’ knowledge, attitude, and practice of malocclusion for their children. Data were collected by self-administered questionnaire type Google Form survey with the convenient sampling technique. The online survey was approximately 20-30 minutes long. The survey invitation stated the objective of the study and notified participants that their participation was anonymous and their information was kept confidential and will only be utilized for the research purpose. Participants were informed that completing the survey implied their consent and agreement to participate in the study. In order to get the adequate amount of sample, the survey was distributed through social medias and 10 dental clinics located in 10 districts of Yangon, Myanmar.

2.4. Statistical Analysis

Obtained data were cleaned and coded onto Microsoft Excel and were entered into SPSS version 28.0. Frequency distributions were computed for parents’ demographic characteristics and responses to survey questions. The mean and frequency distribution of parents’ knowledge and attitude level scores were calculated. Simple Linear regression analysis was performed to determine the association factors at 95% Confidence Interval (95% CI). A significance level of 0.05 was used in all analyses.

2.5. Ethical Consideration

Ethical approval [COA 216/66] for this study was obtained from the Ethical Committee for Research Involving Human Subjects in the Health Science Group of Chulalongkorn University before the data collection. The respondents received a clear explanation of consent prior to answer the questionnaire from the Google Form. This study mainly prioritized participants’ privacy. Google form did not record participants’ email addresses, and names and detailed information of the participants were not necessary to answer within the questionnaire. Moreover, respondents took part with their own consent whether they wished to proceed and complete the Google Form until the end. They had their own rights to answer it without further notice.

3. Results

3.1. Parents’ demographic characteristics

The total number of participants was 103, including 36 fathers (35%) and 67 mothers (65%). The average age of the participants was 37.3 years old. The largest proportion of the participants (53.4%) was between the age of 31 – 40 years, followed by 41 – 50 years of age group with 28.2%. Nearly three-third of the parents (73.8%) were employed. The majority (69.9%) of the participants were at graduate levels. In terms of previous history of orthodontic treatment, nearly all the participants (96.1%) did not receive any types of orthodontic treatment and most of them (67%) have no malocclusion (Table 1).

3.2. Parents’ knowledge, attitude, and practice on children’s malocclusion

The mean score of overall knowledge, attitude and practice scores of parents were 8.97, 15.23 and 8.13, respectively. When it comes to knowledge regarding causes of malocclusion, most of the participants (52.4%) thought genetic factor is not the cause of malocclusion, and 57.3% of participants thought malocclusion was not caused by dietary factor. Most of the participants knew that malocclusion could lead to oral health problems such as esthetic problem (90.3%), social problems (50.5%) and functional problems (71.8%). Over two-third (70.9%) of the participants
Table 1. Demographic characteristics of parents (n=103)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male (Father)</td>
<td>36 (35.0)</td>
</tr>
<tr>
<td>Female (Mother)</td>
<td>67 (65.0)</td>
</tr>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
</tr>
<tr>
<td>20 – 30</td>
<td>19 (18.4)</td>
</tr>
<tr>
<td>31 – 40</td>
<td>55 (53.4)</td>
</tr>
<tr>
<td>41 – 50</td>
<td>29 (28.2)</td>
</tr>
<tr>
<td>Minimum - Maximum</td>
<td>23 – 50</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>37±0.68</td>
</tr>
<tr>
<td><strong>Education Level</strong></td>
<td></td>
</tr>
<tr>
<td>Undergraduate Level</td>
<td>15 (14.6)</td>
</tr>
<tr>
<td>Graduate Level</td>
<td>72 (69.9)</td>
</tr>
<tr>
<td>Post-graduate level</td>
<td>16 (15.5)</td>
</tr>
<tr>
<td><strong>Status of Employment</strong></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>27 (26.2)</td>
</tr>
<tr>
<td>Employed</td>
<td>76 (73.8)</td>
</tr>
<tr>
<td><strong>Monthly Household Income</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 600,000 MMK</td>
<td>38 (36.9)</td>
</tr>
<tr>
<td>600,001 – 2,000,000 MK</td>
<td>37 (35.9)</td>
</tr>
<tr>
<td>&gt; 2,000,000 MMK</td>
<td>28 (27.2)</td>
</tr>
<tr>
<td><strong>History of previous orthodontic treatment</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>99 (96.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (3.9)</td>
</tr>
<tr>
<td><strong>History of malocclusion</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>67 (67)</td>
</tr>
<tr>
<td>Yes</td>
<td>33 (33)</td>
</tr>
</tbody>
</table>

thought that early tooth loss due to caries is the risk factor to malocclusion. Regarding prevention of malocclusion, most of the participant parents knew the preventive measures such as changing diet habits (63.1%), serial extraction (65%), avoiding oral bad habits (79.6%) and starting the orthodontic treatment before the puberty (78.6%).

In parental attitude, 53.4% of the participants agreed to take their children to dental clinics when they found out dental misalignment and oral bad habits. Positive attitudes can be found as 58.3% that will take their children to dental clinics regularly to check up for overall oral health and 52.4% of parents agreed to start orthodontic treatment if needed (Table 2).

According to routine observation, 85% of the parents notice the alignment of their child’s teeth and observe their children’s oral bad habits and, 69% of the parents know if the children have the jaw problem. 61.2% of parents agreed to take their children to the dental clinics for the malocclusion check-up once a year.

The simple linear regression results showed that educational level, knowledge and attitude of parents were significant predictors of practice

Table 2. Parents’ attitude on children’s malocclusion

<table>
<thead>
<tr>
<th>Questions</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>i) If my children have thumb sucking habit, I will take them to the dentist to evaluate dentofacial abnormalities.</td>
<td>11 (10.7)</td>
<td>55 (53.4)</td>
<td>30 (29.1)</td>
<td>5 (4.9)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>ii) Due to the oral habits, for example, thumb sucking, tongue thrusting, I take my children to the dental clinic as soon as possible to prevent dentofacial problems.</td>
<td>11 (10.7)</td>
<td>56 (54.4)</td>
<td>31 (30.1)</td>
<td>3 (2.9)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>iii) It is necessary to take the child for regular dental visits once a year.</td>
<td>28 (27.2)</td>
<td>60 (58.3)</td>
<td>13 (12.5)</td>
<td>1 (1.0)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>iv) To begin orthodontic treatment for our children, we will not wait until their wisdom teeth erupt.</td>
<td>17 (16.5)</td>
<td>54 (52.4)</td>
<td>25 (24.3)</td>
<td>7 (6.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>v) If my child has mandibular deformities, I will wait til he or she becomes an adult. After that, we try for surgical intervention.</td>
<td>4 (3.9)</td>
<td>37 (35.9)</td>
<td>42 (40.8)</td>
<td>15 (14.5)</td>
<td>5 (4.9)</td>
</tr>
<tr>
<td>vi) If my child needs orthodontic management, I will do that even if he or she resists.</td>
<td>5 (4.9)</td>
<td>47 (45.6)</td>
<td>34 (33.0)</td>
<td>15 (14.6)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>vii) To begin orthodontic management, I will not wait till all his or her permanent teeth erupt completely.</td>
<td>2 (1.9)</td>
<td>58 (56.4)</td>
<td>30 (29.1)</td>
<td>13 (12.6)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Table 3. Simple linear regression analysis of parents’ practice regarding children’s malocclusion

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SE</th>
<th>β</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.06</td>
<td>0.038</td>
<td>-0.015</td>
<td>-0.082 – 0.07</td>
<td>0.879</td>
</tr>
<tr>
<td>Gender</td>
<td>0.062</td>
<td>0.529</td>
<td>0.012</td>
<td>-0.987 – 1.111</td>
<td>0.907</td>
</tr>
<tr>
<td>Education Level</td>
<td>2.723</td>
<td>0.661</td>
<td>0.379</td>
<td>1.411 – 4.035</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Status of Employment</td>
<td>0.623</td>
<td>0.57</td>
<td>0.108</td>
<td>-0.908 – 1.753</td>
<td>0.277</td>
</tr>
<tr>
<td>History of Malocclusion</td>
<td>-0.627</td>
<td>0.533</td>
<td>-0.116</td>
<td>-1.684 – 0.429</td>
<td>0.241</td>
</tr>
<tr>
<td>Monthly Household Income</td>
<td>0.2</td>
<td>0.522</td>
<td>0.038</td>
<td>-0.836 – 1.236</td>
<td>0.703</td>
</tr>
<tr>
<td>Knowledge</td>
<td>0.482</td>
<td>0.43</td>
<td>0.747</td>
<td>0.397 – 0.566</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Attitude</td>
<td>0.642</td>
<td>0.099</td>
<td>0.541</td>
<td>0.445 – 0.839</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

p-value <0.05; B = Unstandardized B; SE = Coefficients Standard Error; β=Standardized Coefficients Beta

Fig. 1. Parental knowledge and practice of children’s malocclusion

parents regarding malocclusion in children (p-value <0.05). The results indicated that level of education (β = 0.379), knowledge of parents regarding malocclusion (β = 0.747) and attitude of parents regarding malocclusion (β = 0.541) were the most significant factors with parental practice of children’s malocclusion. The simple linear regression table is showed in Table 3.

4. Discussion

Our study aims to investigate the parental knowledge, attitude, and practice of children’s malocclusion in Yangon, Myanmar. To the best of our knowledge, this is the first study of this kind in the population of Myanmar. In this study, adequate knowledge and practice on children’s malocclusion were found in 64% and 74% of the participants, respectively (Fig.1). Similarly, in the previous study, good knowledge and positive attitude were found in majority of the population [13]. The lowest knowledge score was detected in the dietary factor (57.3% wrong answer) and genetic factor (52.4% wrong answer). According to Mossey PA, genetic factor is irrefutable in many dental and occlusal variations. However, the impact of genetics varies depending on the trait is still under consideration and is often still not well understood [14]. This finding is similar to the previous study in India [15].

Unlike the previous studies, fathers have better knowledge of children’s malocclusion and they practice more positive than mothers, yet, mothers have better attitude than fathers. It could be assumed that children are more rely financially and decisively on fathers than mothers even children are more rely emotionally on mothers than fathers [13].

Only 3.9% of the participants have had at least one kind of orthodontic treatments once in their lives but, they have higher knowledge, attitude and practice than those who have not had orthodontic treatments. In this present study, we also observed that those parents who had orthodontic treatment had good knowledge, positive attitude and good practice regarding malocclusion in their children. This finding is similar with the previous study in Iran [16].

In this present study, among the independent variables, parental knowledge and attitude were significantly associated with parental practice on malocclusion. The more the parents have knowledge and positive attitude towards the malocclusion, the better practice they will adopt for their children’s malocclusion and the uptake of orthodontic treatment. Moreover, educational level is also significantly associated with the parental practice of malocclusion in children. In this study showed that level of education of parents is also significantly associated with
practice of malocclusion. The higher the education level, the greater the awareness of their children’s malocclusion. In the previous studies, education level of parents is not usually mentioned in the association of parental knowledge, attitude, and practice of malocclusion. Similar study showed that moderate to high parental knowledge and attitude towards their children’s malocclusion problems and practice of children’s malocclusion such as treatment needs [13]. Moreover, another study had shown that poor knowledge and attitude of the mothers regarding children’s oral health can predict the parental practice. Therefore, oral health behavior of both the parents can affect oral health behavior of their own children [17]. This indicates that these factors play a substantial role in predicting parental practices concerning children’s malocclusion.

We made effort to minimize bias, such as including subjects from various public areas with no formal dental qualifications and the use of clear well-structured questionnaire in Myanmar language format. However, the total response was below required. Additionally, the survey was limited to people who lived in the Yangon region, Myanmar. Therefore, as a result, the findings cannot be applied to the entire Myanmar population. More studies involving different regions of Myanmar with different classes of population are required.

5. Conclusion
Parents demonstrated good knowledge, positive attitude and good practice regarding their children’s oral bad habits, malocclusion and orthodontic need and care. Males and parents with higher education level were more sensitive and proactive than females and lower level of education parents. The more the parents have knowledge and attitude regarding children’s malocclusion the more they have a better practice.

6. Recommendations
Further studies with more sample size are required to represent the Myanmar population. Moreover, malocclusion assessment is also recommended as there is no study in Myanmar concerning with malocclusion. The implementation of health insurance companies and charity programs could help fund treatment such as dental check-ups and malocclusion assessment for children and should get referred to orthodontists if urgent treatments are needed.

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References
[8] Cenzato N, Nobili A, Maspero C. Prevalence of dental malocclusions in different...


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Abstract

Background: Since the beginning of the Covid-19 pandemic, there has been a global increase in Tuberculosis service disruptions. However, the impacts of the pandemic on Tuberculosis Prevention Treatment (TPT) implementation have not been explored further. This study is aimed to identification the trend of TPT Coverage three period before, during and after the Covid-19 Pandemic.

Method: This study used descriptive quantitative study with Trend Analysis approach using secondary Data. Data collected through the Global Tuberculosis Report from 2016 to 2021 in Asia. Data processing is done using trend analysis with linear and quadrat models. MSE, MAPE, MAD and MSD were required to determine the best model for the forecasting trend analysis.

Results: Linear Yt: 198,287.5 + 26,283.1 (X), MSE= 1550927073.2, MAPE= 0.019, MAD= 23470, and MSD= 1033951382. Linear trend analysis is the best model for TPT Coverage trend analysis. Result shows TPT coverage has a positive trend around 2016 to 2019, hence decline in 2020 and increase again in 2021. Forecasting for 2022-2024 there are an expand constantly, with an average increase of 144,557 individuals.

Conclusion: TPT administration trend analysis yields positive results. The TPT trend increased prior to the Covid-19 Pandemic, but reduced during the Covid-19 Pandemic. TPT provision is expected to increase following the Covid-19 Pandemic.

Keywords: Tuberculosis Preventive Treatment (TPT), Trend Analysis, Covid-19 Pandemic

1. Introduction

Tuberculosis (TB) is a communicable disease with a high number of cases and deaths worldwide [1]. TB is caused by Mycobacterium tuberculosis which is spread into the air and infected from sick person to others (e.g. by coughing) [1, 2] About a quarter of the world’s population has been infected with TB germs. In 2021, 10.6 million people (95% UI: 9.9-11 million) were estimated fell ill with TB and increased about 4.5% (10.1 million) in 2020 (95% UI: 9.9-10.7 million). The incidence rate (new cases per 100.000 population/year) rose by 3.6% between 2020 and 2021. The burden of drug-resistant TB (DR-TB) also estimated have increased until 2021 [2].

As a communicable disease, TB has a Latent Tuberculosis Infection (LTBI). LTBI occurs when the infected immune system can no longer eliminate Mycobacterium Tuberculosis bacteria from the body completely and can control TB bacteria so that no symptoms appear [3]. People with LTBI when the Tuberculin Skin Test (TST) or Interferon Gamma-Release Assay (IGRA) examination are performed will be positive, but the results of the thorax X-ray examination are normal and the results of sputum examination and X-pert MTBC/Rif are negative [4, 5]. People who have been exposed to LTBI can activate TB germs

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when their immunity is decreased and can transmit these germs to others, especially in close contact [6]. Global LTBI burden by 2014 has reached 1.7 trillion people [5, 7].

As part of the END Tuberculosis strategy, WHO recommends provision of Tuberculosis Prevention Treatment (TPT) to LTBI. TPT will be focused on TB household contacts, especially children, persons living with HIV, health workers who have close contact with TB patients and high-risk groups. The WHO has pursued TPT as a global prevention strategy to END TB [5].

The coverage of TPT all age is 12.5 million (42%) with the bridging, people living with HIV 10.3 million (>100%), household contacts aged under 5 years old 1.6 million (40%) and household contacts aged 5 years old and above 0.60 million (3%). Need a special concern from related fields [1, 2]. Asia as the contributor of the most TB cases, has a corresponding number of close domestic contacts. However, the number of close domestic contacts that started the TPT did not meet expectations. Besides, the treatment completion rate is also far too low. In fact, 18 of the 47 countries on the Asian continent, have no TPT completion figures (null) [2]. It is certainly a challenge for TB prevention and control globally [2, 5, 7].

According to the data above, prior to the Covid-19 pandemic, TPT is increasing every year. However, since Tuberculosis program was affected by Pandemic Covid-19, TPT coverage has decrease with a huge number [6-8]. As we know, in December 2019, the WHO has confirmed that Covid-19 was first detected in Wuhan, China [9]. Since it was first discovered, the virus has spread very rapidly to attack all over the region including Asia. By March 2020, Global cases have reached 100,000 cases [9, 10]. Furthermore, the WHO has defined the health situation as a Pandemic. By September 2021, almost 2 years after Covid-19 identified, there had been more than 200 million confirmed cases and over 4.6 million lives lost to the disease.

The global health main focus of this situation is the control of pandemics. Nevertheless, many other health problems are neglected. One of the implications is Tuberculosis. TB disease has been decreasing in numbers during pandemics, according to Global Data; yet, it has been examined as a result of pandemics [8].

Furthermore, there is no analysis related to the impact of the Covid-19 Pandemic on TPT coverage before, during and after. Trend analysis is needed to prepare the best plan to improve program achievement after Covid-19 Pandemic. Trend analysis can be used for forecasting TPT coverage after Covid-19 Pandemic [11]. Forecasting or prediction is the use of past data from a variable or set of variables to estimate its value in the future and important for decision-making [11-13]. Several predictive methods available, the problem arises for researchers in understanding how the characteristics of a prediction method will fit into a particular decision-making situation. Predictive situations vary widely in predictive time horizons, factors that determine actual outcomes, types of data patterns, and many other aspects [12].

This study is aimed to identification the trend of TPT Coverage three period before, during and after the Covid-19 Pandemic. The results of this study are expected to be a forecasting of improving the provision of TPT.

2. Methods

2.1. Study area and population

The region selected is Asia with three regions namely the Eastern Mediterranean, South East Asia and the Western Pacific with total is 47 countries. The population in this study is TPT Coverage Data in the Asian region between 47 countries.

As part of the END Tuberculosis strategy, WHO recommends provision of Tuberculosis Prevention Treatment (TPT) to LTBI. TPT will be focused on TB household contacts, especially children, persons living with HIV, health workers who have close contact with TB patients and high-risk groups. The WHO has pursued TPT as a global prevention strategy to END TB [5].

The coverage of TPT all age is 12.5 million (42%) with the bridging, people living with HIV 10.3 million (>100%), household contacts aged under 5 years old 1.6 million (40%) and household contacts aged 5 years old and above 0.60 million (3%). Need a special concern from related fields [1, 2]. Asia as the contributor of the most TB cases, has a corresponding number of close domestic contacts. However, the number of close domestic contacts that started the TPT did not meet expectations. Besides, the treatment completion rate is also far too low. In fact, 18 of the 47 countries on the Asian continent, have no TPT completion figures (null) [2]. It is certainly a challenge for TB prevention and control globally [2, 5, 7].

According to the data above, prior to the Covid-19 pandemic, TPT is increasing every year. However, since Tuberculosis program was affected by Pandemic Covid-19, TPT coverage has decrease with a huge number [6-8]. As we know, in December 2019, the WHO has confirmed that Covid-19 was first detected in Wuhan, China [9]. Since it was first discovered, the virus has spread very rapidly to attack all over the region including Asia. By March 2020, Global cases have reached 100,000 cases [9, 10]. Furthermore, the WHO has defined the health situation as a Pandemic. By September 2021, almost 2 years after Covid-19 identified, there had been more than 200 million confirmed cases and over 4.6 million lives lost to the disease.

The global health main focus of this situation is the control of pandemics. Nevertheless, many other health problems are neglected. One of the implications is Tuberculosis. TB disease has been decreasing in numbers during pandemics, according to Global Data; yet, it has been examined as a result of pandemics [8].

Furthermore, there is no analysis related to the impact of the Covid-19 Pandemic on TPT coverage before, during and after. Trend analysis is needed to prepare the best plan to improve program achievement after Covid-19 Pandemic. Trend analysis can be used for forecasting TPT coverage after Covid-19 Pandemic [11]. Forecasting or prediction is the use of past data from a variable or set of variables to estimate its value in the future and important for decision-making [11-13]. Several predictive methods available, the problem arises for researchers in understanding how the characteristics of a prediction method will fit into a particular decision-making situation. Predictive situations vary widely in predictive time horizons, factors that determine actual outcomes, types of data patterns, and many other aspects [12].

This study is aimed to identification the trend of TPT Coverage three period before, during and after the Covid-19 Pandemic. The results of this study are expected to be a forecasting of improving the provision of TPT.
Table 1. Region scope

<table>
<thead>
<tr>
<th>Region</th>
<th>Frequency</th>
<th>%</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Mediterranean</td>
<td>22</td>
<td>46.8</td>
<td>24139</td>
<td>31297</td>
<td>38142</td>
<td>45753</td>
<td>37634</td>
<td>45308</td>
</tr>
<tr>
<td>South Eastern Asia</td>
<td>11</td>
<td>23.4</td>
<td>30071</td>
<td>70917</td>
<td>131132</td>
<td>178864</td>
<td>142087</td>
<td>281475</td>
</tr>
<tr>
<td>West Pacific</td>
<td>14</td>
<td>29.8</td>
<td>9390</td>
<td>15973</td>
<td>16570</td>
<td>22820</td>
<td>31529</td>
<td>36624</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>100.0</td>
<td>63600</td>
<td>118187</td>
<td>185844</td>
<td>247437</td>
<td>211250</td>
<td>363407</td>
</tr>
</tbody>
</table>

consists of Brunei Darussalam, Cambodia, China, Hong Kong, Macao, Japan, Laos, Malaysia, Mongolia, Philippines, Republic of Korea, Singapore, Tokelau and Vietnam. Especially for the Western Pacific, we limit areas in the Pacific such as Australia, etc. So that the total countries that we chose for the Western Pacific are 14 countries.

2.2. Study design

This study used quantitative study with descriptive approach using secondary data. Data collected through the Global Tuberculosis Report. The data used are Contact Tuberculosis Preventive Treatment data from 2016 to 2021. That period was chosen 3 years before Covid-19 (2016-2018), 3 years during Pandemic Covid-19 (2019-2021) and its forecasting after Pandemic Covid-19 (2022-2024).

2.3. Data collection and measurement tools

Data processing is done using trend analysis with linear and quadrat models. “y” as TPT coverage is the dependent variable and “x” as time period is the independent variable of this study. Both of linear and quadrat are compared to choose the best model to predict the nearest number of TPT in the future. Before conducting data analysis, an assumption test is needed to see data on the effect of time series on TPT Coverage. Test the classical assumptions of simple regression using the Durbin-Watson Autocorrelation Test. The results of DU < DW < 4-DU were obtained at 1.4002 < 1.984 < 2.5998. It can be concluded that there is no autocorrelation in the data, so there is an influence between the x and y variables.

2.4. Data analysis

Data analysis using regression linear analysis using trend analysis model to find MSE, MAPE, MAD and MSD number. Those value were required to determine the best model for the forecasting trend analysis. Afterwards, the results are presented in the form of tables and line graphic.

2.5. Ethical issues

Ethical approval was not required because this is an anonymized databank that is publicly available in the World Health Organization’s Global Report Tuberculosis.

3. Results

The results of this study have shown in the Table 1 as a region scope and Table 2 as linear and quadratic trend analysis.

3.1. Region scope

Based on the Table 1, it is known that the number of countries in Asia involved in this study amounted to 47 countries. The country is divided into 3 regions, Eastern Mediterranean (46.8%), South East Asia (23.4%) and West Pacific (29.8%). The Eastern Mediterranean consists of Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Palestine, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates and Yemen, with a total of 22 countries. The South East Asia region consists of Bangladesh, Bhutan, North Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste, with a total of 22 countries. The South East Asia region consists of Bangladesh, Bhutan, North Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste, with a total of 22 countries. The South East Asia region consists of Bangladesh, Bhutan, North Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste, with a total of 11 countries. West Pacific consists of Brunei Darussalam, Cambodia, China, Hong Kong, Macao, Japan, Laos, Malaysia, Mongolia, Philippines, Republic of Korea, Singapore, Tokelau and Vietnam. Especially for the Western Pacific, we limit areas in the Pacific such as...
Table 2. TPT trend analysis

<table>
<thead>
<tr>
<th>No.</th>
<th>Period</th>
<th>Years</th>
<th>TPT Coverage</th>
<th>Linear (Yt= a + bX)</th>
<th>Quadratic (Yt= a + bX + cX²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yt</td>
<td>Yt</td>
</tr>
<tr>
<td>1.</td>
<td>Pre-Pandemic</td>
<td>2016</td>
<td>63600</td>
<td>66872</td>
<td>167778,4</td>
</tr>
<tr>
<td>2.</td>
<td>Pre-Pandemic</td>
<td>2017</td>
<td>118187</td>
<td>119438,2</td>
<td>220344,6</td>
</tr>
<tr>
<td>3.</td>
<td>Pre-Pandemic</td>
<td>2018</td>
<td>185844</td>
<td>172004,4</td>
<td>272910,8</td>
</tr>
<tr>
<td>4.</td>
<td>Pandemic</td>
<td>2019</td>
<td>247437</td>
<td>224570,6</td>
<td>325477</td>
</tr>
<tr>
<td>5.</td>
<td>Pandemic</td>
<td>2020</td>
<td>211250</td>
<td>277136,8</td>
<td>378043,2</td>
</tr>
<tr>
<td>6.</td>
<td>Pandemic</td>
<td>2021</td>
<td>363407</td>
<td>329703</td>
<td>430609,4</td>
</tr>
</tbody>
</table>

Abbreviations: Yt= equation of independent variable y to time period result, a= y-intercept, b= the slope, X= independent variable.

Australia, etc. So that the total countries that we chose for the Western Pacific are 14 countries.

We know that the South East Asia (SEA) area is the major donor to TPT coverage. According to Table 1, prior to the Covid-19 pandemic, SEA region TPT coverage rose from 2016 to 2019. However, when the pandemic struck in 2020, access to TPT was promptly revoked. This is also true in the Eastern Mediterranean Region (EMR). The West Pacific (WP) region, on the other hand, has mostly escaped the pandemic, despite rising numbers. TPT coverage in the three SEA, EMR, and WP regions surged prior to the Pandemic from 2016 to 2019, but has dropped as the pandemic continues in 2020.

3.2. TPT coverage trend analysis

The results of trend analysis using linear and quadratic models are shown in Table 2.

Linear and Quadratic models are used to formulate the best models to be used for TPT coverage predictions in three Asian regions. This model needs to be compared to assess the accuracy of the predictions.

The Yt results shown above were generated using regression in the SPSS statistical program version 25.0. The linear result “a” is generated from the coefficients (constant), whereas “b” is acquired from the coefficients of the time period. While quadratic “a” is derived from coefficients (constant), “b” is derived from time period coefficients, and “c” from quadratic time periods. “X” reflects the time given by the number of even numbers’ t model. The result of Yt is obtained with the numbers in Table 2. Linear and quadratic line graphs are available in Fig. 1.

According to Fig. 1, TPT had a good tendency before Covid-19 Pandemic (2016-2018), however the positive trend ended in 2019. TPT trend fell from 2019 to 2020, then increased again in 2021. There was a decrease in TPT coverage when the Pandemic took place in the interval from 2019 to 2021. The decline occurred in the second year of the Pandemic (2020) then gradually increased in 2021.

3.1. TPT coverage forecasting

Before forecasting, we establish the optimal model to utilize first. The forecasting time period was set to be three years following the Pandemic (2022-2024), hence the time series happens in multiples of three. Table 3 contains statistical results for MSE, MAPE, MAD, and MSD.
**Table 3. Linear and Quadratic Model comparison**

<table>
<thead>
<tr>
<th>No.</th>
<th>Model Trend</th>
<th>MSE</th>
<th>MAPE</th>
<th>MAD</th>
<th>MSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Linear</td>
<td>1550927073.2</td>
<td>0.019</td>
<td>23470</td>
<td>1033951382</td>
</tr>
<tr>
<td>2.</td>
<td>Quadratic</td>
<td>2047059586.98</td>
<td>0.084</td>
<td>100906.44</td>
<td>11216062715</td>
</tr>
</tbody>
</table>

Regression error metrics are necessary to find out the best model to forecast the future TPT trend. Abbreviations: MSE= Mean Square Error, MAPE= Mean Absolute Percentage Error, MAD= Mean Absolute Deviation, MSD= Mean Absolute Deviation.

**Table 4. TPT Coverage Forecasting**

<table>
<thead>
<tr>
<th>No.</th>
<th>Year</th>
<th>TPT Coverage Asia</th>
<th>Eastern Mediterranean</th>
<th>South East Asia</th>
<th>West Pacific</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2022</td>
<td>198288</td>
<td>50292</td>
<td>290917</td>
<td>41060</td>
</tr>
<tr>
<td>2.</td>
<td>2023</td>
<td>434836</td>
<td>54077</td>
<td>334296</td>
<td>46462</td>
</tr>
<tr>
<td>3.</td>
<td>2024</td>
<td>487402</td>
<td>57862</td>
<td>377675</td>
<td>51865</td>
</tr>
</tbody>
</table>

Forecasting trend 2022, 2023 and 2024, after Covid-19 Pandemic

Choosing the best trend model is used a measure of accuracy i.e. how precise a forecasting tool predicts the actual event. The more precise the tool will have a good degree of error smaller. To measure accuracy, the value of the difference between each data is needed the smallest forecasting. Table 3 shows that the approach with the lowest MSE, MAPE, MAD, and MSD values is the best for forecasting. The best model is the linear trend model with the equation: Yt = 198,287.5 + 26,283.1 (X). With this equation, the TPT Coverage forecast for 3 years after the Pandemic (2022-2024) is obtained as Table 4.

Table 4 displays the results of the TPT Coverage prediction. If the prognosis is correct, Asia TPT Coverage will approach a positive trend with a decline number in 2022, and improvement in achievement from 2023 to 2024 with average improvement is 144.557. The line graphic shown in Fig. 2.

![Fig. 2. TPT coverage forecasting linear trend analysis](image-url)
Based on the forecast of post-pandemic TPT coverage, the three regions (SEA, EMR, WP) will experience increased coverage from 2022 to 2024. These results are different if calculated globally (Asia). The difference lies in 2022. Global forecasts, the coverage of TPT will decrease by 2022. Hence, each region in 2022 experience increased coverage of TPT.

4. Discussion

Forecasting is an integral part of decision-making, because whether a decision is effective or not generally depends on factors that are not visible at the time of the decision [11]. With several predictive methods available, the problem arises for researchers in understanding how the characteristics of a prediction method will fit into a particular decision-making situation. Predictive situations vary widely in predictive time horizons, factors that determine actual outcomes, types of data patterns, and many other aspects [12]. To face such widespread use, several techniques have been developed, one of which is the trend method. Trend analysis can be used for forecasting. Forecasting or prediction is the use of past data from a variable or set of variables to estimate its value in the future [11-13].

4.1. Region scope

According to the study’s findings, the South East Asian region is the largest contributor to the TPT Program. However, records reveal that during the Covid-19 pandemic, which lasted from 2019 to 2021, this region saw a significant reduction from 2019 to 2020. That year was the first year that the Covid-19 Pandemic became present and expanded globally. According to the findings, the South East Asia region had a reduction in the number of TPT coverage from 2019 to 2020. Reduced TPT coverage by 20.5%. In the meantime, the Eastern Mediterranean and West Pacific regions are quite steady.

Globally, 40% of the nations that participated in a WHO research, experienced disruptions in health services, particularly TB services. Of 66% percent of these nations attributed disruption to medical leave or workforce displacement to Covid-19 services, affecting TB metrics such as the number of notifications. In several countries, there was a partial rebound in 2021, with more susceptible and drug-resistant TB diagnoses than in 2020, but this is still below pre-pandemic levels [2, 9].

As a highlight region, South East Asia (SEA) experienced a lot of target drops from 2019 to 2020. In 2019, 33% of the children under 5 years who are household contacts of persons with infectious TB disease and 32% of the PLHIV newly initiated on HIV care received TPT [13]. This case is related to policy changes that exist in several SEA countries in 2020. Out of the seven countries included in the situational study (Bangladesh, India, Indonesia, Myanmar, Nepal, Thailand, and Timor-Leste) have changed their NSPs and modified their TPT policies. All seven nations have included adolescents and adult household contacts of bacteriologically proven TB patients in the expanded target categories for TPT. In addition to the high-risk clinical groups advised by WHO, five nations have included them in their TPT target population [13]. The assessment for TPT eligibility in the target categories in all seven countries follows the algorithms provided in the most recent “WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment” [5, 7, 13]. Because chest radiography and tuberculosis infection (TBI) testing are optional, their availability and accessibility are unlikely to represent a major obstacle to TPT scale-up. However, the efficacy of this method is contingent on good TB symptom screening practices to prevent those with TB disease from taking TPT inadvertently. The seven nations have now included at least one of the four shorter TPT regimens, most typically the rifapentine-based 3 HP regimen, in their national guidelines [7].

4.2. TPT coverage trend analysis

According to the data analysis of the findings, TPT Coverage has a positive trend despite a one-time decline in 2019 to 2020. According to previous research, it was found that there was a disruption of global health care included in the Tuberculosis program during the Covid-19 pandemic (2019-2022). Unlikely, the TPT trend
tends to be decline in 2022 and then decrease from 2023 to 2024. Though falling in 2020, it could rise back in 2021 and the number is bigger than in 2019.

Different gap data from older research in Brazil, its show that the second wave of pandemics was accompanied by a large decline in TPT prescriptions, which we did not detect in a primary analysis of TB notifications. The decrease was significantly greater than the drop in TB disease notifications, which had reduced by 11.3% in 2021 [8]. However, the drop in TPT prescriptions cannot be explained just by a fall in the number of TB patients. Furthermore, the proportion of treatment finished remained stable, indicating that, while service supply to new patients was disrupted, those previously enrolled in the health system were able to obtain medication and complete their TPT provision [14, 15]. Although just a portion of the mandated TPT is reported in the database, we have no reason to suppose that the same phenomenon was not observed for non-notified TPT because TPT reporting is not necessary and many localities did not use the information system throughout the study period [16, 17].

TPT related recording and reporting methods are included into routine TB monitoring systems in all countries. However, gaps in the data captured and provided appear to exist in terms of completeness and correctness. TPT care cascade analysis is not frequently performed in all countries to assess the adequacy of TPT uptake and completion in target populations. All countries must examine whether TPT related adherence and adverse medication effect monitoring and treatment methods are adequate and patient-friendly, and improve them (if needed) to guarantee optimal TPT completion rates [13]. Finally, as expected, the timing of the reductions differed across Regions. Differences in pandemic burden and local government response may explain this heterogeneity situation, although the federal government never imposed any restrictions on the country [15, 18, 19].

