INDONESIAN JOURNAL OF
CLINICAL PATHOLOGY AND MEDICAL LABORATORY
Majalah Patologi Klinik Indonesia dan Laboratorium Medik

PAGE 161
2022 March; 28(2): 161-164
p-ISSN 0854-4263 e-ISSN 2477-4685
Available at www.indonesianjournalofclinicalpathology.org

Correlation between Inflammatory Markers of Platelet Index and Vitamin D with Body Mass Index

Grace Yuni Soesanti Martieka Harviendo, Ariosta, Meita Hendrianingtyas

Department of Clinical Pathology, Faculty of Medicine, Diponegoro University/Dr. Kariadi Hospital, Semarang, Indonesia. E-mail: grace.soesanti@gmail.com

ABSTRACT

Weight loss remains a worldwide health problem and a risk factor for chronic disease. Decreased serum vitamin D levels in excessive body weight lead to low-grade inflammation. This study aimed to determine the relationship between the platelet index such as Mean Platelet Volume (MPV), Platelet Large Cell Ratio (P-LCR) as an inflammatory marker, and vitamin D as an anti-inflammatory marker with body mass index (BMI). This study was a cross-sectional study of 78 female patients at the Diponegoro National Hospital with an overweight (BMI> 23) state from July to September 2020. Data analysis was performed using Pearson and Spearman tests and p <0.05 was significant. Of the 78 research samples, there was a significant relationship between BMI and MPV (r=0.404; p=0.000); P-LCR (r=0.425; p=0.000) and 25(OH) D (r= -0.231; p=0.04). Low vitamin D levels in obesity and low-grade inflammation increase proinflammatory cytokines. Increased leptin levels in obesity contribute to platelet hyperreactivity. Increased platelet activity compensates for the platelets so that the MPV and P-CLR values increase. This study found a moderate significant positive relationship between MPV, P-CLR, and BMI but a weak significant negative relationship between 25(OH) D and BMI.

Keywords: Mean platelet volume, P-LCR, vitamin D, body mass index

INTRODUCTION

Both obesity and overweight are worldwide problems. The World Health Organization (WHO) 2016 found that more than 650 million people were obese, equivalent to 13% of the world's population.[1] This study linked inflammatory markers such as platelet index, and obesity, with vitamin D as an anti-inflammatory marker. One of the frequently used inflammatory markers is CRP or IL-6. However, those inflammatory markers are not available in all laboratories. Mean platelet volume can be used as an inflammatory marker due to its inexpensive cost and wide availability. Research by Melisa *et al*. found that there was a significant relationship between IL-6 as a marker of inflammation and MPV in children with pneumonia.[2] Research by Lee *et al*., stated that MPV can be used as an inflammatory marker in urinary tract infection and showed a significant relationship with CRP (r=0.199; p=0.031).[3]

Body Mass Index (BMI) is a simple anthropometric measurement by dividing the body weight (in kilograms) by the square of height in meters (meter^2). The Asia-Pacific body mass index classification assigns a weight limit of >23 for the Asian population.[4] The accumulation of fat in overweight people causes continuous low-grade inflammation. Platelet index is a parameter of inflammation that can be indicated from a complete blood count including MPV and P-LCR. Mean Platelet Volume (MPV) indicates the average size of platelets in the blood with a normal value of 7.2-11.7 fL, while the Platelet Large Cell Ratio (P-LCR) is an indicator of the presence of large platelets (> 12 fL) in circulating platelets with normal values 15-25%. Both are inflammatory markers.[5]

Riyahi *et al*. in their research suggested that MPV levels were higher in obese than in overweight. Obese subjects were more likely to have increased platelet activation compared to those with normal BMI. This is due to the higher levels of soluble CD4 ligand (sCD40L) in obesity than in overweight and normal BMI, indicating a proinflammatory state in obese individuals.[6] Different studies from Çeçen *et al*., stated that the decrease in MPV is directly proportional to the increase in BMI and Fat Masses (FM). Mean platelet volume may not be suggested as an inflammatory marker in obesity because no significant relationship was found between MPV and FM, fat percentage, and Fat Mass Index (FMI).[7] As far as researchers are concerned, studies regarding bodyweight about P-LCR have not been conducted.

Vitamin D is a fat-soluble compound and is responsible for increasing intestinal absorption of

calcium, secretion, and release of hormones. Vitamin D receptors are distributed in body tissues and are involved in the pathogenesis of several diseases, such as obesity.[8] Vitamin D has an important role in calcium homeostasis, bone mineralization, immunity, proliferation, cell differentiation, anticoagulation, and anti-inflammation.[9]

Pereira *et al.* found that the prevalence of vitamin D deficiency in obesity was 35% higher than the eutrophic group and 24% higher than the overweight group.[10] Jawad *et al.* in their study of 300 obese participants, most of them had vitamin D deficiency. The obese and overweight elderly respondents had significantly lower serum vitamin D levels than the non-obese group ($p < 0.05$).[11] Different studies by Oommen *et al.* found that 84% of 100 female obese respondents had vitamin D deficiency and 69.6% of overweight respondents had vitamin D deficiency. However, the study found no significant relationship between obesity and vitamin D deficiency.[12] Based on the research above, the researchers were interested to determine the relationship between platelet index, obesity as inflammatory markers with vitamin D as an anti-inflammatory marker, and BMI.

METHODS

The research method was cross-sectional involving females aged 25-45 years old with normal body temperature as the research subjects. This study was carried out from July to September 2020 at the Diponegoro National Hospital Semarang involving 78 people with BMI >23 (obesity). Subjects with increased temperature increased leukocytes, and liver disease were excluded. Ethical clearance was obtained from the Institute of Medical and Health Research Ethics Committee, Faculty of Medicine, Diponegoro University Semarang, no: 32/EC/KEPK/FK-UNDIP/III/2020. Body mass index was determined by dividing body weight and height squared (kg/m^2). Complete blood count was performed using the Sysmex XS-500i hematology analyzer with the impedance method to obtain platelet count. Golzarand *et al.* in his study stated that the amount of body fat mass is related to vitamin D, especially in the active form of 25-hydroxyvitamin D (25(OH) D).[13] Serum 25(OH) D levels were measured using a combination method of competitive enzyme immunoassay and Enzyme-Linked Fluorescent Immunoassay (ELFA). Normal values for 25(OH) D are 30-100 ng/mL.

RESULTS AND DISCUSSIONS

The results of the study were 78 samples with an age range of 25-45 years, BMI >23. Statistical analysis using the Kolmogorov-Smirnov test was carried out to determine the normality of the data. The characteristics of the research subjects can be seen in the Table 1. Scatter plot and correlation of MPV, P-LCR and vitamin D with BMI can be seen in Table 2 and Figure 1.

The data from the study showed that 32% of respondents were exposed to sunlight for more than one hour a day, 28% of respondents were exposed to sunlight for less than one hour a day, and 40% of respondents were rarely exposed to sunlight.

The results of data analysis with the Spearman test showed a moderate significant positive relationship between MPV, P-LCR, and BMI and a significant weak negative relationship between 25(OH) D and BMI. This suggested that there was a relationship between the platelet index

Table 1. Characteristics of research subjects

Variable (n=78)	Mean±SD	Median (min-max)
Age (years)	34.99±6,458	34.5 (25-50)
Bodyweight (Kg)	77.49±12,834	73.5 (958-127)
Height (cm)	154,99±5,273	154,5 (145-170)
BMI (Kg/m^2)	32,296±5,1022	30.85 (25.3-52)
Waist (cm)	94.27±9.77	92 (79-120)
Hip circumference (cm)	110,42±10,167	110 (90-150)
Waist to hip ratio	0,85494±0,060175	0,85750 (0,702-1,000)
Platelet (x10^3/uL)	330,58±66,746	314,5 (184-522)
MPV (fL)	10,213±0,8311	10.2 (8,5-11.8)
P-LCR (%)	26,167±6,8126	25.9 (12-39.3)
25(OH) D (ng/mL)*	11,722±3,4901	11.2 (8-25)

Note: SD (Standard Deviation); min (minimum); max (maximum), * Abnormal data distribution

Table 2. Correlation of MPV, P-LCR, and vitamin D with BMI

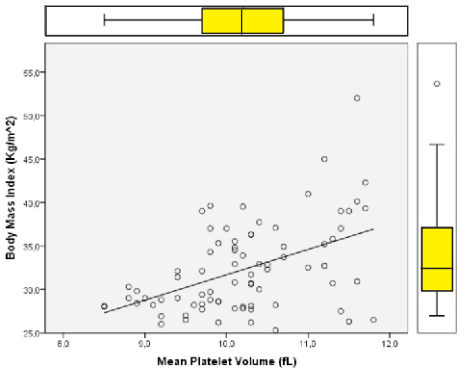
Variable	BMI	
	p	R
MPV	0.000**	0.404
P-LCR	0.000**	0.425
Vitamin D	0.042	-0.231

Spearman's Rho test, *p< 0.05

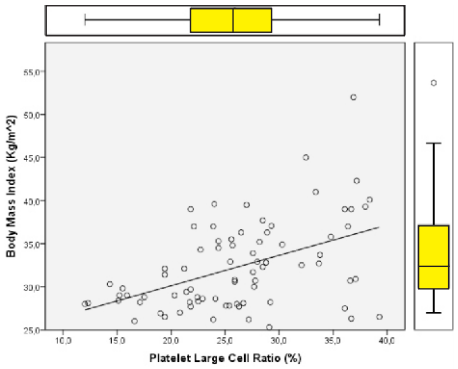
as an inflammatory marker with vitamin D as an anti-inflammatory marker and BMI.

The results in this study were in line with the research of Pinto *et al*., which found that MPV was positively related to body mass index.[14] Vitamin D in healthy individuals is synthesized in the skin or ingested from food and enters the systemic circulation and undergoes 2 stages of hydroxylation. the first stage occurs in the liver to form 25(OH) D3 and in the kidney to form 1,25(OH) 2D. 1,25(OH) 2D affects the pancreas by increasing insulin secretion and sensitivity but decreasing oxidative stress and insulin resistance. 1,25(OH) 2D inhibits chronic inflammation due to obesity, inhibits proinflammatory cytokines such as IL-1β, IL-6, IL-8, and IL-12, reduces the inflammatory activity of adipose tissue, and reduces inflammation in visceral adipose tissue.[15]

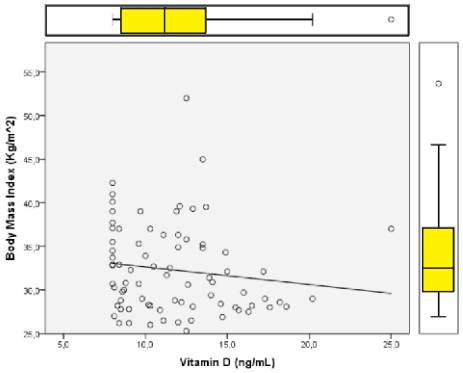
The pathogenesis of low levels of vitamin D is explained using 2 theories, such as the sequestration theory suggesting that the failure of obese individuals to convert previtamin D to vitamin D makes excess fat tissue take up fat-soluble vitamins, leading to low serum 25(OH) D3 levels. Another theory of degradation states that excess fat tissue stimulates the infiltration of activated immune cells resulting in inflammation of adipose tissue and degradation of vitamin D.[16] Adipose tissue in obesity experiences low-grade inflammation, resulting in the increased proinflammatory cytokines in obesity.[17] Leptin hormone increases in obese individuals, contributing to platelet hyperactivity that plays an important role in the development of atherothrombosis. Atherothrombosis is the result of the interaction of insulin resistance, inflammation, oxidative stress, and endothelial dysfunction. The increase in platelet activity compensates for platelet products such as young and large platelets in the circulation, increasing the MPV and P-CLR values as inflammatory markers.[18] This study was in line with the research of Özkan *et al*., a controlled study of children aged 6-16 years, which found that obese children with non-alcoholic fatty liver had a significantly higher MPV compared to children without obesity.[19]



a. Correlation between MPV and BMI



b. Correlation between P-LCR and BMI



c. Correlation between vitamin D and BMI

Figure 1. Scatter plot of correlation of MPV, P-LCR, and vitamin D with BMI

CONCLUSIONS AND SUGGESTIONS

There was a moderate significant positive relationship between MPV and P-CLR as an inflammatory marker with BMI and a significant weak negative relationship between 25(OH) D as an anti-inflammatory marker and BMI. However, homogenization of female subjects with obesity in reproductive age, the absence of another measurement of fat mass markers, no exposure to sunlight, and dietary patterns remained the limitations of this study. Further research can be carried out using other fat mass markers and considering the gender characteristics.

