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Abstract

Background: Triglycerides (TG) and high-density lipoprotein (HDL) levels were significantly higher in children and adolescents with dyslipidemia. Elevated low-density lipoprotein (LDL) levels have been linked to clinical cardiovascular disease. This study aimed to examine the relationship between serum TG and LDL cholesterol levels with nutritional status in adolescents.

Methods: This observational, cross-sectional study was carried out from December 2021 to April 2022. The research participants were 145 teenagers aged 13–18 years old living in the Special Region of Yogyakarta, Indonesia. Participants were chosen by consecutive sampling. At baseline, each participant’s nutritional status and TG and LDL serum levels were measured. Using CDC body mass index guidelines for teenagers, we assessed the nutritional status of all the participants and divided them into 2 groups (normal versus obese/overweight).

Results: Borderline and high levels of LDL were found in 33 participants (22 %) in the obese/overweight group; in addition, in the obese/overweight group, 38 participants (26 %) had borderline or high TG levels. Based on a chi-square test, there was a statistically significant relationship between serum LDL levels and the nutritional status of adolescents (p = 0.009). The difference in serum TG levels based on nutritional status was not statistically significant (p = 0.081).

Conclusion: There was a positive relationship between nutritional status and serum LDL levels, but not TG levels. Serum levels of LDL can be used as cardiometabolic markers associated with obesity and overweight status among adolescents.

Keywords: Obesity, Dyslipidemia, Nutritional status, Adolescents, Indonesia

1. Background

Obesity is a public health problem that requires special attention due to its high prevalence and negative health consequences. Obesity impairs physiological function and raises the risk of cardiometabolic disease. Obesity in children is becoming more common, as well as comorbidities such as high blood pressure, atherosclerosis, left ventricular hypertrophy, obstructive sleep apnea, asthma, polycystic ovary syndrome, type 2 diabetes mellitus, fatty liver, abnormal blood lipid levels (dyslipidemia), and metabolic syndrome. Obesity in children and adolescents is also linked to obesity later in life \[1,2\].

Obesity for adolescents can be determined using the Centers for Disease Control and Prevention (CDC) growth chart based on age and sex. Obesity
in adolescence is defined as having Body Mass Index (BMI) higher than 95th percentile based on adolescents of the same age and sex in the year 2000 CDC growth chart, while being overweight is defined as having a BMI between the 85th and 95th percentiles in the 2000 CDC growth charts.

The incidence of obesity has increased yearly worldwide, including in Indonesia. Abarca-Gómez et al. [3] evaluated trends in body mass index in children, adolescents, and adults in parts of Asia by collecting data from 2416 population-based studies measuring height and weight in 128.9 million participants aged 5 years and over. In this study, there were 31.5 million participants who were aged 5–19 years. There is also growing concern about the rise of obesity among adolescents. A 2009 research study conducted in Shanghai found that the prevalence of being overweight and obese among high school students were 16.3 % and 8.5 %, respectively [3].

Indonesia has a high prevalence of overweight and obesity. The prevalence varies by region, but it is quite concerning. Obesity was prevalent in 7.2 % of junior high school students in urban areas and 2 % in rural areas [4]. Several studies conducted in Indonesia have documented obesity rates among adolescents. Suryaputra and Nadhiroh [5] found the obesity rate (7.8 %) among all adolescents in Surabaya was 10.5 %, which was higher than the obesity rate (7.8 %) among all adolescents in Surabaya. Another study by Putra et al. [6] found that 10.4 % of children aged 13–18 years old who had a body mass index (BMI) of more than the recommended WHO threshold (Tables 1 and 2). Screening adolescent students at a high school in Semarang by Nuraini and Murbawani [7] showed that 12.87 % were overweight and 11.46 % were obese. The number of obese adolescents in the age range of 13–15 years in the Special Region of Yogyakarta were quite large, according to the 2018 Basic Health Research [8].

Metabolic syndrome is an important comorbid condition for obese children and adolescents. The Indonesian Pediatrician Association (IPA) [9] set the criteria for metabolic syndrome, which includes: 1) abdominal obesity as indicated by a waist circumference in the 80th percentile or higher; and 2) two or more additional parameters, namely: 1) hypertension, 2) high-density lipoprotein (HDL) cholesterol levels of 40 mg/dl, 3) triglyceride (TG) levels of 110 mg/dl, and 4) fasting blood glucose level of 100 mg/dl or type 2 diabetes mellitus (T2DM) [10].

