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PUBLICATION TYPE

Journals

ISSN

1394035X

COVERAGE

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INFORMATION

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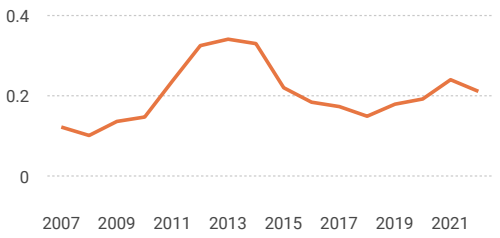

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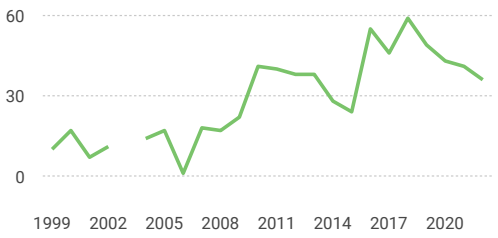

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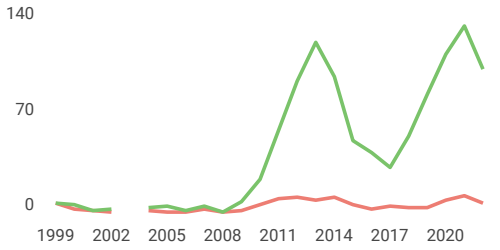

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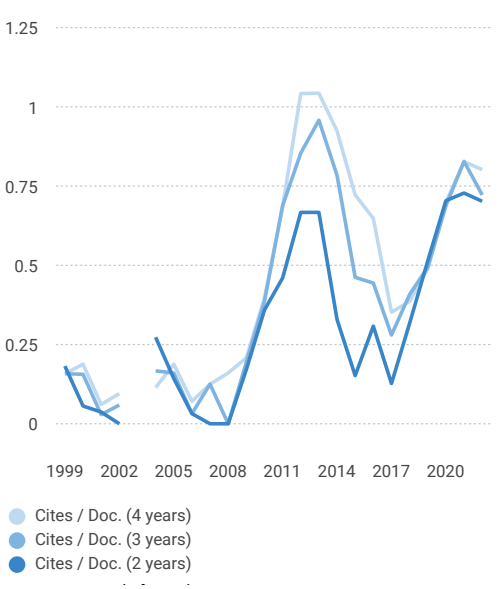

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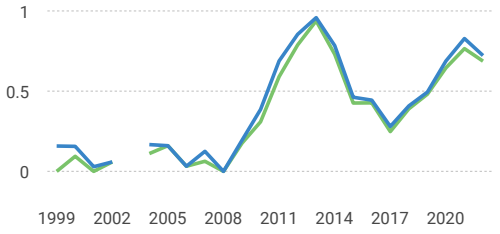

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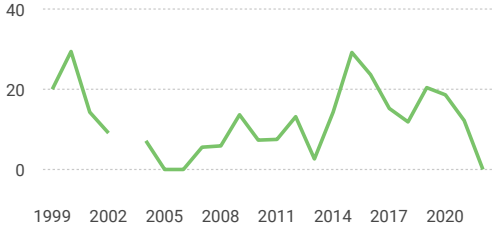

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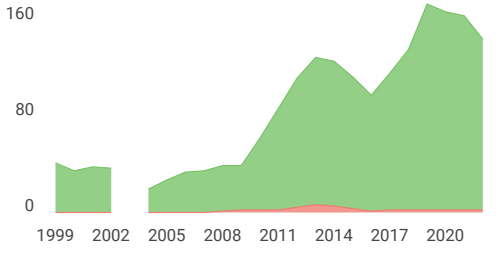

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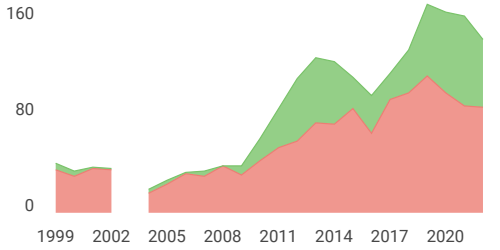

