Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 874–880

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Relationship of leukocytes, platelet indices and adipocytokines in metabolic syndrome patients

Adel Abdel-Moneim [a,*], Basant Mahmoud [b], Eman A. Sultan [c], Rania Mahmoud [b]

[a] Physiology Division, Zoology Department, Faculty of Science, Beni-Suef University, Egypt
[b] Biochemistry Division, Chemistry Department, Faculty of Science, Beni-Suef University, Egypt
[c] Endocrinology and Metabolism Department, National Nutrition Institute, Cairo, Egypt

ARTICLE INFO

Article history:
Received 24 November 2018
Accepted 19 December 2018

Keywords:
Metabolic syndrome
White blood cells indices
Platelets indices
Leptin
Adiponectin

ABSTRACT

Aims: The current study aimed to explore the correlation between leukocytes and platelets indices with adipocytokines (leptin and adiponectin) and MetS components.
Methods: A total of 100 healthy subjects and 200 patients diagnosed with different MetS components were enrolled in the study. Eligible patients were allocated into four groups (50 patients). Group1 include patients with 2 criteria of MetS components, group 2 with 3 criteria, group 3 with 4 criteria and group 4 had patients with 5 criteria.
Results: Regarding white blood cell indices, data showed that total leukocyte and neutrophil count as well as neutrophil/lymphocyte (N/L) ratio were significantly increased in all groups of MetS patients when compared to the healthy group. Additionally, platelets count, platelet distribution width (PDW), and main platelet volume (MPV) levels and platelets/lymphocyte (P/L) ratio were significantly higher in all patients with MetS as compared to the healthy subjects. