Chulalongkorn Medical Journal

Volume 64
Issue 2 *April 2020*

Article 6

4-1-2020

Prevalence of vitamin D deficiency in patients with schizophrenia at King Chulalongkorn Memorial Hospital (P. 159)

Thanaporn Phengkaew

Atapol Sughondhabirom

Follow this and additional works at: https://digital.car.chula.ac.th/clmjournal

 Part of the Medicine and Health Sciences Commons

Recommended Citation

Phengkaew, Thanaporn and Sughondhabirom, Atapol (2020) "Prevalence of vitamin D deficiency in patients with schizophrenia at King Chulalongkorn Memorial Hospital (P. 159)," *Chulalongkorn Medical Journal*: Vol. 64: Iss. 2, Article 6.
Available at: https://digital.car.chula.ac.th/clmjournal/vol64/iss2/6

This Article is brought to you for free and open access by the Chulalongkorn Journal Online (CUJO) at Chula Digital Collections. It has been accepted for inclusion in Chulalongkorn Medical Journal by an authorized editor of Chula Digital Collections. For more information, please contact ChulaDC@car.chula.ac.th.

Chula Med J Vol. 64 No. 2 April - June 2020;159-165 DOI : 10.14456/clmj.2020.20

Original article

Prevalence of vitamin D deficiency in patients with schizophrenia at King Chulalongkorn Memorial Hospital

Thanaporn Phengkaew, Atapol Sughondhabirom*

Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Background: Vitamin D is considered a neurosteroid hormone which can impact brain development and normal brain function, as well as inflammatory and immunological process. Several risk factors of schizophrenia such as season of birth, latitude and migration are linked to vitamin D deficiency. This study aimed to investigate the prevalence of vitamin D deficiency in patients with schizophrenia and investigate relationship between vitamin D levels and schizophrenia.

Objective: To study the prevalence of vitamin D deficiency among patients with schizophrenia at King Chulalongkorn Memorial Hospital.

Methods: Cross-sectional descriptive study, data were collected from schizophrenic patients at King Chulalongkorn Memorial Hospital. Questionnaire on personal data and sun exposure, assessment of psychological illness based on Positive and Negative Syndrome Scale in Thai version (PANSS-T) were obtained and blood 25-hydroxy vitamin D (25 (OH) D) levels were analyzed. The prevalence of vitamin D deficiency was assessed and presented in frequency and percentage, Chi-square test was used to identify factors contributing to vitamin D levels. Pearson's correlation was used to identify factors relating to vitamin D levels. Spearman's rank correlation was used to assess the relationship between vitamin D levels and PANSS-T score. Multiple linear regression analysis was used to identify factors predicting vitamin D levels.

Results: There were 88 subjects who participated in this research project: mean age of 40.8 ± 10.8 years old; 62.5% male; mean vitamin D level of 21.53 ± 8.568 ng/ml. The prevalence of vitamin D deficiency is 45.5% - mean PANSS-T score of 45.56 ± 9.56. Based on the correlation analysis, vitamin D levels are negatively correlated with body mass index (BMI) (r = - 0248, P = 0.017). Vitamin D levels are not related to PANSS-T scores. In addition, Factors predicting vitamin D levels are BMI, sex and duration of illness ($P < 0.05$).

Conclusions: The study reveals that 45.5% of schizophrenic patients treated at King Chulalongkorn Memorial Hospital had vitamin D deficiency. There is a negative correlation between vitamin D levels and BMI, sex and duration of illness. Factors predicting vitamin D levels are BMI, sex and duration of illness. The study demonstrates no relationship between vitamin D levels and PANSS-T score,

Keywords: Vitamin D deficiency, schizophrenia, Positive and Negative Syndrome Scale in Thai version (PANSS-T).