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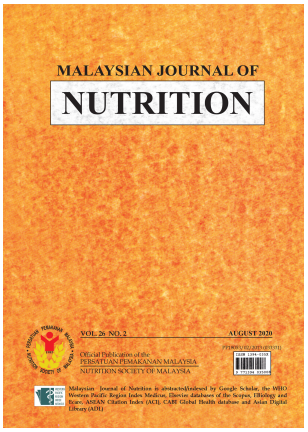

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ABSTRACT

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Methods: A cross-sectional study was performed on 59 obese adolescents aged 13–16 years. Obesity was established on the basis of the Centers for Disease Control and Prevention (CDC) curve (2000). Insulin and blood glucose level measurements were carried out using an enzymatic kit. Adiponectin levels were assayed using enzyme-linked immunosorbent assay (ELISA). The relationships between variables were evaluated by correlation analysis using SPSS.
Results: Statistical tests showed a positive correlation between waist circumference (r=0.421; p=0.001) and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) (r=0.396; p=0.002). Waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) had a weak positive correlation with insulin (r=0.343; p=0.008 and r=0.311; p=0.017) and HOMA-IR (r=0.306; p=0.018). There was a weak negative correlation between adiponectin and insulin in obese adolescents (r=-0.278; p=0.033).
Conclusion: Anthropometric measurements (waist circumference, WHR and WHtR) and adiponectin can be used for early detection of insulin resistance and hyperinsulinemia in obese adolescents.
Key words: Adiponectin, insulin, HOMA-IR, adolescents, obesity

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Mal J Nutr 26(2): 165-172, 2020

Adiponectin, anthropometric measurements and insulin resistance in adolescence with obesity

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ABSTRACT

Introduction: Obesity in adolescents can cause metabolic syndrome. Insulin resistance increases the risk of metabolic syndrome, which then increases the risk of premature death. Studies about anthropometric measurements and adiponectin levels as early markers of insulin resistance in obese adolescents are still limited. **Methods:** A cross-sectional study was performed on 59 obese adolescents aged 13–16 years. Obesity was established on the basis of the Centers for Disease Control and Prevention (CDC) curve (2000). Insulin and blood glucose level measurements were carried out using an enzymatic kit. Adiponectin levels were assayed using enzyme-linked immunosorbent assay (ELISA). The relationships between variables were evaluated by correlation analysis using SPSS. **Results:** Statistical tests showed a positive correlation between waist circumference (r=0.421; p=0.001) and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) (r=0.396; p=0.002). Waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) had a weak positive correlation with insulin (r=0.343; p=0.008 and r=0.311; p=0.017) and HOMA-IR (r=0.306; p=0.018). There was a weak negative correlation between adiponectin and insulin in obese adolescents (r=-0.278; p=0.033). **Conclusion:** Anthropometric measurements (waist circumference, WHR and WHtR) and adiponectin can be used for early detection of insulin resistance and hyperinsulinemia in obese adolescents.

Keywords: Adiponectin, insulin, HOMA-IR, adolescents, obesity

INTRODUCTION

Obesity is a global problem. The number of obese individuals is increasing in Asia (Mazidi *et al.*, 2018). Obesity is associated with various complications, including metabolic syndrome, cardiovascular disease and type 2 diabetes mellitus (Asghar & Sheikh, 2017). These complications have varied effects, ranging from an increased risk of premature death to a reduction in quality of life (Hirko *et al.*, 2015; Morrison *et. al.*, 2015).

In obesity, an increase in the size of fat cells is associated with inflammatory conditions. Visceral fat plays an important

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doi: https://doi.org/10.31246/mjn-2019-0100

role in the production of adipocytokines and other pro-inflammatory cytokines to cause inflammation. Pro-inflammatory cytokines are associated with insulin insensitivity (Asghar & Sheikh, 2017). Insulin resistance plays a role in the pathogenesis of type 2 diabetes mellitus (Tangvarasittichai, 2015), metabolic syndrome (Banerji, Lam & Chaiken, 2017) and cardiovascular disease (Ormazabal *et al.*, 2018).

