The correlation of High-Density Lipoprotein (HDL) with adiponectin levels among obese adolescents in Denpasar, Bali, Indonesia

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ABSTRACT

Background: Obesity is a state of Body Mass Index (BMI) above or equal to 25 kg/m2. In obesity, dyslipidaemia can occur alone or together with other comorbid. This situation could affect pro-inflammatory and anti-inflammatory cytokines that lead to health problems. Several parameters assessed in dyslipidaemia conditions include High-Density Lipoprotein (HDL) and adiponectin. This study aims to evaluate the correlation between HDL and adiponectin levels in obese adolescents.

Methods: A cross-sectional observational study was conducted among 33 obese adolescence (0-18 years) who met the inclusion criteria at Junior and Senior High School in Denpasar during August 2018-January 2019 period. Variables evaluated in this study were age, sex, weight, height, BMI, HDL, and adiponectin. The correlation assessment of HDL and adiponectin levels was conducted by Partial Correlation test after controlling age and sex using SPSS version 23 for Windows.

Results: Males (66.7%) were predominant than females (33.30%) with a ratio of 2:1. The average age of respondents was 15.51±0.70 years old. The mean body weight was 91.04±15.40 kilograms, followed by height (163.09±7.40 cm), BMI (34.08±3.90 kg/m²), HDL (43.40±8.00 mg/dl), and adiponectin (4.55±2.1 µg/ml). There was a very weak and not significant correlation by Partial correlation test (r=0.143; p=0.444) between HDL and adiponectin levels.

Conclusion: Our study found there was a very weak and not significant correlation between HDL and adiponectin levels among obese adolescent in Denpasar, Bali, Indonesia.

Keywords: Obese, Adolescents, HDL, Adiponectin

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INTRODUCTION

The number of obese adolescents is increasing notably in morbidity due to obesity such as metabolic syndrome which is characterized by the occurrence of dyslipidaemia.1 Dyslipidaemia is an imbalance of lipid profile, namely increased levels of triglycerides (TG), Low-Density Lipoprotein (LDL), total cholesterol (TC), and decreased levels of High-Density Lipoprotein (HDL).2 In dyslipidaemia, an inflammatory process occurs, which increases pro-inflammatory cytokines and suppression of anti-inflammatory cytokines.3 One of the anti-inflammatory cytokines is adipocytokines in adipose tissue, adiponectin. Adiponectin levels are associated with HDL levels, abdominal fat index, body mass index (BMI) and insulin sensitivity.4

Obese adolescents are adolescents who have the condition, the BMI is at or above the 95th percentile on the CDC 2000 growth curve according to age and sex.5 Obesity can occur at any age, but the most often occurs in the first year of life, ages 5-6 years, and in adolescence.6 The previous study showed that the prevalence of adolescents from 2010 was 1.4%, rising to 7.3% in 2013.6 Centres for Disease Control and Prevention (CDC) obtained data where the percentage of adolescents aged 12 to 19 years who are obese in the United States increased from 5% in 1980 to 21% in 2012.7 8

Bali Province has an overweight and obesity prevalence above the national prevalence for adolescents aged 13-15 years and aged 16-18 years.9 The prevalence of obesity in Denpasar in 2002 was 11% in adolescents aged 11-17 years.9 The prevalence of obesity is 15% in children aged 10-12 years.7 Obese adolescents have elevated TC levels, increased LDL values, decreased HDL values, increased levels of TG and TG: HDL ratio.7 Adiponectin is one of the adipokines that are widely produced and secreted by adipose tissue and has anti-diabetic, anti-inflammatory, anti-atherogenic, and cardioprotective effects.9 11 In obesity conditions, there is an increase in pro-inflammatory cytokines and a decrease in anti-inflammatory cytokines. A study conducted by Hendarto A found that in obese adolescents found variations in adiponectin levels were low and normal, but no significant relationship was found between obesity and adiponectin...
levels.\textsuperscript{12} Other studies have found that adiponectin levels are lower in obesity than others.\textsuperscript{13-15}

Several studies have been conducted to determine the relationship between adiponectin levels and dyslipidemia, but there are not many studies in adolescents. Besides, there were inconsistent results from the previous studies regarding the correlation between HDL and adiponectin levels among obese adolescents. Based on those mentioned above, this study aims to determine the correlation between HDL and adiponectin levels among obese adolescents in Denpasar, Bali, Indonesia.

METHODS

An observational analytical study by the cross-sectional approach has been conducted among 33 obese-adolescents who met the inclusion and exclusion criteria from August 2018 until January 2019 at Junior High School and Senior High School in Denpasar. The inclusion criteria were adolescents aged 0-18 years old, obese, registered at High school in Denpasar, and parents agree to participate in the study. The student who has illnesses of autoimmune disease, chronic disease, malignancy, and use of medication were excluded.

Subjects were enrolled by two-stage random sampling until complete the required sample size. Bodyweight (kg) and height (meters) were examined to calculate the Body Mass Index (BMI). The High-Density Lipoprotein (HDL) (mg/dl) and adiponectin (µg/ml) levels examination was carried out by the Clinical Pathology Laboratory, Sanglah Hospital Denpasar, Bali, Indonesia.

The characteristic of respondents, HDL, and adiponectin levels were recorded and analyzed using SPSS version 23.0 software for Windows. Descriptive data are presented in a frequency distribution, percentage and mean. The normality of data was analyzed with Kolmogorov-Smirnov. The correlation test analyzed with the Pearson test, followed by Partial Correlation test by adjusting the age and sex variables.

RESULTS

The baseline characteristic of the respondents was showed in Table 1. We found that male subjects were predominant (66.70%) compared to female subjects (33.30%). The median age of respondents was 16 (13-17) years old. Based on the anthropometric measurements, the average weight of respondents was 91.00±15.40 kg, followed by height (163.00±7.40 cm), and BMI (34.08±3.90 kg/m\textsuperscript{2}) (Table 1).

This study found that the mean HDL levels in subjects were 43.49±7.9 mg/dl, with 12 (36.40%) subjects were <40 mg/dl (Table 1). The mean of adiponectin levels of respondents was 4.55±2.1 µg/ml. However, the mean adiponectin

| Table 1 | Baseline characteristic of respondents |
|---------|-----------------------------------------|
| Parameter | N=33 |
| Age (year), median (min-max) | 16 (13-17) |
| Sex | |
| Male, n (%) | 22 (66.70) |
| Female, n (%) | 11 (33.30) |
| Weight (kg), mean±SD | 91.00±15.40 |
| Height (cm), mean±SD | 163.00±7.40 |
| BMI (kg/m\textsuperscript{2}), mean±SD | 34.08±3.90 |
| HDL (mg/dL) | |
| < 40, n (%) | 12 (36.40) |
| ≥ 40, n (%) | 21 (63.60) |
| Adiponectin (µg/ml), mean±SD | 4.55±2.10 |
| Male | 4.73±2.43 |
| Female | 4.18±1.61 |

BMI: Body Mass Index; HDL: High-Density Lipoprotein; SD: Standard Deviation

| Table 2 | Bivariate analysis correlation between HDL and Adiponectin |
|---------|---------------------------------|
| Variable | Normality test | Mean ± SD | Correlation coef. (r) | p |
| HDL (mg/dL) | 0.868 | 43.5±7.90 | 0.111 | 0.537 |
| Adiponectin level (µg/ml) | 0.348 | 4.55±2.10 | | |
levels in male subjects were 4.73±2.43 µg/ml and 4.18±1.61 µg/ml in females (Table 1). The bivariate analysis using a Pearson Correlation test was performed and suggested a very weak positive correlation and not statistically significant between HDL and adiponectin levels (r=0.111; p=0.537) (Table 2). Following Pearson analysis, the Partial Correlation test was also carried out by adjusting the age and sex variables. The recent study found a very weak correlation and not statistically significant between HDL land adiponectin levels (r=0.143; p=0.444) (Table 3).

**DISCUSSION**

In this study, the respondents were adolescents (aged 13-17 years) with obesity and dominated by males. This result is different from the study by Nem et al., which found that adiponectin levels were lower in males than in females. This difference in results is likely due to the different number of respondents in the male subjects was higher compared with female. The mean level of adiponectin obtained in this study was higher in males. A large cohort study involving 1193 children without obesity in Denmark showed that in children aged 13 to 17 years had a 50th percentile of adiponectin levels such as 5.1 µg/ml, 4.7 µg/ml, 5.1 µg/ml, 2.9 µg/ml, and 3.1 µg/ml respectively with 25th percentile values were 1.6 µg/ml, 0.9 µg/ml, 1.5 µg/ml, 1.4 µg/ml, and 1.5 µg/ml in a row. Our findings suggest that the adiponectin levels in normal children age 13 to 17 years ranged from 1.38 µg/ml to 16.98 µg/ml, which shows a higher range than the range in the previous study. However, a different result was also found from the earlier study that showed the average adiponectin level in normal children aged 5 to 18 years was 12.62±6.2 µg/ml while in obese children was significantly lower at 9.09±3.9 µg/ml. Consistent results were also shown from studies conducted by Savolainen MJ et al., involving 180 obese children aged 10 to 18 years and found that the average level of adiponectin was 4.55 µg/ml in the group of children without metabolic syndrome and 2.95 µg/ml in the children with metabolic syndrome.

In vitro study showed adiponectin produce mostly in visceral adipose tissue. Girls have a central fat mass more than boys, although they have bigger waist circumference. With increasing BMI or waist circumference, girls showed a significantly steeper fall in HDL cholesterol levels than boys. It is possible that the decline in adiponectin levels with BMI, only seen in girls, could contribute to these sex differences.

In this study, a not statistically significant of a very weak positive correlation between adiponectin and HDL levels in obese adolescents at Junior and Senior High School in Denpasar. Based on the mean difference test, no significant difference in adiponectin levels was found in the normal or decreased HDL group. However, it can be seen that the average adiponectin level in the lower HDL group was slightly lower than the normal HDL group (4.48±2.10 µg/ml vs 4.58±2.20 µg/ml).

Although these results differ from most previous studies, studies conducted by Eslamian M et al. also showed an insignificant positive correlation between adiponectin levels and HCL levels (r=0.151; p=0.08). They also found that a significant correlation of adiponectin levels to a new lipid profile would be achieved in patients who had 3 metabolic components of the syndrome. These components include abdominal obesity with a waist circumference >90 cm, an increase in blood pressure >130/85 mmHg and or consumption of anti-hypertensive drugs, an increase in fasting glucose plasma >110 mg/dl. The author also revealed that the small sample size of his study involving 173 participants also became one of the factors of the insignificant correlation. It is assumed that adiponectin levels may not play an important role in depicting specific lipid metabolism due to considerable effects on metabolic processes according to the underlying conditions of these patients. This might answer the reason behind the insignificance of the results of this study, where the children in the study sample had not been diagnosed as metabolic syndrome. However, the study uses adult samples that may be less reliable for reference in this study.

Another study with a sample of obese children in Egypt also supports the reason that they show a significant difference in adiponectin levels between obese children with metabolic syndrome (5.29±1.9 µg/ml) and obese children without metabolic syndrome (8.57±2.1 µg/ml). They also said that adiponectin could predict lipid profiles better in obese children with metabolic syndrome compared with normal obese.

The study conducted by Klünder-Klünder M also supports this theory, which found no significant relationship between adiponectin levels in adolescents without obesity and obesity without

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**Table 3 Partial Analysis correlation between HDL and Adiponectin after age and sex variables adjustments**

| Variable | r     | p value |
|----------|-------|---------|
| HDL      | 0.143 | 0.444   |

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metabolic syndrome. However, in adolescents with obesity and diagnosed with metabolic syndrome, there was a significant positive correlation between adiponectin levels and HDL levels based on the study by Kopelman PG. These results are consistent with the existing literature that obesity represented through BMI levels has an association with low HDL concentrations, poor HDL distribution patterns and abnormalities in HDL particle metabolism. This can illustrate the indirect role of adiponectin levels which tend to be lower in samples with higher BMI, as explained in the previous paragraph. However, it turns out that high BMI can affect HDL levels through various mechanisms, one of the primary mechanisms is through hypertriglyceridemia and insulin resistance which causes the release of free fatty acids from adipose tissue into the circulation. The release of fatty acids into the circulation causes an increase in the formation of VLDL by the liver, which causes high amounts of triglycerides to be transferred to HDL particles. Triglyceride-rich HDL is preferred by the liver lipase enzyme which in turn hydrolyzed HDL and increases HDL transport to the liver. This is what causes lower HDL levels in individuals with a higher BMI. Another way is by increasing cholesterol influx into hypertrophic adipocyte tissue, where this can cause HDL to be selectively sent to cells without internalization and degradation of lipoprotein which causes a decrease in HDL plasma levels. In addition to influencing HDL levels, high BMI can also affect the quality of HDL where HDL in patients with higher BMI tends to lose its ability to provide protection against atherogenesis and inflammation as well as can lead to metabolic disease. HDL in advanced obese patients was found to be unable to inhibit monocyte chemotaxis like HDL in the normal population, instead, its increased chemotaxis monocytes which in turn increased inflammatory reactions. Despite the explanation above, a cross sectional design used in this study was one of the study limitations due to could not do long-term observation to evaluate the causal effect between both variables assessed. This study also not include physical or supporting examination to detect the respondents who are risk of metabolic syndrome that may contribute to the bias of study results.

CONCLUSION

Our study found that most of the obese-adolescents involved in this study were male and having HDL levels ≥ 40 mg/dL. There was a very weak correlation using Pearson and Partial Correlation test and statistically not significant between HDL levels and adiponectin levels in obese adolescents.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

ETHICS CONSIDERATION

Ethical clearance No.1733/UN.14.2.2/PD/KEP/2018 has approved this study from the Ethics Committee of Faculty of Medicine, Universitas Udayana, Sanglah General Hospital, Bali, Indonesia prior to the study being conducted.

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AUTHOR CONTRIBUTION

All of the authors are equally contributed to the study from the conceptual framework, data gathering, data analysis, until reporting the results of the study.

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