REFERENCES

1. World Health Organization. Obesity and overweight. Report of WHO expert consultation, April 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (accessed Sept 28, 2020).
2. Melisa L, Heda NM, Dida GA. Serum interleukin-6 and mean platelet volume in pediatric pneumonia. Paediatrica Indonesiana, 2016; 56(1): 57-61.
3. Lee IR, Shin J Il, Park SJ, Oh JY, Kim JH. Mean platelet volume in young children with urinary tract infection. Sci Rep, 2015; 5(June): 1-6.
4. Matthias Helble, Kris Francisco, The imminent obesity crisis in Asia and the pacific: First cost estimates, Asian Development Bank Institute, June 2017. Available from: https://www.adb.org/imminent-obesity-crisis-asia-and-pacific-first-cost-estimates (accessed Sept 28, 2020).
5. Budak YU, Polat M, Huysal K. The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: A systematic review. Biochem Medica, 2016; 26(2): 178-93.
6. Riyahi N, Tohit ERM, Thambiah SC, Ibrahim Z. Platelet-related cytokines among normal body mass index, overweight, and obese Malaysians. Asia Pac J Clin Nutr, 2018; 27(1): 182-8.
7. Çeçen S. Platelet activation is a risk factor for obesity. Turkish J Endocrinol Metab, 2020; 24(2): 132-7.
8. Dos Santos LR, Lima AGA, Braz AF, de Sousa Melo SR, Morais JBS, *et al.* Role of vitamin D in insulin resistance in obese individuals. Nutrire, 2017; 42(1): 1-6.
9. Park YC, Kim J, Seo MS, Hong SW, Cho ES, Kim JK. Inverse relationship between vitamin D levels and platelet indices in Korean adults. Hematology, 2017; 22(10): 623-9.
10. Pereira-Santos M, Costa PRF, Assis AMO, Santos CAST, Santos DB. Obesity and vitamin D deficiency: A systematic review and meta-analysis. Obes Rev, 2015; 16(4): 341-9.
11. Jawad IH, Baiee HA. Prevalence of vitamin D deficiency and its correlate with overweight and obesity in community-dwelling old adults. Med J Babylon, 2020; 17(2): 36-40.
12. Oommen A, Al-Zahrani I. Association of obesity with vitamin D deficiency and the clinical implications. Int J Res Med Sci, 2015; 3(11): 3262-5.
13. Golzarand M, Hollis BW, Mirmiran P, Wagner CL, Shab-Bidar S. Vitamin D supplementation and body fat mass: A systematic review and meta-analysis. Eur J Clin Nutr, 2018; 72(10): 1345-57.
14. Pinto RVL, Rodrigues G, Simões RL, Porto LC. Analysis of post-sample collection EDTA effects on mean platelet volume values in relation to overweight and obese patient status. Acta Haematol, 2019; 142(3): 149-53.
15. Zakharova I, Klimov L, Kuryaninova V, Nikitina I, Malyavskaya S, *et al.* Vitamin D insufficiency in overweight and obese children and adolescents. Frontiers in Endocrinology, 2019; 10(103): 1-13.
16. Sundari LPR. Defisiensi vitamin D pada obesitas. Sport Fit J, 2018; 6(1): 1-5.
17. Castro AM, Macedo-de la Concha LE, Pantoja-Meléndez CA. Low-grade inflammation and its relation to obesity and chronic degenerative diseases. Rev Médica del Hosp Gen México, 2017; 80(2):101-5. Available from: http://dx.doi.org/10.1016/j.hgmx.2016.06.011 (accessed Sept 28, 2020).
18. Batista TR, De Figueiredo RC, Rios DRA. Platelets volume indexes and cardiovascular risk factors. Rev Assoc Med Bras, 2018; 64(6): 554-9.
19. Özkan EA, Khosroshahi HE, Serin H, Özdemir ZT, Kiliç M, *et al.* The evaluation of carotid intima-media thickness and mean platelet volume values and correlation with cardiac functions in obese children. Int J Clin Exp Med, 2015; 8(12): 22557-63.