Waist circumference is one of the indices used to assess a person's risk of metabolic syndrome (Prakaschandra & Naidoo, 2017). The associations of waist circumference, thigh circumference, waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) with insulin resistance have been studied previously. However, most studies were conducted in adult subjects of normal weight (Benites-Zapata *et al.*, 2019) or those with type 2 diabetes mellitus (Yoon *et al.*, 2016).

Adiponectin is an adipocytokine known to have anti-inflammatory, anti-atherogenic and insulin-sensitising effects (Achari & Jain, 2017; Orlando *et al.*, 2019). Adiponectin levels are known to decrease in obese adolescents (Orlando *et al.*, 2019). Adiponectin has been studied as a protective factor against complications of obesity, such as diabetes mellitus, metabolic syndrome, hypertension, dyslipidaemia and cardiovascular disease (Sharma, McClung & Abraham, 2016; Orlando *et al.*, 2019). The protective mechanism of adiponectin has been explained through various adiponectin signalling pathways (Ruan & Dong, 2016). However, clinical research on adiponectin as a marker of insulin resistance has mostly been conducted in adults and patients with type 2 diabetes mellitus (Aleidi *et al.*, 2015).

Studies on adiponectin and anthropometric measurements as initial markers for detecting insulin resistance in obese adolescents are still limited in developing countries. This study aims to analyse the association of anthropometric measurements and adiponectin levels with fasting glucose, insulin and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) levels in obese adolescents.

MATERIALS AND METHODS

Study design

This was a cross-sectional study conducted on obese adolescents. Respondents were considered obese if their Body Mass Index (BMI) was above the 95th percentile on the Centers for Disease Control and Prevention (CDC) 2000 BMI curve according to age and sex. The inclusion criteria were age 13–16 years, obese, and consent obtained from a parent/guardian to participate in the study. Respondents suffering from infections, inflammation, autoimmune diseases, cancer, chronic diseases and endocrine disorders, those who were smokers and who consumed alcohol were excluded from this study. This study was conducted after obtaining ethical approval from the ethics committee of the Dr Soetomo General Academic Hospital, Surabaya (No. 0411/KEPK/VII/2018).

Physical examinations

Respondents were examined for weight, height, waist circumference and thigh circumference. Weight was measured using a digital scale (Seca, Germany) accurate to 0.1kg. Height was measured with a portable stadiometer (Seca, Germany) accurate to 0.1cm. Body weight was measured with respondents standing straight and not wearing footwear or other accessories. Height was measured from the vertex of the head to the heel with respondents in standing position and not wearing footwear or a hat. BMI was calculated with the

formula of body weight (kilogrammes) divided by height squared (meter squared) and plotted onto the BMI curve according to age and sex (CDC, 2000). Waist circumference was measured using a tape measure accurate to 0.1cm at the midpoint between the lowest rib and the endpoint of the iliac crest upon expiration. Hip circumference was measured using a tape measure at the widest area of the hip at the point of the greatest gluteal protuberance. WHR was calculated as waist circumference (cm) divided by hip circumference (cm). WHtR was calculated as waist circumference (cm) divided by height (cm).

Biochemistry examinations

Blood measurements were performed, including adiponectin, fasting blood glucose levels, insulin and HOMA-IR. Blood collection was carried out in the morning after a 12-hour fast. Blood was drawn from the vena mediana cubiti. Blood was centrifuged, and the serum was removed and stored at –70°C until an adiponectin examination was performed. The adiponectin examination was carried out using enzyme-linked immunosorbent assay (ELISA) in accordance with manufacturer's instructions. The examination of insulin and fasting blood glucose levels was carried out with an enzymatic kit according to standard procedures. HOMA-IR was used to describe insulin resistance.

Statistical analysis

Adiponectin, fasting blood glucose, insulin and HOMA-IR levels were expressed as medians and percentiles due to skewed distributions. A normality test was performed on each variable using the Kolmogorov–Smirnov test. The associations between fasting blood glucose, insulin and HOMA-IR with anthropometric measurements and adiponectin levels were analysed by Pearson's and Spearman's rho correlation. Data analysis was performed using SPSS statistics software version 21.0.

RESULTS

In this study, there were 59 obese adolescents aged 13–16 years. A total of 32 (54.2%) adolescents were males and 27 (45.8%) were females. The median fasting insulin level and HOMA IR value were 16.09mU/ml and 2.85, respectively, in obese adolescents (Table 1).

A weak positive correlation was obtained between waist circumference (r=0.421; p=0.001) and HOMA-IR (r=0.396; p=0.002). WHtR also had a weak positive correlation with HOMA-IR (r=0.306; p=0.018) (Table 2). WHR and

Table 1. Characteristics of obese adolescents

Variable	*Median (25^{th}–75^{th})*
Body Mass Index (kg/m^2)	31.25 (29.20–33.70)
Waist circumference (cm)	97.20 (94.00–107.00)
Hip circumference (cm)	105.00 (99.00–110.00)
WHR	0.95 (0.91–0.99)
WHtR	0.62 (0.59–0.66)
Adiponectin (ng/ml)	6841.90 (5204.66–10044.31)
Fasting blood glucose (mg/dl)	79.00 (75.00–84.00)
Insulin (mU/ml)	16.09 (10.87–22.82)
HOMA-IR	2.85 (2.07–4.24)

25^{th}: percentile 25; 75^{th}: percentile 75
WHR: Waist-to-hip ratio; WHtR: Waist-to-height ratio; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance

Table 2. Correlation between anthropometric measurements and insulin resistance

Variable	*Fasting blood glucose*		*Insulin*		*HOMA-IR*	
	r	*p*	*r*	*p*	*r*	*p*
Body Mass Index‡	0.168	-0.182	0.111	0.401	0.068	0.608
Waist circumference†	0.029	0.830	0.421	0.001*	0.396	0.002*
Hip circumference‡	-0.094	0.480	0.034	0.276	0.152	0.251
WHR‡	0.105	0.213	0.343	0.008*	0.159	0.230
WHtR†	0.108	0.416	0.311	0.017*	0.306	0.018*

†Spearman's rho correlation
‡Pearson's correlation
*significant at $p<0.05$
WHR: Waist-to-hip ratio; WHtR: Waist-to-height ratio

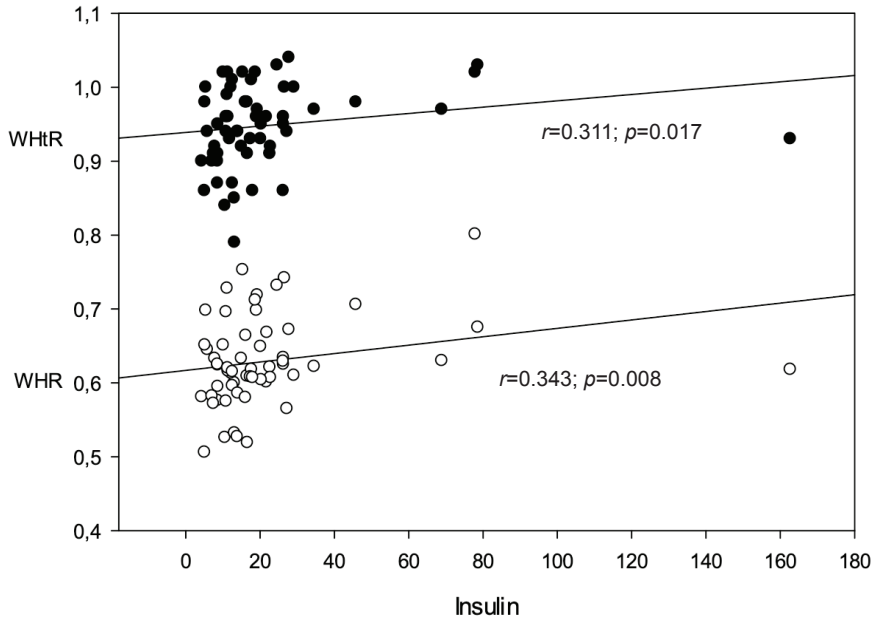

Figure 1. Correlation of insulin with WHR and WHtR

WHtR had a weak positive correlation with insulin (r=0.343; p=0.008; r=0.311; p=0.017) (Figure 1).