4.3. **TPT coverage forecasting**

Quantitative methods require information from the past to be quantified in the form of numerical data, and quantitatively predictive methods base their predictions on statistical and mathematical methods [11, 12]. The results show a decline number from 2021 to 2022, hence increase in 2023 and 2024. The decline number in 2022 with the assumption of the impact of Pandemic Covid-19, however further research necessary. Increase number forecasting in 2023 and 2024 is very good for global TPT access, in Asia. In line with the global target, TPT coverage should reach 40% of total households for END TB strategy in 2024 [20, 21].

If these predictions are correct, then the global will be beneficial. Nevertheless, there are challenges ahead. Logistical preparations including regimes, procurement, distribution, monitoring and evaluation must be well planned. Previous research has shown that there is a weak recording and reporting on the tasks of monitoring and evaluation of TB program [8, 13, 18]. So, if the TPT coverage trend rises, it is expected that there will be an increase in preparedness also globally.

5. **Conclusion**

Trend analysis for multiples of three TPT coverage period among the Covid-19 Pandemic in Asia from 2016 to 2024 are using linear and quadratic models. The best model is the linear model with the equation \( Y_t = 198,287.5 + 26,283.1 \times X \), MSE= 1550927073.2, MAPE= 0.019, MAD= 23470, and MSD= 1033951382. According to the Covid-19 pandemic, TPT coverage in Asia had increased coverage rates, but as the Pandemic took place especially in 2020, access to TPT declined drastically. Forecasting using a linear model reveals that the population will expand constantly over the following three periods post Covid-19 Pandemic, with an average increase of 144,557 individuals in Asia.

6. **Recommendations**

During the Covid-19 Pandemic (2019 to 2020), there was a decline in TPT coverage in regions of Asia, particularly South East Asia, according to this research funding. More study on techniques to boost TPT coverage is required. As a result, the TPT program can have a global
impact on reducing the incidence of tuberculosis in at-risk communities. Strengthening collaboration and more massive efforts are needed so that the provision of TPT can be carried out optimally. For Primary Health Facilities throughout the region, it is expected to encourage contact household and close contact of TB index cases to consume TPT so that the latent TB infection present in his body does not become active. Primary health facilities are expected to play an active role in improving TPT coverage. It is expected that the entire territory will be fully equipped for mass procurement of TPT with optimal TPT logistical management.

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Conflict of Interest
The authors have no conflict of interest to declare.

References


Prostaglandin I₂ Inhibit Platelet Activation and Preserve Ultrastructure during Platelet Isolation by Centrifugation

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Abstract

Background: Platelets play role in hemostasis, therefore, either decreasing or increasing in platelet structure/function affects hemodynamic disorders. Platelet structural abnormalities and platelet dysfunction can cause bleeding disorder. In contrast, an increasing in α-granules and mitochondria, increased circulating reticulated platelets and platelet hyperfunction which led to hypercoagulable state that contribute to thrombosis. Therefore, ultrastructural and platelet function analysis are required for diagnosis, determining molecular abnormalities, and exploring novel therapeutic approaches.

Method: Platelet rich plasma (PRP) was collected from citrate-anticoagulated blood samples from healthy donors (n = 3), then being centrifuged at 150 x g for 10 min. Platelets were then isolated from PRP with or without prostaglandin I₂ (PGI₂, 2.5 - 10 μg/mL) by centrifugation at 25°C, either at low-speed (400 x g for 20 min) or high-speed (14,000 x g for 2 min). Flow cytometric analysis was used to determine platelet activation (CD41a⁺CD62P⁺). Transmission electron microscope was used to determine ultrastructure of platelets.

Results: Platelet activation was not significantly difference between whole blood (3±1%) and PRP (5±2%). Notably, centrifugation of PRP increased platelet activation at both low-speed (51±23%) and high-speed (66±21%). At high-speed centrifugation, PRP treated with PGI₂ at 10 μg/mL was 1.5- to 5-fold reduced in platelet activation compared to untreated PRP. However, PGI₂ had no effect in preventing platelet activation by low-speed centrifugation. Ultrastructure analysis of platelets is isolated by high-speed centrifugation with 10 μg/mL PGI₂ present with preserved platelet ultrastructure contain α-granules, dense granules, mitochondria and open canalicular system.

Conclusion: Therefore, 10 μg/mL PGI₂ was suitable for inhibiting platelet activation during high-speed centrifugation.

Keywords: Flow cytometry, Platelets, Platelet isolation technique, Prostaglandins I₂, Transmission electron microscope

1. Introduction

Platelets are mainly playing a role on hemostasis, wound healing and inflammation [1, 2]. The decrease in number of platelets (thrombopenia), platelet structural abnormalities and platelet dysfunction can lead to bleeding.

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disorder such as Bernard Soulier syndrome. In contrast, increased number of platelets (thrombocytosis), reticulated platelets and platelet hyperfunction can leading to hypercoagulable state that can contribute to thrombosis. Ultrastructural and platelet function analysis are required for diagnosis, determining molecular abnormalities, and exploring novel therapeutic approaches. Platelets are easily activated during blood collection, storage and centrifugation. Routine blood bank for platelet concentration is generally performed by centrifuged whole blood donors in citrate phosphate dextrose adenine solution (CPDA-1) anticoagulant at 1,000-1,500×g for 10 min to collect platelet rich plasma (PRP), and consequent centrifuged PRP at 3,000-5,000×g for 20 min to collect platelets and storage in 22±2°C for use within 72 h or immediately frozen at -80°C for cryopreservation [3-6]. Anticoagulant, speed of centrifugation, temperature and storage length are associated with quality of platelets for transfusion [5]. Special purification technique without artifacts is crucial for studying molecular mechanisms, functional properties of platelets and their impact on several diseases such as inherited platelet disorders, cardiovascular disease and sepsis.

Platelets are small (2-3 μm in diameter), anucleate cells derived from bone marrow megakaryocytes and have a lifespan of approximately 7-10 days in blood circulation. Structure of platelets including phospholipid bilayer form as plasma membrane, the open canalicular system (OCS), endoplasmic reticulum to form as the dense tubular system (DTS), spectrin-based membrane skeleton, actin-based cytoskeletal network, microtubules, α-granules, dense granules, peroxisomes, lysosomes and mitochondria. α-Granules present dominantly ~50-80 granules per platelet, which contain proteins essential for platelet adhesion during vascular repair such as glycoprotein (GP)IIb/IIIa (CD41a), fibrinogen and von Willebrand factor (vWF). α-Granules (200-500 nm in diameter) preset spherical shapes with a dark central core [7]. Dense granules or dense bodies (250 nm in diameter) are presented as electron-dense cores when investigate with electron micrographs and contain catecholamines, serotonin, calcium, adenosine 5'-diphosphate (ADP) and adenosine 5'-triphosphate (ATP) that released during platelet activation [8]. Freshly platelets released from bone marrow contain enrichment of mRNA that called “reticulated platelets” [9, 10]. mRNA in reticulated platelets had short time that degraded within ~24 hours, then, non-mRNA in platelets are called “platelets” which have 10 days as the average lifespan in blood circulation [10]. Reticulated platelets are enriched in mRNA leads to rapidly synthesize and express P-selectin or CD62P during activation after being treated with ADP as a weak agonist and thrombin as a strong agonist than non-reticulated platelets [9]. Moreover, reticulated platelets have increased amounts of α-granules and mitochondria compared to non-reticulated platelets. Increased amounts of reticulated platelets in diabetes mellitus have been evidence to play a critical role on increased platelet activation, platelet-leukocyte aggregation that can lead to initiation and progression of atherosclerosis, that associated with an increased risk for cardiovascular disease [10, 11]. Therefore, abnormalities of platelets either number, structure or function affects hemodynamic disorders. Defects of platelet structure including disorders of the platelet storage granules such as dense granule deficiency, α-granule deficiency, combined dense and α-granule deficiency and defective platelet adhesion such as decreased or absent expression of GP are related to abnormal function of platelets.

In this study, we applied the use of prostaglandins I2 (PGI2) or prostacyclin to acts as platelet inhibitors in order to prevent platelet activation and platelet aggregation [12] and to preserve platelet morphology during platelet purification from peripheral blood samples using centrifugation. Flow cytometry is an easy and rapidly method to screening platelet activation by using P-selectin (CD62P) as platelet activation marker, and the used of transmission electron microscope is a standard method for ultrastructural analysis of platelets. Herein, we demonstrated the approach to purified platelets from human peripheral blood samples using low- and high-speed centrifugation while preserve platelet
Fig. 1. Experimental design. Flow chart to study the effect of prostaglandins $I_2$ on inhibit platelet activation during low- and high-speed centrifugation. $PGI_2$: prostaglandins $I_2$, $PRP$: platelet rich plasma.

morbidity and limited artifact by treated PRP with $PGI_2$ upon the induction of platelet activation from centrifugation.

2. Methodology

2.1. Blood sample collection and platelet isolation

This study was performed in accordance with the Helsinki declaration and was approved by the Mahidol University Central Institutional Review Board (MU-CIRB), approval number 2021/069.2503. Written informed consent was obtained from all individual participants included in the study. The first 2 mL of blood samples from healthy donors ($n = 3$) were discarded to avoid platelet activation, and then individual sample was collected into 3.2% sodium citrate anticoagulant tube. Platelet rich plasma (PRP) was collected from citrate-anticoagulated blood samples from healthy donors by centrifuged at 150 $x$ g for 10 min (Fig. 1). Platelets were then isolated from PRP by centrifugation at 25°C, either at low-speed (400 $x$ g for 20 min) or high-speed (14,000 $x$ g for 2 min). In order to decreased platelet activation, 2.5 - 10 $\mu$g/mL of $PGI_2$ was added to PRP before centrifugation. Pellet platelets were washed one with Tyrode’s-HEPES buffer (145 mM NaCl, 2.9 mM KCl, 1 mM MgCl$_2$ and 5 mM D(-)-glucose), pH 7.4 at the same speed and used to investigate platelet activation by using flow cytometry and morphological analysis by using transmission electron microscope.

2.2. Platelet activation using flow cytometry

Whole blood, PRP and isolated platelets were stained with fluorochrome conjugated monoclonal antibody specific to CD41a (GPIIb/IIa, common platelet marker) and CD62P (P-selectin as platelet activation markers) and measured by FACScan flow cytometer (BD Bioscience) as described in previous study [13]. Percentages of platelet activation (CD41a$^+$CD62P$^+$) were analyzed by BD CellQuest software (Fig. 2), briefly, platelet population in R1 region was gated and analyzed CD41a as common protein on platelets as platelet marker in R3 region. Then, CD41a$^+$ platelets in R3 region were analyzed CD41a$^+$CD62P$^+$ as platelet activation marker (upper right of the quadrant analysis in Fig. 2F). BD CellQuest software was calculated the percentages of platelet activation from positive events in CD41a$^+$CD62P$^+$ multiply
Fig. 2. Flow cytometric analysis of platelet activation. (A-C) Whole blood sample from healthy donor was diluted in phosphate buffer saline as negative control for analysis of platelet activation; (A) density plot of platelet population in FSC-Height and SSC-Height in R1 region that gated to analysis of (B) CD41a negative cells in R2 region and used for (C) determine dual positive signal by using quadrant analysis. (D-F) Whole blood sample from healthy donor was diluted and stained with FITC conjugated anti-CD41a and PE conjugated with anti-CD62P for determine platelet activation. (D) Gated platelet population in R1 region were further investigate (E) CD41a⁺ platelets in R3 region and consequent to analysis of (F) platelet activation as dual positive signal of CD41a⁺CD62P⁺platelets.

by 100 and divide by total events in R3 region as CD41a⁺platelets. All antibodies and reagents were purchased from BD Bioscience.

2.3. Platelet morphology analysis using transmission electron microscope (TEM)

Platelet morphology was performed by the modification from previous study [14]. Isolated platelets were fixed with 2.5% glutaldehyde solution in 0.5 M phosphate buffer and stained with osmium tetra-oxide, then, wash with distill water and dehydration with sequential 50%, 70%, 90%, absolute ethanol solution and acetone. Platelets were embedding in Epon for section. Thick section was stained with toluidine blue to select the investigated zone before performed thin section, which further stained with uranyl and lead for the analysis of ultrastructure using Hitachi TEM System HT7700 (Hitachi High-Technologies Corporation, Japan).

2.4. Statistical analysis

Statistical analysis was performed by SPSS Version 18.0 (IBM, Chicago, USA) and platelet morphology were analyzed by using ImageJ software (National Institutes of Health, USA). Comparisons between parameters was evaluated with independent samples T-Test at P < 0.05.

3. Results

3.1. PGI₂ inhibit platelet activation as dose dependent manner during high-speed centrifugation

In order to evaluate the effect of centrifugation on platelet activation, flow cytometric analysis was performed to determine platelet activation (CD41a⁺CD62P⁺) in citrate-whole blood, PRP and isolated platelets from centrifugation at low- and high-speed. No significantly different of platelet activation was observed between whole blood (3±1%) and PRP (5±2%) as the baseline control in healthy donors (n = 3). Notably,
Fig. 3. Effect of centrifugation and PGI$_2$ concentration on platelet activation. (A) Percentages of platelet activation were analyzed by flow cytometry in whole blood (WB), platelet rich plasma (PRP), low-speed centrifugation (400×g for 20 min) and high-speed centrifugation (14,000×g for 2 min). Effect of different doses of prostaglandins I$_2$ (PGI$_2$) to inhibit platelet activation during centrifugation at (B) low-speed and (C) high-speed. *Significant difference between groups, $P < 0.05$.

Fig. 4. Ultrastructural Morphology of platelets under TEM analysis. (A) Electron micrograph of platelets from healthy donor. (B) A color labeling organelle; α-granules (blue), dense granules (orange), mitochondria (green) and open canaliculi system (yellow).

Centrifugation had affected to increased platelet activation at both low-speed (51±23%) and high-speed (66±21%) when compared with whole blood and PRP ($P < 0.05$) (Fig. 3A). In order to prevent platelet activation during centrifugation, PGI$_2$ at different concentration (2.5, 5 and 10 μg/mL) was used to pretreated PRP samples before centrifugation. Untreated and PGI$_2$-treated PRP samples were centrifuged at either low-speed centrifugation (400×g for 20 min) or high-speed centrifugation (14,000×g for 2 min) at 25°C to collected pellet platelet and dissolved in Tyrode’s-HEPES buffer. Surprisingly, no effect of PGI$_2$ in inhibiting platelet activation was observed during low-speed centrifugation in platelets treated with PGI$_2$ at 2.5, 5, 10 μg/mL (44±20%, 48±31% and 47±21%, respectively) compared to baseline control (51±23%) (Fig. 3B). While PGI$_2$ inhibit platelet activation during high-speed centrifugation was observed as dose dependent manner in platelets treated with PGI$_2$ at 2.5, 5, 10 μg/mL (52±7%, 39±21% and 28±25%, respectively) compared to baseline control (66±21%) (Fig. 3C). Therefore, PGI$_2$ at 10 μg/mL was recommended for inhibiting platelet activation during centrifugation. However, percentages of platelet activation in PGI$_2$-treated platelets were still higher than fresh PRP before performing high-speed centrifugation.

3.2. PGI$_2$ acts as preservative for investigate platelet morphology
Ultrastructural analysis is a standard method to evaluate the defect in platelet structure. Therefore, the suitable concentration of PGI₂ at optimal speed of centrifugation could not affect the morphology of platelets. In this study, PRP sample was treated with 10 μg/mL of PGI₂ before centrifugation, then, pellet platelets were washed and fixed with 2.5% glutaraldehyde solution and process samples for analysis morphology by using TEM. Electron micrographs were captured and identified organelle including α-granules (blue), dense granules (orange), mitochondria (green) and OCS (yellow) in platelets using Image J software (Fig. 4). The ultrastructure of the individual platelet was clearly identified. Resting platelets are generally presented α-granules as back circular form, dense granules as black dot surrounded by halo in the circular or oval shape and OCS as conduits like tunnel throughout the interior part of the platelet. Resting platelets had a few or not present mitochondria, characterized by oval-circular shapes present with fold of cristae.

4. Discussion

Diagnosis of platelet disorders in structural defect, discovery on biology, functional analysis, pathology and novel treatments of platelets required purified platelets from blood circulation without artifacts from isolation technique. Herein, isolated platelets using PGI₂-treated PRP and double centrifugation is easy and not expensive technique for investigate platelet morphology. Prostaglandin has been established as platelet activation inhibitor to preserved platelet morphological change, inhibit platelet release their granules and aggregation [14]. Prostaglandins are a group of physiologically active lipid compounds, eicosanoids which having diverse hormone-like effects that found in many tissues and organs and synthesized in cell from arachidonic acid via cyclooxygenase pathway or lipoxygenase pathway. There are 4 types of bioactive prostaglandins generated in vivo that are including PGI₂, prostaglandin D2 (PGD₂), prostaglandin E2 (PGE₂) and prostaglandin F2α (PGD₂α) [15]. PGI₂ is generally release from endothelial cells to regulate vasodilation, inhibit platelet aggregation, leukocyte adhesion and vascular smooth muscle cell proliferation. In this study, we found that the PGI₂ had effect to inhibit platelet activation, however, it is no ability to inhibit platelet activation during low-speed centrifugation at 400×g for 20 min. It might be cause of time consumed for sediment of platelets. As demonstrated by aggregometry, PRP was treated with 5 μM ADP at time 0 shown no platelet aggregation. After incubation, the platelet aggregation was increased up to 50% for 1.5 min and 100% for 3 min. The ultrastructural analysis of 10 μM ADP-treated platelets for 7 min was showed macroaggregated platelets without isolated platelet. In the clump, most of platelets had no organelle remain while few platelets had α-granule [16]. Therefore, the ultrastructural analysis of platelets isolated from untreated PRP at both low- and high-speed centrifugation and PGI₂-treated PRP at low-speed centrifugation was not investigated in this study. Because of all those conditions affect to increased platelet activation as determined by flow cytomtery. It could induce ADP release from activated platelets during centrifugation, then, soluble ADP might activate other resting platelets to activated platelets leading to clump. Not only PGI₂ is commonly used for inhibiting platelet activation, PGE₁ has been reported to use as antiplatelet therapy, common use in infants with congenital heart defects, by mediated P2Y1-platelet receptor [17] and also use as preservative to prevent loss and alteration of platelets during specimen collection such as cardiopulmonary bypass [14]. PGE₂ is also abundant in cells and tissues and mainly involving in anti-inflammation to regulate immune cell function [18]. PGE₁ is biologically active at low concentration (0.1-0.3 μM), rapidly metabolized by lung and its effects potentially are reversible. Therefore, PGE₁ might be another biological molecule that useful for further investigation of inhibit platelet activation during centrifugation.

The centrifugation affect to quality of platelets, the speed of centrifugation at 100-250×g for 10 min had no effect to activate platelets while at 1,000-10,000-g for 10 min had increased platelet activation [19]. In addition, we investigated effect of different speeds of
centrifugation at 400×g for 20 min [9] and 14,000×g for 2 min [20] that widely used for platelet isolation but not reported the effect on platelet activation. Moreover, PRP and platelet concentration are commonly used for transfusion in patients with bleeding disorder as the standard therapeutic approach. However, protocol for PRP and platelet concentration in routine blood bank is used at 1,000 – 5,000×g without preservative that could be effect to induce platelet activation during centrifugation. The low-speed of centrifugation might be trigger platelets as weak agonist that could reverse to resting platelets during storage in few minutes [19]. Additionally, platelets had sequential to response against to different stimuli. Weak agonists such as low dose of ADP (1.5 μM) trigger a primary wave of aggregation without degranulation which means platelets can reverse to resting stage after platelet activation and aggregation. By contrast, strong agonists such as thrombin, collagen, high dose of ADP (8 μM) trigger both primary and secondary waves of aggregation leading to irreversible of platelets [21, 22]. Therefore, it needs to concern the preservative and the speed of centrifugation for the quality of platelets in routine blood bank.

Ultrastructural analysis of platelets required special technique for sample preparation. Importantly, the key factors that need to be concerned for platelet preparation are isolation technique such as centrifugation and perseverative solution that use for preventing loss and alteration of platelets during purification. In this study, we demonstrated the effect of speed of centrifugation on platelet activation and optimize the suitable dosage of PGI₂ to prevent artificial platelet activation by centrifugation. However, there are other techniques for sample preparation such as agar sandwich technique by using agar in a polyethylene terephthalate tube with 1-2 mm diameter [9] and gel-filtered platelets with aspirin [23] that could be used for platelet preparation for TEM analysis.

5. Conclusion

PGI₂ at 10 μg/mL was suitable for inhibiting platelet activation during high-speed centrifugation to preserved platelet ultrastructure. This study is useful for improve the quality of platelet purification without the artifact that could be investigate the morphology and function of platelets in the specific diagnosis and research.

6. Recommendations

Speed of centrifugation affect to increased platelet activation, however, centrifuged whole blood samples at 150×g for 10 min, 25°C to collect PRP had recommended to avoid platelet activation. Platelet isolation for further research study or functional assay could be treat PRP with 10 μg/mL PGI₂ before high-speed centrifugation at 14,000×g for 2 min, 25°C to collect platelets and dissolved in Tyrode’s-HEPES buffer, pH 7.4 or fixed with preservative such as 2.5% glutaldehyde solution in 0.5 M phosphate buffer.

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Authors’ contributions
PU performed the experiments, analyzed the data and drafted the manuscript. RP and SC were responsible for platelet activation and analyzed the data. CP were responsible for performed and captured illustration using transmission electron microscope. KP contributed to the concept of the study and specimen collection. SW and SS contributed to the concept of the study and interpretation. PC was the principal investigator and takes primary responsibility for the conception, research design, data analysis, drafting and editing the manuscript. All authors reviewed and approved the final version to be published.

Conflict of interest
None

References


[22] Zhou L, Schmaier AH. Platelet aggregation

Description of Values in Nursepreneurship Services in the East-North Kalimantan Region of Indonesia: Cross-Sectional Study

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Abstract

Background: Nursepreneurship support with modern nursing services. Through expanding access and independent nursing practice models that pay attention to value (product quality, financial value, emotional value, social value) is important in realizing optimal care services with relevant capabilities. This study aims to provide an overview of the value that includes product quality, financial value, emotional value, social value that exists in nursepreneurship services in the East-North Kalimantan region.

Method: Cross sectional with 32 nurses as respondents, using closed questionnaire instruments and descriptive analysis to see the description of the variables studied.

Result: 32 nursepreneurs in the East-north Kalimantan region filled the value questionnaire. Questionnaire answers describe product quality with 3 indicators: quality (mean: 37.9, SD: 2.4), quality standards (mean: 37.87, SD: 3.36), consistent (mean: 18.56, SD: 2.5), financial value with 3 indicators: economy (mean: 18.56, SD: 2.5), effectiveness (mean: 11.00, SD: 1.13), efficiency (mean: 14.7, 1.81). Emotional value with 4 indicators; motivation (mean: 31.18, SD: 1.42), interest (mean: 29.75, SD: 2.01), customer response (mean 64.31, SD: 3.13), service experience (mean: 19.68, SD: 0.89). Social value with 3 indicators; solution (mean: 25.5, SD: 1.52), perception (mean: 52.87, SD: 7.05), recognition (mean: 25.43, SD: 1.26).

Conclusion: Nursepreneurship is expected to pay attention to value in services with new knowledge. Created through a sustainable directed system to support the optimization of nursing services. Mastery of knowledge management competencies in nursepreneurship services that are an element in every nursing care action with optimal nursing services and measurable value.

Keywords: Nurse practitioner, Private practice, Entrepreneurship

1. Introduction

Nursepreneurship is an entrepreneurial activity carried out by a nurse entrepreneur (nursepreneur) in independent nursing practice with accountable integrity values based on education and skills in the field of nursing and the ability to manage a business [1]. Nursepreneurship is an idea that focuses on innovation decisions with the nursing care process in appreciation, recognition and improvement of work in the social context of experiences, expectations and perspectives carried out by nursing professionals [2]. The support of nursepreneurship with modern nursing services [1] through expanding access and independent nursing practice models that pay attention to value (product quality, financial value, emotional value, social value) [3] has an effect on improving the quality of health services [4] in realizing optimal care services with relevant capabilities [5].

Global data on nursepreneurship in service delivery activities amount to 0.5-1% of all working nurses [6]. In 2021, nursepreneurship in the form of independent nursing practice services in

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Indonesia amounted to 1941 and in East-North Kalimantan amounted to 84 [7]. The low value of nursepreneurship risks an adverse situation because it is considered not in accordance with the service needs desired by patients [8]. The short-term impact causes the number of nursepreneurship to decrease one by one, and it is feared that it will not get support from policy holders. The long-term impact is that the development of personal and professional quality of nursing in strengthening nursepreneurship to support the improvement of the quality of health services cannot be realized [9].

This problem needs to be highlighted to what extent the description of the value that exists in nursepreneurship in East-North Kalimantan in facing the challenges of a more formal role to create changes in modern nursing with expanded access for patients with increasing needs [10]. It is expected that the better the value, the quality of health services tends to improve with increased patient satisfaction [11].

2. Methods

This research design with a cross sectional study approach with stages carried out without any intervention and carried out at the same time in the East-North Kalimantan region. We administered the questionnaire to nursepreneurship groups in East and North Kalimantan with 80 members, and 32 people completed and returned the questionnaire. Using non probability sampling technique and purposive sampling method with predetermined inclusion criteria [12].

In the next stage, we administered a non-intervention questionnaire developed by the researchers based on [3] to the nursepreneurship group in the East-North Kalimantan region, and 32 nurses completed the questionnaire. The sample criteria for this study are as follows:

1. Inclusion criteria
   a. Male or female nurses over the age of 23 years
   b. Have a minimum education of diploma nursing
   c. Running independent nursing practice as nursepreneurship
   d. Able to communicate well

2. Exclusion criteria
   a. Nurses who only work in health care facilities or in academia
   b. Nurses who run independent nursing practice as nursepreneurship but are experiencing illness, or in emergency conditions.

3. Results

Data were collected using a closed question questionnaire instrument and descriptive analysis to see the description of the variables studied.
This stage begins with a literature review on various data bases with the keywords used nurse practitioner, private practice, entrepreneurship, nursing service. The PRISMA diagram presents the results of the literature search (Fig. 1.).

Some of the research studies that underlie this research are [9] that the patient’s point of view shows the highest priority in the perspective of nursepreneurship services that present important challenges in nursepreneur behavior [13] where the accompanying values (product quality, social value, financial value and emotional value) have a reciprocal relationship between these types of values have shown the dominance of extrinsic-intrinsic and self-other [14]. The gaps found from the aforementioned studies are that the antecedent factors are not the same, the research designs are different and the explanation of the results only corresponds to one keyword each. References on the description of nursepreneurship with value are also still minimal so there is no previous research as a comparison and research questions have not been answered.

Measurement of variable results in this study was carried out indirectly, namely by measuring several indicators, Table 1.

Table 1, Table 1, it can be explained that the product quality with 3 indicators, namely quality (mean: 37.9, SD: 2.4), quality standards (mean: 37.87, SD: 3.36), consistent (mean: 18.56, SD: 2.5). The opinion that can be given is that there are unmet customer desires regarding detailed information related to services, payments and basic customer service that is still low, as well as problems with compliance with SOPs. Information provided on services through explanation of options can ensure greater acceptance from others [10].

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4. Discussion

The description of the value of product quality in nursepreneurship services in the East Kalimantan region with the value of product quality with 3 indicators, namely quality (mean: 37.9, SD: 2.4), quality standards (mean: 37.87, SD: 3.36), consistent (mean; 18.56, SD; 2.5). The opinion that can be given is that there are unmet customer desires regarding detailed information related to services, payments and basic customer service that is still low, as well as problems with compliance with SOPs. Information provided on services through explanation of options can ensure greater acceptance from others [10].

Financial value with 3 indicators, namely economy (mean; 18.56, SD; 2.5), effectiveness (mean; 11.00, SD; 1.13), efficiency (mean; 14.7, SD; 1.81). Financial arrangements, goals and targets that are not yet appropriate, management of resources and funds that are not maximized are likely to be a contributing factor to the low financial value picture. Financial literacy is
needed with the ability to make judgments, make effective decisions in using and managing finances [15].

Emotional value with 4 indicators, namely motivation (mean; 31.18, SD; 1.42), interest (mean; 29.75, SD; 2.01), customer response (mean 64.31, SD; 3.13), service experience (mean; 19.68, SD; 0.89). These test results illustrate the desires, beliefs and expectations that have not been achieved with the skills and knowledge possessed. Activities that are still focused on achieving material targets, there are still many service complaints, there has been no evaluation of service testimonials, the application of customer oriented is still minimal, there is also no application of lost customer analysis. The results of research [16] show that it is important to make efforts to improve care services while the results of research [17] show that the expectation score of health service users is 4.97 and while the perception is 3.26, and the quality gap in the same type of service provided is 1.7.

Problem solving ability, service process, how to serve is reflected in social value with 3 indicators; solution (mean 25.5, SD; 1.52), perception (mean; 52.87, SD; 7.05), recognition (mean; 25.43, SD; 1.26). The overview of these test results shows that good service design is needed by applying design thinking to all aspects of service in improving customer experience and understanding [4].

5. Conclusion

This study only describes the value that exists in nursepreneurship services in the East-North Kalimantan region in one measurement time, with a limited number of samples, providing recommendations for phenomena and not a core solution to the problem at hand. The lack of research on value in nursepreneurship is a limitation in comparing this study with previous research results. From the results of the questionnaire, it can be concluded that the current reality of nursepreneurship is still not in accordance with the expected [1] and it is feared that it will give a perception of poor service quality, with indicators that need attention, which is shown by a mean value < 50 low in product quality, financial value, emotional value, and social value. Although the value of customer responses and perceptions shows a mean value > 50, it has not been able to represent a good value on nursepreneurship. It is feared that this will lead to complaints with sharp criticism, and the nursepreneur is considered unable to complete the job perfectly.

The suggestions to improve knowledge to explore entrepreneurial ideas and opportunities, validity analysis, business planning, supported by good management are expected to increase the value of nursepreneurship which is still low [18]. Nursepreneurship that has a good value will have an impact on the quality of health services. These indicators influence the identification of influence on the quality of health services [19]. The development of value-based nursepreneurship is expected to have an impact on the quality of health services with elements of responsiveness, assurance, tangibles, empathy, reliability. This is an integration of nursing focused on health services with customer loyalty as the end result. Freedom to innovate in nursepreneurship must be a driving force towards success in the world of nursing as a supporter of the quality of health services [20].

Nursepreneur as a business development actor in independent nursing practice is a trend in the field of private nursing, with nursing services produced in the form of goods and services, or home care with their expertise [21]. The changes and developments in the world of nursing with the needs of the global community prove that in the history of nursing shows the ability of nurses to do so, by utilizing knowledge and experience to face challenges [10]. Global development requires innovation and creativity in various industries, not least in nursepreneurship with the support of management knowledge that has an impact on the formation of trust and motivation [5].

Nursepreneurship with value is expected to collaborate, with the creation of technology and smart advanced policies that support nursepreneurs as market players [22]. A nursepreneur must be able to interact by putting themselves forward as agents of change, combining strong entrepreneurial motivation with...
clinical skills, business knowledge in providing solutions [20]. The application and real work of nurses in carrying out their activities as nursepreneurs is an experience that is presented as motivation. Career transition into a nursepreneur requires challenges and strategies with the increasing need for privacy care in the community as well as self-reflection on negative issues found in other work environments [23].

6. Recommendations
The need for a nursepreneurship development model based on value (product quality, financial value, emotional value, social value) owned by nursepreneurs with management knowledge in an effort to provide optimal care services that have an impact on the quality of health services. In the future, nursepreneurship is expected to face the biggest challenges for success faced in service delivery [23]. The impact of nursepreneurship is that the quality of health services. Nursepreneurship services must always be considered and measured because of course patients and families want the best and tangible services [24]. Nursepreneurship must be able to respond to changes in the globalization dimension of society through technological developments. Services must include better dimensions of professional pride and competence centered on patient center care [25].

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Conflict of Interest
The authors declare that there are no conflicts of interest.

References


Radiosynthesis of Novel $^{68}$Ga-labeled $\alpha$-Cyclodextrin for PET Imaging

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Abstract

**Background:** Cyclodextrins (CDs) are cyclic oligosaccharides composed of glucose units linked by $\alpha$-1,4 glycosidic bond. Recently, CDs have been promising for the application of medical imaging, especially nuclear medicine imaging. Herein, we aim to simply radiosynthesize $^{68}$Ga-alpha-cyclodextrin ($^{68}$Ga-αCD) by directly radiolabeling Ga-68 to αCD.

**Method:** Ga-68 was eluted from the $^{68}$Ge/$^{68}$Ga generator. αCD solution was prepared and added to the reaction vial. The vial was heated at 100 °C for 20 min. After that, the reaction was allowed to cool down at room temperature. Radioactivity was measured using instant thin layer chromatography (iTLC) and the obtained iTLC paper was scanned by a TLC scanner. The radiochemical purity (RCP) was calculated. The pH of the resulting solution was measured using a pH meter and its mass to charge ratio was measured using mass spectrometry (MS). The radiosynthesis process was then optimized to increase the RCP of $^{68}$Ga-αCD.

**Result:** Initially, RCP of the $^{68}$Ga-αCD was very low (0.236 ± 0.02%, n=3). Upon the optimization using sodium ascorbate as radiostabilizer together with 1 mg/ml αCD solution and purified by C-18 cartridge, the RCP is increased. Ultimately, we have successfully achieved an RCP of 18.4 ± 1.1%.

**Conclusion:** In this study, we successfully radiosynthesized $^{68}$Ga-αCD by directly radiolabeling Ga-68 with αCD. Although our findings reveal significant possibilities, further investigation of biodistribution studies using PET imaging is required to thoroughly understand the potential of these novel radiopharmaceuticals.