There have been various studies examining the prevalence of metabolic syndrome internationally and in Indonesia. A meta-analysis by Friend et al. [11], in all, 378 studies published since 2003 were identified, and of these 85 research studies reported that the prevalence of metabolic syndrome was 3.3 % of the general population, 11.9 % of the obese children, and 29.2 % of the children with obesity. The Indonesian Pediatrician Association (IPA) [12] cited two studies on the prevalence of metabolic syndrome using the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria. First, there was a study in Jakarta found a 34 % prevalence in 50 obese adolescents aged 10–19 years old. Second, a study in Manado documented a 23 % prevalence in 2000 overweight or obese children and adolescents aged 10–14 years old [12].

Castro et al. [13] explained why obesity is a risk factor for several diseases. Obesity causes chronic low-grade inflammation or parainflammation. Parainflammation has been shown to be a risk factor in type 2 diabetes mellitus (DM2). Proinflammatory cytokine levels also affected cardiovascular risk. Adipose tissue, apart from functioning as a store of energy reserves, also functions as an endocrine organ. This tissue produces adipocytokines, including IL-1, IL-6, IL-8, IFN, TNF, leptin, and resistin. Adipocytokine production and release of these cells induce chronic inflammation and affect other systems, leading to various diseases [13].

Thus, obesity has been linked to an increased risk of hypertension, diabetes, cardiovascular disease, dyslipidemia, kidney failure, and inflammatory responses [14]. The main causes of increased atherosclerosis and cardiovascular disease in patients with dyslipidemia are high levels of total cholesterol, TG, low-density lipoprotein (LDL), and low levels of HDL [15]. Long-term obesity and excessive food consumption cause metabolic system disorders in the form of hypercholesterolemia. The regulation of cholesterol metabolism runs normally if the amount of cholesterol in the blood is sufficient and does not

| Table 1. Baseline characteristics of study participants (N = 145). |
|----------------|---------------|----------------|
| Sex            | Total         | Percentage (%) |
| Male           | 49            | 33.8           |
| Female         | 96            | 66.2           |
| Education      |               |                |
| Junior high school | 32            | 22.0           |
| Senior high school | 113           | 78.0           |
| Nutritional status |              |                |
| Normal         | 79            | 54.5           |
| Overweight and obese | 66           | 45.5           |

*a Normal nutritional status: BMI was <85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.*

*b Overweight and obese: BMI was ≥85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.*

Thus, obesity has been linked to an increased risk of hypertension, diabetes, cardiovascular disease, dyslipidemia, kidney failure, and inflammatory responses [14]. The main causes of increased atherosclerosis and cardiovascular disease in patients with dyslipidemia are high levels of total cholesterol, TG, low-density lipoprotein (LDL), and low levels of HDL [15]. Long-term obesity and excessive food consumption cause metabolic system disorders in the form of hypercholesterolemia. The regulation of cholesterol metabolism runs normally if the amount of cholesterol in the blood is sufficient and does not...
exceed the normal amount needed by the body. However, obesity in children can cause disruptions in the regulation of fatty acids, which raises TG and cholesterol levels. Children who are overweight usually have higher blood cholesterol levels than normal weight children [15]. Shah et al. [15] reported that obese people tended to have high total cholesterol levels.

Comorbidities in obesity are primarily caused by oxidative stress which are a result of increased oxygen consumption and the production of reactive oxygen species (ROS) via excessive mitochondrial respiration leading to cell damage. Demerdash [16] described the role of ROS and oxidative stress in obesity. Oxidative stress includes inflammatory cell infiltration into adipose tissue and excessive ROS production by inflammatory cells. Adipocyte dysfunction occurs and adipokines are secreted, which contribute to the development of several metabolic diseases by disrupting lipid and glucose homeostasis [16]. Excess free fatty acids released from adipose tissue causes lipotoxicity by producing reactive oxygen species (ROS) in the endoplasmic reticulum and mitochondria. The storage of free fatty acids in adipocytes as triglycerides (TG) prevents fatty acid toxicity. Excess storage of TG in adipose tissue ultimately leads to fatty acid release due to increased lipolysis, which is amplified by an increase in sympathetic status that usually occurs in obesity [17].