Schizophrenia is one of the severe mental disorders that cause disability, and subsequently cause health and economic, and social impacts. According to a recent study, the prevalence of schizophrenia is 3.3 per thousand in the world population.[1] Global Epidemiology and Burden of Schizophrenia reports that schizophrenia accounts for a total of 13.5 million years lost due to illness and disability (95% UI: 9.9 – 16.7), based on the global population of schizophrenia.[2]

At present, attempts have been made to investigate the relationship between vitamin D levels and schizophrenia, following the discovery of the role of vitamin D as a neurosteroid hormone which can impact brain development and normal brain function, as well as inflammatory and immunological process. There are many risk factors linked with vitamin D deficiency, including season of birth, latitude and migration.[3]

Studies conducted overseas reports high prevalence of vitamin D deficiency in patients with schizophrenia.[4] Vitamin D deficiency is associated

***Correspondence to: Atapol Sughondhabirom**, Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Received: March 6, 2019
Revised: May 14, 2019
Accepted: June 25, 2019

with schizophrenia. In Thailand, there have been a number of studies on vitamin D deficiency among the general population; however, none of these have yet explored vitamin D deficiency among schizophrenia. It is an intention of this research project to address this research gap. The findings obtained from this research will be applied in the future.

Materials and methods

This is a cross-sectional descriptive study that focuses on patients with schizophrenia who were treated at the Department of Psychiatry, King Chulalongkorn Memorial Hospital.

The sample size is calculated by the formula

$N = Z^2pq/d^2$

$P = 0.653$ (according to Valipour G, *et al*.[6])

After calculation, the adequate sample size is 88.

Inclusion criteria was used in selecting participants: people aged between 18 - 60, clinically diagnosed of schizophrenia according to the DSM- 5 criteria, treated at the Department of Psychiatry, King Chulalongkorn Memorial Hospital, who are capable of listening, speaking, reading and writing Thai.

Data were collected between May 2018 and January 2019, after the research ethics approval was granted by the Research Ethics Committee of the Faculty of Medicine, Chulalongkorn University (COA 205/2018). Prior to data collection, each participant was informed about the research objectives and gave their written consent to participate in this research voluntarily.

The questionnaire comprises three parts including: 1) personal data; 2) sunlight exposure; and 3) assessment of psychological illness based on Positive and Negative Syndrome Scale in Thai version (PANSS-T) assessment.

The questionnaire collected the subjects' personal data including sex, age, weight, height, body mass index (BMI), treatment status, marital status, current occupation, housing, personal illness and medications used, duration of illness, history of drug use, and family history of schizophrenia.

The questionnaire also collected data on sunlight exposure, including sunlight exposure time (min), time of sunlight exposure and the season when the questionnaire is responded.

The Thai version of Positive and Negative Syndrome Scale (PANSS) was translated by Tana Nilchaikovit MD, *et al*., from Kay, Fiszbein and Opler (1987)'s Positive and Negative Syndrome Scale (PANSS), a standard tool widely used in assessing the symptom severity of the schizophrenia. It comprises of 3 subscales including 7 positive scales, 7 negative scales, and 16 general psychopathology scales. Each symptom question is rated on a 7-point scale. Each scale indicates the degree of symptom severity. It is also found that each subscale shows good internal consistency: alpha coefficients ranging from 0.78 to 0.83 ($P < 0.001$).

Blood samples were collected from patients after responding to the questionnaire. Venipuncture was used to collect blood specimens; 5 ml of blood (equivalent to 1 teaspoon) was drawn from vein in the inner side of the upper arm and then inserted in tube containing anticoagulant before being sent to the Center for Medical Diagnostic Laboratories, King Chulalongkorn Memorial Hospital to measure serum 25-hydroxy vitamin D. (25 (OH) D) levels.

Statistical analysis

Statistical data were analyzed by statistical package for the social sciences (SPSS) for Window Version 22.0 which reports the prevalence of vitamin D deficiency in frequency and percentage. Data were expressed as mean ± standard deviation (SD). Then, Chi-square test, Pearson's correlation, Spearman rank correlation and multiple linear regression were used respectively to identify factors related to vitamin D levels.