**Keywords:** Cyclodextrin, Gallium-68, Radiochemical purity, Radiopharmaceuticals

1. Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of glucopyranose units linked by $\alpha$-1,4 glycosidic bonds. They possess cone-shaped structures capable of forming inclusion complexes, resulting in enhanced aqueous solubility of poorly water-soluble drugs. The natural CDs are $\alpha$-cyclodextrin (αCD), $\beta$-cyclodextrin (βCD) and $\gamma$-cyclodextrin (γCD), which are composed of 6, 7, or 8 glucose units, respectively [1]. The natural CDs and their guest/CD complexes have limited aqueous solubility. Various CD derivatives, such as hydroxypropyl and randomly methylated CDs, have been introduced to improve their solubility and that of their complexes [2]. CDs are enabled excipients in pharmaceutical products, and they offer versatile benefits in many industries, such as food, textiles and packaging, cosmetics and...
personal care, and the separation process. Recently, CDs have been interesting for the application of medical imaging, especially in nuclear medicine imaging [3].

Hajdu et al. [4] studied the in vivo distribution of hydroxypropyl-β-cyclodextrin (HPβCD) in normal mice by radiolabeling with 68Ga-1,4,7-triazacyclononane-1,glutaric acid-4,7-acetic acid (NODAGA). 68Ga-NODAGA-HPβCD has high radiochemical purity, stability, favorable pharmacokinetics in a mouse model and partition coefficient (log P value) at -3.07. One year later, the same research group investigated the biodistribution of the prostaglandin E2 (PGE2)/randomly methylated β-cyclodextrin (RMβCD) complex in normal mice and PGE2 positive tumor-bearing mice by radiolabeling with 68Ga-NODAGA [5]. The log P value of 68Ga-NODAGA-RMβCD is -3.63. A high standard uptake value (SUV) and accumulation of 68Ga-NODAGA-RMβCD at the tumor site were observed in the tumor-bearing mice group. In mid-2022, Csige et al. [6] investigated the in vivo distribution of RMβCD in normal mice and tumor-bearing mice by radiolabeling with 68Ga-1,4,7,10-tetraazacyclododecane-1-(glutaric acid)-4,7,10-triacetic acid (DOTAGA), and 205/206Bi-DOTAGA. The log P value of [68Ga-DOTAGA-RMβCD and 205/206Bi-DOTAGA are -3.47 and -3.45 respectively. Again, in the tumor-bearing mice, high SUV and accumulation of 68Ga-DOTAGA-RMβCD at the tumor site were also detected. In late 2022, Szabo et al. [7] evaluated the in vivo PET imaging of 68Ga-NODAGA-RMβCD and 68Ga-NODAGA-HPβCD compared with [18F] Fluorodeoxyglucose ([18F-FDG) in a tumor model. 68Ga-NODAGA-RMβCD and 68Ga-NODAGA-HPβCD uptake at the tumor site. However, the accumulation and SUV of both radiopharmaceuticals were lower than those of [18F-FDG.

As aforementioned above, CD-based radiopharmaceuticals have the potential for PET imaging and can be further developed and expanded for other applications in nuclear medicine. For example, tracking the biodistribution of drugs in a formulation containing CD as an excipient, the synergistic or additive effects of chemotherapy drug/CD complexes, and radiolabeled with β- or α-emitting radionuclide for tumor killing. The previous studies reported that the radiosynthesis require chelator molecules such as 1,4,7-triazacyclododecane-1,4,7,10-tetraazacyclododecane (NOTA) or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) to link CD together with radionuclide [5-7]. To the best of our knowledge, there are no reports regarding direct radiolabeling between CDs and radionuclides (i.e., without chelator). Thus, the aim of this study was to fabricate and characterize αCD labeled with Ga-68 (68Ga-αCD) by directly radiolabeled Ga-68 with αCD and optimize a radiosynthesis of (68Ga-αCD) for PET imaging. Ga-68 was selected as radionuclide due to its commonly used in clinic and it primary emit β+, making ideal for PET imaging [8]. Simultaneously, αCD was selected as a ligand due to its high aqueous solubility and can be used in various pharmaceutical dosage forms, especially in parenteral solutions [9]. Additionally, the effect of radiostabilizers (i.e., ascorbic acid and sodium ascorbate), the concentrations of ligand (i.e., αCD) and the purification step using C-18 cartridge were determined for the optimization process.

2. Methods

2.1. Radiosynthesis of 68Ga-DOTA and 68Ga-αCD

The radiosynthesis procedure is modified based on the clinical use of the PSMA-11 radiolabeling protocol [10]. In this study, αCD was used as a ligand due to its high aqueous solubility and can be used in various pharmaceutical dosage forms, especially in parenteral solutions. Briefly, 250 mg of αCD was accurately weighed, dissolved, and adjusted with sterile water to 100 mL (2.5 mg/ml). Further dilution was prepared by pipetting 1 ml of obtained αCD solution into a 10-ml volumetric flask and then adjusting the volume with sterile water to obtain the final concentration (0.25 mg/ml). After that, 100 µl of αCD solution was pipetted and mixed with 2 ml of 0.05 M HCl in a syringe. To compared with the reference DOTA, the most commonly used as a chelator for Ga-68 [11] was prepared with the same procedure as described above.
For the Ga-68 eluting process, the reaction vial was put in shielding and connected to the \(^{68}\)Ge\(^{68}\)Ga generator. Then, Ga-68 was eluted from the generator by using 4 ml of 0.05M HCL as an eluent. Radioactivity was measured immediately after the elution. The obtained \(^{68}\)GaCl\(_3\) solution was divided into two reaction vials. DOTA and \(\alpha\)CD solutions that were previously prepared were separately added to the reaction vial. Both vials were heated at 100°C for 20 minutes. After that, the reaction was allowed to cool down at room temperature for 5 minutes. Finally, the radioactivity was measured using instant thin layer chromatography (iTLC), and the presenting result data was radiochemical purity (RCP) (Fig. 1). Each sample was performed in triplicate.

The effect of radiostabilizer on the RCP of \(^{68}\)Ga-DOTA and \(^{68}\)Ga-\(\alpha\)CD was determined. Sodium ascorbate and ascorbic acid were selected as radiostabilizers. These two radiostabilizers have been reported as effective radiostabilizers for many radiopharmaceuticals [12]. Each compound was separately prepared by dissolving 0.04 g in 2 ml of sterile water. Each solution was mixed with 100 µl of DOTA or \(\alpha\)CD solutions and was used as a ligand sample. Radiolabeling of \(^{68}\)GaCl\(_3\) and the most potent radiostabilizer (without ligand) was also conducted to confirm the absence of any reactions between them. The radiosynthesis process was conducted as described above. Each sample was performed in triplicate.

2.2. Optimization of \(^{68}\)Ga-\(\alpha\)CD radiosynthesis

2.2.1. Effect of \(\alpha\)CD concentrations

A stock solution of \(\alpha\)CD was prepared by dissolving 500 mg of \(\alpha\)CD in 100 ml of sterile water (5.0 mg/mL). Serial dilutions of \(\alpha\)CD solutions were prepared, and the concentration range from 0.5 mg/mL to 5.0 mg/mL were given. 100 µl of each \(\alpha\)CD solution was mixed with 2 ml of sodium ascorbate. The radiosynthesis process was conducted as described above.

2.2.2. Purification of \(^{68}\)Ga-\(\alpha\)CD

\(^{68}\)Ga-\(\alpha\)CD was purified by C-18 cartridge, a widely used cartridge for Ga-68 radiopharmaceuticals purification [13]. Firstly, C-18 was washed with 2 ml ethanol prior before radiosynthesis process. After the radiosynthesis, waste vial was put in shielding and connected to the C-18. \(^{68}\)Ga-\(\alpha\)CD solution in reaction vial was drawn via syringe and connected to product vial. C-18 was slowly flushed with 3 ml of 1:1 ethanol:water. Finally, the radioactivity of solution from product and waste vials were measured using iTLC.

2.3. Characterization of \(^{68}\)Ga-DOTA and \(^{68}\)Ga-\(\alpha\)CD

2.3.1. TLC and RCP determination

0.2 ml of sample (\(^{68}\)Ga-DOTA or \(^{68}\)Ga-\(\alpha\)CD) were drawn in 1-ml syringe. Five small drops of the sample solution were dropped on iTLC paper. The paper was placed in a mobile phase tank.
containing 1 ml of 1:1 ammonium acetate; methanol. To determine TLC, the iTLC papers were scanned by TLC scanner (Gamma BGO-V-Detector, Raytest®, Isotopenmessgeraette, GmbH, Germany). For RCP measurement, the paper was cut into eight sections and put in eight separate tubes. After that, the activity of iTLC paper was measured in a well-chambered γ-counter. The RCP of the obtained product was calculated using the following equation:

\[ \text{RCP} = \left( \frac{\text{Product}}{\text{Product + Free Ga-68}} \right) \times 100 \]

2.3.2. **Mass spectrometry (MS)**

To observe the mass of ⁶⁸Ga-αCD, MS was determined in form of ⁶⁸Zn-αCD after 3 days of radiolabeling. This time frame ensured the complete decay of all Ga-68 into Zn-68. The sample analyzed by ESI (+) triple quadrupole MS (QTRAP6500, Sciex, Framingham, MA, USA). ⁶⁸Ga-αCD was placed directly at ESI source and the analysis conditions were as follows: electrospray ionization (ESI) positive mode; scan, 200–1050 m/z; temperature, 350 °C; capillary voltage, 4500 V; and collision energy, 40 eV.

2.3.3. **pH determination**

pH of the obtained samples was determined by pH meter (FE20 FiveEasy, Mettler Toledo, Switzerland) at 25 °C. Prior to analysis, the pH meter was calibrated with the standard solutions at the pH of 4, 7 and 10.

2.4. **Statistical analysis**

All quantitative data are presented as the mean ± standard deviation (SD). The statistical significance of the difference in mean was calculated by paired T test or one-way ANOVA followed by Post Hoc test. A \( p < 0.01 \) was considered as statistical significance.

3. **Results**

3.1. **Radiosynthesis of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD**

Table 1 displays the pH and the RCP of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD. In the absence of radiostabilizer, the RCP of both samples are relatively low. The RCP of 13.68 % for ⁶⁸Ga-DOTA and 0.24 % for ⁶⁸Ga-αCD. The pH of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD was 1.55 and 1.56, respectively.

3.2. **Effect of radiostabilizer**

The RCP obtained from sodium ascorbate as a radiostabilizer yields significantly higher than those of ascorbic acid and without radiostabilizer in both cases (DOTA and αCD). In the presence of ascorbic acid, the pH of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD solutions were 2.02 and 2.07, respectively. The pH of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD containing sodium ascorbate were significantly higher (3.83 and 3.93, respectively) compared to the former cases. Because ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD using sodium ascorbate as a radiostabilizer showed a promising RCP result, their iTLC papers were scanned by TLC scanner (Fig. 2A and B). The products (⁶⁸Ga-DOTA and ⁶⁸Ga-αCD) were shown in red, while free Ga-68 was shown in green. Retention factor (RF) of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD were 0.77 and 0.72, respectively. Radiolabeling of ⁶⁸GaCl₃ and

**Table 1. pH and the RCP of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD**

<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>Radiostabilizer</th>
<th>pH</th>
<th>Radiochemical purity (RCP, %)</th>
<th>RCP ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>⁶⁸Ga-DOTA</td>
<td>-</td>
<td>1.55 ± 0.03</td>
<td>13.68 ± 0.69%</td>
<td>-</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>2.02 ± 0.12</td>
<td>60.57 ± 5.68%*</td>
<td>4.43</td>
<td></td>
</tr>
<tr>
<td>Sodium ascorbate</td>
<td>3.83 ± 0.29</td>
<td>94.56 ± 1.34%*</td>
<td>6.91</td>
<td></td>
</tr>
<tr>
<td>⁶⁸Ga-αCD</td>
<td>-</td>
<td>1.56 ± 0.02</td>
<td>0.24 ± 0.03%</td>
<td>-</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>2.07 ± 0.23</td>
<td>0.59 ± 0.29%</td>
<td>2.46</td>
<td></td>
</tr>
<tr>
<td>Sodium ascorbate</td>
<td>3.93 ± 0.19</td>
<td>4.19 ± 0.25%*</td>
<td>17.46</td>
<td></td>
</tr>
</tbody>
</table>

* Ratio of RCP of the sample in presence of radiostabilizer/the absence of radiostabilizer

*p Statistical difference (* \( p < 0.01 \)) when compared to the absence of radiostabilizer.
sodium ascorbate (without ligand) was carried out. The result of radiolabeling of $^{68}$GaCl$_3$ and sodium ascorbate (without ligand) reveal that there was barely any activity on the product section of iTLC paper (RCP $\approx$ 0.01%) alongside a pH value of 2.

3.3. Mass spectrometry

Fig. 3 shows the full ESI (+) triple quadrupole MS spectrum of $^{68}$Zn-αCD. No other complexations, e.g., 1:2 or 1:3 complex was found.

3.4. Optimization of $^{68}$Ga-αCD radiosynthesis

3.4.1. Effect of αCD concentrations

Fig. 4 exhibits the optimization of $^{68}$Ga-αCD radiosynthesis by varying the concentrations of αCD. The RCP was increased with increasing αCD until its concentration of 1 mg/ml, which yielded the highest RCP (6.18 ± 0.16%) and then levelling off. Further increasing its concentrations, there was no significantly different RCP was observed ($p > 0.01$).
3.4.2. Purification of $^{68}$Ga-$\alpha$CD

Following the utilization of a C-18 cartridge for purification, there is a notable increase in the RCP. The final product demonstrates a pH value of 4.90 and RCP of 18.42 ± 1.07%. It demonstrates that the obtained RCP after purification provided significantly higher RCP compared to the unused C-18 (6.18 ± 0.16%), (p<0.01).

4. Discussion

In recent years, CDs have gained interest in medical imaging role especially in nuclear medicine. Firstly, Hadju and co-workers fabricated the CD-based nuclear medicine using $^{68}$Ga-NODAGA-HPβCD for biodistribution study in normal mice [4]. Further studies have been conducted so far, but all studies still require chelator molecules such as NOTA or DOTA to link CD together with radionuclide [5-7]. In this study we successfully radiosynthesis $^{68}$Ga-$\alpha$CD without requiring chelator molecule by directly radiolabeled Ga-68 with $\alpha$CD. However, the RCP of $^{68}$Ga-$\alpha$CD was relatively low (0.24%, n=3) compared to $^{68}$Ga-DOTA, which was commonly practiced in clinical settings.

Upon the complete decay of Ga-68 decay to Zn-68, we decided to confirm the result by measuring m/z of sample by MS which is ESI (+) triple quadrupole MS. The result from MS was supported that $^{68}$Ga-$\alpha$CD was formed with the stoichiometry ratio of 1:1 complex of $^{68}$Zn-$\alpha$CD in the final solution.

Thus, to increase the RCP, the radiosynthesis process was further optimized. When adding radiostabilizer (i.e., ascorbic acid or sodium ascorbate), RCP values of both $^{68}$Ga-DOTA and $^{68}$Ga-$\alpha$CD were significantly improved. This indicates that radiostabilizer has a strongly positive effect on radiolabeling process. A radiostabilizer also known as radioprotectant, is a radical scavenger that can prevent the formation of free radicals which are induced by radiation emitted from radionuclide. These free radicals can degrade compounds or prevention formation of desired product [13-16]. Baudhuin et al. [14] investigate the effect of various radiostabilizers on $^{68}$Ga-NOTA-single-domain antibodies (sdAb) radiolabeling. Their result indicates ascorbic acid and gentisic acid are not well compatible with Ga-68. Based on our results, it clearly demonstrated that ascorbic acid was less potent than sodium ascorbate. This was assumed that the obtained RCP possibly be related to the pH of the sample. Optimal pH range for Ga-68 radiolabeling is 3–5 [17, 18]. At pH lower than 3, the solution is too acidic for radiolabeling, whereas at pH above 5, $^{68}$GaCl$_3$ forms complex with hydroxide and become $^{68}$Ga(OH)$_3$, which is incapable of radiolabeling [17]. In our case, the pH of the samples that comprise of sodium ascorbate are 3.83 for $^{68}$Ga-DOTA and 3.93 for $^{68}$Ga-$\alpha$CD which are suitable for Ga-68 radiolabeling. In order to confirm that sodium ascorbate does not compete with $\alpha$CD or DOTA, radiolabeling of...
GaCl₃ and sodium ascorbate (without ligand) was carried out. The result showed that the pH of final solution was about 2, which was not the optimal pH for radiolabeling and there was barely any activity on the product section of iTLC paper (RCP ≈ 0.01%). This indicates that sodium ascorbate did not interact with GaCl₃. For supporting the RCP data, the iTLC papers of ⁶⁸Ga-DOTA and ⁶⁸Ga-αCD containing sodium ascorbate were scanned by TLC scanner. The results are aligned with the RCP, ⁶⁸Ga-DOTA shows a high amount of product and some free Ga-68. In contrast to ⁶⁸Ga-αCD, it exhibited a large amount of free Ga-68 together with low product yield. This observation is similar to the result obtained by RCP measurement.

For the optimum condition of ⁶⁸Ga-αCD radiosynthesis, the various αCD concentrations and the purification step were included. Increasing the starting αCD concentration can improve RCP of product up to 1 mg/ml (Figure 4). At the higher αCD concentrations (> 1 mg/ml) the RCP gradually dropped, which assumed that the solution might be saturated. αCD concentrations at 0.5 mg/ml and 1 mg/ml did not show a significant difference in RCP. However, 1 mg/ml αCD was selected for further studies because it yielded the highest RCP. To further increase the RCP of ⁶⁸Ga-αCD, a C-18 cartridge was used to purify ⁶⁸Ga-αCD solution. C-18 cartridge is a widely use solid phase extraction cartridge for Ga-68 purification in clinic [13]. Utilizing a C-18 cartridge significantly increases RCP of ⁶⁸Ga-αCD, resulting in a three-fold increase compared to no further purification step (18.42 ± 1.07% versus 6.18 ± 0.16%).

5. Conclusion

In this study, we achieved the successful radiosynthesis of ⁶⁸Ga-αCD without the use of a chelator molecule, demonstrating the first pioneer of direct radiolabeling of Ga-68 with αCD. Initially, the RCP of ⁶⁸Ga-αCD is very low; however, the RCP is increased when using the appropriate radiostabilizer and optimized process. It was suggested that using sodium ascorbate as a radiostabilizer, the concentration of 1 mg/ml αCD and the C-18 cartridge for purification were the optimal parameters for radiolabeling ⁶⁸Ga-αCD. Overall, we have successfully synthesized ⁶⁸Ga-αCD and achieved RCP of 18.42 ± 1.07%.

Further investigation of biodistribution studies using PET imaging is needed to gain a comprehensive understanding of the potential of these innovative radiopharmaceuticals.

6. Recommendations

αCD is a commonly used pharmaceutical excipient known for its ability to form inclusion complexes with variety of drug molecules. In this study, we focus exclusively on the formation of complexation between Ga-68 and αCD. Our findings indicate that Ga-68 has a low affinity for αCD. Therefore, the radiosynthesis of ⁶⁸Ga-αCD needs extensive optimization to purify the product for further elucidation and application in nuclear imaging. Due to the radiosynthesis process of ⁶⁸Ga-αCD being performed in diluted solutions, quantitative analysis was limited and not fully implemented. However, for a comprehensive exploration of the application of CDs in the field of nuclear medicine, the investigation of radiolabeling of Ga-68 with αCD derivatives, as well as βCD and γCD, along with their respective derivatives, will be considered for further studies.

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Funding

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Conflict of Interest

The authors declare no conflict of interest.

References


[18] Bauwens M, Chekol R, Vanbilloen H, Bormans G, Verbruggen A. Optimal buffer choice of the radiosynthesis of (68)Ga-Dotatoc...
Factors Associated with Prevention Behaviors of Family-Based Pulmonary Tuberculosis Transmission: A Literature Review

Christiawan Rinaldo *, Bagoes Widjanarko, Zahroh Shaluhiyah

Department of Health Promotion, Faculty of Public Health, Diponegoro University, Indonesia

Abstract

Background: Pulmonary tuberculosis (TB) is a major health problem worldwide, characterized by high morbidity, disability, and mortality rates. The family is the smallest unit within a community that is at risk of transmitting pulmonary TB. In 2020 there are 5.8 million TB cases reported globally and it is increased to 6.4 million in 2021. Indonesia has the second highest incidence of TB in the world (312 per 100,000 population) and accounts for 8.5% of global cases in 2019. There are several efforts that families can undertake to prevent the spread of pulmonary TB. The behavior of pulmonary TB patients within the family influences the containment of TB bacteria transmission. This article aims to review the factors associated with prevention behaviors of family-based pulmonary tuberculosis transmission.

Methods: Data was collected using literature from Google Scholar, PMC, and ScienceDirect. There are only 10 articles suitable for this review. After reviewing the suitable articles, to conclude the finding factors of pulmonary TB based on PRECEDE-PROCEED framework. The scope of the articles are not limited only in Indonesia, but also from other countries, such as India and Philippines. The keywords used in the literature search for articles in Indonesian were “Perilaku” AND “Pencegahan Tuberkulosis” AND “Keluarga”. For articles in English, the keywords used were “Behavior” AND “Tuberculosis Prevention” AND “Family”. The collected articles were those published within 2013 and 2023.

Results: Several factors are associated with the behavior of preventing the transmission of pulmonary tuberculosis within the family context. These factors can stand alone or be interconnected. A total of 10 articles were found for this article. Results are according to the theory of health behavior developed by Lawrence Green, several factors influencing prevention behaviors of pulmonary TB transmission within the family were identified, including knowledge and attitudes as predisposing factors, tendency to overlook early TB symptoms, preference for herbal medicines, family history of diabetes mellitus, larger number of family member as enabling factors, and educational interventions as reinforcing factors.

Conclusion: Based on the results and discussion, several factors are associated with prevention behaviors of family-based pulmonary tuberculosis transmission. Therefore, it is believed that intervening in one of these factors can significantly reduce the transmission of pulmonary tuberculosis within the family.

Keywords: Tuberculosis, Behavior, Transmission, Family

1. Introduction

Pulmonary tuberculosis (TB) is a major problem in the healthcare world as an infectious disease with high morbidity, disability, and mortality rates. Prevention of pulmonary TB transmission is important and it is including focusing on promotive and preventive aspects, reducing morbidity or mortality rates, breaking the chain of transmission, avoiding antibiotic resistance, and minimizing the adverse effects of pulmonary tuberculosis. The Indonesian National Tuberculosis Control Program aims to eliminate

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tuberculosis by 2035 and achieve zero tuberculosis cases by 2050 [1].

According to the Global Tuberculosis Report 2022 by the World Health Organization (WHO), tuberculosis mortality remains high and is one of the top five deadly diseases for women aged 20-59. In 2020 there are 5.8 million TB cases reported globally and it is increased to 6.4 million in 2021. Indonesia has the second highest incidence of TB in the world (312 per 100,000 population) and accounts for 8.5% of global cases in 2019. Pulmonary tuberculosis is the leading cause of death compared to other infectious diseases and ranks third after cardiovascular diseases and acute respiratory infections [2].

Mycobacterium tuberculosis is transmitted through droplets or airborne sputum when confirmed bacteriological pulmonary TB patients cough or sneeze [3, 4]. As the smallest unit within a community, families are at risk of transmitting pulmonary TB. Unintentional spitting and keeping the mouth open while coughing or sneezing are examples of behaviors that can increase the spread of pulmonary tuberculosis [5]. Guwatudde et al. [6] found a 6% prevalence of positive bacteriological TB among household contacts in Kampala, Uganda from 1995 to 1999.

There are several efforts that families can undertake to prevent the spread of pulmonary TB. Previous studies have identified the following measures: improving the air circulation around the house, proper disposal of sputum, using masks, covering the nose and mouth while coughing, regular medication intake, regular monitoring at health centers, and family supervision during medication intake [7]. The behavior of pulmonary TB patients within the family influences the containment of TB bacteria transmission. Some preventive behaviors that can be practiced by pulmonary TB patients include covering the mouth when sneezing and coughing, disposing of saliva in disinfected areas, staying away from cold temperatures, ensuring sunlight enters the bedroom, and consuming carbohydrate and protein-rich foods [8].

Several factors influence the health of individuals, groups, and populations, as described by HL. Blum, including the surrounding area encompassing physical, social, cultural, political, and economic aspects; behavior; healthcare services; and genetics. Each factor is interrelated as they do not exist independently [9]. The success of disease control programs and prevention of pulmonary TB transmission can be attributed to various factors such as knowledge, attitudes, and actions. These factors play a crucial role and have a significant impact on determining the health status of individuals and communities [8].

2. Method

In this literature review, data was collected from Google Scholar, PMC, and ScienceDirect. The keywords used in the literature search for articles in Indonesian were “Perilaku” AND “Pencegahan Tuberkulosis” AND “Keluarga” in the title and abstract. For articles in English, the keywords used were “Behavior” AND “Tuberculosis Prevention” AND “Family” in the title and abstract.

There were only 10 articles suitable for this review. The selected articles discussed ways to prevent the transmission of tuberculosis, because there are 3 articles from Google Scholar, 2 articles from PMC, and 2 articles from ScienceDirect entitled prevention of tuberculosis but did not describe how to prevent it. In most articles did not include instruments and how was the validity and reliability, Fig. 1.

After reviewing them the finding several factors were identified to influence the preventive actions against the spread of pulmonary tuberculosis within the family, and some factors identified did not affect the behavior of preventing the spread of pulmonary tuberculosis within the family.

The factors of pulmonary TB based on the theory of health behavior developed by Lawrence Green, several factors influencing prevention behaviors of pulmonary TB transmission within the family. The factors of pulmonary TB can be influenced by three aspects: predisposing factors, enabling factors, and reinforcing factors.

The articles are not limited only to Indonesia, but cover other countries, such as Ethiopia and Iran. The collected articles were those published within the last 10 years.
3. Results and Discussion

The summary of 10 articles is presented in the Table 1.

From the literature review, several factors were identified to influence the preventive actions against the spread of pulmonary tuberculosis within the family, namely knowledge, attitude, educational interventions, family history of diabetes, and a larger number of family members. Some factors identified did not affect the behavior of preventing the spread of pulmonary tuberculosis within the family, such as socioeconomic status and family support.

Health behavior, according to the theory developed by Lawrence Green, people’s beliefs about whether or not they are at risk for a disease or health problem, and their perceptions of the benefits of taking action to avoid it, influence their readiness to take action [10]. The health behavior can be influenced by three aspects: predisposing factors, which are manifested in knowledge, attitude, beliefs, faith and values, enabling factors which are manifested in physical environment, availability or unavailability of health facilities, and reinforcing factors, which are manifested in the attitude and behavior of health workers or other officers who are a reference group of community behavior [10]. In preventing the occurrence of a disease or seeking treatment, individuals are influenced by predisposition factors, one of which is the attitude that tends to cause a person to perform a behavior [10].

3.1. Predisposing factors

Predisposing factors include age, occupation, education, knowledge, and attitude. In our analysis of the literature review, knowledge was found to be the most frequently identified factor that significantly influences health behavior. According to Notoatmodjo cited from Rogers, knowledge plays a major role in shaping individual behavior (overt behavior), where behavior based on knowledge is more likely to be sustained compared to behavior without knowledge [11]. And also consistent with Agustina and Wahjuni [12] where knowledge is the most dominant factor influencing the behavior of preventing pulmonary tuberculosis within the family [13]. Pampel et al. [14] also reported.
Table 1. Literature search results

<table>
<thead>
<tr>
<th>No.</th>
<th>Authors</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rizana et al. [15]</td>
<td>Quasi-experimental</td>
<td>Behavior, attitude, and knowledge related to the prevention of pulmonary TB were influenced by health education (P&lt;0.000).</td>
</tr>
<tr>
<td>2</td>
<td>Veronika [16]</td>
<td>Cross-Sectional (98 respondents)</td>
<td>Respondents’ knowledge and attitudes were associated with the behavior of preventing pulmonary TB (p=0.009 and p=0.012).</td>
</tr>
<tr>
<td>3</td>
<td>Buang et al. [17]</td>
<td>Quasi-experimental (30 respondents)</td>
<td>Knowledge and healthy living behaviors regarding the prevention of pulmonary TB were influenced by audiovisual health education (P&lt;0.000).</td>
</tr>
<tr>
<td>4</td>
<td>Ayurti et al. [18]</td>
<td>Cross-Sectional (30 respondents)</td>
<td>Knowledge and attitudes towards family behavior in preventing the transmission of TB were not related.</td>
</tr>
<tr>
<td>5</td>
<td>Agustina and Wahjuni [12]</td>
<td>Case-control (50 respondents)</td>
<td>Prevention of pulmonary TB is related to knowledge (p=0.018) and actions (p=0.000). No difference was found in socioeconomic status (p=0.533) and attitudes (p=0.212).</td>
</tr>
<tr>
<td>6</td>
<td>Kaka et al. [19]</td>
<td>Cross-Sectional (30 respondent)</td>
<td>Attitude is positively correlated with preventive actions for the transmission of TB (p=0.000 and r=0.688).</td>
</tr>
<tr>
<td>7</td>
<td>Tahu and Dion [20]</td>
<td>Cross-Sectional (36 respondent)</td>
<td>61% of family behaviors were categorized as good, 22% as moderate, and 17% as poor.</td>
</tr>
<tr>
<td>8</td>
<td>Wulandari et al. [21]</td>
<td>Cross-Sectional (46 respondent)</td>
<td>Family support (p=0.292) did not affect the behavior of preventing TB transmission, while knowledge (p=0.004) did affect the behavior of preventing TB transmission.</td>
</tr>
<tr>
<td>9</td>
<td>Shegaze et al. [22]</td>
<td>Phenomenological research design with 27 respondents from families with TB-related deaths</td>
<td>Poor treatment adherence, lack of TB awareness, stigma, inadequate food consumption, poor healthcare-seeking behavior, and limited access to healthcare facilities were identified as the main causes of death.</td>
</tr>
<tr>
<td>10</td>
<td>Afshari et al. [23]</td>
<td>Cohort (50 respondent)</td>
<td>Significant associations were found between a history of diabetes mellitus in index cases (p=0.043) and a larger number of family members (p=0.026) with an increased risk of TB infection among children.</td>
</tr>
</tbody>
</table>

Limited understanding of the risks of unhealthy behaviors is due to a lack of knowledge. Knowledge about tuberculosis prevention behavior can include an individual’s understanding of pulmonary TB, including its definition, etiology, transmission, clinical manifestations, diagnosis, treatment, and preventive measures [24]. Various sources of knowledge about pulmonary tuberculosis and preventive actions can come from various written and media sources. Hatzenbuehler et al. [25] found that a one time educational intervention about TB prevention programs could improve the identification, testing and treatment of adolescents at risk for TB and also affect an individual’s level of knowledge. According to Notoatmodjo [11], a person will have broad knowledge if they obtain information from various sources.

On the other hand, Kaka et al. [19] indicate that some research subjects already exhibit good attitudes, but it can still be observed that negative attitudes affect TB prevention behavior. Negative attitudes can manifest as habits of unintentionally spitting and leaving the mouth open while...
coughing or sneezing [5]. It is also consistent with Notoatmodjo [11], the function of attitude does not necessarily translate into overt actions but rather serves as a predisposition to those actions, also known as covert actions.

Two other variables within the predisposing factors, which is age and occupation, have not been extensively discussed in the literature review regarding their significant relationship with preventive behavior against TB transmission within the family. Similarly, no significant findings were found in previous literature review regarding specific age groups such as children, adolescents, adults, and the elderly, as well as specific occupations such as healthcare workers and non-healthcare workers.

3.2. Enabling factors

Enabling factors manifest in the physical environment conditions. A study by Shegaze et al. [22] explains that TB patients tend to overlook early symptoms. Families and patients prefer herbal medicines. Other reasons for treatment non-adherence include the expensive cost of travel due to long distances and inadequate nutritional intake. Nutritional intake is related to family behavior in selecting food, which can enhance the immune status of family members in preventing TB transmission. Furthermore, research by Afshari et al. [23] indicates that families with a history of diabetes mellitus can increase the risk of TB infection among children. The choice of nutritional intake indirectly relates to economic status. Families with low or inadequate economic status face difficulties in meeting their nutritional needs. However, the reviewed study conducted by Agustina and Wahjuni [12] showed that economic status was not associated with TB prevention. In addition to discussing nutrition, the reviewed study by Afshari et al. [23] also suggests that another environmental factor, namely the number of family members, influences TB transmission. Families with a larger number of members can affect TB transmission [23]. In Indonesia, the number of family members is still heavily influenced by the stigma stating that “more children, more blessings” and “rejection of contraception programs”.

The living environment is also an important factor in preventing the transmission of pulmonary TB. Families can make efforts to create an optimal environment to prevent TB transmission, such as keeping the house well-ventilated, placing the bed of pulmonary tuberculosis patients under direct sunlight for at least once a week [7]. These efforts aim to allow sunlight to directly kill M. tuberculosis bacteria. This concept aligns with the theory according to the Indonesian Ministry of Health in 2009, where Clean and Healthy Living Behavior becomes a preventive measure against transmission. Clean and Healthy Living Behavior can include sun-drying mattresses, opening windows and doors in the morning, consuming nutritious food, avoiding smoking and alcohol, engaging in regular exercise, cleaning clothes, getting enough sleep, and avoiding sharing personal hygiene items [24].

3.3. Reinforcing factors

Reinforcing factors involve the support provided by families and community leaders. A study by Wulandari et al. [21] indicates that family contributions does not affect the prevention of TB transmission. Other studies conducted by Rizana et al. [15] and Buang et al. [17] that provided health education interventions showed a positive impact on changing health behaviors by improving knowledge. Therefore, community leaders who have the ability to influence policies are expected to provide interventions tailored to the local environmental conditions. Interventions do not always have to be directly provided in the form of health education, but indirect interventions such as facilitating access to and transportation of medication are also important to implement.

Other research also shows that in addition to family support, the role of healthcare workers significantly influences the transmission of pulmonary TB. According to Eliska [26], healthcare workers play a significant role in patients’ adherence to taking their pulmonary tuberculosis medication. Motivational support from healthcare workers encourages patients to consistently obtain medications from health centers and continuously monitor changes in their
health status, enabling patients to receive all the advice from healthcare workers throughout their treatment. Healthcare workers play a crucial role in providing healthcare services to the intended population in order to improve the population’s health status. In fulfilling this role, healthcare workers must create conditions that promote positive patient behaviors towards their health [27].