This study focused on the prevalence of dyslipidemia in overweight and obese adolescents in Indonesia. Specifically, it examined the relationship between LDL and serum TG levels with nutritional status in adolescents. The description of these relationships are expected to provide considerations regarding the measurement of LDL and TG levels in adolescents so that the cardiometabolic risk in adolescents can be examined. The presence of dyslipidemia in adolescents who are overweight and obese may be able to predict cardiovascular risk in these participants.

2. Methods

2.1. Study design

The study had an observational cross-sectional design. The participants were 145 teenagers aged 13 to 18 attending a boarding school located in Yogyakarta's Special Region in Indonesia. Participants were selected from the junior and senior high school clusters, and then from male and female groups within each cluster, employing consecutive sampling. The inclusion criteria for participants included that they were healthy adolescents aged 13–18 years old. Exclusion criteria included participants suffering from acute illness or having a history of liver disorders and other chronic diseases. Age, weight, and height were measured directly on all participants. We calculated the minimum sample size using Equation (1). Assuming that the quantity to be estimated was a binomial proportion and the allowable error was 5 % [18,19], the minimum sample is 183. However, the researchers only got 146 participants because some students withdrew from the study. The boarding school was chosen because students came from various regions/provinces in Indonesia. However, a limitation was that selection of participants was not random. Before sampling, the authors conducted community service in the form of online and offline nutrition education for adolescents. After the adolescents received the education, participants in this activity were offered the opportunity to participate in this research study. Sampling was carried out consecutively.

The sample size calculation formula was:

\[ n = \frac{Z^2 p (1 - p)}{d^2} \]

(1)

Where n is the minimum required sample, Z is the Z-score based on the error rate; assuming a 5 % error rate, the Z-score is 1.96; d is error tolerance, and p is the case proportion in question. In this case, p was the obesity prevalence in Yogyakarta in 2018, which was 14.43 % or 0.14.

We utilized a CDC chart to determine the study participants' nutritional status based on body mass index, age, and sex. Weight and height measurements were carried out by a trained research assistant. Body weight was measured with a digital scale; when being weighed, participants wore minimal clothing. Height was measured using a microtoise, which is a height measuring instrument. When their height was measured, the participants were not wearing shoes and was facing straight ahead. Body mass index was calculated and entered into the CDC chart according to age and sex. The CDC's body mass index (BMI) chart applied to children
aged 2–19 years. This CDC chart was developed in 2000. It was color-coded according to BMI percentiles as follows: 1) red: BMI was < 5th percentile, 2) green: BMI was between 5th-85th percentile, 3) yellow: BMI was between 85 and 95th percentile, and 4) red: BMI was > 95th percentile. Additional graphs have been developed for children aged 2–20 years with severe obesity. The percentile line in this chart was included for BMI measurements between 110 and 190 from the CDC’s 95th percentile.

2.2. Low-density lipoprotein (LDL) cholesterol and triglyceride (TG) level measurement

LDL and TG levels were measured spectrophotometrically with venous blood samples. According to the IPA, normal LDL levels in adolescents are <110 mg/dl; LDL levels are considered borderline in the range of 110–129 mg/dl and high if >=130 mg/dl. Meanwhile, normal TG levels in adolescents aged 10–19 years old are below 90 mg/dl. The threshold for borderline TG levels is 90–129 mg/dl; TG levels are considered high for 130 mg/dl and above [9].

2.2.1. Statistical analysis

The chi-square test was used to examine the relationship between serum LDL and TG levels and adolescents’ nutritional status. Statistical analysis was done using SPSS version 25 with a statistical significance level of less than 0.05.

2.2.2. Ethical issues

Consent statements to participate in the study were collected from the participants and their parents. Teachers were only informed the students participation in this study. This study received ethical approval from the Health Ethics and Research Committee of the Faculty of Medicine and Health Sciences, Muhammadiyah University of Yogyakarta. This study was approved by Health Research Ethics Committee Fakultas Kedokteran dan Ilmu Kesehatan Universitas Muhammadiyah Yogyakarta (No. 310/EC-KEPKFKIK UMY/XII/2021).

3. Results

3.1. Characteristics of participants

This study involved 145 adolescents aged 13–19 years old. Table 1 shows the general characteristics of the participants. There were more female participants (n = 96, 66.2 %), than male participants (n = 49, 33.8 %). The highest levels of education attained by the participants were senior high school (n = 113, 78.0 %) and junior high school (n = 32, 22.0 %). The nutritional status of the participants consisted of two levels: overweight/obese (n = 66, 45.5 %) and normal (n = 79, 54.5 %).

3.2. Serum TG and LDL levels

Data on serum TG and LDL cholesterol levels of 145 participants are presented in Table 2. LDL cholesterol had a minimum level of 11.2 mg/dl, maximum level of 220.0 mg/dl, SD of 28.3, and mean of 105.4 mg/dl. Also, TG had a minimum level of 35.9 mg/dl, maximum level of 289.1 mg/dl, SD of 54.5, and mean of 122.6 mg/dl.

3.3. The relationship between serum LDL levels and nutritional status among adolescents

Data for serum LDL levels by nutritional status is summarized in Table 3. Increased serum LDL levels were found more in obese and overweight participants (n = 35, 24.1 %) compared to participants with normal nutritional status (n = 25, 17.2 %). Results from the chi-square test found a statistically significant relationship between serum LDL levels and the nutritional status of adolescents (p = 0.009).

<table>
<thead>
<tr>
<th>LDL levels</th>
<th>Normal</th>
<th>Obese and overweight</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Above normal level</td>
<td>25</td>
<td>17.2</td>
<td>35</td>
<td>24.1</td>
</tr>
</tbody>
</table>

a Normal nutritional status: BMI was <85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.

b Overweight and obese: BMI was ≥85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.

c Normal LDL level: <110 mg/dl.

d Statistically significant at p-value < 0.05.

e Above normal LDL level: ≥110 mg/dl.
3.4. Relationship between serum TG levels and nutritional status among adolescents

Table 4 summarizes serum TG levels and nutritional status among our study participants. Elevated serum TG levels were also found in more obese and overweight participants than participants with normal nutritional status, 38 (26.2 %) versus 34 (23.4 %) participants. However, the difference was statistically insignificant (p = 0.081).

4. Discussion

In this study, participants with obese and overweight nutritional status had higher serum LDL levels than participants with normal nutritional status. The distinction was statistically significant (p = 0.009). It is consistent with the findings of Lozano et al. [20], who found that the proportion of participants with increased total cholesterol levels differed significantly depending on nutritional status. Lozano et al. [20] found that 10.7 % (95 % CI, 10.2 %–11.3 %) of participants with increased total cholesterol levels were in the obese group, 8.6 % (95 % CI, 7.8 %–9.4 %) were in the overweight group, and 6.7 % (95 % CI, 6.2 %–7.1 %) were in the healthy weight group. Mardiah [21] also found a relationship between total cholesterol and LDL levels with central obesity; but obesity was not associated with TG levels. Kaniawati et al. [22] found a relationship between obesity and levels of LDL cholesterol, apolipoprotein B, and small-dense LDL.

TG levels in this study were not significantly different between obese and overweight participants compared to participants with normal nutritional status. This finding follows the research findings of Farizal and Marlina [23], which showed no significant link between obesity and TG levels among college students. Tandra et al. [24] also showed a difference in total and LDL cholesterol levels between obese and non-obese adolescents; but TG and HDL levels did not differ significantly between these two groups. The opposite result, namely, a relationship between obesity and TG levels but no relationship between obesity and LDL levels has also been found previously [25]. Subandrate et al. [26] found there was no relationship between BMI with total cholesterol, LDL cholesterol, or HDL cholesterol in adolescents; but there was a link between BMI and TG levels.

The difference between this study’s finding with those of other studies may be due to differences in the study populations [26]. Another factor that can affect our findings is that total cholesterol, LDL cholesterol, and HDL cholesterol are not lipid components that make up fat stores in the body. These three measurements (total cholesterol, LDL cholesterol, and HDL cholesterol) are components of fat which function for transport or are precursors of body metabolism [27,28].