There was a weak negative correlation between adiponectin and insulin levels (r=–0.278; p=0.033). Statistical tests did not detect a relationship between adiponectin and HOMA-IR or fasting blood glucose levels (p>0.05) (Table 3). In this study, a negative correlation was found between adiponectin and insulin levels (Figure 2).

DISCUSSION

Pro-inflammatory cytokines are associated with various metabolic complications, such as insulin resistance (Asghar & Sheikh, 2017). As chronic, low-level inflammation occurs in obesity, it is therefore associated with insulin resistance (Lim *et al.*, 2015). There is an increase in fasting insulin levels and HOMA-IR in obese adolescents. HOMA-IR is an index of peripheral insulin sensitivity, which is used to predict

Table 3. Correlation between adiponectin and insulin resistance

Variable	*Adiponectin*	
	r	*p*
Fasting blood glucose‡	0.036	0.789
Insulin†	-0.278	0.033*
HOMA-IR‡	-0.205	0.119

†Spearman's rho correlation
‡Pearson's correlation
*significant at $p<0.05$

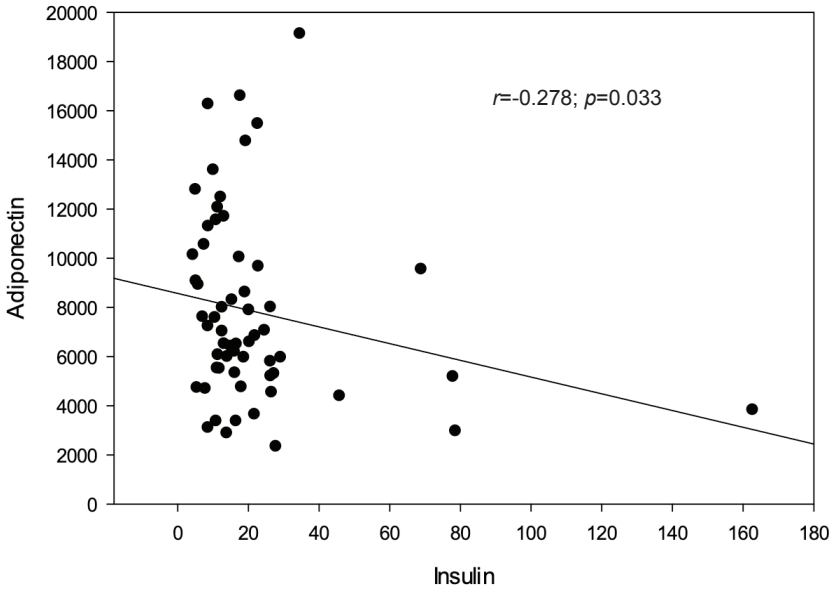

Figure 2. Correlation between adiponectin and insulin

insulin resistance. Increased HOMA-IR is accompanied by increased levels of blood glucose, low-density lipoprotein cholesterol, triglycerides, insulin and glycated haemoglobin (HbA1c), which are risk factors for metabolic syndrome (González-Jiménez *et al.*, 2016). BMI is associated with insulin secretion and insulin sensitivity in obesity (Wang *et al.*, 2016). An increase in HOMA-IR is proportional to an increase in the BMI of adolescents (González-Jiménez *et al.*, 2016), although this increase can also be found in healthy adolescents (Telford *et al.*, 2012). In this study, there was no relationship between BMI and fasting blood glucose levels, insulin or insulin resistance. The findings of this study differed from those of previous studies which showed BMI to be correlated with insulin resistance (Cheng *et al.*, 2017; González-Jiménez *et al.*, 2016; Lim *et al.*, 2015). However, the strength of correlation between BMI with insulin resistance shown by HOMA-IR was found to be weak in adolescents (Convit, Wedin & Diaz-Gimenez, 2012).