Based on the discussion, several factors are associated with the behavior of preventing the transmission of pulmonary tuberculosis within the family context. These factors can stand alone or be interconnected. Therefore, intervention in one of these factors can significantly reduce the transmission of pulmonary tuberculosis within the family. One possible intervention is to increase the knowledge of at-risk communities and families. Educational interventions are expected to enhance health knowledge, thus improving the family’s attitudes towards the transmission of pulmonary tuberculosis. However, further research is needed to explore suitable educational intervention methods for each community, considering the diverse characteristics and strong cultural aspects of the Indonesian population. Additionally, further research is necessary to investigate the significance of socioeconomic status, which was considered inconclusive in this review.

5. Conclusion

Based on the results and discussion, several factors are associated with prevention behaviors of family-based pulmonary tuberculosis transmission, including predisposing factors (knowledge and attitudes), enabling factors (ignoring early symptoms, use of herbal medicine, nutrition, large family size, and history of diabetes mellitus), and reinforcing factors (educational interventions). Therefore, intervention in one of these factors can significantly reduce the transmission of pulmonary tuberculosis within the family.

References


A Qualitative Study on Adolescents Lifestyles Related to Stunting Prevention

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Abstract

Background: Adolescence is an important period for acquiring health- and nutrition-related behaviors. It is known that eating and physical activity behaviors established in adolescence will continue into adulthood and may contribute to nutrition-related chronic diseases in later life. The nutritional status of adolescent girls is a strong determinant of the health, nutrition, well-being, low birth weight and stunting of their future offspring. Because of that, this research focus to describe about adolescent girl lifestyles related to stunting prevention.

Method: This article used a qualitative descriptive method with a case study approach. The informants are from two school, including 11 adolescent girls in the CED (Chronic Energy Deficiency) category, 2 health center teachers and 2 vice principal. Data collection was conducted by in-depth interviews and focus group discussions. Data were analyzed using content analysis methods.

Result: The results showed that the most adolescents didn’t know about the meaning, causes, characteristics, impact and prevention of stunting. The practice of taking iron supplement for adolescents girl are low. The average eating pattern of adolescent is only 2 times a day and they have difficulty eating. Besides that, they’re like to consumed instant food. On average, they didn’t have the habit of physical activity at home and have unhealthy sleeping habits.

Conclusion: Adolescent lifestyle related to stunting prevention are not good. Less sleep, bad diet patterns and lack of exercise. For this reason, it is necessary to educate adolescent about healthy lifestyle especially for stunting prevention.

Keywords: Adolescent lifestyle, Health promotion, Stunting prevention

1. Introduction

Globally, 144 million people are stunted in 2020 [1]. One in four children under the age of 5 is stunted [2]. Stunting is a global issue that urgently needs to be resolved because it has an impact on the quality of human resources in the future [3]. Human resources are a factor the main determinant of a country’s success [4]. With a superior future generation, Indonesia is expected to be able to compete with other countries and survive in the face of future challenges.

According to estimates by UNICEF, WHO and the World Bank, more than half of stunted children <5 years are reported to live in Asia and more than one-third lived in Africa [5]. Indonesia is ranked fifth in the country with the highest stunting burden among children under five in the world [6]. According to Global Nutrition Report 2014 (based on data from 117 countries), Indonesia is one of 17 countries with three main malnutrition problems: stunting, wasting, and obesity [7].

Based on the results of the 2019 SSGI, the prevalence of stunting in Indonesia reached 27.7%, in 2021 it will be 24.4%. Based on the results of SSGI 2022, the prevalence of stunting in Indonesia reached 21.6%, above the WHO target of 20% [8]. In addition, the Indonesian government targets the stunting rate to be 14% by 2024.

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Stunting is one of the problems of malnutrition. Stunting is a length-or height-for-age < 2 SD of a growth standard or reference and is claimed to be caused by repeated infection, poor nutrition, and inadequate psychosocial stimulation [9]. Stunting is a condition of failure in the growth and development of children under five due to chronic malnutrition. Thus the child becomes too short for his age, or a condition when a person's height is shorter than the height of other people (ages) in general. Stunting caused by quite complex, including the health characteristics of children under five, environmental factors and sociodemographic factors [10]. Stunting in children has immediate and long-term impacts [11].

Investing in nutrition in the early years is key to increasing human capital. Investing in nutrition, especially in the first 1,000 days of a person's life, is a cost-effective investment that promises high economic returns. Reducing stunting is not an easy thing. Stunting reduction require a strong commitment and political will from the government and an integrated [12]. One of the Government of Indonesia's top priorities is to reduce stunting with a multi-sectoral and coordinated approach at the national, regional and community levels [13]. Child stunting prevention include specific and sensitive nutrition intervention programmes [14]. One of the nutrition-sensitive intervention programs is about adolescent health.

Adolescence is a crucial period of human life [15]. Adolescence is a critical period for the acquisition of health-and nutrition-related behaviors. It is well accepted that eating and physical activity behaviors established in adolescence continue into adulthood and may contribute to nutrition-related chronic diseases in later life. The nutritional status of adolescent girls is a strong determinant of low birthweight, stunting and the health, nutrition, and well-being of their offspring. Adolescent girls are future brides and mothers of future generations. The quality of future generations depends on today's youth through their knowledge of the factors that influence stunting. Correct knowledge and accompanied by attitudes and healthy living behaviors are expected to help give birth to a higher quality generation [16].

The role of adolescent girls as future mothers to give birth to a new generation is believed to have great potential in carrying out various stunting prevention efforts, such as balanced nutritional food habits, fulfillment of high calcium milk intake, fulfillment of micronutrient intake, and school feeding programs can support optimal growth and development during adolescence [17]. Because of that, this research focus about adolescent girl lifestyles related to stunting prevention.

2. Methods

A descriptive, qualitative approach was used to enable the researchers to learn about adolescents lifestyle related to stunting prevention. Purposeful sampling was used. The purpose of using purposive sampling is to determine the sample of a study that does require certain criteria so that the sample taken is in accordance with the research objectives. Informants were recruited from 2 schools, including 11 adolescent girls in the CED (Chronic Energy Deficiency) category, 2 health center teachers and 2 vice principal. The criterion for informants in this study was simply being an adolescent (between 12 and 16 years old) in the CED (Chronic Energy Deficiency) category and they are representatives of departments or classes in the school. Health center teachers and vice principals are also used as informants to explain whether there are health programs in schools that support stunting prevention. Data collection was conducted by in-depth interviews to 15 informants and focus group discussion to adolescent girls.

The interviews were analysed using the qualitative content analysis method to identify prominent themes and patterns among the themes. Content analysis has an important place in the wide range of investigative tools valuable to investigators of themes and was therefore selected as an appropriate method for the analysis of the study data [18]. Documentation conducted in this research was taking pictures/photos during interviews and focus group discussion where it has gotten approval from the informants and maintains the privacy of the informants.
Table 1. Demographic characteristics of adolescents informants

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>12-13</td>
<td>3 (27)</td>
</tr>
<tr>
<td>14-16</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>3 (27)</td>
</tr>
<tr>
<td>High school</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Total</td>
<td>11 (100)</td>
</tr>
</tbody>
</table>

Table 2. Demographic characteristics of other informants

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Male</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>30-40</td>
<td>2 (50)</td>
</tr>
<tr>
<td>41-50</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Institution</td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>2 (50)</td>
</tr>
<tr>
<td>High school</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Job</td>
<td></td>
</tr>
<tr>
<td>Vice principal</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Health centre teacher</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Total</td>
<td>4 (100)</td>
</tr>
</tbody>
</table>

3. Results

3.1. Informants characteristic
Informants consisted of 11 Adolescents, 2 health centre teacher, and 2 vice principal. Adolescents aged between 12-16 years old. The remaining demographic characteristics of the participants are shown in Table 1 and 2.

3.2. Themes
Content analysis of the transcripts revealed the following six main themes, each of which embraces one to three sub-themes. The informants identified lifestyles related to stunting prevention consisting of:
1. Iron supplementation
2. Eating patterns
3. Exercise habits
4. Sleep habits
5. Knowledge of stunting
6. Programs related to stunting prevention in the schools (see Box.1)

Box 1 Emerged themes and sub-themes
1. Taking iron supplements
   a. Knowledge of hemoglobin, anemia, and iron supplements.
   b. Practice of taking iron supplement
   c. Barriers of taking iron supplements
2. Eating patterns
   a. Knowledge of CED and MUAC <23.5 cm
   b. Knowledge of eating patterns
   c. Eating habits
3. Exercise habits
4. Sleep habits
5. Knowledge of stunting
6. Programs related to stunting prevention in the schools

3.2.1. Theme 1 Iron supplementation
The first main theme was the Iron supplementation, with three sub-themes: knowledge of hemoglobin, anemia, and iron supplements; practice of taking iron supplement; barriers of taking iron supplements.

Knowledge of hemoglobin, anemia, and iron supplements

“I don’t know about or about the importance of hemoglobin. When I checked it, I wasn’t told anything, I just said that it was just because of lack of sleep and then I was told to adjust my sleep pattern and drink more water, that’s all I was told at that time, there was no other information.”

Most adolescents did not know about the importance of hemoglobin and maintaining normal hemoglobin. They also did not know what to do if their hemoglobin is low. Most adolescents did not know the definition of HB and the difference with blood pressure. There is a misperception among adolescents, Adolescents mentioned that that low HB is the same as low blood pressure.
Most adolescents mentioned that the impact of anemia is risky to pregnancy such as lack of blood during pregnancy, causing headache, weakness, and can cause bleeding during birth. Looking at knowledge, most adolescents mentioned that taking iron supplements to increase blood and to avoid blood shortage during menstruation. (There is an inaccurate understanding). While a small proportion mentioned to avoid low blood pressure, prevent anemia and to avoid weakness during menstruation.

Practice of taking iron supplement

“Oh, iron supplement, yes, once, when this was the first time, what was the first time in junior high school, I was given it by the PMR, but I didn’t like it because I was nauseous, the smell was bad, so I didn’t like to drink it usually. I used to taking it once when it was first distributed at that time when it was this or that line and then I was told to taking it and then taking it After that, I immediately vomited and didn’t want to taking anymore, because it doesn’t have good taste because it seems to make you nauseous and the bottom is also not good.”

The practice of taking iron supplement among adolescent girls is still lacking. Most of the informants only taking iron supplement once at school which was distributed by the health center. A small proportion of adolescent girls taking iron supplements during menstruation only and when they had low blood pressure. Adolescent girls claimed that iron supplements that distributed at school had fishy tasted. So most of them did not want to consume it. Meanwhile, according to adolescents, iron supplements obtained from pharmacies such as sangobion had better taste than those obtained from schools.

Barriers of taking iron supplements

Informants mentioned that the barriers they had experience when taking iron supplements are feeling nauseous, headache, bitterness, fishy smell.

3.2.2. Theme 2 Eating patterns

Eating patterns was the second main category with three sub-categories: Knowledge of CED and MUAC <23.5; knowledge of eating patterns; Eating habits.

“often, noodles... yes, not necessarily, if I’m hungry and don’t eat rice, I eat noodles... maybe 4 times a week, mba... make it at night, if it’s tight, if it’s not in the afternoon, if I want it... yes, it’s dangerous for the organs... but I still consume it because it’s delicious, hehehe.”

Knowledge of CED / MUAC <23.5 cm

Most adolescents did not know the definition of Chronic Energy Deficiency (CED). They also did not know the impact and risk of CED / Mid Upper Arm Circumference (MUAC) <23.5 cm on pregnancy and the risk of having CED during marriage or approaching marriage.

Knowledge of eating patterns

All informants thought that it was okay to eat instant food as long as it was not in excessive portions (reasonable), instant food tastes good, and a substitute when hungry, despite knowing the dangers of instant food because it contains preservatives.

Eating habits

On average, informants eat only 2 times a day in normal portions, and they admit to having difficulty eating because they wake up late so they didn’t have time to have breakfast and had a lot of school assignments so they did not have time to eat, as a result there is 1 informant who has acid reflux / gastritis. Most of them like instant foods such as meatballs, shumai, seblak, and fried foods.

3.2.3. Theme 3 Exercise habits

“At school, I do sports once a week. Never at home.”

All informants did sports at school once a week during sports lessons. On average, informants
did not have the habit of exercising at home because they were lazy and preferred to sleep. Despite this, all of them thought that exercise was important for health and immune system. A small proportion of informants have exercise habits at home, such as stretching and cycling.

3.2.4. Theme 4 Sleep habits

“since as student in vocational senior high school, I have been sleeping less, I don’t get enough sleep because I have a lot of assignments and usually when I go on holiday, I sleep for 7 hours.”

On average, informants have unhealthy sleeping habits (7 hours/day), and some even sleep late into the early hours of the morning due to difficulty falling asleep and not fulfilling the recommended sleep time (8-9 hours). The reasons are doing school assignments, and playing cellphones so that they forgot to sleep.

3.2.5. Theme 5 Knowledge of stunting

“I’ve heard about it on TV but I don’t know what stunting is.”

Most informants did not know about the definition, causes, characteristics, impacts and prevention of stunting and even mentioned that they had never heard of stunting. There were informants who had heard of stunting in TV commercials, but even then were unable to explain the concept of stunting.

3.2.6. Theme 6 Programs related to stunting prevention in the schools

The health program includes extra-curricular PMR (Palang Merah Remaja). In addition, there is also a health check program in collaboration with the Community Health Center (Puskesmas) which is held once every 6 months. There is no program that directly prevents stunting, but there is a program to provide iron supplement to female students.

4. Discussion

In general, qualitative research methods search for answers from the broader social context. The closer we get to the natural state in which health research data are collected, the fewer the limitations that will exist in translating the findings into real-life applications.

4.1. Methodological considerations

While this study was conducted in a qualitative manner, potential limitations still exist. The naturalistic paradigm of the study and the deeper meaning of health can limit the generation of the findings. The study also has the limitation, focus on adolescent girls, along with 2 educator and 2 healthcare, the scope appears limited by only considering these 3 stakeholders. The research was not extended to include other important parties, such as parents, who could offer a more important view of the issue at hand.

No data were collected for those adolescents who declined to participate, or who asked for their tapes or their transcripts, because of the informed consent process. Strengths of the study design were by using two data collection models, which are in-depth interviews and focus group discussions with adolescent girls. Prolonged engagement with participants, maximum variation of sampling and good communication skills have contributed to the deep and rich data gathered in this research.

4.2. Themes

4.2.1. Theme 1 Iron supplementation

Iron is needed for the production of hemoglobin, which is an essential ingredient in red blood cells. Hemoglobin is very important, as it carries oxygen from the lungs to the rest of the body. If a person didn’t have enough iron, they can develop anemia, which means they aren’t making enough red blood cells to carry oxygen around their body. The resulting effects are breathless, tired and have a lack of energy, the skin may becomes pale and may have palpitations (noticeable heartbeats) [19].

Many factors influence adherence in taking
iron supplements including: knowledge, attitude, motivation, parental support and teacher support. Based on research conducted by Nuradhiani, the most dominant determinant of adherence to taking iron supplements in adolescent girls is teacher support \((p<0.05; \text{OR}=4.7; 95\%\text{CI}:1.5-14.2)\). This indicates that subjects who received good teacher support significantly increased their adherence to taking iron supplement 4.7 times greater than those who received less support from teachers [20].

Referring to other studies, health promotion is needed to increase knowledge about anemia, the importance of iron and folic acid and regular supervision. Supervision can be done by conducting iron and folic acid drinking movements simultaneously at the same time and day with direct supervision by teachers at school [21]. With high adherence to taking iron supplement, adolescent girls will avoid anemia [22].

4.2.2. Theme 2 Eating patterns

Adolescent girls are a critical period as well as unique among several phases in the human life cycle, including unique nutritional vulnerabilities, however they are almost invisible in many regions of the world including their nutritional status is often overlooked, even though the nutritional status of adolescent girls plays an important role in breaking the cycle of malnutrition intergeneration in society [23].

One of the nutritional problems in adolescent girls is the lack of food intake which in the long run can cause Chronic Energy Deficiency (CED) [24]. Nutritional intake factors show that 32% of adolescent girls in Indonesia in 2017 were at risk of chronic energy deficiency (CED). If the nutrition of adolescent girls is not improved, then in the future there will be more future mothers at risk whose children will be born with low weight and even stunting. Pregnant women with short stature and/or chronic energy deficiency will lead to an increase in the prevalence of stunting in Indonesia [25].

Adolescent nutritional needs need to be considered because in adolescence there is rapid growth and development. Unhealthy eating habits will affect adolescent nutrition. Unhealthy foods such as fast food are consumed by adolescent. At a time when everything is modern like now, teenagers want everything to be fast, including in choosing food. Fast food is also known to the public as junk food. Junk food is defined as food waste or food that does not have nutrients for the body. Eating junk food is not only in vain, but can also damage health [26]. Therefore, adolescents must adopt a healthy diet to build their bodies. The habit of consuming unhealthy food since adolescence will have a negative impact in the future [27].

4.2.3. Theme 3 Exercise habits

Stunting in children is a chronic nutritional problem that is common throughout the world, including in Indonesia. To achieve good health standards, it is necessary to have a process of managing the surrounding environment and daily activities that are reflected in a healthy lifestyle. A healthy lifestyle is a community lifestyle that upholds health aspects such as managing cleanliness and environmental health, maintaining physical and psychological fitness and providing adequate nutrition, so as to achieve good health standards. Physical activity also plays an important role in preventing stunting. Physical activity can help improve bone and muscle quality, and help improve growth and development.

4.2.4. Theme 4 Sleep habits

Sleep is a basic human need that absolutely must be fulfilled by everyone. Everyone needs enough sleep to be able to carry out activities optimally in the future. The benefit of sleep itself is to rest the body, so everyone must need it. Sleep has several positive impacts, namely, repairing damaged cells, improve memory, prevent disease, increase energy, and prevent stress. Therefore, every human being must get maximum rest results in order to get good quality sleep. Most people, especially adolescents who are the target audience, still ignore healthy sleep patterns and use sleeping hours that are not in accordance with their needs to fulfill their sleep quality. This is caused by external disturbances such as late night work, urban lifestyle, using gadgets before bedtime, and lack of understanding of the impact.
of staying up too late. Poor sleep patterns caused by staying up too late can affect daily activities such as reducing endurance, decreased productivity, lack of concentration, and emotional instability. But this can be overcome by reducing night activities outside the home, reducing the use of gadgets at least 1 hour before bed, regular exercise 3-4 times a week for at least 30 minutes, avoiding caffeinated drinks and smoking [28].

4.2.5. Theme 5 Knowledge of stunting

There are also misperceptions among adolescent girl regarding stunting [29]. The research before showed that most (86.6%) respondents did not know that stunting was a nutritional problem for adolescents, and 50.4 percent of respondents had negative perceptions about stunting, especially in aspects of stunting prevention. These results indicate the importance of providing stunting prevention education models for adolescent girl [30].

4.2.6. Theme 6 Programs related to stunting prevention in the schools

There is a program to provide iron supplement from the community health center to schools, but there needs to be some evaluation. Good cooperation between the school and community health center is needed. In addition to improvements in terms of distribution, there is also a need for routine supervision accompanied by appropriate methods, such as using monitoring cards and regular supervision [31].

There is a need for additional education for students on the benefits of taking iron supplement tablets and preventing stunting. In this case, schools can collaborate with community health centers or other private parties such as universities or non-governmental organizations. It’s hoped that by increasing knowledge about the importance of taking iron supplements (Fe), adolescent girls will be able to increase their awareness about stunting, the dangers of stunting and what needs to be done so that stunting does not occur, especially the importance of Fe supplements. Another thing that is expected is that young women are able and aware that free from anemia, they can become prospective mothers who will give birth to children free from stunting [32].

5. Conclusion

Most adolescents did not know about the meaning, causes, characteristics, impact and prevention of stunting. The lifestyle of adolescents related to stunting prevention is still not good. The practice of taking iron supplement for adolescent girl is still low. Most of the informants had taking iron supplement tablets only once at school when distributed by the Student Councils and School Health Unit’s teachers, but it was discontinued because of its unpleasant taste. Most adolescent did not know information about the causes and occurrence of anemia, CED (Chronic Energy Deficiency) and Mid Upper Arm Circumference (MUAC) <23.5 cm and the risks to marriage and pregnancy. The average eating pattern of adolescent is only 2 times a day and they have difficulty eating. Besides that, adolescent like instant food. On average, the informants didn’t have the habit of physical activity at home and has unhealthy sleeping habits.

6. Recommendations

It is necessary to educate adolescents about stunting prevention, because adolescent girls are prospective mothers who are expected to be born not stunted. The material needed by adolescent girl is about anemia, Chronic Energy Deficiency (CED), good diet, physical activity. Keep in mind the preferred educational model or one that suits adolescent girl. The media that adolescent girls like is interesting media such as animated videos with a short duration. Besides that, teenagers also like direct practice such as cooking competitions, gymnastic competitions, role playing, etc.

References


[25] Parinduri SK. Optimalisasi Potensi Remaja...


Development of an Android-Based Wound Care Documentation Application in Support of Management Information Systems in Nursepreneurship: Research and Development

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Faculty of Nursing, Airlangga University, Surabaya East Java, Indonesia

Abstract

Background: The provision of nursing care supported by the application of care documentation is growing rapidly using android. This study aims to develop an android-based wound nursing care documentation application in providing support for management information systems in nursepreneurship.

Method: The development method used as a reference is the development research model; analysis, design, development, implementation, evaluation (ADDIE). 2) Design; Focus group discussion, 3) Development, 4) Implementation; Trial. In Depok City with the number of respondents 22 nursepreneurs using Happines questionnaire.

Results: Participants had a new understanding of Android-based wound care documentation applications (agree; 96.9%, neutral; 3.1%), stating that this application is difficult to use, (agree; 43.8%, disagree; 56.2%), confident in using Android-based wound care documentation (agree; 93.8%, neutral; 6.2%), expect to use the next (agree; 90.6%, neutral; 9.4%) express happiness using the application (agree; 71.9%, neutral; 6.20%). 5) Evaluation stage.

Conclusion: Nursepreneurship requires management information system support in providing services in different areas with hospitals. Information system support with electronic nursing documentation in wound care applies structured nursing standards and principles, can be used and connected to patient files, and accelerates information and utilisation in care service management.

Keywords: Nursing documentation, Wound care, Nurse entrepreneur, System information, App android

1. Introduction

Improving information services is expected to bring convenience in the digital era of entrepreneurship. The purpose of using applications in nursing documentation is for better access, evaluation and information, as well as the support of nursepreneurship service management information systems that support effective decision-making [1]. Nursepreneurs must be able to answer challenges for the fulfillment of management information support that has an impact on improving the quality of nursepreneurship services. The provision of nursing care supported by care documentation applications is currently growing rapidly using Android, nurses need an information system to document their tasks with a more concise time including in wound care [2]. This application was created for the reason that there is no standardized wound nursing documentation using an android.
application that is able to explain the patient's wound condition so that it becomes the basis for providing appropriate intervention. Care services in nursepreneurship must use a higher level of knowledge and a positive attitude in conducting electronic documentation [3].

Another reason for developing Android applications for wound care documentation as management information support in nursepreneurship is because Indonesia is the fourth Android user in the world after China, India, and the United States. Android is relatively affordable, service centers are available in many places, easy to use, making most Indonesians choose to use it, including nurses. The android application allows it to be used with many purposes such as entertainment, business, education, health and others [4]. This is an effective and efficient response needed in the digital era [5].

2. Methods

The design of this research is descriptive with a research and development (R&D) approach, the development method that is referenced is a [6] design, development, implementation, evaluation (ADDIE) model [7].

This study was conducted without intervention simultaneously in Depok City, with the calculation of the study sample size using G*Power software version 3.1.9.7.

The sample size calculation begins with calculating the effect size from previous similar studies, which is 1.06 (mean group 1 = 49.30, mean group 2 = 41.6; SD group 1 = 6.90, SD group 2 = 8.20). The sample size with [8] effect size 1.06, α error prob 0.05, power (1-β error prob) 0.95, and allocation ratio N2/N1 = 1, resulted in a sample size of 22 nurses. With the sample criteria in this study are as follows:

1) Inclusion Criteria
   a. Male or female nurses over 23 years old
   b. Have a minimum education of nursing diploma
   c. Running an independent nursing practice as nursepreneurship
   d. Able to communicate well
   e. Have wound care competency
2) Exclusion Criteria
   a. Nurses who only work in health care facilities or in the academic world
   b. Nurses who practice nursing independently as nursepreneurship but are experiencing illness, or in emergency conditions.
   c. Do not have wound care competency

Data collection was conducted using closed-ended question instruments and descriptive analysis to see the description of the variables studied. Data collection was carried out using a closed question instrument and descriptive analysis to see the description of the variables studied.

3. Results

Prior to this research, a literature study and field study were conducted, which aimed to gather information relevant to the needs of developing an android-based wound care documentation instrument. The steps of this research are as follows:

1. Analysis phase

The analysis carried out consists of two types, namely:

   1) functional needs analysis; is an analysis of the materials needed in the mobile application
   2) analysis of user needs; namely the analysis of the needs of mobile users from the aspects of user friendly, display and can be used as an alternative ease in reporting and documentation.

2. Design phase

This design stage is carried out by focus group discussion (FGD) together with 3 wound care experts, 2 doctors, 1 patient, and input from nursing experts. Produces a design that contains components for the development of applications to be made. The design of the android-based application is described in Table 1.

This design uses nursing documentation and diagnosis guidelines compiled in nursing diagnosis standards (IDHS) [9] using wound assessment with the Bates Jansen scale [10-12]. Odor Intensity Referencing Scale (OIRS) [13] a flowchart has begun to be designed with the Fig. 1.
Table 1. Application design

<table>
<thead>
<tr>
<th>No</th>
<th>ITEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>General patient data: Name, place of birth, address, medical record number, telephone number</td>
</tr>
</tbody>
</table>
| 2  | a. Subject data: cause of wound, duration of wound, factors inhibiting wound healing  
  b. Object data: wound size, wound depth, wound edges, undermaining, necrotic tissue type, amount of necrotic tissue, exudate type, amount of exudate, skin color around the wound, edematous tissue, hardening of the wound edges, granulation tissue, epithelialization |
| 3  | Odor scale |
| 4  | Nursing diagnoses related to wound problems. |
| 5  | Intervention  
  a. Total wound scoring with TIME management  
  b. Wound bed preparation: autolytic, debridement, biological, Conservative sharb wound debridement  
  c. Use of dressings |
| 6  | Supporting laboratories |
| 7  | Medication records |
| 8  | Control plan |

Table 2. Test questionnaire Happines

<table>
<thead>
<tr>
<th>No</th>
<th>Question</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I have a new understanding of wound care applications</td>
<td>96.9%</td>
<td>3.1%</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>I find this app difficult to use</td>
<td>43.8%</td>
<td>-</td>
<td>56.2%</td>
</tr>
<tr>
<td>3</td>
<td>I feel confident when using the wound care application</td>
<td>93.8%</td>
<td>6.2%</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>I hope to use this wound care application next</td>
<td>90.6%</td>
<td>9.4%</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>I am happy using an Android-based wound care application</td>
<td>71.9%</td>
<td>6.20%</td>
<td>-</td>
</tr>
</tbody>
</table>

Fig. 1. Design flow Application development flow chart

3. Development stage
   At this stage, the researcher involves an application developer. The product validation stage is also carried out with wound care experts and IT experts before the product is tested in groups.

4. Implement stage
   The results of the happiness questionnaire trial on the use of the application can be presented as Table 2.
   From the results of the happiness fordyce sixty second questionnaire [14] analyzed using chi square, it can be explained that participants have a new understanding of Android-based wound care documentation applications are (agree; 96.9%, neutral; 3.1%), stating that this application is difficult to use, (agree; 43.8%, disagree; 56.2%), confident in using Android-based
wound care documentation (agree; 93.8%, neutral; 6.2%), hope to use the next (agree; 90.6%, neutral; 9.4%) express happiness using the application (agree; 71.9%, neutral; 6.20%).

5. Evaluation stage

Activities at this stage are to revise (update data on the application) which aims to improve product quality based on revision suggestions from experts, with revised flowchart as Fig. 2.

Fig. 3, the front view of the application made based on the revised results. The display of the documentation results stored in the form of pdf files that can be inserted into existing data on other computers (Fig. 4).

As for the steps to use the application:

1. Download the app
2. User registration
3. Filling in the general data of the patient
4. Filling in subject data
5. Take pictures of wounds
6. Fill in object data according to the condition of the wound
7. Filling odor scale
8. Choosing a nursing diagnosis
9. Filling out a medication record
10. Filling out the control plan
11. Save pdf or print file
4. Discussion

This research stage takes time from January to mid-September 2023 with stages of analysis, design, development, implementation, and evaluation. At the Analysis stage we create our own concept schemes for functional needs and user needs through many descriptions and literature for us to develop. We wanted an application that we could use as wound care documentation with interventions that were tailored to the data, and that we could store and connect to other computers. This creates a formula from experience during our provision of wound care services. The use of terms must be clearly understood so as to avoid confusion and misunderstanding [15].

Focus group discussions are carried out from the design stage which continues to the evaluation stage, even though we realize that perfection belongs only to God, but we still want the best in this process. We listened to the opinions and what was needed from 3 wound care experts, 2 doctors and patients, and was refined by nursing academic experts. Discussions with our academic nursing experts are conducted separately. Wound care experts want the application to be easy and accurate to use, doctors suggest documentation that can be used as communication and intercollaboration with nurses and patients, patients need documentation that can be carried without paper lists. Nursing academy experts advise to stick to the evidence base in nursing with the scientific research process. Data information related to models, knowledge and methods must be extracted so that they can be used as a data integration base [16].

At the development stage, there are several components that are felt unnecessary and eliminated because it is feared to aggravate the use of the application. We work closely with the IT team in conducting the application developer process. We also need advice from graphic design in this regard. This research must consider accuracy, so that it is more effective with comprehensible visual support [17]. The implementation stage with socialization carried out once without intervention concluded how this application was received among nurseprenuers in Depok City. The last evaluation stage that we carried out to update data on the application adjusted service accreditation standards so that we added and changed the form of its appearance, Data components included in application-based wound nursing documentation were carried out continuously and comprehensively [18]. In the future we plan to develop research on how to use this application in wound nursing documentation as a support for management information with a longer and repeatable time. Research related to phenomena and applied is the scientific basis that will play an important role in service activities [19].

We call this application MyWound Care, which can be used on all types of wounds. The results of the study [20] showed six components; debridement, infection control, revascularisation, exudate control, determines chronicity of the wound; and evaluates the top surface of the skin.
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5. Conclusion

The results of this study show that nursepreneurship requires management information system support in providing services in different areas from hospitals [21] where Android application-based nursing documentation is felt to be very important. Management information system support in nursepreneurship through the use of Android-based wound care applications is considered useful because the focus of nursepreneurship services is more on home visits with the wide conditions of different work areas, limited health distribution, the availability of service systems that are felt to be still lacking, and the use of technology is not optimal. This is taken into consideration to achieve the best results by thinking explicitly about the implications of the nursing field [22].

The development of Android-based wound care applications as documentation of care in today's technological era changes the way of view and service. Nursepreneur began to focus on being a user and ensuring effective management of management information systems with technology as the driving force. The creation of a culture of nursing innovation in nursepreneurship ensures effective management with the use of technology ethically and transparently [23]. Android-based wound care applications in information management support can be considered as long as they meet two legal requirements, namely can be used for documentation and evidence-based. This information system with electronic nursing documentation in wound care is used with structured standards and principles that allow information to be connected to patient files, accelerating information and utilization in care service management [24].

6. Recommendations

Management information systems with the use of android-based wound care applications for nursing documentation require an understanding of wound care so training is needed before using it, because nursepreneurs always need knowledge and readiness to conduct service analysis [25]. Wound documentation with the use of android-based wound care applications is an integral part, which contains health data, with interventions that support nursing implementation [26]. Suggestions for developing research on the achievement of wound care competence in the use of Android-based applications are also felt necessary. Evaluation of the use and effectiveness of Android-based wound care applications from the perspective of doctors and patients can also be considered in the future.

Acknowledgements

The authors would like to thank Prof. Nursalam, Head of Nursing Study Program, Faculty of Nursing, Airlangga University, Surabaya, Indonesia; Dr. Vimala Ramoo, Department of Nursing Science, Faculty of Medicine, University of Malaya, Malaysia; Wahyu Kurniawan as the IT team that supports the process of making this application and Nursepreneurs research participants in Depok City, Indonesia.

Funding

None

Conflict of interest

The authors declare that there are no conflicts of interest.

References

[1] Aula AS. Hospital management information systems acceptance at Wonisari Regional Hospital, Gunungkidul, Yogyakarta, Indonesia. Epidemiology and Society Health Review.


[25] Lim JY, Kim J, Kim S. The effects of the Start-

Quality of Care for Children under Five with Malaria Using Integrated Management of Childhood Illness (IMCI) at Public Health Center: A Systematic Review

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b Department of Nursing, Health Polytechnic of Kupang, Ministry of Health, Kupang, Indonesia
c Faculty of Health, Institute of Technology and Health Bali, Denpasar, Indonesia

Abstract

**Background:** Children under five who have a fever in areas where malaria is highly endemic must take a microscope test to ensure that the children have plasmodium malaria. The purpose of this article is to identify the quality of care for children under five with malaria using the Integrated Management of Childhood Illness approach.

**Method:** A systematic review. The search strategy was conducted on data-based Scopus, Web of Science, Pubmed, Science Direct, Proquest and Ebscohost with the keywords “quality of care” AND “IMCI” AND “malaria” AND “children” AND “under five”. Inclusion criteria were: children under five with fever or malaria. Intervention: treatment using IMCI, comparison: none, outcome: assessment, classification, and treatment according to the IMCI chart, study design: quasi experiment, cross-sectional.

**Results:** 156 articles were found. Ten articles meet the inclusion criteria. The results show that IMCI strategies were promotive, preventive, curative, and rehabilitative activities. IMCI services were focused on case management by looking at clinical symptoms and empirical therapy carried out by doctors, nurses, and midwives. Assessment and accurate classification of sick children under five using IMCI guidelines have had a significant impact.

**Conclusion:** Guidelines for managing children under five suffering from malaria using the IMCI approach are very helpful for nurses. This includes serious cases such as malaria with complications. It is highly recommended that healthcare facilities improve the quality of services by training, monitoring, and procuring essential medicines, and conducting microscope testing.

Keywords: Quality of care, IMCI, Children under five, Malaria

1. Introduction

Malaria is a disease transmitted by Anopheles mosquitoes which is greatly influenced by climatic conditions in the form of temperature, rainfall, and humidity [1]. In particular, rainfall and temperature affect mosquito reproduction and development as well as the presence of parasites in the mosquito’s body. Naturally, mosquito breeding is influenced by two seasons, namely the rainy season and the dry season. Malaria is a leading cause of death, especially for babies, children, and pregnant women. Clinical manifestations of malaria in children are difficult to assess because most clinical symptoms are nonspecific and most cases occur in settings where no routine screening is available [2].

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Children under five are vulnerable to malaria because they have low body resistance. They can have severe anemia, hypoglycaemia, and cerebral malaria if proper and timely treatment is not taken. The symptoms of this disease are intermittent high fever, anemia, and splenomegaly. However, for children under five, these typical symptoms do not always present at younger ages. The prominent symptoms are diarrhea, anemia, and inflammation of the respiratory tract. Globally 61% of the 435,000 people who died from malaria were children under the age of five [3]. Malaria is one of the direct causes of malnutrition in children and communities vulnerable to malnutrition. If children are frequently infected with diseases, they may suffer from malnutrition. Regardless of nourished food intake, children lose their appetite which leads to low immunity. If this condition is not treated, it will have an impact on the growth and development of children under five. One of the bad impacts is stunting.

Despite interventions and preventive measures against malaria, this disease remains a major health problem throughout the world, especially in developing countries. Malaria is one of the main causes of morbidity and mortality, especially in Sub-Saharan African countries. The most vulnerable groups to malaria are pregnant women and children [4]. The IMCI approach was first launched by WHO in 1994. This initiative is a collaboration among WHO, UNICEF and other organizations. In 1993, the World Bank reported that IMCI was a cost-effective intervention to overcome the problem of under-five mortality caused by acute respiratory infections, diarrhoea, measles, malaria, and malnutrition. According to WHO data, three out of four sick toddlers often have multiple complaints and suffer from at least 1 of the 5 most common diseases in toddlers. This issue is the focus of IMCI. One of the Sustainable Development Goals (SDGs) is to ensure a healthy life and promote the wellbeing of all people. One of the targets is by 2030 it can end preventable deaths of babies and toddlers, with all countries trying to reduce the number. Neonatal mortality is at least 12 per 1000 live births and the infant mortality rate is 25 per 1000 live births. The results of research in the European region, poor quality of care for children, lack of evidence-based guidelines, misuse of antibiotics, and long hospitalizations necessitate the implementation of systems such as IMCI [5].

IMCI is an integrated guideline that elaborates on the management of illnesses for children under five in detail. IMCI is an approach to managing illness in children under five, which aims to improve their health and quality of service for children. Children brought to health facilities are often found to be suffering from more than one unhealthy condition, making a single diagnosis impossible. Children require combined therapies for successful treatment. IMCI is a holistic approach that focuses on child health and development [6]. IMCI focuses on children aged 0 months to 5 years because they are vulnerable to multiple diseases because their immune system is still low. Initiatives are needed to reduce the high mortality rate in infants and toddlers. One of the best initiatives is IMCI because it is an integrated approach that combines promotion, prevention, and treatment services for the five main causes of death in infants and toddlers in developing countries. The World Health Organization (WHO) has recognized that the IMCI approach is an appropriate initiative for developing countries to reduce mortality, morbidity, and disability in infants and toddlers. The purpose of this systematic review is to identify the quality of services for children under five with malaria using the IMCI approach including assessment, classification, and action/treatment.

2. Methods
2.1. Study design

The purpose of this systematic review is to identify the quality of services for children under five with malaria using the Integrated Management of Childhood Illness (IMCI) approach including assessment, classification, and action/treatment. The research was conducted with a systematic approach using a PRISMA literature study without conducting a meta-analysis test on quantitative data.
2.2. Search strategy

The research method used in this study was a systematic review. The search strategy was conducted on data-based Scopus, Web of Science, Pubmed, Science Direct, Proquest and Ebscohost with the keywords “quality of care” AND “IMCI” AND “malaria” AND “children” AND “under five”. After identification and screening, ten articles were found to meet the inclusion criteria. The selected articles were published between 2019 and 2023. Article exclusion criteria were: not related to IMCI chart, non-malaria patient population and not in public health center, review study design, published under 2019, article not published in a peer-reviewed journal.

2.3. Eligibility criteria

The articles used in the study were articles that met the PICOS inclusion criteria, namely the population: children under five with fever or malaria, intervention: treatment using the Integrated Management of Childhood Illness (IMCI) approach, comparison: none, outcome: assessment, classification, and treatment according to the IMCI chart, study design: RCT, quasi-experimental, cross-sectional, case-control. The selected articles were published between 2019 and 2023. Article exclusion criteria were: not related to IMCI chart, non-malaria patient population and not in public health center, review study design, published under 2019, article not published in a peer-reviewed journal.

2.4. Study selection

There were 156 articles found in international journal databases including Scopus (8), Web of Science (19), Pubmed (9), Science Direct (89), Proquest (16), and Ebscohost (15). Then, the researchers filtered articles according to research objectives by deleting duplicate articles, identifying articles by title, identifying abstracts that matched the inclusion criteria, and reading the full text of the relevant articles according to PICOS. Finally, the researchers found 10 relevant articles (Fig. 1).
Table 1. The results of the article review

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Research design</th>
<th>Sample</th>
<th>Data analysis</th>
<th>Research results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mwanga-Amumpaire et al. [7]</td>
<td>mixed-methods convergent parallel study: cross-sectional design</td>
<td>532 children under five with malaria infection</td>
<td>Descriptive analysis and logistic regression models</td>
<td>Correct assessment 73%, Correct classification 34%, Correct treatment 16%, Appropriately managed overall: n= 14%</td>
</tr>
<tr>
<td>Kilov et al. [8]</td>
<td>concurrent mixed-methods study: cross-sectional design</td>
<td>47 Health facilities and 531 healthcare</td>
<td>Descriptive analysis and Multivariable linear regression analysis</td>
<td>Correct treatment 98%; there was a statistically significant association between knowledge and refresher training</td>
</tr>
<tr>
<td>Mpimbaza et al. [9]</td>
<td>A cross-sectional design</td>
<td>N=3936 patients and 1718 HCW from 392 facilities, 1235 (31.4%) children under five</td>
<td>Descriptive analysis and chi-square test</td>
<td>Availability of IMCI guidelines/charts 136 (34.7%), Malaria test 90.6%, IMCI training in the past 5 years 36.7%</td>
</tr>
<tr>
<td>Mwanga-Amumpaire et al. [10]</td>
<td>a cross-sectional survey</td>
<td>N=110 Urban and rural health facilities that treat children using IMCI charts.</td>
<td>descriptive analysis and Chi-square tests or 2-tailed Fisher’s exact test</td>
<td>Malaria rapid diagnostic tests and microscopes 86%, oral artemether 96%</td>
</tr>
<tr>
<td>Rozelle et al. [11]</td>
<td>a cross-sectional survey</td>
<td>315 health facilities</td>
<td>descriptive analysis</td>
<td>The presence of health assistants and the implementation of IMCI in children with malaria diagnosed 50% by confirmation of RDT and microscopic examination, 51% correct treatment of malaria in children under five years</td>
</tr>
<tr>
<td>Nyaoke et al. [12]</td>
<td>a cross-sectional survey</td>
<td>N=341 children under five</td>
<td>descriptive analysis</td>
<td>Prescription of antimalarial drugs despite negative microscopic results was found in 12.9% of the children, with death reported in 48 (14.1%)</td>
</tr>
<tr>
<td>Getachew et al. [14]</td>
<td>a cross-sectional survey</td>
<td>N=1908 patient</td>
<td>descriptive and regression analysis</td>
<td>Body temperature checks were performed in 92% of children with fever, only 3% of children with fever were referred or treated, and 60% received antibiotics. In children diagnosed with malaria, 51% were assessed for screening with IMCI management and 4% for general danger signs.</td>
</tr>
<tr>
<td>Sarker et al. [15]</td>
<td>a cross-sectional survey</td>
<td>N=100 children</td>
<td>descriptive analysis</td>
<td>a low concordance between physician and IMCI algorithmic diagnosis and very severe diseases is not a diagnosis made by the physician. The IMCI algorithms have to be refined for appropriate management of these</td>
</tr>
<tr>
<td>Candrinho et al. [2]</td>
<td>a cross-sectional survey</td>
<td>A total of 319 health care providers and 1840 patients from 117 health facilities were included</td>
<td>descriptive analysis and a multi variate regression model</td>
<td>the proportion of suspect malaria cases correctly managed was under 50%</td>
</tr>
</tbody>
</table>

2.5. Data extraction

The researchers filtered all abstracts and studies that did not fit the inclusion criteria. The data extraction process was carried out by collecting data on the author, year of publication, study design, basic sample, final size, and duration of intervention. After the data extraction process, it was reviewed by all researchers to check the data accuracy (Table 1).
3. Results

3.1. Characteristic study

The ten articles were all original research that used a cross-sectional study design. 10 articles describing IMCI services for children aged 0 - 59 months. Malaria examination is part of the assessment of children with fever at the age of 2 months - 5 years. Children with fever can be classified as suffering from malaria, measles, and dengue infection. All of article describe the almost universal adoption of Integrated Management of Childhood Illness (IMCI) guidelines for the diagnosis and treatment of sick children under the age of five in low- and middle-income countries.

3.2. Results

The analysis found low compliance with the IMCI protocol established by WHO. Regarding protocols in MTBS include assessment, classification, providing action/treatment, counseling and follow-up services. For children under five with malaria, the protocol flow that must be emphasized is that the administration of action/treatment with antimalarial drugs must be based on the results of blood tests either by RDT or microscope examination.

4. Discussion

The strategy for implementing IMCI includes promotive, preventive, curative, and rehabilitative activities. IMCI services are focused on case management by looking at clinical signs and empirical therapy performed by doctors, nurses, midwives, and other health workers in primary healthcare services such as polyclinics, health centers, clinics, and hospitals. According to the IMCI chart, the process is an interplay between assessment and classification. The implementation of IMCI has to run comprehensively and simultaneously, especially for a developing country like Indonesia. This strategy is significant in achieving children’s health status. Multiple research found that IMCI is an effective approach to improving the quality of child health services.

The first stage in the IMCI protocol is conducting an assessment. Assessing according to the IMCI protocol in children under five with malaria, the child’s body temperature must be checked, malaria endemic areas are determined, asked how long the child has had a fever, whether the child is suffering from malaria or is taking anti-malarial medication, and blood tests are carried out with an RDT or microscope [16]. The assessment must be carried out accurately so that it makes it easier to enforce the classification later. In dealing with sick toddlers, health workers (nurses, midwives or village midwives) who are in basic services are trained to apply the IMCI approach actively and structured to assess the presence of signs or symptoms of disease by asking, looking, listening, touching, making classifications, determine actions and treat children, provide counseling and follow-up services during repeat visits. In implementing IMCI, health workers are taught to quickly pay attention to all the symptoms of a sick child, so that they can determine whether the child is seriously ill and needs to be referred. If the disease is not serious, then health workers can provide treatment according to IMCI guidelines [14, 17].

The second step in the IMCI protocol is to enforce classification based on the results of the assessment that has been carried out by matching the symptom column according to the IMCI guidelines. The IMCI chart states that the classification that can be enforced in children with malaria in high malaria endemic areas is very serious disease with fever. If the child's assessment results have a fever and the RDT or microscope results are positive then the child is classified as malaria and if the RDT or microscope results are negative or there is a cause other than fever, the child is classified as having a fever, perhaps not malaria [5, 13, 16]. Establishing the correct classification will be very helpful in determining the treatment or treatment given to the patient [8, 15, 17-19]. Therefore, health workers must be careful and precise in matching symptoms based on the results of the assessment carried out at the initial stage.

The third step is providing care or treatment according to the classification that has been established in step two. Based on IMCI guidelines, the actions or treatment given if a child is classified as malaria include giving first choice
oral anti-malarial medication; Give one dose of paracetamol for fever ≥ 38°C; Repeat visit in 3 days if fever persists; Advise when to return immediately ; If fever persists for more than 7 days, refer for further assessment. The anti-malarial drugs given to patients are appropriate to the type of plasmodium malaria they suffer from.

Fever in children is one of the typical signs of infectious disease. Fever is also a general clinical sign of an infection of a disease. One study in malaria-endemic countries found that 71.4% of children with fever were caused by malaria. In high malaria endemic areas, it is mandatory to measure temperature and examine blood samples both by RDT and microscopic [16, 20, 21]. Providing appropriate treatment measures is expected to prevent malaria children from recovering and growing according to their age.

IMCI is an evidence-based approach that is widely adopted to prove testing and treatment for children with malaria. The aim is to improve access and quality of services, especially for the diagnosis and treatment of malaria in children [14]. “Fever is a common problem in young children, most episodes of fever are caused by self-limiting infections, but a small number of children will develop life-threatening infections. Each infection has a symptom threshold and other clinical symptoms that can distinguish a sick child from asymptomatic or so-called progenic fever in malaria cases” [22]. Implementation of IMCI is carried out by assessing, classifying diseases, determining action/treatment or follow-up and counseling. This activity requires good ability or work performance from the officers carrying it out. A person’s work performance can be influenced by several internal factors such as knowledge, attitude, motivation, education, length of work. External factors such as incentives and training. The success of implementing IMCI cannot be separated from post-training monitoring, technical guidance for nurses and midwives, complete facilities and infrastructure supporting the implementation of IMCI [23]. In malaria-endemic countries, malaria is suspected mainly based on fever. WHO recommends early malaria diagnosis (within 24 hours of symptom onset) to prevent the occurrence of severe malaria. IMCI screening in febrile children has helped early diagnosis and treatment of uncomplicated malaria, thereby reducing the effects of severe malaria.

5. Conclusion

IMCI is one of the appropriate interventions in screening, diagnostic examinations and providing appropriate action for children under five suffering from malaria. Children are given antimalarial therapy if supported by the results of RDT or malaria microscopy. Overall, it can be concluded that the quality of IMCI services is still lacking and assistance needs to be provided in implementation at community health centers so that it can improve the quality of services for sick toddlers.

6. Recommendations

There needs to be a government commitment to regulating MTBS services as a standard service for sick toddlers at health centers and supported by financing and providing supporting infrastructure to implement standardized MTBS services. Health workers who carry out IMCI need to be trained and have their knowledge updated every time there is a change in WHO guidelines and after the training, they need to be provided with assistance in providing services on a regular basis.

Conflict of Interest

The authors declare that there is no conflict of interest in the publication of this paper.

References


International Conference of Public Health Sciences

HIV Prevention Program with PrEP Focus on Public-Private-Community Partnership (PPCP) in Semarang City

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Abstract

Background: In 2021, Indonesia was estimated to have 540,000 people living with HIV (PLHIV). One of the key HIV prevention programs is the utilization of Pre-Exposure Prophylaxis (PrEP). This research aims to analyze HIV prevention with the PrEP program, within the context of the Public-Private-Community Partnership (PPCP) in Semarang City.

Method: This study employed a mix of qualitative and quantitative research approaches. The qualitative data were collected through FGD with HIV program stakeholders. The quantitative data were collected through the secondary data. The validity and reliability were conducted through triangulation.

Results: The specific protection of the HIV Program is using condoms and PrEP. In Indonesia, the program of using condoms was not as successful as it was expected. In the PrEP program, community members actively referred potential users to healthcare facilities to access PrEP services that are available at four government-owned healthcare facilities: Puskesmas Poncol, Halmahera, Kedungmundu, and Lebdosari. Despite these efforts, Semarang City has achieved only 17.6% (135) of the total target of 765 PrEP users. By 2023, 93% (126) of PrEP users were men who have sex with men (MSM), 3.7% (5) were sex workers, 2.2% (3) were transgender individuals, and 0.7% (1) were people who inject drugs (PWID). Notably, private healthcare facilities have not yet become involved in PrEP services.

Conclusion: The number of PrEP users in Semarang City has increased yearly. Additionally, involving private healthcare to enhance access to PrEP and communities in HIV education and prevention campaigns can reduce HIV.

Keywords: HIV/AIDS, PrEP, Prevention, PPCP

1. Introduction

Indonesia faces a significant challenge in addressing the HIV epidemic. In 2021, Indonesia is estimated to have 540 thousand people living with HIV (PLHIV) [1]. The prevalence of HIV varies across regions, with higher rates observed in certain populations, including men who have sex with men (MSM), transgender individuals, people who inject drugs (PWID), and sex workers [2].

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affected populations, and gaps in implementing evidence-based prevention interventions [4].

HIV prevention programs play a crucial role in reducing new HIV infections and improving communities’ overall health and well-being. Key strategies in HIV prevention include increasing awareness, promoting safer sexual practices, providing access to testing and counseling services, and ensuring timely access to antiretroviral treatment (ART) [5]. While significant progress has been made in HIV prevention, there is a need to strengthen efforts further and explore innovative approaches to reach at-risk populations effectively. One such approach is the utilization of Pre-Exposure Prophylaxis (PrEP), which involves using antiretroviral medication by HIV-negative individuals to prevent HIV transmission [6].

In addressing the HIV epidemic, fostering partnerships between the public, private, and local communities is essential. Public-Private-Community Partnerships (PPCP) offer a collaborative framework to leverage the strengths and resources of each sector and create synergistic interventions that can have a greater impact on HIV prevention. PPCP can facilitate the successful implementation of PrEP programs by tapping into the existing infrastructure and expertise of private clinics, universities, and community organizations. Private clinics can contribute by providing clinical services, while universities can offer research expertise and community engagement. Involving the community, including NGOs and PrEP users, ensures that the program is designed to address the specific needs and challenges faced by key affected populations.

By establishing a PPCP model for HIV prevention, particularly in the context of PrEP, Indonesia can enhance access to comprehensive prevention services, improve community engagement and ownership, and promote sustainable and effective interventions to reduce new HIV infections.

This research was conducted to analyze the HIV prevention programs focusing on PrEP use among key populations in Semarang City. This study also looked at the private sector and community role involvement in supporting the implementation of HIV prevention programs using PrEP in Semarang City.

2. Methods

This was a mix of qualitative and quantitative research approaches. This research was conducted in Semarang City. The population in this study are stakeholders involved in the HIV prevention and control program in Semarang City. The samples taken for in-depth interviews were the Central Java Provincial Health Service, Semarang City Health Service, and Community Health Centers that had provided PrEP services.

Qualitative data was collected by focus group discussion. The informants of the forum group discussion were samplings from the population. Questions in the FGD include information about HIV control and prevention programs at the district level, cross-sector involvement, DHO’s strategy in engaging the community and private sector, DHO’s support for HIV prevention programs with PrEP, financing of the PrEP program, and obstacles in HIV/AIDS prevention efforts through the PrEP program.

The quantitative data were collected through the secondary data of the Central Java PHO and the Semarang DHO. Data sources searched the Infectious Disease Control and Prevention Section Database, and Embase from January 2021 to April 2023. The quantitative data was analyzed descriptively to make it easier for researchers to interpret the data and use it for the triangulation process.

The validity and reliability were conducted through triangulation. Methodology triangulation and data triangulation were applied. The methodology triangulation was done by in-depth interview and observation. Data triangulation was done by descriptive analyzing secondary data from the Central Java PHO and the DHO of Semarang.

3. Results

The number of PrEP use as an HIV prevention effort in Semarang City has increased every year. Nevertheless, this amount has not met the target for PrEP use set nationally by the Ministry of Health. Currently, access to PrEP in
Central Java Province is only available in Semarang City, including the Halmahera, Kedungmundu, Poncol, and Lebdosari Health Centers. That’s because Semarang has the first highest number of HIV cases in Central Java (Fig. 1) and Semarang was chosen as the trial location for PrEP. The four health facilities are public sector. Until now, no private health facilities have been involved in HIV prevention programs using PrEP in Semarang City, both private hospitals and private primary health care facilities (clinics).

The HIV prevention program with PrEP in Semarang City started in 2021 with a target of 398 users from key populations. Table 1, the number of PrEP users each year from 2021 to 2023.

By 2023, 93% (126) of PrEP access by MSM; 3.7% (5) of PrEP access by sex workers; 2.2% (3) of PrEP access by transgender individuals; and 0.7% (1) was accessed by PWID. This number is still far below the target set by the National (Ministry of Health) of 765 PrEP users during 2023. Until July 2023, Semarang had only reached 17.6% (135) of PrEP users out of the total target of 765 users. This requires a strategy to increase the number of PrEP users in Semarang City.

Another obstacle found in HIV prevention programs using PrEP is the high dropout rate. Based on Table 2, Semarang City PrEP Cascade data until July 2023, it is known that the number of key populations accessing in months 1, 3, 6, 9, and 12 after starting PrEP always decreases. The reason for the decrease in the number of PrEP users is due to several reasons, including PrEP users forgetting to consume PrEP so the drugs should run out in a month, the side effects of using PrEP, and boredom in taking PrEP drugs.
Table 2. Cascade Data of PrEP users in Semarang City per July 2023

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential PrEP Users</td>
<td>486</td>
</tr>
<tr>
<td>PrEP Eligibility</td>
<td>216</td>
</tr>
<tr>
<td>Starting PrEP</td>
<td>207</td>
</tr>
<tr>
<td>Month 1</td>
<td>44</td>
</tr>
<tr>
<td>Month 3</td>
<td>23</td>
</tr>
<tr>
<td>Month 6</td>
<td>14</td>
</tr>
<tr>
<td>Month 9</td>
<td>5</td>
</tr>
<tr>
<td>Month 12</td>
<td>4</td>
</tr>
</tbody>
</table>

4. Discussion

Pre-exposure prophylaxis (PrEP) is highly effective at reducing the risk of HIV. PrEP is an effort to prevent HIV by taking medicine according to the rules of use. PrEP reduces the risk of getting HIV from sex by about 99% and PrEP reduces the risk of getting HIV from injection drug use by at least 74%. The type of PrEP drug used in Indonesia is TDF/FTC. There are 2 types of regimens in PrEP: daily regimen and ED (Event Driven) regimen [7]. Expanding PrEP access outside the Semarang City area also needs to be carried out to increase the number of PrEP accesses. It is known that 17.6% of PrEP users are still dominated by key populations living in Semarang City. Meanwhile, key populations outside Semarang City need to come to Semarang City if they want to access free PrEP provided by the government.

Table 1 displays data regarding the number of PrEP users in Semarang City. It is shown that the number of PrEP users in Semarang City is still far below the national target determined by the Indonesian Ministry of Health. From the results of the FGD, it is shown that several factors hinder access to the use of PrEP as an HIV prevention effort in the city of Semarang. There are factors of public knowledge, factors of negative stigma and discrimination in the community and health care facilities, and factors of the small number of private clinics capable of providing HIV screening and HIV prevention care. PrEP as an HIV prevention effort was only introduced and actively used in Indonesia in 2021. While in Semarang City, PrEP was actively used in 2022 and increased the number of users in 2023. In Semarang, users of PrEP are limited because the PrEP program is still in the development stage, and many people don't know about PrEP and how to access it. Using social media to disseminate information about PrEP can be a strategy to increase users of PrEP. Using social media to disseminate information about PrEP can be a strategy to increase users of PrEP services. Over the last two decades, social media has changed the way many people share and consume health information. There is significant potential for social media to help increase knowledge, awareness, and uptake among key groups of young people at risk of contracting HIV. Although a single approach has not been identified, the findings show that various social media platforms can be used to share and disseminate information about PrEP in a way that is appropriate and appealing to a specific audience [8].

Another obstacle in accessing PrEP in Semarang City is the negative stigma and discrimination factors in the community and health workers are still high. It is also in line with previous research that found that the stigma factor was an obstacle to HIV prevention efforts in Indonesia. Stigma makes HIV sufferers ostracized in society, which causes HIV sufferers to be reluctant to take tests and not come to healthcare facilities to find out their health status [9]. Reducing HIV stigma and discriminatory attitudes is essential and necessary for effective HIV prevention and treatment efforts [10]. Several studies have proven that an essential strategy in responding to the HIV epidemic is to increase knowledge of healthy behavior and reduce social stigma [11].

The limited number of health care facilities (private clinics) that provide HIV screening and prevention with PrEP in Semarang City is also an obstacle in itself. Private clinics are health facilities that have a large number of National Health Insurance participants [12]. There is concern that an increase in the number of private clinics capable of providing PrEP services will lead to an increase in PrEP drug users as well as an increase in the number of perpetrators of risky sexual behavior and MSM in Semarang City.
These issues and concerns have caused several private clinics and institutions, especially those operating based on religious principles, to be reluctant to provide PrEP services. However, the Semarang City District Health Office has committed to continuing to involve private clinics regarding access to PrEP services for HIV prevention, especially among pregnant women and serodiscordant couples.

The Public-Private-Community Partnership (PPCP) aims to increase access to prevention, treatment, and care services for key populations and PLHIV. PPCP is a strategy involving all sectors to support HIV prevention programs, including the government sector, private sector, and community/society sector. The government can provide policy support, allocate funds for the PrEP program, coordinate and monitoring and evaluation. The private sector can provide PrEP service facilities. Community organizations can provide outreach, education, and support services to key populations. Multi-sector collaborations through public-private Partnerships are emerging to address complex health issues requiring multidisciplinary approaches [13]. Public-private-community partnerships in global health have rapidly proliferated and are now recognized as an integral component for implementing effective interventions [14]. Governments are seeing the potential for engaging the private sector in improving people’s health [15]. Despite various challenges, PPCP could provide a good opportunity to facilitate access to health care services. However, it should be noted that the success of PPCP depends on the existence of transparency in relationships between partners, PPCP being flexible, having a sustainable financing source, mutual commitment, and the ability of the public sector to monitor and control the quality of services provided by the private sector [16, 17].

Private-sector engagement strategies also need to be developed to increase the number of access to PrEP [18]. Private health services have great potential to increase access to PrEP because they have a large population of consumers. Based on the 2017 Patient Pathway Analysis Study, it is known that 74% of people prefer to come to private health facilities to seek initial treatment, while 24% of people choose to come to public health facilities. This is due to high confidentiality, non-discriminatory services, and more flexibility, but it is believed that the cost of obtaining PrEP services is not small so only people with good economic conditions can access PrEP at private clinics. In Malaysia, differentiated PrEP distribution strategies are needed to provide MSM-friendly and focused services, allowing for PrEP delivery that differs based on dosing, location, provider, and frequency of engagement [19].

The free community setting model in accessing PrEP was most commonly adopted in the Asia-Pacific [20]. Community involvement in increasing access to PrEP in key populations also needs to be strengthened. Not only the key population community itself but also other communities such as university academics or students to participate in campaigns on HIV education and prevention that can also reduce HIV rates in an area. The involvement of key communities is also very influential in PrEP service use. The government needs to collaborate with communities in reducing HIV rates in Indonesia. Community positions can support peers who are at high risk of experiencing HIV, assist in accessing PrEP services, and accompany patients in obtaining PrEP services. Meanwhile, communities in various places have jointly served PrEP and community-based clinics.

5. Conclusion
PrEP reduces the risk of getting HIV from sex and injection drug use. Access and PrEP users increase every year from 2021 until 2023 in Semarang City. PrEP is accessed by MSM; sex workers; transgender individuals; and PWID. However, the number of PrEP users always decreases in the following months. The reason for the decrease in the number of PrEP users is due to several reasons, including PrEP users forgetting to consume PrEP so the drugs should run out in a month, the side effects of using PrEP, and boredom in taking PrEP drugs. A strategy involving the roles of various government, private and community sectors needs to be carried out to continue to increase the number of PrEP
users in Semarang City, especially key and at-risk groups. Until now, no private health facilities have been involved in HIV prevention programs using PrEP in Semarang City, both private hospitals and private primary health care facilities (clinics). Semarang was chosen as the location for the PrEP service trial because it has the highest number of HIV cases in Central Java. The strategy of PPCP (Public-Private-Community Partnership) is a model for HIV prevention, particularly in the context of PrEP, Indonesia can enhance access to comprehensive prevention services, improve community engagement and ownership, and promote sustainable and effective interventions to reduce new HIV infection.

6. Recommendations
From the results of this study, the authors provide several strategic recommendations to stakeholders/government to increase the number of PrEP users to prevent HIV in the city of Semarang:

1. Involve the private sector and community in providing PrEP services in Semarang City;
2. Identify the needs of the private sector and the community sector, including the benefits that will be obtained by the private sector and community if they are involved in providing PrEP services;
3. Design a strategy for implementing a health service network between the public and private sectors (referral network; logistics network; capacity building; and assessment);
4. Expanding PrEP access outside the Semarang City area also needs to be carried out to increase the number of PrEP accesses.

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The research team would like to thank all parties who have been involved and helped in the research process until completion. Thank you to the District Health Office of Semarang and the Province Health Office of Central Java for providing supporting data for this research. Thank you to UNAIDS Indonesia for supporting funding for the development of HIV/AIDS research in Indonesia, especially in the city of Semarang.

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References


The Influence Factors of Client Satisfaction on Recommendations among Abortion Seekers at Planned Parenthood Association of Thailand

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b The Planned Parenthood Association of Thailand under the Patronage of Her Royal Highness the Princess Mother (PPAT)

Abstract

Background: Abortion is a crucial aspect of women's reproductive health services. In response to changes in Thailand's abortion laws in 2021, the Planned Parenthood Association of Thailand (PPAT) extended abortion services through affiliate clinics. Alongside providing these services, PPAT has sought feedback from patients regarding satisfaction with the care received and their willingness to recommend the service to others. This study aims to identify the client satisfaction factors that influence the willingness to recommend among abortion seekers at PPAT-affiliated clinics.

Method: This research constitutes a secondary data cross-sectional survey conducted from February 2022 to December 2022, in response to legal amendments. The questionnaire was distributed and collected by PPAT’s staff. The survey included a range of questions, covering sociodemographic information, satisfaction evaluations, and clients’ willingness to recommend PPAT’s clinic. Both descriptive analysis and simple linear regression analyses were performed.

Result: In our study comprising 368 respondents, one significant factor emerged: a positive satisfaction level with the abortion services (β = 0.356, p < 0.001) was linked to an increased likelihood of clients expressing their willingness to recommend PPAT's clinic.

Conclusion: Our study’s findings, it is evident that a positive level of client satisfaction with abortion services emerged as a potent catalyst for enhancing willingness to recommend PPAT’s clinics. In conclusion, diligently maintaining high levels of client satisfaction should be prioritized in the ongoing efforts of PPAT and similar organizations to ensure the provision of safe and accessible abortion services.

Keywords: Abortion, Abortion Seekers, PPAT, Satisfaction, Thailand

1. Introduction

Abortion is a pivotal part of women’s reproductive health services, serving as an indispensable role in meeting women’s health needs and has a profound impact on all aspects of a woman’s life. First of all, abortion has the potential to fulfill a supportive role in the realization of a woman’s personal aspirations and goals. According to Upadhay’s research, women frequently view abortion as an aid, a family plan aid, in deciding whether or not they want to have a child based on the situation at the time while pursuing academic or professional ambitions [1].

Secondly, abortion contributes positively to women's reproductive health [2]. Abortion provides women with a safe and legal option when faced with unintended pregnancies of their own and non-self-inflicted causes, which can safeguard women’s physical and mental health. In addition, although women from different backgrounds have different needs when seeking abortion services, a good, safe abortion...
service can make women feel respected and willing to accept and seek abortion-related health services [3]. In conclusion, it can be argued that abortion has both short-term and long-term benefits for women’s lives.

Thailand, as a leader in health, especially women’s health, in the South-East Asian region, has been clear and effective in its efforts to address abortion in recent times. In the past, the overall environment in Thailand has been relatively strict on abortion. As a result, women had difficulties in accessing abortion as a health service. In 1957, the Thai Penal Code was amended from prohibiting any form of abortion to allowing abortion under certain circumstances [4]. Sections 301 to 303 of the Penal Code stipulate the circumstances under which a woman may have an abortion. However, there are still many difficulties in practical implementation. Notably, the possibilities and accessibility of abortion services for Thai women have improved significantly in the 21st century through the concerted efforts of both official Thai governmental and non-governmental organizations. In 2005, the Medical Council of Thailand (MCT) gave doctors part of the right to perform abortions for their patients by establishing supervisory measures [4]. Later, the Thai parliament removed part of the abortion law from the penal code after the Constitutional Court ruled it unconstitutional in 2020. With the change in the law, in 2021 and February, the abortion limit was relaxed to 12 weeks [5]. Moreover, two years later, in February 2023, abortion services were made available to pregnant women up to 20 weeks of pregnancy. From this, we can see that the efforts made by various sectors in Thailand towards the accessibility of abortion services are meaningful.

As a member of the above non-governmental organizations, the Planned Parenthood Association of Thailand (PPAT) has made a valuable contribution [6]. PPAT is a pioneer in family planning in Thailand and the only member organization of the International Planned Parenthood Federation (IPPF) in Thailand [7]. PPAT has been working to support and guarantee access to sexual and reproductive health services in Thailand. Following a change in the law in 2021, PPAT began providing abortion services to Thai women at its affiliated facilities, including three clinics in Bangkok (Din Daeng, Bang Khen, and Pin Klao). In previous studies, it has been found that patients’ recommendation of hospitals is a sign of high satisfaction with the quality of services, as it indicates that patients are delighted with the services they received and are confident enough to recommend the services to others. According to a study with the participation of 1,366 patients [8], staff behavior, atmospherics, information, examination comfort, and perceived worth were suggestively associated with patient satisfaction. Another study [9] also showed that patients who acquired adequate quality healthcare services were more likely to demonstrate higher satisfaction levels and to recommend the hospital or clinic for which the healthcare provider worked. This conclusion holds even after controlling for these patients’ socio-demographic and health-related factors. Thus, patient, or client, satisfaction with an organization can influence whether and to what extent the organization is ultimately recommended to others. Higher recommendations then allow more women to learn about locations where they can obtain safe and quality abortion services, which reduces the likelihood of choosing an unsafe abortion option. However, since abortion-related laws have been changed in less than three years, abortion-related services are very unexplored to Thai health service providers. This fact has also led to a deficiency of local research on satisfaction and recommendation willingness with abortion-related services. Consequently, understanding the aspects of the healthcare organization that patients are satisfied explicitly with has important implications for how to improve overall patient satisfaction and willingness to recommend. To identify the client satisfaction factors influenced the willingness to recommend among abortion seekers at PPAT-affiliated clinics, this research was conducted.

2. Methods
2.1. Participants and Setting

This research was a cross-sectional study. The questionnaire was collected by PPAT staff from February 2021, after the law changed, to
December 2021. All abortion seekers who fully reported the questionnaire and whose responses met the inclusion criteria were included in this research. The inclusion criteria for this secondary data research were as follows: 1) report their gender as female 2) the age of the participant was not older than 50 years old. The exclusion criteria for this secondary data research were as follows: 1) who did not fully answer the questionnaire.

2.2. Data collection

The questionnaire was distributed by PPAT’s staff after the client get abortion service at PPAT’s clinic. Then the PPAT’s staff collected the data from questionnaire, input and clean the data.

2.3. Sample size and technique

In this research, all participants met the inclusion criteria and did not meet the exclusion criteria were included.

2.3. Measurement

2.3.1. Sociodemographic variable

In this study, sociodemographic variables included age, occupation, and location.

2.3.2. The satisfaction questionnaire

This questionnaire was designed by PPAT and included questions to investigate patients’ satisfaction with the services they received after receiving them, patients’ willingness to recommend the clinic, and the ways in which patients were informed. The satisfaction is collected by rating scale. For scales, very good, good, ok and not satisfaction were adopted. In this study, patient satisfaction and willingness to recommend will be examined.

2.4. Data analysis

SPSS 28(IBM) was adopted as the data analysis tool. By using descriptive analysis, the characteristics of clients can be established. For the liner regression analysis, it was used to perform and evaluate the impact of the satisfaction to the recommendation wiliness. The significance of statistical analysis was set as <0.05.

2.5. Reliability and validity

Regarding to the validity, the PPAT had sent their questionnaire to three experts for validity evaluation to insure reliability of questionnaire. For the reliability, according to the reliability statistic, the Cronbach’s Alpha equal to 0.865. This result proofs that the reliability of this questionnaire is high.

3. Results

3.1. Descriptive statistics

A total of 368 people who met the criteria were involved in this study. The age range of participants was from 14 to 48, with a mean age of 28.45 years old (SD 5.94). The smallest group, the under 24 group, had 107 persons, accounting for 29.1% of the total. Comparatively, the most numerous group, 25-35, had 135 people, or 26.7% of the total.

People who work for state enterprise (118, 32.1%) occupied the largest number of total clients, and the general labor group (67, 18.2%) are 13.9% fewer than the first group. The general labor and the business owner share nearly the same number of people (62, 16.8%) in the population. Next is the student group. There were 51 students who received abortions at PPAT clinics in 2021, representing 13.9% of the total abortion clients that year. The number of abortion patients who reported as unemployed was 30, or 8.2% of the total number of patients. Housewives made up a small percentage, with only 14(3.8%) housewives seeking abortion services at PPAT’s clinics in 2021. The agriculture group occupied the lowest part, only 1 person (0.3%) of abortion service clients at PPAT’s clinics.

Regarding the location, most clients visit Bang Khen (40.2%) and Din Daeng (34.2%) clinics for service, and only 25.5 percent of clients seek service at Pin Klao clinic (Table 1).

3.2. Simple liner regression analysis

According to the result, the p-value for all satisfaction-related items was less than 0.001. The 2.3, Ability to provide services/suggestions clients are looking for, which have the highest standardized $\beta$ (0.442) and R2(0.196) and was the strongest predictor of recommendation wiliness.
Table 1. Characteristics of PPAT's clients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 24</td>
<td>107</td>
<td>29.1</td>
</tr>
<tr>
<td>25-30</td>
<td>135</td>
<td>36.7</td>
</tr>
<tr>
<td>Over 30</td>
<td>126</td>
<td>34.2</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>25</td>
<td>6.8</td>
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<tr>
<td>State enterprise</td>
<td>118</td>
<td>32.1</td>
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<tr>
<td>General labor</td>
<td>67</td>
<td>18.2</td>
</tr>
<tr>
<td>Business owner</td>
<td>62</td>
<td>16.8</td>
</tr>
<tr>
<td>Agriculture</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Housewife</td>
<td>14</td>
<td>3.8</td>
</tr>
<tr>
<td>Student</td>
<td>51</td>
<td>13.9</td>
</tr>
<tr>
<td>Unemployed</td>
<td>30</td>
<td>8.2</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Din Daeng</td>
<td>126</td>
<td>34.2</td>
</tr>
<tr>
<td>Bang Khen</td>
<td>94</td>
<td>25.5</td>
</tr>
<tr>
<td>Pin Klao</td>
<td>148</td>
<td>40.2</td>
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</table>

Table 2. Hierarchical linear regression analysis for satisfaction

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>β</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>P-value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1. The procedure of service</td>
<td>0.9</td>
<td>0.1</td>
<td>0.3</td>
<td>0.64</td>
<td>1.12</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>1.2. Service provided according to order</td>
<td>0.8</td>
<td>0.1</td>
<td>0.3</td>
<td>0.52</td>
<td>1.02</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>1.3. The speed of service provision</td>
<td>0.7</td>
<td>0.1</td>
<td>0.4</td>
<td>0.55</td>
<td>0.95</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>1.4. Appropriate time allocated for service provision</td>
<td>0.7</td>
<td>0.1</td>
<td>0.3</td>
<td>0.53</td>
<td>0.95</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>2.1. Their hospitality</td>
<td>0.9</td>
<td>0.1</td>
<td>0.4</td>
<td>0.65</td>
<td>1.11</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>2.2. Ability to listen to clients well during counseling session</td>
<td>1.0</td>
<td>0.1</td>
<td>0.4</td>
<td>0.72</td>
<td>1.19</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>2.3. Ability to provide services/suggestions clients are looking for</td>
<td>1.1</td>
<td>0.1</td>
<td>0.4</td>
<td>0.90</td>
<td>1.37</td>
<td>&lt;0.001</td>
<td>0.2</td>
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<tr>
<td>3.1. The cleanness</td>
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<td>0.1</td>
<td>0.3</td>
<td>0.47</td>
<td>0.96</td>
<td>&lt;0.001</td>
<td>0.1</td>
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<tr>
<td>3.2. Sufficient equipment</td>
<td>0.6</td>
<td>0.1</td>
<td>0.3</td>
<td>0.36</td>
<td>0.93</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>3.3. Visibility of PR board</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.31</td>
<td>0.76</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
<tr>
<td>3.4 Parking space</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
<td>0.15</td>
<td>0.42</td>
<td>&lt;0.001</td>
<td>0.0</td>
</tr>
<tr>
<td>4. Overall satisfaction level</td>
<td>0.9</td>
<td>0.1</td>
<td>0.4</td>
<td>0.63</td>
<td>1.10</td>
<td>&lt;0.001</td>
<td>0.1</td>
</tr>
</tbody>
</table>
On the contrary, 3.4. Parking space shows a weakness in predicting the recommendation willingness significantly due to the low $\beta$ (0.210) and $R^2(0.210)$.

For the other projects, there are four projects, including 1.3 The speed of service provision, 2.1 Their hospitality, 2.2 Ability to listen to clients well during counseling session, and 4 Overall satisfaction level, that have a standard beta above 0.4, but not more than 0.442 for 2.3 Ability to provide services/suggestions clients are looking for. Item 3.3 Visibility of PR board has a lower standard beta, less than 0.3, but not less than 0.310 for 3.4 Parking space. The remaining projects, including 1.1 The procedure of service, 1.2 Service provided according to order, 1.4 Appropriate time allocated for service provision, 3.1 The cleanliness and 3.2 Sufficient equipment are between 0.3 and 0.4 (Table 2).

4. Discussion

This study was conducted to identify the association between the clients’ willingness to recommendation and satisfaction. In this study, the findings indicated the association between the satisfaction level of service and recommendation level. According to the result, clients show a positive view towards the satisfaction level in all dimensions and have a high recommendation willingness to recommend other women to get service at PPAT’s clinic. The $P$-value of all satisfaction fact are smaller than 0.01.

By comparing the data from each part, it can be seen that being able to provide patients with the services that patients need has the most significant impact on patients’ willingness to recommend. This fact is caused based on the following aspects. First and most importantly, providing services that are suitable for the customer can effectively address the patient’s needs [10]. Customers seek health services because they have concerns about their health, and providing the services they seek can effectively address their problems and needs, thus increasing patient satisfaction.

The second is that appropriate healthcare services can make patients feel respected [3], and being respected is an essential prerequisite for high patient satisfaction with services. First, the provision of appropriate healthcare services demonstrates that the healthcare provider cares about and has the desire to fulfill the patient’s needs, thus making the patient feel respected [11]. Moreover, appropriate service means that the provider has an effective interaction with the customer and understands and agrees with the decisions the patient makes about her health. Such likewise allows patients to feel respected and thus satisfied with the services they receive [12]. At the same time, like childbirth, abortion services are not a one-time service. Abortion services include pre-abortion counseling, diagnosis, abortion performance, and post-abortion review and return visits. Providing the proper service improves the continuity of service and gives the patient the desire to complete the entire abortion service process at the same provider. Not only is this good for the patient’s health, but the increased willingness of the patient to recommend the service to others is more remarkable when high-quality services are provided each time over a long period of time compared to a single visit.

Third, appropriate services can be effective in alleviating patient anxiety about health concerns, [10]. Abortion patients tend to feel less supported than clients seeking other reproductive health services for reasons such as legal and social stigma [13, 14]. Less support means that patients are left to deal with their own issues in seeking healthcare services, including abortion services, which can create anxiety [15]. Therefore, providing timely, accurate, and effective services to patients can create a supportive environment for clients, which can alleviate anxiety and improve their quality of life. A client with a lower level of anxiety and a higher quality of life has a greater likelihood of being satisfied with the attendant they receive and is more likely to recommend the service received to others.

As for why the parking lot has the least impact on patient satisfaction, it may be caused by the fact that the clinic’s accessibility in terms of transportation has been met by public transportation system. The following two aspects could explain this situation: high motorcycle ownership and Bangkok’s relatively well-
developed public transportation system. Motorcycles are a popular mode of transportation in Bangkok [16] and, compared to cars, parking a motorcycle does not require much space. This feature means that whether patients drive their own motorcycles or take a motorcycle cab, a unique taxi-type ride in Bangkok, it is easy to find a place to park and get off the bike near the clinic. As for public transportation, as a in which tourism had been one of the major priorities for its development, Bangkok has variety public transportation system including rail transportation including BTS (Bangkok Mass Transit System), MRT (Metropolitan Rapid Transit), etc., public transportation boats and buses, and people do not necessarily need to drive their own cars to get around [17, 18]. Hence, clients can readily reach the clinic from most city locations without needing to factor in transportation concerns. These two reasons together contribute to the low sensitivity of patients to the size of clinics equipped with parking space.

However, based on the study design and sample, the following limitations exist in this study. First, this study was a cross-sectional study that sampled one year after PPAT began providing abortion services to clients following the changes in the law related to abortion. Clients who visited PPAT clinics for services during this period were knowledgeable about PPAT relative to clients in the period afterward. The reason for this fact is that PPAT was unable to conduct large-scale promotions prior to the change in the law, including client-to-client promotions or promotions that were not explicitly targeted. As a result, the majority of clients who visited PPAT during this period were seeking abortion services at PPAT clinics even though they were aware of the quality of the services in advance, leading to relatively high levels of satisfaction.

Second, according to previous research, most service providers have relatively high service quality in the early stages of service delivery. In contrast, retention in the later stages of service delivery varies depending on the service provider. However, as a cross-sectional study, it is not possible to measure the impact of service changes over time on patient service satisfaction. This issue limits the study’s ability to compare satisfaction and willingness to recommend over time.

In addition, although this study used all customer satisfaction questionnaire data, all samples that did not answer the questionnaire completely were removed to ensure the reliability of the study data. For this reason, it may have resulted in the removal of content from customers who were valuable but did not answer the questionnaire completely. Reproductive health services, especially abortion services, remain relatively sensitive to society and patients compared to other health services. Thus, customers may refuse to respond to specific questions based on ethical, cognitive, and literacy reasons. Therefore, this behavior is understandable during the questionnaire period. To ensure the validity and reliability of the statistical results, it is feasible to exclude the data of these customers from the statistical analysis.

5. Conclusion
Our study shows that overall customer satisfaction is high, a higher willingness to satisfy will have a positive effect on the willingness of patients to make referrals.

6. Recommendations
PPAT’s clients should maintain their high-quality service in the future to fulfill clients’ needs, which may ensure more patients have the willingness to promote PPAT clinics’ high-quality services and help more women in need of help to seek services at PPAT’s clinics. As the law continues to open up and publicity continues to grow, the number of patients visiting PPAT clinics will undoubtedly continue to increase in the future. How to maintain customer satisfaction while increasing the number of customers will be an issue to be observed in the long run. Accordingly, PPAT should continue to collect data on patient satisfaction and add more socio-demographic information on patients, such as average monthly or annual income and marital and childbearing status. These data can better target patient service programs to different patient profiles, thus ensuring high service satisfaction.
and high willingness to recommend.

Furthermore, given the high sensitivity of the topic of abortion in Thailand, a substantial portion of clients who took part in the questionnaire did not provide complete answers to all the questions within it. In order to collect further complete patient information, PPAT may adopt the following three steps. First, state and emphasize privacy protection measures for patients strongly. Before the client fills out the questionnaire, the doctor, nurse, or other staff member declares to the patient the ways in which the PPAT protects the client’s privacy and re-emphasizes these efforts in the questionnaire. This measure will reduce the patient’s concerns about privacy breaches in the questionnaire.

Second, provide questionnaire responses that are relaxing to the patient and have a high level of privacy. For example, provide the patient with a separate, undisturbed cubicle to complete the questionnaire. Such a cubicle will assist the client in fending the questionnaire information from potential interference by individuals in proximity to the client.

Third, offer patients a variety of ways to collect the questionnaire. Different patients have different privacy preferences. Multifarious questionnaire collection methods can be provided to patients, including paper questionnaires, on-site electronic questionnaires, and mobile application questionnaires. Multiple reporting methods will ensure that most patients with privacy concerns get the questionnaire they prefer to complete. Thus, more fully responded and valid questionnaires can be collected.

References
[14] Ireland S, Belton S, Doran F. ‘I didn’t feel judged’: exploring women’s access to


The Expression of miR-30b-5p during Erythropoiesis

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Abstract

Background: Erythropoiesis, a process in which hematopoietic stem cells differentiate into mature red blood cells, is controlled by multiple molecular pathways. GATA-1 is a major erythroid transcription factor, which regulates erythroid differentiation and anti-apoptosis. The cleavage of GATA-1 by caspase-3 results in erythroid maturation arrested and apoptosis. To prevent the cleavage of GATA-1, the chaperone Heat Shock Protein 70 (Hsp70) translocates to the nucleus, enabling continued terminal maturation. The accumulation of Hsp70 in the nucleus is regulated by exportin-1 (XPO1), a nuclear export receptor, responsible for exporting Hsp70. Thus, targeting the Hsp70 nuclear translocation by blocking XPO1 could be a novel therapeutic option for dyserythropoiesis. microRNAs (miRNAs), small non-coding RNAs, regulate gene expression at the post-transcriptional level. Therefore, identifying miRNAs responsible for regulating XPO1 could offer a novel therapeutic approach.

Method: The bioinformatic-based approaches (miRDB, miRmap, and miRTarBase) were utilized to identify potential miRNAs targeting XPO1. Among these miRNAs, miR-30b-5p was identified as a candidate for regulating XPO1. Subsequently, the expression pattern of miR-30b-5p was determined by RT-qPCR.

Result: The results showed that the trend of miR-30b-5p expression was high on day 7 in which the main population was polychromatic erythroblast and markedly decreased on day 11, when orthochromatic erythroblasts were the main population.

Conclusion: The differential expression of miR-30b-5p during erythropoiesis suggested that miR-30b-5p might play a role in the regulation of XPO1 expression. Regulation of miR-30b-5p expression could be a potential target for a novel therapeutic option for dyserythropoiesis. However, further study of XPO1 expression modulation by miR-30b-5p in dyserythropoiesis is required.

Keywords: Erythropoiesis, miRNA, XPO1

1. Introduction

Erythropoiesis is a tightly regulated process that involves multiple molecular pathways governing the stepwise differentiation of hematopoietic stem cells into mature red blood cells (RBCs) [1]. GATA-1 is a master erythroid transcription factor that regulates promoters of anti-apoptotic and erythroid-specific genes [2]. Levels of GATA-1 protein during erythropoiesis are tightly controlled and vary significantly depending on the stage of differentiation. During the early stage of erythroid maturation, it is important to maintain high levels of GATA-1 protein, whereas a downregulation of GATA-1

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protein is necessary during terminal erythroid differentiation. Cleavage of GATA-1 by caspases-3 causes erythroid precursors apoptosis. Importantly, Hsp70 is constitutively expressed during erythroid differentiation. The translocation of Hsp70 to the nucleus leading to the protection of GATA-1 cleavage by caspase-3 and reducing apoptosis, thereby allowing continued terminal maturation [3].

The nuclear localization of Hsp70 is essential for maintaining the viability of erythroblasts. The accumulation of Hsp70 in the nucleus is regulated by exportin-1 (XPO1), a nuclear export receptor responsible for exporting various proteins, including Hsp70, in human erythroid progenitors [3]. Targeting Hsp70 nuclear translocation by inhibiting XPO1 could represent a novel therapeutic option for dyserythropoiesis. Interestingly, in β-thalassemic erythroblasts, Hsp70 is sequestered in the cytoplasm by the excess of free α-globin chains preventing it from entering the nucleus, which resulted in the cleavage of GATA-1 by caspase-3. Consequently, this led to maturation arrest and apoptosis. Inhibition of Hsp70 nuclear accumulation by XPO1 inhibitor could rescue GATA-1 expression and improve terminal differentiation of β-thalassemic erythroblasts [4].

miRNA has emerged as a key player in post-transcriptional regulators of gene expression. These 19-25 short nucleotide sequences are accomplished through the RNA-induced silencing complex (RISC), activating a complex to target messenger RNA (mRNA) specified by miRNA. The degree of base complementary between miRNA and their target determines the translational inhibition or mRNA degradation [5]. Several miRNA mimics and anti-miRNAs showed promise in preclinical development and clinical trials. For example, a mimic of miR-16/15 (TargomiR) [6] and miR-155 inhibitor (MRG-106) was performed in clinical trials [7]. Remarkably, the liposomal formation of miR-34a (MRX34) is an miRNA mimic cancer therapy involving the downregulation of oncoproteins and tumor immune evasion. The trial of MRX34 treatment in a man with kidney cancer showed a significant reduction in the tumor size after three months discontinuing MRX34 [8]. With this capacity, thousands of mature miRNAs have been discovered in the human genome that could potentially be the regulators of gene expression in several cellular pathways, notably in erythropoiesis [9]. Therefore, the identification of miRNAs responsible for regulating XPO1 could offer a novel therapeutic option for dyserythropoietic anemia. In this study, three bioinformatic tools were used to predict XPO1-regulating miRNAs. Among these miRNAs, one notable candidate, miR-30b-5p, was selected for investigation and the expression pattern of miR-30b-5p showed the differential expression during erythropoiesis.

2. Methods

2.1. Subjects

This study was conducted with approval from the Mahidol University Central Institutional Review Board, under the approval numbers MU/MOU 2022/129.0812 and MU/MOU 2023/126.2508. The written informed consent was obtained from each participant. All participants were selected based on inclusion criteria and normal hematological data. A total of four healthy donors, ranging in age from 18 to 50 years old with normal complete blood count (CBC) and hemoglobin typing were recruited in this study. The characteristics of all participants included a hemoglobin level ranging from 12-15 g/dL, a Mean Corpuscular Volume (MCV) within 87±5 fL, a Mean Corpuscular Hemoglobin (MCH) of 29±2 pg, a Mean Corpuscular Hemoglobin Concentration (MCHC) of 34±2 g/dL, and a Red Cell Distribution Width (RDW) between 11.5-14.5%. Additionally, the hemoglobin typing of the participants was predominantly Hb A at approximately 97%, with Hb A2 constituting around 2.5%, and Hb F being less than 1% [10].

2.2. Erythroid progenitor isolation and culture

Peripheral blood samples were collected into blood collection tubes with an anticoagulant, CPDA-1. To isolate the peripheral blood mononuclear cells (PBMCs), the whole blood samples underwent gradient centrifugation with
Fig. 1. Erythroid differentiation analysis by flow cytometry. Cells were labeled with three specific antibodies for a white blood cells marker (CD45), and other markers for erythroblasts including CD71 and GPA. Cells in the A1 gate was sorted based on their side scatter (SSC) and forward scatter (FSC) characteristics. The A1 area was then subdivided into two groups: CD45- erythroblasts (A2) and CD45+ white blood cells (A3). Subsequently, the A2 area was further evaluated using CD71 and GPA expression, enabling the identification of erythroid progenitors as basophilic erythroblasts (R1), polychromatic erythroblasts (R2), and orthochromatic erythroblasts (R3) regions.

Lymphoprep (Axis-Shield, Oslo, Norway), with a 1.077 g/mL density. The subsequent step involved culturing the PBMCs in a two-phase liquid culture system [11]. In phase I, known as the expansion phase, the PBMCs were cultured in Iscove’s Modified Dulbecco’s Medium (IMDM; Gibco-Invitrogen, Carlsbad, CA) supplemented with 30% fetal bovine serum (FBS; Sigma-Aldrich, St. Louis, MO), 25 ng/mL recombinant human interleukin-3 (rHuIL-3; Cell Signaling Technology, Danvers, MA), 50 ng/mL recombinant human stem cell factor (rHuSCF; Cell Signaling Technology), 50 mg/mL cyclosporin A (CSA; Sigma-Aldrich), and 0.1 U/mL recombinant human erythropoietin (rHuEPO; Janssen-Cliag, New Brunswick, NJ). This stage was cultured at 37˚C, 5% CO₂ for a duration of 7 days. Subsequently, the erythroid progenitor cells were transitioned to the differentiation phase (phase II). During this phase, the cells were cultured in IMDM supplemented with 30% FBS, 0.1 ng/mL rHuIL-3, and 3 U/mL rHuEPO under the condition of 37˚C, 5% CO₂ for 11 days.

2.3. Erythroid differentiation by light microscopic analysis and flow cytometry

To determine the erythroid differentiation during a two-phase liquid culture system, erythroid progenitor cells were collected at three different time points during the differentiation phase: days 7, 9, and 11. The cell differentiation stage was assessed using both a light microscope and flow cytometry. For the light microscope analysis, 1x10⁵ cells were spun onto a glass slide and stained with Wright-Giemsa. Cell morphology, including proerythroblasts, basophilic erythroblasts, polychromatic erythroblasts, and orthochromatic erythroblasts, were examined and one hundred nucleated red blood cells were counted under the light microscope. As for the flow cytometric analysis (Fig. 1), 1x10⁵ cells were stained with three different antibodies including FITC conjugated with anti-human CD45 monoclonal antibody (BD Bioscience, San Jose, CA) as a leukocyte marker, PerCP/Cy5.5 conjugated with anti-human CD71 monoclonal antibody, and PE conjugated with anti-human Glycophorin A (GPA) monoclonal antibody (BD Bioscience) as a late stage of erythrocyte marker.

2.4. miRNA target prediction

The miRNA target of XPO1 was predicted using online bioinformatic tools which included miRDB (www.mirdb.org) [12], miRmap (https://mirmap.ezlab.org) [13], and miRTarBase (https://
Fig. 2. Bioinformatic prediction of XPO1-regulating miRNAs. (A) The Venn diagram represents the miRNAs target predictions for XPO1 obtained from 3 databases: miRmap, miRDB, and miRTarBase. Among these miRNA targets, 6 miRNAs were predicted by all 3 databases. (B) The miR-30b-5p targeted site at XPO1 3′-UTR were conserved among species. The white box represents miR-30b-5p binding site.

mirtarbase.cuhk.edu.cn) [14]. The process begins by inputting the gene target or gene symbol into each program. Then, the target of interest was selected, specifying “Human” as the organism. Subsequently, the programs used various algorithms specific to each tool, including seed matching, conservation score, and site accessibility, to search for miRNA targets of XPO1. Additionally, the conservation among species of the interaction between XPO1 and predicted miRNA target was studied by TargetScan (version 8) [15].

2.5. miRNA expression analysis by RT-qPCR

To investigate the expression of miR-30b-5p in erythroid progenitor cells obtained from healthy donors, the cells were collected on days 7, 9, and 11 of the differentiation phases. For RNA isolation, 1x10⁶ cells were collected in 1 mL of TRIzol reagent (Thermo Fisher Scientific, Carlsbad, CA), following the manufacturer’s protocol. Subsequently, the RNA concentrations were determined using a Nanodrop spectrophotometer (Thermo Fisher Scientific). For cDNA synthesis, the TaqMan advanced miRNA cDNA synthesis kit (Applied Biosystems, Foster City, CA) was utilized, and 100 ng of RNA was used for cDNA synthesis. Additionally, the TaqMan miRNA reverse transcription kit (Applied Biosystems) was employed to synthesize U6 snRNA from cDNA templates, serving as the endogenous control. miRNA quantification was conducted using qPCR with TaqMan universal master mix (Applied Biosystems) and TaqMan specific miRNA assay probes (Applied Biosystems). These reactions were carried out in a CFX96 real-time PCR instrument (Bio-Rad, laboratories, Hercules, CA). The relative miRNA expression levels were determined using the comparative 2⁻⁴Ct method and the U6 snRNA was used as the normalizing gene.

2.6. Statistical analysis

The data was displayed as mean ± standard error of the mean (SEM). The differential expression of miR-30b-5p at days 7, 9, and 11 were analyzed and compared using one-way ANOVA. For non-parametric data sets, Tukey’s multiple
comparisons test was applied to determine differences between groups. A $P$-value $\leq 0.05$ was set as the threshold for considering differences as significant. All statistical analysis was performed using GraphPad Prism software (version 8.0; GraphPad Software, San Diego, CA).

3. Results

3.1. XPO1 is targeted by miRNAs

Bioinformatics-based approaches, namely miRmap, miRDB, and miRTarBase were utilized to investigate the putative predicted miRNAs regulating XPO1. The results revealed 6 common miRNAs that target XPO1 (Fig. 2A) including miR-30a-5p, miR-30b-5p, miR-30c-5p, miR-30d-5p, miR-30e-5p, and miR-4495. Importantly, the predicted recognized site at 3’untranslated regions (UTR) of XPO1 mRNA by miR-30b-5p (5’-UGUAAACAUCUCACUCAGCU-3’) was conserved among species (Fig. 2B). Therefore, the miR-30b-5p was selected to further investigate the expression level during erythropoiesis.

3.2. Erythroid progenitor culture

The white blood cells contamination in erythroid progenitor culture was determined by analysis of CD45 expression, which showed CD45$^+$ cells on days 7, 9, and 11 were 7.2±2.4%, 6.1±2.8%, and 4.6±2.1%, respectively. Flow cytometry and light microscopic were used to investigate the differentiation of erythroid progenitor cells during erythropoiesis. The cells were examined on days 7, 9, and 11 of phase II culture. For flow cytometry analysis, the stage of erythroid progenitors was determined by the expression levels of GPA and CD71. At the early stage of erythroid maturation, CD71 expression was increased, coinciding with a low GPA expression. While, at the late stage of erythroid maturation, CD71 expression was decreased, coinciding with an increase in GPA expression. The population of erythroid progenitors in R1, R2, and R3 represented the stage of basophilic erythroblast, polychromatic erythroblast, and orthochromatic erythroblast, respectively (Fig. 3A).
The results showed that the main population on day 7 of phase II culture was polychromatic erythroblast (46.7±6.4%). Subsequently, CD71 expression was decreased through erythroid maturation and the cells were differentiated to orthochromatic erythroblasts which were the main population on day 11 of phase II culture. As erythroid maturation proceeded, the cells differentiated into polychromatic (37.9±9.6%) and orthochromatic erythroblasts (53.3±7.6%), which predominated on day 9. On day 11, the main population was orthochromatic erythroblasts (74.1±8.1%).

For light microscopic analysis, the predominant population on day 7 consisted of polychromatic erythroblasts with approximately 61.0±2.1% of the total population. Meanwhile, the proportions of basophilic and orthochromatic erythroblasts were 7.0±1.6% and 32.0±2.6%, respectively (Fig. 3B). On day 9, the predominant population shifted to orthochromatic erythroblasts with approximately 72.3±2.5%. Additionally, the proportion of basophilic and polychromatic erythroblasts on this day was 3.5±0.8% and 24.3±1.9%, respectively. Finally, on day 11 of phase II culture, the proportion of orthochromatic and polychromatic erythroblasts were 85.5±3.1% and 14.0±2.6%, respectively. The results from flow cytometry and light microscopic analysis were consistent. This demonstrated that the culture system could support proliferation and differentiation of erythroid progenitors, and could be used for the study of erythropoiesis and dyserythropoiesis.

3.3. Expression of miR-30b-5p during erythropoiesis

The erythroid progenitors were collected on days 7, 9, and 11 of phase II culture to examine the expression pattern of miR-30b-5p during erythropoiesis by RT-qPCR. The results revealed that the levels of miR-30b-5p on day 7 and 9 were not significantly different. The miR-30b-5p was significantly decreased on day 11 when compared to day 7 and day 9 (P < 0.05) (Fig 4).

4. Discussion

Erythropoiesis is a highly regulated process by which the mature red blood cells are generated [1]. Deregulation of the erythropoiesis can have significant consequences on physiological function [16]. The nuclear accumulation of Hsp70, which is regulated by XPO1, is essential for terminal erythropoiesis as it protect against caspase-3-mediated cleavage of GATA-1 [17]. Downregulation of XPO1 and reduced Hsp70 transport from nucleus could be a novel therapeutic option for dyserythropoiesis. miRNAs that regulate XPO1 might be a potential for a novel therapeutic option. Herein, XPO1-regulating miRNAs were predicted by three bioinformatic tools. The expression pattern of the candidate miR-30b-5p during erythropoiesis was revealed, suggesting its potential involvement in regulating erythroid maturation.

Three bioinformatic tools were used for prediction of miRNA that regulating XPO1. The predicted miRNA from miRTarBase, miRDB, and miRmap, were 21, 126 and 356, respectively. This suggested the difference algorithms of the 3 bioinformatic tools. Although miRNA is about 22 nucleotides in length, the mRNA recognition site is primarily mediated by the seed region, nucleotides 2 to nucleotide 8 in the miRNA. This makes precise prediction of miRNA and mRNA target difficult. Thus, more than one bioinformatic tool is normally used for prediction. Here 6 miRNAs were predicted by all 3 databases. Five
miRNAs were from miR-30 family, miR-30a-5p, miR-30b-5p, miR-30c-5p, miR-30d-5p, and miR-30e-5p, which were conserved among different species. Previous studies showed that five of miR-30 family were identified in in vitro human erythroblasts (Day 8), but not for miR-4495 [18]. In addition, dysregulation of miR-30b-5p can have a consequence in various physiological functions contributing to the development of dyserythropoietic conditions [19, 20]. Thus, miR-30b-5p was selected to determine its expression during erythropoiesis.

In this study, the PBMCs were isolated from the peripheral blood sample were used as the starting material for erythroid progenitor cell culture by a two-phase liquid culture system. Erythroblast differentiation was examined by flow cytometry and light microscopic analysis, which showed consistence results from both techniques. The culture system could promote erythroid differentiation to the latter stage of erythropoiesis, providing a reliable platform for investigating and understanding the role of miRNAs during erythropoiesis. The contamination of white blood cells was determined by flow cytometry. Although PBMCs were used as starting cells for erythroid progenitor cells culture, at the time of miR-30b-5p expression was assessed on day 7-11 of phase II culture, less than 10% of the cells exhibited the CD45+ marker. After 7 days of incubation in phase I, nonadherent cells, mainly macrophages, were removed and transitioned to cultivation in differentiation phase (phase II). During this phase, it was conducted in the absence of essential cytokines required for the development of white blood cells. Consequently, there was a notable reduction in CD45+ cells in the Phase II culture. Therefore, this system was suitable for studying the expression pattern of miR-30b-5p during erythropoiesis.

During erythropoiesis, GATA-1 is required for erythroid differentiation and terminal erythroid maturation [21]. GATA-1 deficiency arrests erythropoiesis at an early stage and induced apoptotic cell death. Knockdown of GATA-1 in embryonic mice showed extraordinary paleness and die between embryonic stages due to severe anemia [22]. Importantly, caspase-3 showed transient activation during erythropoiesis, which seems to occur at the transition between proerythroblasts and basophilic erythroblast. This activation of caspase-3 leads to the cleavage of several proteins that are involved in nucleus integrity (lamin B) and chromatin condensation (acinus) without inducing cell apoptosis and cleavage of GATA-1. Unfortunately, when erythroid progenitors are dying due to a lack of cytokines or exposure to death receptor signals, GATA-1 is degraded by caspase-3 resulting in apoptotic cell death. However, in normal differentiating erythroblasts, GATA-1 remains intact and is protected [23]. Therefore, the expression level of caspase-3 during erythroid differentiation is needed to be elucidated in both erythropoiesis and dyserythropoiesis for a better understanding of caspase-3 activity in this study.

Previous studies found that GATA-1 is protected by Hsp70 that translocates to the nucleus at onset of caspase activation [3]. As expected, Hsp70 is detectable in the nucleus of normal cells from basophilic to polychromatic and orthochromatic erythroblasts. However, during dyserythropoiesis, Hsp70 is absent from the nucleus of polychromatic and orthochromatic erythroblasts, and the ratio of nuclear to cytosolic Hsp70 expression is reduced in dyserythropoietic erythroblasts [17]. The disruption in the regulatory interaction among Hsp70, GATA-1, and caspase-3 might be a contributing factor to the development of anemia observed in myelodysplastic syndrome (MDS) and β-thalassemia [24]. Hence, targeting the Hsp70 nuclear translocation could be a novel therapeutic option for dyserythropoiesis.

In human erythroblast, XPO1 was found to be the main nuclear exporter of Hsp70 during normal and pathological erythropoiesis [4]. Thus, maintaining Hsp70 in the nucleus by blocking XPO1 could be useful in the pathologies of erythropoiesis where Hsp70 is not localized in the nucleus. The higher expression of miR-30b-5p on day 7 and 9 compared to day 11 of phase II culture was demonstrated in this study. This suggested that the polychromatic erythroblasts express miR-30b-5p higher than orthochromatic erythroblast. The expression of XPO1 was reported to be
highly expressed in proerythroblasts and remained consistently low in orthochromatic erythroblasts [4]. This showed no correlation with the expression of XPO1 reported previously. The expression of XPO1 could be regulated by many mechanisms such as transcription, translation and post-transcription. Previous studies have confirmed that the expression of the miR-30 family results in a marked decrease in XPO1 expression. This indicates that a coordinated action of several miR-30 family is more effective in regulating XPO1 expression rather than a particular miRNA [25]. It is well-known that a miRNA can target and regulate numerous genes, conversely, a specific mRNA can be modulated by multiple miRNAs. The expression of miR-30b-5p during erythropoiesis suggested that it would play a role in erythropoiesis. However, for a better understanding of the association between XPO1 and miR-30b-5p, it is necessary to elucidate the expression pattern of XPO1 during erythroid differentiation in this study. Furthermore, the decrease in of miR-30b-5p level in orthochromatic erythroblasts suggests that increasing the expression level of miR-30b-5p could be a therapeutic option for dyserythropoiesis diseases, facilitating Hsp70 nuclear localization and consequently promoting erythroid terminal differentiation. However, to prove the correlation between miR-30b-5p, GATA-1 and XPO1 in this study, the expression pattern of XPO1 and GATA-1 during erythropoiesis is required.

5. Conclusion
In summary, we demonstrated the differential expression of miR-30b-5p during erythropoiesis suggesting its potential involvement late stage of erythroid maturation. This study provides the basic knowledge of the differential expression of miR-30b-5p during erythropoiesis in healthy donors. Regulation of XPO1 using miR-30b-5p would be the novel therapeutic approach of dyserythropoiesis diseases.

6. Recommendations
We demonstrated the differential expression of miR-30b-5p during erythropoiesis. This suggests the potential use of miR-30b-5p for regulating erythroid maturation. However, verification of interaction between miR-30b-5p and XPO1 in erythroblast is needed. In addition, further study about the expression of miR-30b-5p in diserythropoiesis diseases such as thalassemia is required.

Acknowledgments
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Conflict of Interest
No potential conflict of interest was reported by the authors.

References
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Screening of Curcuminoid Analogs as Potential Hemoglobin F Inducer in K562::Δ^{Gγ-Aγ} EGFP Cells

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Abstract

Background: β-Thalassemia is a hereditary hematological disease resulting from a defect in β-globin chain production. The reduction or absence of β-globin chain production causes an excess of unbound α-globin chains in erythroid progenitors. This leads to pathologies in thalassemia patients, including chronic anemia, iron overload, and other complications. Stimulating γ-globin chain production, which can be assembled with excess unbound α-globin chains to form hemoglobin F (HbF, α2γ2) and compensate for the reduced amount of β-globin synthesis, can ameliorate disease severity. Currently, hydroxyurea (HU) is the only USFDA-approved drug to treat β-hemoglobinopathies. However, only 30-50% of patients respond to HU. Therefore, a novel HbF inducer as an alternative treatment is needed.

Method: In this study, we evaluated HbF-inducing properties of 3 curcuminoids derived from Curcuma longa and their 17 analogs in a reporter cell line carrying enhanced green fluorescent protein (EGFP) gene under control of γ-globin promoter, K562::Δ^{Gγ-Aγ} EGFP cells.

Results: The results showed that curcuminoids and 8 analogs significantly enhanced HbF production with low toxicity. Particularly, compound 16 exhibited the most potent EGFP expression with a 4.4 ± 0.3-fold increase.

Conclusion: This study provides the potential of compound 16 to be developed as a new HbF inducer for treatment of β-thalassemia patients.

Keywords: β-Thalassemia, Fetal hemoglobin, HbF inducer, Hydroxyurea, Curcuminoid analogs

1. Introduction

β- Thalassemia is a hereditary anemia resulting from a defect in β-globin chain production, while α-globin chains are normally synthesized, leading to an imbalance of α- and β-globin chain production. The accumulation of excess α-globin chains in erythroid progenitors leads to pathologies of β-thalassemia, including anemia, iron overload, an enlarged spleen, slowed growth rates, and cardiac dysfunction [1]. Currently, the treatment for β- thalassemia includes blood transfusion and iron chelators. However, chronic blood transfusion is complicated by high rates of allo-immunization, blood-borne
infectious disease and iron overload. Stem cell transplant is the only curative treatment, but it has limitations, such as the requirement for a human leukocyte antigen (HLA) match donor, high costs and the need for long-term immunosuppressive drugs to prevent graft-versus-host disease [2].

The pathology of β-thalassemia is caused by an excess of α-globin chains. Reducing the excess α-globin chains by inducing γ-globin expression, which can combine with excess α-globins to form fetal hemoglobin (HbF, α2γ2) and compensate for the reduced amount of β-globin synthesis. This can significantly alleviate the severity of β-thalassemia symptoms [3]. Pharmacological stimulation of HbF production is a potential alternative treatment. However, hydroxyurea (HU) is the only USFDA-approved HbF inducer drug to treat β-hemoglobinopathies. Unfortunately, only 30-50% of patients respond to HU, leading to a reduced need for regular blood transfusion [4]. Therefore, the development of HbF inducers as alternative treatments with high efficacy and low toxicity for β-thalassemia patients is of great interest.

Curcuminoids, which include curcumin (CUR; 1), demethoxycurcumin (DMC; 2) and bisdemethoxycurcumin (BDMC; 3), are the major constituents of Curcuma longa, providing several therapeutic properties such as anti-inflammatory and anti-oxidant activities. Our previous studies have demonstrated that curcuminoids, along with their reduced and trienone analogs could induce γ-globin mRNA expression and HbF production in K562::ΔG-γ-A-γ EGFP cells and human erythroid progenitor cells [5, 6]. These results prompt us to investigate other curcumin analogs as new alternative HbF inducers. In this study, curcuminoids were conducted by chemical modification and were evaluated for their HbF-inducing effect.

2. Methods

2.1. Curcuminoids and curcuminoid analogs

Curcuminoids (1–3) were isolated from the rhizomes of C. longa, by silica gel column chromatography, using a gradient solvent system of dichloromethane, dichloromethane-methanol and methanol. Curcuminoid analogs were synthesized by conventional chemical methods [7, 8]. Their structures were characterized through spectroscopic techniques, including nuclear magnetic resonance spectrometry (NMR; Bruker ASCEND 400 FT-NMR spectrometer) and high-resolution mass spectrometry (HR-MS; Bruker micrOTOF-QII mass spectrometer) and by comparison with reported values. The curcuminoids and their analogs were prepared as 10 mM stock solutions in dimethyl sulfoxide (DMSO).

2.2. K562::ΔG-γ-A-γ EGFP cell culture and treatment

A stable reporter cell line, K562: ΔG-γ-A-γ EGFP cells, consists of modified cells that harbor the enhanced green fluorescent protein (EGFP) in replacement of G-γ and A-γ-globin coding sequence under the control of G-γ-globin gene promoter.
Fig. 2. Chemical structures of curcuminoids and analogs

intact human β-globin locus [9]. The induction of EGFP expression represents the activation of the endogenous γ-globin gene. The K562::Δ^Gγ-Δγ EGFP cells were cultured in RPMI 1640 media supplemented with 20% fetal bovine serum and 1% penicillin/streptomycin. The cells were treated with various concentrations of tested compounds, specifically at 0.1, 0.3, 1, 3, 10, 30, 40 and 50 µM, for 3 days. HU (250 µM) was used as the positive control, while DMSO (0.5%) and untreated cells were used as negative controls.

2.3. Analysis of EGFP expression

The induction of EGFP expression K562::Δ^Gγ-Δγ EGFP cells was determined and analyzed using mean fluorescence intensity (MFI) measured with the BD Accuri™ C6 Plus flow cytometer (BD Bioscience) and C6 Plus Analysis software (BD Bioscience) (Fig. 1). The MFI of the treated cells was used to calculate the fold change in EGFP expression by multiplying it with the MFI of DMSO-treated cells.

2.4. Cytotoxicity measurement

The viability of K562::Δ^Gγ-Δγ EGFP cells was assessed using propidium iodide (PI) staining (Sigma-Aldrich). Positive PI (PI+) cells were detected by BD Accuri™ C6 Plus flow cytometer and analyzed with C6 Plus Analysis software (Fig. 1). The percentage of cell viability was calculated by subtracting the percentage of PI+ cells from 100%.

2.5 Statistical analysis

Data were presented as the mean ± standard error of the mean (SEM). One-way ANOVA was
used for the statistical analysis of EGFP expression and the percentage of cell viability based on three independent measurements. The values of significance were considered at $P < 0.05$. All statistical analyses were performed using GraphPad Prism software (Version 9.1; GraphPad Software).

3. Results

The induction of EGFP expression was evaluated in K562::$\Delta^G\gamma$-A$\gamma$ EGFP cells. These cells were treated with curcuminoids and 17 analogs to investigate their potential as HbF-inducing agents (Fig. 2). This cell line is characterized by increased EGFP expression which is associated with the activity of $\gamma$-globin promoter. Briefly, the cells were treated with various concentrations of compounds (0.1–50 $\mu$M) for 3 days. After the treatment period, the results revealed that curcuminoids and 8 of their analogs significantly increased EGFP expression levels with more than 80% cell viability when compared to DMSO (0.5%) treated cells at the highest EGFP-inducing potency (Fig. 3). Noticeably, CUR (1), DMC (2) and BDMC (3) increased EGFP expression in a dose-dependent manner. The results showed that compounds 1–3 significantly enhanced EGFP expression at $30 \mu$M with $2.0 \pm 0.1$, $1.9 \pm 0.1$ and $3.6 \pm 0.3$ fold changes, respectively (Fig. 3a). Cell viability of the cell treated with compounds 1–3 was $92.6 \pm 1.3\%$, $85.0 \pm 2.5\%$ and $92.0 \pm 2.5\%$, respectively (Fig. 3b). However, this result was comparable or less active than the positive control, HU ($3.3 \pm 0.2$ folds). This study is in agreement with our previous studies that found BDMC (3) to have the highest EGFP expression among other major of curcuminoids in K562::$\Delta^G\gamma$-A$\gamma$ EGFP cells [5, 6]. We also found that curcuminoid diacetates (4–6) highly induced EGFP expression with fold increases of $2.1 \pm 0.2$ ($40 \mu$M), $2.1 \pm 0.2$ ($30 \mu$M) and $3.8 \pm 0.3$ ($30 \mu$M), respectively, compared to

Fig. 3. EGFP expression of active curcuminoids and analogs (a, c, e and g) and cell viability (b, d, f and h) of EGFP reporter cells. The augmentation of EGFP mean fluorescent intensity as a dose-dependent manner in treated cells compared to DMSO (0.5%) was observed. The cell viability was determined by PI staining. HU (250 $\mu$M) was used as positive control. The fold changes in EGFP expression and the percentage of cell viability showed as mean $\pm$ SEM of three independent experiments. *$P < 0.05$ and **$P < 0.01$ statistically analyzed by comparing to DMSO (0.5%) treated cells. Un, untreated; DM, DMSO (0.5%); HU, hydroxyurea.
DMSO-treated cells (Fig. 3c). In addition, compounds 4–6 enhanced EGFP expression more than 1–3. Importantly, compound 6 enhanced EGFP expression more than HU. Cell viability of the cell treated with compounds 4–6 was over 80% cell viability (Fig. 3d). The cells treated with tetrahydrobisdemethoxycurcumin (THBDMC, 9) and hexahydrobisdemethoxycurcumin (HHBDMC, 12) at 30 μM showed that the induction of EGFP expression increased by 3.6 ± 0.3 and 4.1 ± 0.1 fold changes, respectively, when compared with DMSO-treated cells (Fig. 3e). Furthermore, cells treated with these compounds at the most effective concentration, the cell viability was higher than 80% (Fig. 3f). The highest induction of EGFP expression was observed in compound 16 (4.4 ± 0.3 folds at 10 μM) among trienone analogs of curcuminoids (14–16), compared to DMSO-treated cells (Fig. 3g). However, the EGFP expressions of compounds 14 and 15 treated cells were also significantly induced with fold increases of 2.1 ± 0.1 (30 μM) and 3.8 ± 0.2 (10 μM). Moreover, cell viability of the cells treated with these compounds was more than 80% (Fig. 3h). Compounds 7, 8, 10, 11, 13, 17, 18, 19 and 20 were inactive to the test. Hence, our study has the potential to improve HbF-inducing properties from curcuminoid and their analogs that could serve as HbF inducers.

4. Discussion

In β-thalassemia patients, an imbalance of α-globin and β-globin chain synthesis is a key factor in pathophysiology and clinical severity. Augmenting γ-globin production is an alternative therapy that can improve globin synthesis imbalance and clinical manifestations [1]. Several pharmacological HbF inducing agents continue to lack specificity, have limited potency and remain safety concerns. HU is the only medicine approved by the USFDA to treat β-hemoglobinopathies. However, it exhibits many side effects, including cytopenia and myelosuppression [10]. Moreover, it results in variable response magnitudes, with approximately 20% of patients showing no response. These non-responders remain dependent on blood transfusion to increase hemoglobin levels [11, 12]. Thus, several researches are making efforts to find new HbF inducing agents with greater efficiency, higher specificity, and lower toxicity. A large number of plant extracts have been reported to induce HbF synthesis. For example, labdane diterpenes from *Curcuma comosa* [13] and quercetin from *Anaxagorea luzonensis* [14] have been shown to induce γ-globin mRNA expression and HbF production in a reporter cell line, K562::Δγγγ EGFP cells and human erythroid progenitors. Through our research, the three parent curcinoids (1–3) derived from *C. longa* and 17 chemically modified analogs were assessed for HbF inducing properties by stimulating γ-globin gene expression. The results showed that BDMC (3) gave the highest EGFP expression in K562::Δγγγ EGFP cells when compared to DMSO-treated cells, which was more active than the two parent curcuminoids (1–2).

This result was consistent with previous studies that found BDMC significantly enhanced EGFP expression and HbF production in K562::Δγγγ EGFP cells, K562 cells and human primary erythroid progenitor cells [5, 6]. At this point, it seemed that an increase in polarity in the molecule resulted in increased activity. A decrease in oxygenated (hydroxy or alkyl groups) substituents in the aromatic rings of parent curcuminoids tended to generally increase HbF-inducing activity. However, curcuminoids are poorly absorbed and undergo low water solubility. With the framework of the most active compound 3, modifications of the α,β-unsaturated diketo moiety and the methylene group (1–3) to reduced analogs (7–13) should improve their solubility and reduced analogs were found to be more active than the parent curcuminoids. In addition, mono-oxygenated analogs of the heptyl linker chain, and additional olefinic function (14–19) generally tended to increase activity. This result was in agreement with a previous study by our group [5]. Recently, the previous report revealed that trienone analog 16 increases HbF synthesis through demethylation at 16γ-globin promoter in primary human erythroid cells. However, further studies on the regulation of DNA methylation are needed to clarify the mechanism of γ-globin inducer [6]. Additionally,
the acetate analogs of curcuminoids (4–6) were subjected to biological evaluation. The results demonstrated that the activity of these acetate analogs was higher than that of their respective parent curcuminoids. Furthermore, there were no previous reports on HbF-inducing effect and cytotoxicity against K562::Δαγ-γ EGFP cells of compounds 4–6.

Mechanistically, curcuminoids have been published to act as epigenetic modifying agents, such as histone deacetylases (HDAC), histone acetyltransferase (HAT), and DNA methyltransferase I (DNMT1) [15]. In contrast, the exact mechanism of HU, the only USFDA-approved drug, is still unclear due to its role as an HbF inducer operating several pathways, including signal transduction pathways, post-transcriptional pathways, and epigenetic modifications. It not only has the ability to induce HbF production and γ-globin mRNA expression but also causes damage to cells, similar to that caused by chemotherapeutic agents [16]. Therefore, the plant extracts represent a suitable alternative treatment known for their low-risk factors of side effects and reduced toxicity.

In this study, we continued to investigate the effects of HbF-inducing agents of curcuminoids and their analogs, which have been previously shown in other studies to enhance γ-globin expression and HbF synthesis. The results show that not only BDMC but also its analogs can enhance EGFP expression levels in K562::Δαγ-γ EGFP cells. However, this study only focuses on the EGFP reporter cells for compound screening, with no report about the bioavailability and pharmacokinetic activity of curcuminoids and analogs. Therefore, further investigation in human erythroid progenitor cells and in vivo studies of these compounds are warranted.

5. Conclusion
In summary, this study investigated the structure modification of curcuminoids derived from C. longa with the objective of stimulating HbF synthesis. We found that 11 curcuminoids and analogs significantly enhanced EGFP expression with low toxicity. Consequently, our research has successfully provided new HbF inducers for potential use as an alternative treatment for β-thalassemia patients. Further studies are necessary to validate the effects of these compounds on human erythroid progenitor cells.

6. Recommendations
To clarify the effect of HbF production by these compounds, human erythroid progenitor cells that obtained from healthy donors and β-thalassemia patients are needed for further study. Subsequently, these compounds will be investigated to understand the molecular mechanism underlying γ-globin induction, with the aim of developing a new therapeutic approach for β-hemoglobinopathies.

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Conflict of Interest
No potential conflict of interest was reported by the authors.

References


Association between Factors Related and Mask-Wearing Behavior among Chinese Tourists Toward Post COVID-19 in Beijing, China: A Preliminary Study

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Abstract

**Background:** The global travel and tourism landscape has been profoundly affected by the COVID-19 pandemic, necessitating the adoption of preventive measures to ensure the safety of both travelers and local communities. In this context, comprehending the factors that shape mask-wearing behavior among Chinese tourists, especially in bustling destinations like Beijing, China, holds great significance. This preliminary study delves into the intricate association between knowledge, attitudes, gender, and communication factors that influence mask-wearing behavior among post-COVID-19 Chinese tourists. This preliminary study aims to investigate the association between factors related and mask-wearing behavior among Chinese tourists in Beijing, China, during the post-COVID-19 era.

**Method:** This is a cross-sectional design. The participants comprise 124 Chinese nationals from different cities in China, all of whom visited Beijing for a minimum of two days. Data were gathered through an online questionnaire. Descriptive statistics and binary logistic regression were used for analysis.

**Results:** The findings indicated that tourists who consistently received reliable information regarding COVID-19 preventive measures from local authorities in Beijing were more inclined to wear masks compared to those without such information (OR = 3.34, 95% CI = 1.18-9.47). Additionally, males exhibited a significantly higher tendency to wear masks, being 7.10 times more likely than females (OR = 7.10, 95% CI = 2.90-17.40).

**Conclusion:** The study revealed that tourists who received consistent and reliable information and knowledge about COVID-19 prevention measures from local authorities in Beijing were more likely to wear masks. This highlights the pivotal role of effective information dissemination in promoting responsible behavior. It also reveals a significant gender disparity, emphasizing the need for gender-specific strategies. Policymakers, public health authorities, and tourism management should collaborate on comprehensive, to promote consistent mask-wearing behavior among tourists, safeguarding public health and ensuring the vitality of the tourism industry in the post-pandemic era.

**Keywords:** Chinese tourists, Post-COVID-19, Beijing, Wear masks

1. Introduction

The outbreak of the COVID-19 pandemic has resulted in unparalleled global challenges, profoundly affecting individuals, economies, and societies [1]. Among the myriad of countermeasures, the wearing of face masks emerged as a key preventive measure, becoming especially prevalent in China, where the pandemic initially surfaced. Here, rigorous public health directives, inclusive of mask mandates and expansive health campaigns, played a pivotal role in shaping public behavior, particularly among tourists traveling both domestically and internationally [2]. As the world continues to
navigate the aftermath of the pandemic, the landscape of international tourism, notably in areas like Beijing, has witnessed considerable transformation [3].

Extant literature offers multiple insights into mask-wearing behaviors. Positive perceptions of mask-wearing often correlate with consistent usage, whereas negative perceptions can deter consistent adherence [4]. Additionally, individuals informed about the benefits and significance of mask-wearing are generally more compliant [5]. Gender, too, emerges as an influential factor in shaping health behaviors, including mask-wearing practices [6, 7]. Communication dynamics, particularly during health crises, play a crucial role in information dissemination and in influencing public attitudes and behaviors [8]. However, a notable gap persists in the current literature. Many studies, while comprehensive, focus predominantly on general populations or healthcare professionals, often sideling the unique behaviors and contexts of Chinese tourists.

To bridge this research lacuna, our study endeavors to understand the between knowledge, attitudes, gender, and communication factors and their collective influence on mask-wearing behavior among Chinese tourists in Beijing in the post-COVID-19 context. By exploring the attitudes of Chinese tourists, discerning gender-based variances in mask-wearing tendencies, gauging the impact of diverse communication strategies, and understanding their interrelationships, this study aims to furnish invaluable insights. These insights will be particularly beneficial for policymakers, public health officials, and tourism agencies, equipping them to craft effective strategies to promote mask-wearing and other preventive measures, keeping in view the multifaceted factors at play.

2. Methods

This research adopts a quantitative cross-sectional design. The study, centered around prominent tourist locales in Beijing such as the Great Wall, is set to transpire from April to August 2023. Its foundational intent is to amass data via meticulously tailored online survey questionnaires [9, 10]. These instruments, designed to probe into tourists’ insights, attitudes, and practices concerning COVID-19 preventive measures, target Chinese tourists from diverse urban and rural backgrounds visiting Beijing with a stay of at least two days. Unlike the previous study, this investigation shifts its geographical focus to prominent tourist locales in Beijing, including the Great Wall. However, considering the distinct cultural and behavioral nuances that may differentiate their responses from Indian participants. Eligibility hinges on several criteria, including age (18 years and above), proficiency in the Chinese language, and adeptness with online platforms like WeChat and QQ, with a projected sample size of 124 participants (Fig. 1). This study was approved for ethical considerations, COA No. 193/66.

The survey is meticulously structured to evaluate key variables: sociodemographics, Knowledge, Attitude, Communication, and Behavior. Each section of the questionnaire is clearly delineated to ensure precise measurement and analysis. The Knowledge section assesses understanding of COVID-19 precautions through a ternary format: True, False, or Not Sure. This approach allows for a nuanced grasp of the participants’ awareness levels. Attitude is gauged through responses that reflect personal perspectives on the pandemic. The Communication section is further elaborated upon, defining specific factors such as the frequency and effectiveness of information exchange about COVID-19. Other aspects, including Attitude, Communication, and Behavior, are measured using a 5-point Likert scale. Responses on this scale are categorized with clear cut-off points: scores of 1 to 3 indicate a low level, while scores of 4 to 5 denote a high level in the respective variable.

To ensure the survey’s credibility and robustness, The research instrument, integrating items from previously validated studies, was subjected to a rigorous translation process. It was then pretested on a smaller cohort to ascertain its reliability, yielding a notable Cronbach’s alpha value of Knowledge (0.924), Attitude (0.849), Communication (0.909), and mask-wearing behavior of Beijing tourists after COVID-19 (0.939). This alpha value is indicative of the high
**Fig. 1. Target Chinese tourists**

**Table 1. Demographic characteristics (n=124)**

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
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<tr>
<td>Early working age (≤30)</td>
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<tr>
<td>Middle working age (31-45)</td>
<td>44(35.5)</td>
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<tr>
<td>Late working age (≥46)</td>
<td>38(30.6)</td>
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<tr>
<td>Mean(sd)</td>
<td>38.4(10.2)</td>
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<tr>
<td>Range</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
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<tr>
<td>Female</td>
<td>63(50.8)</td>
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<tr>
<td>High school Diploma or equivalent</td>
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<tr>
<td>Vocational school</td>
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<tr>
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Table 1. Demographic characteristics (n=124) (cont.)

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<td>More than 10001 ¥</td>
<td>16(12.9)</td>
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<td>Residence</td>
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<td>Kidney disease</td>
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Table 2. Association between sociodemographic characteristics and mask-wearing behavior analyzed through binary logistic (n=124)

<table>
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<th>Related factors</th>
<th>Unadjusted OR</th>
<th>(95% CI)</th>
<th>p-value</th>
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<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early working age (30 ≤ Age)</td>
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<tr>
<td>Middle working age (31 – 45)</td>
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<td>(0.28-1.67)</td>
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<td>(0.22-0.35)</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
<td>7.10</td>
<td>(2.90-17.40)</td>
<td>&lt;0.001***</td>
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<td>Female</td>
<td>Ref</td>
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<tr>
<td>Educational Level</td>
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<tr>
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<td>Ref</td>
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<td>High school Diploma or equivalent</td>
<td>1.42</td>
<td>(0.29-6.91)</td>
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<tr>
<td>Vocational school</td>
<td>1.73</td>
<td>(0.39-7.76)</td>
<td>0.47</td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>0.98</td>
<td>(0.23-4.24)</td>
<td>0.98</td>
</tr>
<tr>
<td>Master’s degree or higher</td>
<td>0.67</td>
<td>(0.05-8.64)</td>
<td>0.76</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>0.50</td>
<td>(0.19-1.35)</td>
<td>0.17</td>
</tr>
<tr>
<td>Widowed and Divorced</td>
<td>0.41</td>
<td>(0.07-2.53)</td>
<td>0.34</td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less and equal 10000 ¥</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than 10001 ¥</td>
<td>0.46</td>
<td>(0.12-1.72)</td>
<td>0.25</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.78</td>
<td>(0.75-4.21)</td>
<td>0.19</td>
</tr>
<tr>
<td>Physical illness history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.74</td>
<td>(0.33-1.65)</td>
<td>0.46</td>
</tr>
<tr>
<td>COVID-19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unchecked</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Checked</td>
<td>0.74</td>
<td>(0.36-1.65)</td>
<td>0.46</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unchecked</td>
<td>Ref</td>
<td>(0.63-6.49)</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Table 2. Association between sociodemographic characteristics and mask-wearing behavior analyzed through binary logistic (n=124) (cont.)

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Unadjusted OR</th>
<th>(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Checked</td>
<td>2.03</td>
<td>(0.19-2.08)</td>
<td>0.45</td>
</tr>
<tr>
<td>Unchecked</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Checked</td>
<td>0.63</td>
<td>(0.20-1.28)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unchecked</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Checked</td>
<td>0.16</td>
<td>(0.24-9.22)</td>
<td>0.65</td>
</tr>
<tr>
<td>Kidney disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unchecked</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Checked</td>
<td>1.48</td>
<td>(0.19-2.08)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Table 3. Communications characteristics (n=124)

<table>
<thead>
<tr>
<th>Communications characteristics</th>
<th>N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communications from local authorities in Beijing regarding COVID-19 precautions have been consistent.</td>
<td></td>
</tr>
<tr>
<td>Consistent</td>
<td>33(26.6)</td>
</tr>
<tr>
<td>Inconsistent</td>
<td>91(73.4)</td>
</tr>
</tbody>
</table>

Table 4. Association between communication and mask-wearing behavior analyzed through binary logistic (n=124)

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Unadjusted OR</th>
<th>(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communications from local authorities in Beijing regarding COVID-19 precautions have been consistent.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consistent</td>
<td>3.34</td>
<td>(1.18-9.47)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Inconsistent</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

reliability of the questionnaire. The culmination of this research endeavor involves a rigorous data analysis process using licensed IBM SPSS version 28, where findings with a p-value below 0.05 will be treated as statistically significant, providing a nuanced understanding of factors influencing mask-wearing behaviors among Chinese tourists post-COVID-19.

3. Results

Table 1, the participants were between 23 and 59, with a median age of 38.4 and a standard deviation of 10.16. The data showed that married participants accounted for 77.4% of the total participants. Also, 54% of participants had a lower than Bachelor’s degree, and 87.1% of the total participants had a monthly household income of less than 100,000 ¥, pointing to a mid-range income bracket for the majority.

As shown in Table 2. In a binary logistic regression analysis assessing the association between sociodemographic characteristics and mask-wearing behavior among Chinese tourists in Beijing, it was observed that males were 7.10 times more likely to wear masks compared to females (Unadjusted OR = 7.10, 95% CI: 2.90-17.40, p < 0.001), indicating a statistically significant higher propensity for mask-wearing among females. While individuals with higher educational levels and incomes displayed certain tendencies in mask-wearing behavior, these trends were not statistically significant. Among the examined factors, only gender demonstrated a significant relationship with mask-wearing practices.
Table 5. Association between knowledge and mask-wearing behavior analyzed through binary logistic(n=124)

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Unadjusted OR</th>
<th>(95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of knowledge about COVID-19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not sure and False (Low Knowledge Level)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>True (High Knowledge Level)</td>
<td>2.06</td>
<td>(0.91-4.66)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 6. Analysis of the association between attitude and mask-wearing behavior through binary logic (n=124)

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Unadjusted OR</th>
<th>(95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of knowledge about COVID-19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low attitudes</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High attitudes</td>
<td>2.17</td>
<td>(0.58-8.09)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Tables 3 and 4, in a sample of 124 participants assessing the reliability of communications from Beijing’s local authorities on COVID-19 precautions, 26.6% deemed the communications consistent and reliable, while 73.4% found them inconsistent and unreliable. Logistic regression revealed a significant association between these perceptions and mask-wearing behavior: those viewing the communications as reliable were 3.34 times more inclined to wear masks (Unadjusted OR = 3.34, 95% CI: 1.18-9.47, p-value = 0.02).

In a sample of 124 participants, those with accurate knowledge about COVID-19 had a 2.06-fold increased likelihood of mask-wearing, though this was not statistically significant (p=0.08, CI: 0.91-4.66), Table 5. Similarly, Individuals who highly regard COVID-19 precautions are approximately 2.17 times more likely to wear masks compared to those with lower attitudes towards these precautions, yet this association also lacked statistical significance (p=0.25, CI: 0.58-8.09), Table 6.

4. Discussion

The unprecedented challenges posed by the COVID-19 pandemic have brought to the fore the criticality of preventive health measures, notably the consistent adoption of mask-wearing. Delving into the intricacies of this behavior, our study has presented several noteworthy findings. Most strikingly, gender-based variations in mask-wearing emerged, with males displaying a more pronounced inclination towards this preventive measure compared to females. Such an observation, while finding resonance in prior studies [6, 7], accentuates the multifaceted nature of health behaviors, influenced by a matrix of sociocultural, psychological, and individual factors. Given this, it’s imperative for public health initiatives to adopt a more inclusive approach, ensuring that health messages and interventions cater to the diverse needs and perspectives of all individuals, irrespective of gender.

In the realm of communication, our study underscored its pivotal role in shaping health behaviors. Tourists who viewed communications from Beijing’s local authorities as consistent and dependable exhibited a higher likelihood to wear masks. This insight aligns seamlessly with established paradigms of crisis communication, which highlight the imperativeness of clear, accurate, and timely information in navigating public behaviors during health emergencies [8]. As we grapple with the evolving contours of the pandemic, the trustworthiness and reliability of health advisories become cornerstone elements in influencing public responses and fostering adherence to recommended practices.

On the fronts of knowledge and attitude, while our study observed a trend suggesting that those with a more accurate understanding of COVID-19 and a positive disposition towards precautions were more inclined to wear masks, these associations weren’t statistically significant. Nevertheless, these observed inclinations cannot be dismissed. They suggest a potential trajectory that can be further explored in future research, perhaps with more extensive sample sizes or...
varied demographics. In essence, the link between knowledge dissemination and behavioral adherence underscores the continuous need for evidence-based public health education.

However, as with any study, ours is not devoid of limitations. The cross-sectional design prevents us from establishing causative relationships. The focus on Chinese tourists in Beijing, while providing in-depth insights into this demographic, may not necessarily be generalizable to other populations or contexts.

5. Conclusion

Drawing from these findings, it becomes evident that an inclusive and holistic approach to public health messaging is essential. Tailoring campaigns that cater to the diverse needs of all individuals, irrespective of gender, while emphasizing the importance of credible and timely information, can optimize compliance with preventive measures. While the associations between comprehensive knowledge about COVID-19 and mask-wearing did not reach statistical significance, they underscore the importance of public health education in guiding community responses.

In essence, our study aims to provide critical insights and guidance as we adapt to the changing realities of the post-COVID era. By examining the behavior and attitudes toward COVID-19 precautions, our research offers valuable benchmarks and informs strategies for effective public health communication and intervention in this new context. They not only elucidate the current behavioral patterns but also offer guidance for shaping robust, evidence-driven, and inclusive public health interventions in the future. As we move forward, harnessing these insights will be crucial in fostering a well-informed, proactive, and resilient global community.

6. Recommendations

Our study on Chinese tourists in Beijing has shed light on pivotal factors influencing mask-wearing behaviors, emphasizing the need for targeted and effective public health strategies. In our study, we emphasize the need for a gender-sensitive approach to health aimed at increasing mask-wearing among tourists. This involves using targeted messaging tailored to different gender preferences, engaging with influencers who appeal to diverse demographics, and setting up interactive educational installations at tourist sites. Reliable and transparent communication from local authorities stands out as a determinant for preventive behaviors, underscoring the importance of bolstering communication channels and ensuring timely, accurate dissemination of information. Moreover, while the study did not find a statistically significant direct correlation between extensive knowledge about COVID-19 and the practice of mask-wearing (Table 6), the trend observed suggests that consistent, evidence-based public health education could potentially influence mask-wearing behaviors [11].

Our study, while focused primarily on mask-wearing behaviors, has revealed nuanced insights into public attitudes and compliance regarding COVID-19 precautions. For instance, we observed that certain demographics, despite showing awareness of mask-wearing as a preventive measure, exhibited varying degrees of compliance. This observation raises questions about their attitudes and practices towards other preventive measures like hand hygiene and vaccination. Additionally, the correlation, though not statistically significant, between COVID-19 knowledge and mask-wearing behavior suggests that increased awareness might similarly influence other health behaviors. These findings underscore the importance of exploring a wider array of preventive behaviors in future research, as understanding the factors influencing one behavior, like mask-wearing, could provide valuable insights into how best to encourage other critical health practices such as regular hand washing and vaccine uptake [12]. Longitudinal studies could offer a dynamic view of evolving health behaviors over time. To enhance the generalizability and depth of insights, diversifying the sample base to include a wider range of demographics and regions is essential. Lastly, integrating feedback mechanisms can offer local authorities real-time insights into public perceptions, enabling them to tailor their
communications more effectively, ultimately driving better compliance with recommended health protocols in the face of global health challenges [13].