TGs are fat components consisting of three fatty acids and glycerol. TG levels in the blood mainly come from a diet high in fat and carbohydrates. When the stomach is full, the hormone insulin regulates the metabolism of TG to be stored as reserves in adipocytes. This causes high levels of TG in the blood to be transported and stored in adipocyte tissue, which further increases body weight [27,28].

A limitation of this study was that it did not distinguish between small- and normal-sized LDL cholesterol; small and dense LDL is more atherogenic than normal-sized LDL.

In patients with obesity, hyperlipidemia is considered an independent risk factor for developing Non-alcoholic Fatty Liver Disease (NAFLD). Increased levels of triglyceride (TG) and low-density lipoprotein-cholesterol (LDL-C) are thought to be responsible for the disease. NAFLD may be a clinical finding of primary hypolipidemia characterized by decreased plasma lipids and lipoproteins levels. In a meta-analysis covering a general population of children and young adults published in 2015, the

Table 4. Relationship between serum triglycerides (TG) levels and nutritional status in adolescent study participants.

<table>
<thead>
<tr>
<th>TG levels</th>
<th>Normala</th>
<th>Obese and Overweightb</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Normalc</td>
<td>45</td>
<td>31.0</td>
<td>28</td>
<td>19.3</td>
</tr>
<tr>
<td>Above normal leveld</td>
<td>34</td>
<td>23.4</td>
<td>38</td>
<td>26.2</td>
</tr>
</tbody>
</table>

*Statistically significant at p-value < 0.05.

a Normal nutritional status: BMI was < 85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.

b Overweight and obese: BMI was ≥ 85th percentile for same age and sex as year 2000 Centers for Disease Control (CDC) growth chart.

c Normal TG level in adolescent: < 90 mg/dl.

d Above normal LDL level: ≥ 90 mg/dl.
incidence of non-alcoholic fatty liver disease was found to be 7.8% and 34.2% in obese people [6]. NAFLD in children has steadily become more common, in parallel to the rise in obesity-related cases. In Indonesia, children with obesity were reported as having an incidence of NAFLD of 23–62% [29].

Lipid abnormalities in children and adolescents play an important role later in life in the development of coronary heart disease. Lipid abnormalities are a major cause of morbidity and mortality in Western societies. The American Academy of Pediatrics recommends screening for high cholesterol levels only in children with a family history of hypercholesterolemia or premature coronary heart disease [30].

The role of triglyceride (TG) in cardiovascular disease has long been controversial, at least partially due to the high within-person variability. An elevated TG level is a known biomarker of cardiovascular risk; and hypertriglyceridemia is a component of metabolic syndrome. Recent genetic studies suggest that TGs and TG-rich lipoproteins (TRLs) are related to cardiovascular disease (CVD) rather than simply being a biomarker. The prevalence of hypertriglyceridemia in children and adolescents was 5.9%–8.6% in the general population, which is comparable to other components of dyslipidemia. However, among overweight or obese youth, the prevalence of hypertriglyceridemia increased to 13.8%–31.8% [31].

Physical activity was not included as a variable in this study. It is a risk factor for being overweight and obese, while the independent variable examined in this study was nutritional status. Physical activity of students in boarding schools is relatively the same. Physical activity is a variable that affects nutritional status, but it does not directly affect laboratory parameters.

A limitation of this study was that we assumed the participants' physical activity was similar. Physical activity is a factor for nutritional status. The main research question analyzed in this study was the association between nutritional status and LDL levels. Physical activity has an indirect effect on serum LDL level, which we did not measure in this study. An additional limitation is that the number of participants in our study did not reach the minimum sample size calculated for this study. Furthermore, study participants were not randomly selected.

5. Conclusion

There was a link between nutritional status and serum LDL levels, but there was no link between serum TG levels and nutritional status among adolescent participants in our study. The relationship may provide considerations regarding measuring LDL and TG levels in adolescents to understand cardiometabolic risk in adolescents. Our results suggest that LDL serum levels can be used as cardiometabolic markers associated with obesity and overweight among adolescents. Future study could include more participants and more heterogeneity among participants to achieve more comprehensive results. The suggestion to always measure serum LDL levels in obese patients is relatively new idea; it is not always done in health services. Thus, the presence of increased serum LDL levels in obese children and adolescents, which can impact cardiovascular problems, need to be emphasized in medical education.

Acknowledgments

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Conflicts of interest

None.

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