Results

The research project comprises of a sample of 88 schizophrenic patients: 78 (88.6%) outpatients, 10 (11.4%) inpatients; 55 (62.5%) males, 33 (37.5%) females; their mean age was 40.8 ± 10.8 years, mean BMI of 26.0 ± 4.3 kg/m^2; 78.4% single; 59.1% unemployed, 59.1% with others underlying disease, mean duration of illness 11.5 ± 8.7 years; 56.8% with no history of substance abuse, 69.3% with no family history of schizophrenia (Table 1).

Among the participants, the most common sunlight exposure time is less than 30 minutes (40.9% of the whole sample) and the most common time of sunlight exposure is the morning time (30.7% of the whole sample). Data were collected from 73 participants (83.0%) in the rainy season (mid-May to mid-October) and 15 (17.0%) participants in winter.

Regarding vitamin D levels, it is found that 40 subjects (45.5%) are vitamin D deficient, 34 participants (38.6%) are vitamin D insufficient, and 14 subjects (15.9%) have sufficiency vitamin D levels (Table 2). There is a statistically significant difference in the vitamin D levels between schizophrenics and the general population[8]: differential value = 10.270; 95% confidence interval = 8.4635 - 12.0765; $P < 0.0001$.

Table 1. Demographic characteristics of schizophrenia patients (n = 88).

Characteristics	n (%) or n (mean ± SD)
Sex	
Male	55 (62.5)
Female	33 (37.5)
Age (years)	40.8 ± 10.9 (Min 18, Max 60)
Marital status	
Single	69 (78.4)
Married	13 (14.8)
Widowed	3 (3.4)
Divorced	3 (3.4)
Body weight (kg)	72.0 ± 14.6 (Min 45.7, Max 119)
Height (cm)	165.8 ± 8.7 (Min 148, Max 185)
BMI (kg/m^2)	26.0 ± 4.3 (Min 17.48, Max 38.05)
Setting	
Outpatient	78 (88.6)
Psychiatric inpatient	10 (11.4)
Employment status	
Unemployed	48 (54.5)
Civil servant	4 (4.5)
Company employee	5 (5.7)
Business owner	15 (17.0)
Employee	9 (10.2)
Other	7(8.0)
Address	
Bangkok Metropolitans region	72 (81.8)
Others	16 (18.2)
Underlying disease	
Yes	52 (59.1)
No	36 (40.9)
Other medications	
Yes	68 (77.3)
No	20 (22.7)
Drug allergy	
Yes	12 (13.6)
No	76 (86.4)
Duration of illness (years)	1.5 ± 8.7 (Min 1, Max 40)
History of substance use	
Yes	38 (43.2)
No	50 (56.8)
Family history of psychiatric illness	
Yes	27 (30.7)
No	61 (69.3)
Sunlight exposure time (mins)	
None	14 (15.9)
< 30	36 (40.9)
31 - 60	23 (26.1)
61 - 180	15 (17.0)
>180	0 (0.0)
Time of sunlight exposure	
None	14 (15.9)
Morning	27 (30.7)
Midday	17 (19.3)
Evening	12 (13.6)
Morning and midday	10 (11.4)
Morning and evening	8 (9.1)
Season of sampling	
Summer	0 (0.0)
Rainy	73 (83.0)
Winter	15 (17.0)

Table 2. Percentage of volunteers by 25 (OH) D levels.

25 (OH) D levels (ng/ml)	n (%)
25 (OH) D level	21.5 ± 8.6 (min 4.0, max 48.3)
< 20 (deficiency)	40 (45.5)
20 - 29.99 (insufficiency)	34 (38.6)
≥ 30 (sufficiency)	14 (15.9)

The sample's mean score is 45.6 ± 9.6 (min 30, max 75): PANSS positive = 11.5 ± 4.2 (min 7, max 24); negative = 10.0 ± 2.8 (min 7, max 22); general psychopathology = 24.0 ± 4.9 (min 16, max 41).

There is a negative correlation between vitamin D levels and BMI (r = - 0.294, P = 0.006) and body weight (r = - 0.223, P = 0.036) (Table 3). According to Chi-square test, there is no other factor linking with vitamin D levels. Also, no correlation between vitamin D levels and PANSS-T scores is found, in spite of the variation of vitamin D according to BMI (Table 4).