Acknowledgments

I extend profound gratitude to Dr. Mehrolia and Dr. Yesuf, among others, for allowing me to utilize their meticulously crafted questionnaire. Their previous work and contributions have significantly influenced the framework of my research. Recognizing the cultural and contextual differences, I further suggest the modification and validation of this questionnaire to suit Chinese populations. This step is crucial to ensure its relevance and effectiveness in accurately capturing the attitudes and behaviors of Chinese respondents. Their generosity in sharing these valuable resources has been pivotal to the success of this study.

Special thanks go to the dedicated participants of this research, whose insights and time have been essential in bringing depth and authenticity to our findings. I am also grateful to Chief Physician Xiaofeng Huang from Beijing Hospital for checking my translation of the Chinese version from the English version questionnaire.

References


Phenomenological Study: Breast Cancer Survivors’ Experience to Improving Quality of Life

Della Zulfa Rifda *, Zahroh Shaluhiyah, Antono Surjoputro

Faculty of Public Health, Diponegoro University, Central Java, Indonesia

Abstract

**Background:** Cancer is often considered a deadly disease. In almost all countries, breast cancer is the most common type of cancer suffered by the community. Nevertheless, it is not impossible for breast cancer patients to survive the disease, commonly known as “survivors”. Ken Saras Hospital is a private hospital located in Central Java, Indonesia. Ken Saras Hospital also has excellent one-stop cancer services and a community of cancer survivors, namely Oncology Ken Saras Community. So, the researcher wants to explore deeply of a person’s experience from being diagnosed with breast cancer until being as a breast cancer survivor.

**Method:** The research design used is a qualitative study using a phenomenological approach. Data collection was done by in-depth interviews and observation. The informants of this research were 11 breast cancer survivors using purposive sampling technique with inclusion criteria. The data will be analyzed with thematic analysis.

**Results:** Several themes in this research; a) coping mechanism that happened to breast cancer survivor; b) hope of breast cancer survivors such as be healed/cured, doesn’t pass their diseases to their children, be useful to others; c) factors that affect the quality of life of breast cancer survivors such as motivation for life, the role of medic staff, spiritual approach, the role of other cancer patients, implementation of healthy lifestyle.

**Conclusion:** There is a need for counseling, especially on the psychological problems of breast cancer patients, given the importance of handling patients’ mental health.

**Keywords:** Phenomenology, Breast cancer survivors, Quality of life

1. Introduction

Cancer is a disease on the body due to abnormal growth and development of cells (malignant) [1]. This disease is one of the noncommunicable diseases and can attack anyone [2]. According to the WHO, it is estimated that by 2030 there will be 26 million cases, and 17 million of them are expected to die. Meanwhile, cancer cases in 2018 in Indonesia ranked 8th in Southeast Asia and 23rd in Asia [3]. In almost all countries, breast cancer is the most common type of cancer. Globocan in 2020 stated that the number of new cases of breast cancer in Indonesia reached 68,868 cases (16.6%) of the total 396,914 cancer cases [4].

The incidence of breast cancer will increase above the age of 35 and decrease at the age of menopause [5]. In line with the Indonesian Breast Cancer National Strategy in the National Cancer Action Plan 2022-2024, which targets its programs for ages 30–50 years old [6]. In Indonesia, the treatment of breast cancer patients is often late. Whereas about 43% of deaths from breast cancer can be avoided by early detection and avoiding risk factors [4]. The delay in handling breast cancer is causing sufferers to experience a decrease in their quality of life. Many problems are found in breast cancer patients’ daily lives.

First, there are psychological problems. There are 5 stages that breast cancer patients commonly go through, which are denial, anger, bargaining, depression, and acceptance. However, not all patients can reach the final stage [7].

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Second, physiological problems. Such as nausea, vomiting, loss of appetite, the appearance of lumps, ulcers, and pain [8]. During the treatment process, breast cancer patients also have the possibility of losing some or all of their breasts.

Third, social problems. Some cancer patients distance themselves from society due to fears about their mental and physical changes [9]. But on the other hand, cancer patients also need help, which makes them reliant on people around them.

Fourth, spiritual needs. Cancer patients need a considerable amount of spiritual intervention [10]. Spiritual needs can also affect the patient's perception of the meaning of life and how the patient appraises his life after being diagnosed with cancer.

All these problems can actually be handled holistically at the hospital. The hospital is a place that is expected to provide comfort for breast cancer patients. Ken Saras Hospital is a hospital in Central Java, Indonesia, that has excellent one-stop cancer services. From the data of patient visits in the last 7 years, it was found that malignant neoplasm of breast were in the first place. Not only focusing on cancer treatment, Ken Saras Hospital also provides promotive, preventive, rehabilitative, and even palliative care services.

There is also a cancer survivor community, namely the Oncology Ken Saras Community. With the limitations that cancer patients have, it is not impossible for them to survive, we usually call them as “a survivors”. We often assume that medicine is the main thing to recovery, so we ignore the other needs. In fact, there are several factors that can affect their recovery. Until the end, breast cancer survivors managed to go through it all and strive to improve their quality of life.

Therefore, the experiences that occur in breast cancer patients to become breast cancer survivors, attract researchers’ empathy to do research on “Phenomenological Studies: Experiences of Breast Cancer Survivors in Improving Quality of Life”.

2. Methods

The research design used was a qualitative study using a descriptive phenomenological approach. The data collection method was conducted using the in-depth interview method with the instrument of the interview guideline form, and observation was done during the in-depth interview.

The informants of this research were breast cancer survivors at Ken Saras Hospital, using purposive sampling technique, with criteria:

a. Breast cancer survivors with stage 2 and/or 3 when first diagnosed with breast cancer and have been declared as breast cancer survivors in the last 5 years
b. Age 26–59 years old
c. Have undergone mastectomy

The data obtained from this research was analyzed by thematic analysis using the ATLAS.ti application with the following steps:

a. Transcribe the in-depth interviews and read the entire data
b. Coding by giving meaning to the inductive - deductive transcript data
c. Grouping the codes into categories/ themes
d. Create a network by linking all categories/ themes from the coding results into one meaningful concept

The research were done in the following steps:

a. The introduction study and interview with Mrs. Vero as the Head of the Emerald Room, a nurse who specializes in treating cancer patients at Ken Saras Hospital
b. Discussion with the advisor
c. Obtain research license and ethical clearance letter
d. After the research permit was received, the researcher met key informants obtained through introductory interviews with Mrs. Vero, namely Mrs. Ety (Leader of OKC - Oncology Ken Saras Community) with the aim of assisting in providing data on breast cancer survivors at Ken Saras Hospital. After that, the researcher contacted one by one the candidate informants who fit the criteria of this study to ask for their willingness to do in-depth interviews about their experiences as breast cancer survivors in improving their quality of life.
Table 1. Informant characteristics

<table>
<thead>
<tr>
<th>Informant</th>
<th>Age when diagnosed with breast cancer (years old)</th>
<th>Stage</th>
<th>Metastases</th>
<th>Treatment Period (start of diagnosis until completion of treatment)</th>
<th>Profession</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>III</td>
<td>-</td>
<td>2019 – 2020</td>
<td>Housewives</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>III</td>
<td>-</td>
<td>2014 – 2018</td>
<td>Director of a local radio station</td>
</tr>
<tr>
<td>3</td>
<td>48</td>
<td>III</td>
<td>√</td>
<td>2020 – 2023</td>
<td>Advertising</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>III</td>
<td>√</td>
<td>2016 – 2021</td>
<td>Laundry</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>II</td>
<td>-</td>
<td>2017 – 2018</td>
<td>Security</td>
</tr>
<tr>
<td>6</td>
<td>52</td>
<td>III</td>
<td>-</td>
<td>2016 – 2018</td>
<td>Housewives</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>II</td>
<td>-</td>
<td>2020 – 2022</td>
<td>Housewives</td>
</tr>
<tr>
<td>8</td>
<td>51</td>
<td>III</td>
<td>√</td>
<td>2016 – 2023</td>
<td>Housewives</td>
</tr>
<tr>
<td>9</td>
<td>51</td>
<td>II</td>
<td>-</td>
<td>2016 – 2017</td>
<td>Nun</td>
</tr>
<tr>
<td>10</td>
<td>49</td>
<td>III</td>
<td>-</td>
<td>2017 – 2018</td>
<td>Laundry</td>
</tr>
<tr>
<td>11</td>
<td>53</td>
<td>II</td>
<td>-</td>
<td>2018 – 2019</td>
<td>Civil Servants</td>
</tr>
</tbody>
</table>

Table 2. Triangulation informants characteristics

<table>
<thead>
<tr>
<th>Triangulation Informant</th>
<th>As a...</th>
<th>Profession</th>
<th>Education</th>
<th>Age (years old)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Head of Emerald Room</td>
<td>Nurse</td>
<td>Bachelor’s Degree</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>Emerald Room Nurse</td>
<td>Nurse</td>
<td>Associate Degree</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>Lead of OKC (Oncology Ken Saras Community)</td>
<td>Self-employed</td>
<td>Associate Degree</td>
<td>55</td>
</tr>
</tbody>
</table>

In-depth interviews were conducted with 11 (eleven) main informants (Table 1). Interviews were conducted in the morning and afternoon at their homes, workplaces and at the Ken Saras Hospital Canteen. In-depth interviews were conducted with a duration of 45 - 120 minutes.

Before the interview, the researcher attached an informed consent form that had to be signed as an agreement to be used as a research subject. After that, the researcher explained the purpose and objectives and apologized if during the interview there were sensitive questions. Researchers give informants the freedom to answer or not answer if they feel the question is too sensitive.

This research has received approval from the Health Research Ethics Commission, Faculty of Public Health, Diponegoro University, with number: 445/EA/KEPK-FKM/2023.

3. Results

In-depth interviews with 11 main informants and 3 triangulation informants were used to perform in this research, who are the leaders of the cancer community and nurse at Ken Saras Hospital (Table 2).

Table 1, the age of informants is between 38–56 years old, first diagnosed with breast cancer at stage III with different treatment periods (start of diagnosis until completion of treatment). Informants with stage II have a shorter treatment period. Some informants with stage III also have metastases. However, with these conditions, some informants are still working either as employees or housewives.

The concept map of breast cancer survivors’ experiences to improve quality of life as shown in Fig. 1.

3.1. Coping mechanisms in breast cancer survivors

Coping mechanisms are the behavioral and cognitive efforts of cancer patients in dealing with physical and psychosocial threats due to their illness.
Fig. 1. Concept map of breast cancer survivors’ experiences to improve quality of life

3.1.1. Denying the situation

It was found that the first response when the patient was diagnosed with breast cancer by the doctor was not to accept or deny. Six out of 11 informants revealed that they were surprised and did not expect to be diagnosed with breast cancer.

“Why would I? I am a Servant of God (as a Nun), I have served the people, why did I get this?”

(Informant 9)

3.1.2. Regretting

Feelings of regret are the next stage expressed by the research subjects (3 out of 11 informants). This feeling of regret is indicated by the informant’s answer that says “if only” or “what if” and is supported by the results of observations during in-depth interviews, there are expressions of disappointment when the informant remembers her past.

What I regret is why I didn’t get it checked earlier, maybe the treatment would have been easier, the pain wouldn’t have been as painful as it was back then.

(Informant 10)

3.1.3. The fear of cancer and sadness

Fear of cancer was another response shown by the research subjects (7 out of 11 informants).

What I feel is fear and worry, because cancer is something horrible for most people.

(Informant 4)

Furthermore, the feeling of sadness is an expression that is often spoken by informants. Even during in-depth interviews, there were informants who shared their experiences while struggling to become “cancer survivors” while bursting into tears.

...I was shocked, I cried. I am a single parent, I have one child. I thought a lot that day, I couldn’t sleep.

(Informant 10)

This was also confirmed by one of the triangulation informants who is a specialist nurse for cancer patients at Ken Saras Hospital, that she found patients who felt sadness related to their illness during treatment at the hospital.

I’ve cared for patients who cried when
they were here, because of their illness, they thought “What will happen to their children if they get sick? Can’t I get well? What if in the middle of the treatment I don’t finish and then I die?”

(Triangulation 2)

3.1.4. Accepting the situation

The stage of accepting the situation is the final stage of someone who is grieving when faced with a chronic disease that changes their life. Most of the research subjects (9 out of 11 informants) said they could accept their current condition even though it took time to adapt.

I believe in God, God must have a meaning for all of this. I am now more motivated to live my life, to share my faith with others. I am grateful that with this illness I know what it feels like to be sick, what it feels like to struggle, I’m just feeling grateful

(Informant 9)

3.2. Breast survivor’s hope

3.2.1. Be healed

Most of the research subjects (8 out of 11 informants) hoped to be given a cure for their illness. Generally, wanting to be with the child is one of the reasons informants want to be cured.

I wanted to be cured, because at that time my son was still in junior high school, so I wanted to see his growth.

(Informant 9)

3.2.2. Useful to others

In addition to hoping for a cure and not passing on the disease to their children, informants also hope that even with their condition they can still be useful to others.

After I knew the tightness due to cancer, I collected the nebulizer that was still feasible to lend to people. Hopefully I can continue to be a useful person for others.

(Informant 3)

3.3. Factors affecting the quality of life of breast cancer survivors

3.3.1. Motivation for life

Half of the research subjects (5 out of 11 informants) thought that their husbands’ support such as motivation, attention and guidance had a positive impact on improving the patient’s quality of life.

My husband was the most influential during my illness, after all the treatments were finished I said “Thank you, Dad, for accompanying me until the treatment was finished.”

(Informant 2)

3.3.2. The role of medc staff

3.3.2.1. Doctor’s advice

Eight out of 11 informants) thought that following all the doctor’s advice could improve their quality of life.

Whatever Dr. Bi suggested, I actually took it all. Alhamdulillah, I never missed a single treatment. Until now, Alhamdulillah, there has never been a relapse.

(Informant 4)

This is also supported by the confession of triangulation informants about the role of doctors at Ken Saras Hospital. Not only for advice, motivation, attention and even costs are also provided by doctors at Ken Saras Hospital.

Doctors often help provide cost relief for patients who cannot be covered by Health Insurance, such as giving discounts on treatments, or free of charge, helping to find donators to help with the lack of costs.

(Triangulation 3)

3.3.2.2. Nurse support

Four out of 11 informants said that the nurses’ help during their hospitalization left a positive impression on them.

After my mastectomy I chose homecare from a nurse at Ken Saras, she helped me a lot. Qodarullah, she is a very positive person. I was told by the nurse that my wound was not bad and would get better quickly.

(Informant 3)
3.3.3. Spiritual approach

Improving the quality of prayer is one of the things that most research subjects (7 out of 11 informants) do to get closer to God. This is accomplished such as sunnah prayers, umrah and increasing the sincerity of prayer.

...Spiritual changes, since I got cancer and because I'm at this age I have to get closer to God. Starting to wake up at night regularly for tahajud.

(Informant 2)

3.3.4. The role of other cancer patients

Most of the research subjects (7 out of 11 informants) felt helped by the role of other survivors of cancer at Ken Saras Hospital, (OKC - Oncology Ken Saras Community). The roles provided include motivation, material, drug support, assistance during treatment and many more.

It is also known from in-depth interviews that there are several hospital events for OKC members, such as health education, social services, and gatherings to celebrate OKC’s anniversary. It is these activities that increase the spirit of cancer patients to recover.

I join OKC events because I enjoy meeting my friends in arms. I have also borrowed medicine from other friends (cancer patients), because the stock at the pharmacy is still on indent, later when my medicine is available, I replace the medicine with my medicine.

(Informant 1)

3.3.5. Implementation of healthy lifestyle

The adoption of a healthy lifestyle such as routine control, regular medical check-ups, regulating diet, exercise, getting enough rest and avoiding stress has been carried out by all research subjects.

...I still go for regular check-ups, I still get breast x-ray, thoracic and abdominal ultrasounds every year.

(Informant 1)

4. Discussion

4.1. Informant description

4.1.1. Age

The age of informants is between 38–56 years old. Age is also one of the risks of breast cancer. The incidence of breast cancer will increase as you get older, which is after the age of 30 years. Then it will increase significantly at the age of 40 years and enter the peak age at 70 to 80 years [11]. In line with the research of Satya et al. [12], breast cancer cases are dominated by the age group >40 years. This caused by hormone exposure and tumor formation in a woman’s body, which takes a long time to become malignant [13].

4.1.2. Stage of cancer

Informants first found out that they were diagnosed with breast cancer at stage III (6 out of 9 informants). The higher the grade/stage, the greater of severity will cause [2]. In this research, some informants with stage III tend to have metastasized.

In the literature, the life expectancy in the next 5 years for stage I is 87%; for stage II it is 75%; for stage III it is 46%; and for stage IV it is 13% [14]. In line with Lee Caplan’s research, it shows that someone who is late in breast cancer treatment is often found at an advanced stage. This causes a low life expectancy, a complex and longer treatment [15].

4.1.3. Job

All informants in this research were diagnosed with breast cancer at a productive age. According to the Ministry of Health of the Republic of Indonesia, grouping ages 20–59 years is in the productive category [16].

This age is considered a suitable to complete formal education, find and build a career, build a new family, etc. [17]. However, in this research, it was found that some informants remained productive with their various jobs.

4.2. Coping mechanisms in breast cancer survivors

Homoestatic is a person’s continuous effort to maintain a state of balance to sustain life using coping mechanisms that have or have not been tried before [18]. Coping mechanisms consist of problem focused coping and emotion focused coping [19]. In this case, although the research
subject initially denied his illness. In accordance with the Kubler-Ross theory of loss and grief which consists of 5 stages, such as denial, anger, bargaining, depression and acceptance [20]. However, in the end, most of the research subjects took adaptive actions, which were proven by acceptance of their condition. Likewise, regarding problem focused coping, it is known that the research subject followed all the treatments that had been scheduled and in emotion focused coping it was known that the research subject had begun to accept and make peace with his current situation.

4.3. Breast survivor’s hope

Cancer patients who have positive aspects such as hope, regardless of what the hope is, can encourage patients to have resilience in dealing with the disease that brings better medical outcomes [21]. One of the hopes of research subjects hopes not to pass on the disease to their children. Where it is common knowledge that cancer can be inherited by parents to their children. The existence of this hope factor is in accordance with the research of Babacan et al. [22] there is a positive and significant relationship between hope and quality of life in 55 female patients with breast cancer.

4.4. Factors affecting the quality of life of breast cancer survivors

4.4.1. Motivation for life

Family support, such as spouses and children, shows that the support system of the people around them is working well. This support system is needed to provide physical assistance and psychological strengthening to the research subjects. So that it helps patients to make decisions, monitor treatment compliance, help change lifestyles to be healthier and accelerate the process of acceptance of their condition [23]. This also happened to most of the research subjects who received support from their families so as to increase their motivation.

4.4.2. The role of medical staff

Watson’s theory known as the Theory of Human Caring can explain that the role of medical personnel in providing care is a type of relationship between medical personnel and patients to improve and protect patients as human beings, so as to accelerate the healing process [24]. It was found in this study that the form of attention given from medical staff (doctors and nurses) was in the form of attention, motivation, assistance and even financial assistance. In practice, healing a patient with a caring environment has significant results holistically in patients.

4.4.3. Spiritual approach

A spiritual approach is relevant in all aspects of care for patients with any illness. It has been shown to have a favorable impact during treatment as well as helping patients to deal with their past problems, current problems and likely future problems [25]. The spiritual approach in this study is shown in the behavior of the research subjects who began to improve the quality of their worship by performing sunnah worship, regularly reading or watching religious material. A hope in God gives the patient a sense of hope and optimism in life.

4.4.4. The role if other cancer patients

Smet (1994) reveals that social support as an interpersonal reciprocal relationship by providing assistance to others in the form of actions, attention, support. This support can have a positive effect on individual health [26]. In accordance with this study, it is said that social support, especially from other cancer survivors who are members of a community called OKC, provides positive effects for its members.

4.4.5. Implementation of healthy lifestyle

Coping mechanism is a way that a person does in solving problems by adapting to changes and responding to threatening situations [27]. One example of a form of coping mechanism is by adapting a healthy lifestyle. All of informants tried to adopt a healthy lifestyle such as maintaining a diet, managing stress, getting enough rest, doing physical activity, consuming herbal drinks. In line with Amelia et al.’s research, some informants admitted to taking
herbal medicines, to increase their strength because they could provide positive self-treatment rather than just relying on doctors [28].

5. Conclusion
In this study, the research subject was able to reach the end of the coping mechanism stage by accepting her condition. Cure, be useful to others and the willingness not to pass on the disease to their children are the hopes of the research subjects. Some factors that can improve the quality of life of breast cancer survivors include high motivation to live, the role of medical staff at the hospital, a spiritual approach by improving the quality of prayer, social support and adaptation of a healthy lifestyle that has now been carried out by all subjects of this study.

6. Recommendations
Although most of the research subjects admitted that they have accepted their current condition, there is a need for psychological counseling for both patients and families (as care givers). Considering that not all patients and families of patients can finally accept their condition. Handling a person's mental health, especially in someone suffering from chronic illness is very necessary.

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Conflict of Interest
No potential conflict of interest was reported by the authors.

References


Preliminary Survey on Knowledge, Attitudes, and Practices about Indoor Air Pollution among Myanmar Residents

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Abstract

Background: Indoor air pollution (IAP) is a growing public health threat, but little is known about knowledge, attitudes, and practices among urban residents in Myanmar. Rapid development in cities like Yangon and Mandalay might exacerbate pollution while increasing time spent indoors. This study aims to assess the knowledge, attitudes, and practices (KAP) related to Indoor Air Pollution (IAP) among residents of Yangon and Mandalay.

Methods: A preliminary cross-sectional survey was conducted with 150 participants, with 58% from Yangon and 42% from Mandalay. Sociodemographic details, knowledge, attitudes, and self-reported practices related to Indoor Air Pollution (IAP) were assessed using an online self-reported questionnaire. Knowledge was scored based on correctly identifying sources, possible health effects, and mitigation approaches. Attitude questions utilized 4-point Likert scales, while practice questions employed a binary response (yes/no). Frequencies were used as summaries for sociodemographic, knowledge, attitudes, and practices.

Results: Most participants correctly identified cooking fuel (80%), poor ventilation (69.33%), and mold (62%) as sources of pollution. Furthermore, 82.67% of respondents identified eye, nose, and throat irritation as health effects of prolonged exposure to indoor air pollution. Regarding management systems, the highest response (95.33%) indicated opening doors and windows for ventilation. 68.67% strongly agreed that air quality is important but 60.7% felt they lacked control over home air quality. Many participants reported opening windows for ventilation (92.96%) and avoiding indoor smoking (79.33%), while only 28% used air purifiers.

Conclusion: The majority of respondents could identify sources of Indoor Air Pollution (IAP) in the house, possible health effects, and IAP management strategies. Few respondents identified furniture and home renovation as sources. Respondents agreed that air quality is important. However, only a few of them reported using an air purifier. An educational intervention related to Indoor Air Pollution (IAP) should be provided to enhance a better understanding of IAP in Myanmar.

Keywords: Indoor air pollution, Knowledge, Attitudes, Practices, Myanmar

1. Introduction

Most of the global population around 50% now lives in cities, a proportion projected to rise to 68% by 2050 [1, 2]. Air pollution has short and long-term health effects [3]. Though lower risk than direct exposures, indoor air pollution is linked to lung cancer. Nearly 3 billion worldwide use solid fuels, implicated in over 4 million premature deaths in 2012 [4].

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though little comparative data exists on risks versus global scenarios. More research is needed on pollution levels and impacts in Myanmar’s rapidly urbanizing context [5].

Indoor air pollution is contributed by the presence of harmful pollutants within infrastructures or buildings such as offices, school, etc. The pollutants (IAP) are comprised of physical, chemical, and biological pollutants [6]. Physical pollutants refer to elements like particulate matter, smoke, and dust particles. In contrast, chemical pollutants may include compounds such as carbon monoxide, nitrogen and sulfur oxides, volatile organic compounds, formaldehyde, and radon. These stem from everyday household day to day items like cleaning agents, solvents, and paints, or from combustion activities linked with domestic appliances like heaters, stoves, or fireplaces [7]. Biological pollutants typically constitute living organisms or derivatives of living organisms that can compromise indoor air quality. These incorporate bacteria, viruses, molds, pollen, pet dander, dust mites, and fragments of insects. These contaminants can originate from diverse sources, such as humans, pets, indoor plants, and various indoor surfaces or objects [8].

Existing research on indoor air quality in Myanmar is limited. This research aimed to assess the knowledge, attitudes, and practices (KAP) related to Indoor Air Pollution (IAP) among residents of Yangon and Mandalay.

2. Method

A pilot online self-reported questionnaire was distributed through an online platform for 3 consecutive days. The total number of respondents was 165. After applying inclusion and exclusion criteria, 150 participants were eligible for analysis. The selected study areas is urban and densely populated regions of Yangon and Mandalay, Myanmar. Given their relatively high levels of urbanization as compared to other regions of Myanmar and predominant use of solid fuels for cooking, Yangon and Mandalay were selected as the focus cities for this KAP study. They were selected as the primary focus because they are major urban regions with Yangon region having greatest urban population accounting for 70% of the total region while Mandalay is the third largest urbanized population accounting for 36% of the total region population. The targeted population was adults, specifically those over the age of 18 years regardless of their social status or role in their household, residing in the identified areas. This demographic is chosen based on the assumption that adults are typically the decision makers on household practices affecting IAP. This study was approved by The Research Ethics Review Committee for Research Involving Human Research Participants, Group I, Chulalongkorn University (COA No. 249/66).

Sociodemographic details, knowledge, attitudes, and self-reported practices related to IAP were assessed using a self-reported questionnaire. Sociodemographic details include gender, house status, having children aged under 5 years old in house, highest educational attainment, region of stay and having air conditioner (cooling system) and air purifier in house. Knowledge was scored for correctly identifying sources (9 items), health effects (5 items) and mitigation approaches (5 items). Attitude questions (4 items) used 4-point Likert scales. Each item was applied 4-likert scale (Disagree-1, Neutral-2, Agree-3, and Strongly Agree-4). Practice questions (6 items) used a binary response format, with ‘Yes’ and ‘No’. Descriptive statistical analysis was performed. Frequencies were summarized sociodemographic, knowledge, attitudes, and practices.

3. Results

Table 1 shows sociodemographic profile of participants. The study included 150 participants, with 58% (n=87) from Yangon region and 42% (n=63) from Mandalay region. Half of respondents were female (53.3%, n=80). Most respondents had completed graduate education (53.3%, n=80), followed by postgraduate education (29.3%, n=44). Eighty-four percent of respondents did not have children aged under 5 years old in their homes. The majority of participants (86.67%) reported having an air conditioner as their cooling system. However, only 28% had an air purifier in their homes.
Table 1. Sociodemographic profile (n=150)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Variables</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>80</td>
<td>53.33%</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>67</td>
<td>44.67%</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>3</td>
<td>2.00%</td>
</tr>
<tr>
<td>House status</td>
<td>Owner</td>
<td>124</td>
<td>82.67%</td>
</tr>
<tr>
<td></td>
<td>Rental</td>
<td>26</td>
<td>17.33%</td>
</tr>
<tr>
<td>Children aged under 5 years old</td>
<td>No</td>
<td>126</td>
<td>84.00%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>24</td>
<td>16.00%</td>
</tr>
<tr>
<td>Highest educational attainment</td>
<td>Graduate</td>
<td>80</td>
<td>53.33%</td>
</tr>
<tr>
<td></td>
<td>High School</td>
<td>6</td>
<td>4.00%</td>
</tr>
<tr>
<td></td>
<td>Postgraduate</td>
<td>44</td>
<td>29.33%</td>
</tr>
<tr>
<td></td>
<td>Undergraduate</td>
<td>20</td>
<td>13.33%</td>
</tr>
<tr>
<td>Region of stay</td>
<td>Mandalay region</td>
<td>63</td>
<td>42.00%</td>
</tr>
<tr>
<td></td>
<td>Yangon region</td>
<td>87</td>
<td>58.00%</td>
</tr>
<tr>
<td>Air conditioner (cooling system)</td>
<td>No</td>
<td>20</td>
<td>13.33%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>130</td>
<td>86.67%</td>
</tr>
<tr>
<td>Air purifier in house</td>
<td>No</td>
<td>108</td>
<td>72.00%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>42</td>
<td>28.00%</td>
</tr>
</tbody>
</table>

Table 2. Knowledge related to indoor air pollution of participants (N=150)

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Identifying sources of Indoor air pollution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning products</td>
<td>60</td>
<td>40.00%</td>
</tr>
<tr>
<td>Cooking</td>
<td>120</td>
<td>80.00%</td>
</tr>
<tr>
<td>Poor ventilation</td>
<td>104</td>
<td>69.33%</td>
</tr>
<tr>
<td>Mould/fungus</td>
<td>93</td>
<td>62.00%</td>
</tr>
<tr>
<td>Furniture</td>
<td>42</td>
<td>28.00%</td>
</tr>
<tr>
<td>Outdoor air (e.g. haze)</td>
<td>61</td>
<td>40.67%</td>
</tr>
<tr>
<td>Paint / glue</td>
<td>69</td>
<td>46.00%</td>
</tr>
<tr>
<td>Renovation works</td>
<td>45</td>
<td>30.00%</td>
</tr>
<tr>
<td>Smoking indoors</td>
<td>89</td>
<td>59.33%</td>
</tr>
<tr>
<td><strong>Identifying the possible health effects of prolonged exposure to indoor air pollution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>50</td>
<td>33.33%</td>
</tr>
<tr>
<td>Skin rashes</td>
<td>100</td>
<td>66.67%</td>
</tr>
<tr>
<td>Headaches / Dizziness</td>
<td>97</td>
<td>64.67%</td>
</tr>
<tr>
<td>Eye, nose and throat irritation</td>
<td>124</td>
<td>82.67%</td>
</tr>
<tr>
<td>Reduced productivity/ Lethargy</td>
<td>94</td>
<td>62.67%</td>
</tr>
<tr>
<td><strong>Identifying the indoor air pollution management system at home</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using air cleaner</td>
<td>103</td>
<td>68.67%</td>
</tr>
<tr>
<td>Avoid using cleaning products</td>
<td>21</td>
<td>14.00%</td>
</tr>
<tr>
<td>Regularly maintenance the air condition</td>
<td>100</td>
<td>66.67%</td>
</tr>
<tr>
<td>Open door and window</td>
<td>143</td>
<td>95.33%</td>
</tr>
<tr>
<td>Using plant</td>
<td>108</td>
<td>72.00%</td>
</tr>
</tbody>
</table>

Table 2 presents the knowledge related to indoor air pollution of respondents. The majority correctly identified cooking (80.00%, n=120), poor ventilation (69.33%, n=104), and mold/fungus (62.00%, n=93) as sources of indoor pollution. The most commonly known health effects of indoor air pollution included eye, nose, and throat irritation (82.67%, n=124), headaches/dizziness (64.67%, n=97), and reduced productivity/laziness (62.67%, n=94). The majority of respondents
(95.33%, n=143) identified ‘Open door and window’ as the main indoor air pollution management system, while the least indoor management was ‘Avoidance of using cleaning products’ (14.00%, n=21).

Table 3 presents the attitudes of respondents towards indoor air pollution. The majority of respondents (68.67%) strongly agreed that ‘good air quality is important’. Additionally, 48.67% disagreed with having poor indoor air quality in their homes sometimes. A significant portion (60.67%) agreed that they have little control over indoor air quality at home. Only 38% expressed a strong willingness to make changes in their lifestyle to reduce indoor air pollution. In the practice related to indoor air pollution
management (Fig. 1), 92.67% of respondents reported regularly opening windows or doors for ventilation. Moreover, 56.67% tried to avoid using dirty cooking fuel and 79.33% reported not smoking indoors. However, only 28% of them used an air purifier.

4. Discussion

Most respondents correctly identified cooking, poor ventilation, and would growth as contributors to indoor air quality issues. Eye, nose, and throat irritation, headaches/dizziness, and reduced productivity/lethargy were commonly identified as possible health effects. Most of them agreed the air quality is important but had less control over indoor air quality at home. The main practice was opening windows or doors for ventilation, followed by not smoking indoor.

Air pollution becomes a major public health concern in Myanmar. Outdoor PM2.5 and PM10 levels in residential and commercial areas in Myanmar were exceeded the WHO reference values [9]. Previous study in Myanmar also demonstrate that the indoor use of cooking fuels that cause indoor air pollution, such as firewood and charcoal, is a considerable risk factor for human health [10]. Our results found that 92.67% of respondents regularly open windows or doors for ventilation, and 79.33% report not smoking indoors. These findings align with the study by Aung et al. [11], which assessed outdoor and indoor air quality in Yangon, Myanmar. The study found that 2 out of 3 houses in crowded areas use natural ventilation systems and air conditioning. Additionally, only 1 out of 3 houses reported tobacco smoking. Gaps existed regarding more severe and less obvious risks like lung cancer and formaldehyde emissions from pressed wood furniture. Only around half were cognizant of cancer risks, while just 28% knew about risks from common furnishings. This demonstrates that despite a baseline understanding of IAP’s basic impacts, knowledge deficiencies persist surrounding specific major contributors to indoor pollution. As demonstrated in previous study that household characteristics plays a pivotal role in indoor exposure, this could lead to concern-able risks that have a big impact [12]. Public messaging and educational initiatives must emphasize these formaldehyde and carcinogen risks to build comprehensive IAP awareness.

In terms of attitudes, the majority agreed indoor air quality is important and expressed willingness to allocate more resources towards home improvements for better air. This coincide with the previous study conducted in China [13]. However, over 60% simultaneously felt they have little control over their home air quality. This disconnects between valuing air quality and perceiving capacity to act reveals a critical barrier. People perceiving little control over IAQ will not act significantly to improve IAQ as perception plays a pivotal role in practice [14]. Even when armed with information and concern, people may feel constrained by external factors like housing quality, costs, infrastructure, and accessibility. Enhancing perceived control through small feasible changes like ventilation during cooking could be pivotal.

These preliminary findings reveal a population with a base knowledge and generally positive attitudes regarding the importance of indoor air quality, yet facing barriers in perceived capacity to mitigate risks, as well as gaps in translating awareness into the frequent adoption of preventive practices. However, the willingness expressed by many residents signals receptiveness to interventions aimed at converting positive intentions into actual behaviors. There remain substantial opportunities to build upon the existing foundations through synergistic awareness-raising, community empowerment, motivational, and policy strategies.

References


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