Body fat composition has a larger effect on insulin resistance than body fat percentage (Cheng *et al.*, 2017). In this study, waist circumference and WHtR were positively correlated with insulin and HOMA-IR. Previous studies have suggested that waist circumference is

correlated with increased insulin levels (Cempaka & Sidiartha, 2017) and HOMA-IR (da Silva *et al.*, 2018; Lim *et al.*, 2015). Waist circumference is more strongly correlated with HOMA-IR than with BMI (Convit *et al.*, 2012). In a similar study, adolescents stated that BMI, along with increased waist circumference and systolic blood pressure, were risk factors for insulin resistance (González-Jiménez *et al.*, 2016).

This study found that WHR has a positive correlation with insulin, similar to studies conducted in China. A study on respondents with normal weight showed that WHR was associated with hyperinsulinemia after tests of glucose tolerance and insulin resistance (Benites-Zapata *et al.*, 2019). Hyperinsulinemia in obesity occurs due to compensatory insulin secretion under conditions of insulin resistance (Wang *et al.*, 2016). WHR has also been shown to have a positive correlation with HOMA-IR (Lim *et al.*, 2015). However, in this study, there was no relationship between WHR and HOMA-IR. One possible explanation may be the similarities in pancreatic beta-cell function disorders between obese and non-obese respondents with impaired glucose tolerance (Takahara *et al.*, 2013).

Adiponectin is produced by fat tissue. The concentration of adiponectin in plasma is 2–30µg/ml (Sharma *et al.*, 2016). Although adiponectin is produced by fat tissue, but its level is decreased in obesity. Adiponectin is negatively correlated with metabolic syndrome (Ntzouvani *et al.*, 2016), prevents cardiovascular disease and improves insulin sensitisation (Stern, Rutkowski & Scherer, 2016). In this study, low levels of adiponectin were obtained. Adiponectin had no correlation with blood glucose and HOMA-IR levels, but had a negative correlation with fasting insulin levels.

The differences between our results and those of previous studies may have been due to several factors. The relationship between anthropometric measurements and insulin resistance can vary between study populations, influenced by ethnicity (Yoon *et al.*, 2016) and age (Chandler-Laney *et al.*, 2010). Similarly, adiponectin levels are also influenced by ethnicity and gender (Sharma *et al.*, 2016; Aleidi *et al.*, 2015). However, combinations of anthropometric measurements can be used to predict cardiometabolic risk in adolescents (Samouda *et al.*, 2015). In addition, adiponectin and anthropometric measurements are also useful for early detection of insulin resistance and hyperinsulinemia in obese adolescents.

This study has several limitations. Firstly, the sample size was limited and there were no non-obese subjects with normal BMI included as a comparison group in this study. Secondly, no serial measurements of adiponectin, blood glucose and insulin levels were performed in this study. This could have affected the accuracy of the results as blood glucose can be affected by dietary consumption and physical activity.

CONCLUSION

There was a positive correlation in waist circumference, WHR and WHtR with insulin, while a positive correlation was observed between waist circumference and WHtR with HOMA-IR. There was no correlation between adiponectin and blood glucose levels or HOMA-IR. Adiponectin had a negative correlation with fasting insulin levels. Adiponectin, waist circumference, WHR and WHtR can be used for early detection of insulin resistance and hyperinsulinemia in obese adolescents. This can be one step towards preventing metabolic syndrome in adulthood.

Acknowledgement

The authors thank Universitas Airlangga and Dr. Soetomo Academic General Hospital, Surabaya, Indonesia for supporting this research.

Authors' contributions

NAW, principal investor, conceptualised and designed the study, prepared the draft of the manuscript and reviewed the manuscript; RAP, led the data collection, data analysis and wrote the manuscript; MHH, reviewed the manuscript; RI, led the data collection and reviewed the manuscript; IDGU, reviewed the manuscript; RH, reviewed the manuscript.

Conflict of interest

The authors declare no conflict of interest in this study.

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