It is found that BMI, sex, and duration of schizophrenia ($P < 0.05$) are factors predicting vitamin D levels of schizophrenics ($P < 0.05$) (Table 5).

Table 3. Pearson's correlation between vitamin D levels and variable factors.

Variable factors	Vitamin D levels	
	Pearson's correlation coefficiency	*P* - value
Age	0.410	0.707
Body weight	- 0.223	0.036*
Height	0.101	0.351
Body mass index	- 0.294	0.006**
Duration of illness	0.207	0.053

*$P < 0.05$, **$P < 0.01$

Table 4. Association between serum total vitamin D levels and clinical evaluation (Spearman rank correlation).

PANSS-T	Vitamin D levels (adjusted)	
	Correlation coefficiency	*P* - value
Positive scale	0.184	0.086
Negative scale	-0.120	0.915
General psychopathology scale	0.128	0.234
PANSS-T total score	0.164	0.127

*$P < 0.05$, **$P < 0.01$

Table 5. Factors predicting vitamin D levels by multiple linear regression.

	Unstandardized coefficients		Standardized coeffocients	*t*	Sig.	95% CI	
	B	Std. Error	Beta			Lower bound	Upper bound
BMI	- 0.490	0.201	- 0.248	- 2.432	0.017*	- 0.891	- 0.089
Gender	4.880	1.860	0.277	2.623	0.010*	1.177	8.583
Duration of llness	0.297	0.110	0.305	2.691	0.009**	0.077	0.516

*$P < 0.05$, **$P < 0.01$

Discussion

The study found the prevalence of vitamin D deficiency among patients with schizophrenic patients treated at King Chulalongkorn Memorial Hospital is 45.5%, with a mean vitamin D levels of 21.5 ± 8.6 ng/ml. When compared with the prevalence of vitamin D deficiency in the Thai population according to the 2008 national health survey in Thailand, (5.7%, mean vitamin D levels of 31.8 ± 8.5 ng/ml[8]), it can be concluded that schizophrenic patients have more tendency of experiencing vitamin D deficiency than the general population. Based on the mean difference calculation, there is a significant difference in vitamin D levels between schizophrenic patients and the general population, corresponding with an earlier research conducted overseas which reports the prevalence of vitamin D deficiency among schizophrenic patients as 65.3%. It is also found in the research that those with vitamin D deficiency has a 2.16 higher risk of schizophrenia. Also, the findings in the research agree with a study conducted by Akinlade KS, *et al*.[9] which reveals that a vitamin D deficiency symptom is more common among schizophrenics than the general population. However, to date, the causal relationship between vitamin D deficiency and schizophrenia and the relationship between vitamin D deficiency and duration and period of light exposure are not yet found.

Regarding factors associating with vitamin D deficiency, this study found that vitamin D levels is negatively associated with BMI and body weight, which corresponded to an earlier study conducted by Lagunova Z, *et al*. [10], which reported a negative relationship between vitamin D and BMI, and indicated a high prevalence of vitamin D deficiency among people with BMI ≥ 40 kg/m^2. People with higher vitamin D deficiency are likely to have more body fat, being a secondary storage of lipid soluble vitamins (including vitamin D). As animal model studies confirm, it is found that adipose tissue can store between 10 and 12.0% of the total of vitamin D supplement taken. Also, to be noted, the release of vitamin D from adipose tissue is a slow process- a mechanism preventing toxic effects of vitamin D in the active form and maintaining vitamin D at an adequate level.

The study found no relationship between vitamin D levels and each subscale (comprising of positive scale, negative scale and general psychopathology scale) of the PANSS-T assessment. This corresponded with a study conducted by Kehinde, *et al*. which found no relationship between vitamin D levels and PANSS results, being classified into mildly, moderately, moderately and severely ill. The findings in this study partially correspond with what is discovered by Nerhus M.[11]: the relationship between vitamin D levels and the excitement and the disorganize (positive) syndrome is not identifiable. However, Nerhus concludes that low vitamin D levels is responsible for negative syndromes.

Also, the study contradicts with Prasanty N, *et al*. [12] who found a negative relationship between vitamin D levels and PANSS total score; lower vitamin D levels corresponding with higher total PANSS score. To explain, the relationship between vitamin D levels and negative syndromes is attributed by the neuroprotective effect of vitamin D that prevents oxidative stress. [13] It is also hypothesized that negative symptoms are contributed by oxidative stress. [14, 15] Based on multiple linear regression, the research found that BMI, sex and duration of illness are factors that are significantly related to vitamin D levels.

The role of BMI found in this study agrees with a number of studies made earlier, such as a study conducted by Kannan S, *et al*.[16] that pinpoints the role of BMI in determining vitamin D levels among obese children (where BMI Z- score e" 2.5SD implies higher risk of vitamin D deficiency). Similarly, in a study conducted by Delle MS, *et al*. [17] on dependent elderly women, it is concluded that BMI is a significant factor predicting vitamin D levels. It is founded that people with a high BMI level have more tendency to experience vitamin D deficiency than those with a normal BMI.

The research finds that sex is a factor responsible for low vitamin D levels, yet incapable of pinpointing which one has a more significant impact. According to Verdoia M, *et al*. [18], sex is a significant factor determining vitamin D levels: females tending to have a lower vitamin D levels than males. On the contrary, the research conducted by AlQuaiz AM, *et al*. [19], males have a lower vitamin D levels than females. However, this differing outcomes are possibly derived from different types of population involved in each research study.

The research findings do not match with another research conducted by Lally J, *et al*. [20] on vitamin D deficiency among patients with psychosis syndrome, where duration of illness is not related to vitamin D levels. Based on a study of Yüksel RN, *et al*.[21], after investigating the relationship vitamin D levels and

psychotic psychopathology, it is concluded that vitamin D levels is not linked with the duration of illness, although acutely psychosis patients have lower vitamin D levels than those during the remission stage.

There are some limitations in this study. Due to the nature of the research design, this study can only reveal the prevalence of vitamin D deficiency and factors linked with vitamin D levels. It does not provide sufficient data for determining causal relationships between these elements. The findings only cover schizophrenic patients treated at King Chulalongkorn Memorial Hospital, which is insufficient for representing other population groups. Another shortcoming of this research is the absence of the data on psychiatric drugs used by patients. It is also noted that some drugs can impact BMI values, a significant factor leading to vitamin D deficiency. More studies can be done on other variables determining vitamin D levels such as skin tone, amount of body fat, dietary consumption, personal syndromes that affects vitamin D levels such as digestion diseases, liver diseases, kidney diseases, etc. Further investigations are needed on vitamin D supplementation among schizophrenic patients with vitamin D deficiency. Ideally, this could be a comparative study on pathological changes in patients before and after vitamin D supplementation.

Conclusion

The study reveals that the prevalence of vitamin D deficiency among patients with schizophrenia in King Chulalongkorn Memorial Hospital is 40.0%. Vitamin D deficiency is related to BMI. BMI, sex and duration of schizophrenia are factors predicting vitamin D levels, and no correlation between vitamin D levels and PANSS-T scores is found. Therefore, it can be suggested from the research that schizophrenic patients should have their vitamin D levels checked, since vitamin D deficiency is commonly found among schizophrenic patients.

Acknowledgements

The researchers would like to thank Assistant Professor Dr. Tana Nilchaikovit for his permission to use the Thai version of Positive and Negative Syndrome (PANSS-T).

Conflict of interest

The authors, hereby, declare no conflict of interest.

References

1. Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. PLoS Med 2005;2:e141.
2. Charlson FJ, Ferrari AJ, Santomauro DF, Diminic S, Stockings E, Scott JG, et al. Global epidemiology and burden of schizophrenia: findings from the global burden of disease study 2016. Schizophr Bull 2018;44: 1195-203.
3. Chiang M, Natarajan R, Fan X. Vitamin D in schizophrenia: a clinical review. Evid Based Ment Health 2016;19:6-9.
4. Boerman R, Cohen D, Schulte PF, Nugter A. Prevalence of vitamin D deficiency in adult outpatients with bipolar disorder or schizophrenia. J Clin Psychopharmacol 2016;36:588-92.
5. Chaiyodsilp S, Pureekul T, Srisuk Y, Euathanikkanon C. A cross section study of vitamin D levels in Thai office worker. Bangkok Med J 2015;9:8-11.
6. Valipour G, Saneei P, Esmaillzadeh A. Serum vitamin D levels in relation to schizophrenia: a systematic review and meta-analysis of observational studies. J Clin Endocrinol Metab 2014;99:3863-72.
7. Nilchaikovit T, Uneanong S, Kessawai D, Thomyangkoon P. The Thai version of the Positive and Negative Syndrome Scale (PANSS) for schizophrenia: criterion validity and interrater reliability. J Med Assoc Thai 2000;83:646-51.
8. Chailurkit L, Aekplakorn W, Ongphiphadnakul B. Regional variation and determinants of vitamin D status in sunshine-abundant Thailand. BMC Public Health 2011;11:853.
9. Akinlade KS, Olaniyan OA, Lasebikan VO, Rahamon SK. Vitamin D levels in different severity groups of schizophrenia. Front Psychiatry 2017;8:105.
10. Lagunova Z, Porojnicu AC, Lindberg F, Hexeberg S, Moan J. The dependency of vitamin D status on body mass index, gender, age and season. Anticancer Res 2009;29:3713-20.
11. Nerhus M. Migration and vitamin D in psychotic disorders-Across sectional study of clinical and cognitive correlation [Thesis]. Oslo, Norway: University of Oslo; 2017.
12. Prasanty N, Amin MM, Effendy E, Simbolon J. Low vitamin D serum level increases severity symptoms in schizophrenic patients measured by Positive and Negative Symptoms Scale (PANSS) in Batak Tribe Sumatera Utara, Medan-Indonesia. Bali Med J 2018;7: 249-54.

13. Wrzosek M, £ukaszkiewicz J, Wrzosek M, Jakubczyk A, Matsumoto H, Piątkiewicz P, et al. Vitamin D and the central nervous system. Pharmacol Rep 2013;65: 271-8.
14. Albayrak Y, Ünsal C, Beyazyüz M, Ünal A, Kuloğlu M. Reduced total antioxidant level and increased oxidative stress in patients with deficit schizophrenia: a preliminary study. Prog Neuropsychopharmacol Biol Psychiatry 2013;45:144-9.
15. Sullivan EM, O'Donnell P. Inhibitory interneurons, oxidative stress, and schizophrenia. Schizophr Bull 2012;38:373-6.
16. Kannan S, Visintainer P, Ganguri HB, Conroy R, Gudala M, Wittcopp C. Body mass index is a strong predictor of vitamin D deficiency in multiethnic obese children. Obes Res Open J 2016;4:11-8.
17. Delle MS, Di Fulvio P, Iannetti E, Valerii L, Capone L, Nespoli MG, et al. Body mass index represents a good predictor of vitamin D status in women independently from age. Clin Nutr 2018 pii: S0261-5614(18)30089-X.
18. Verdoia M, Schaffer A, Barbieri L, Di Giovine G, Marino P, Suryapranata H, et al. Impact of gender difference on vitamin D status and its relationship with the extent of coronary artery disease. Nutr Metab Cardiovasc Dis 2015;25:464-70.
19. AlQuaiz AM, Kazi A, Fouda M, Alyousefi N. Age and gender differences in the prevalence and correlates of vitamin D deficiency. Arch Osteoporos 2018;13:49.
20. Lally J, Gardner-Sood P, Firdosi M, Iyegbe C, Stubbs B, Greenwood K, et al. Clinical correlates of vitamin D deficiency in established psychosis. BMC Psychiatry 2016;16:76.
21. Yüksel RN, Altunsoy N, Tikir B, Cingi Külük M, Unal K, Goka S, et al. Correlation between total vitamin D levels and psychotic psychopathology in patients with schizophrenia: therapeutic implications for add-on vitamin D augmentation. Ther Adv Psychopharmacol 2014;4:268-75.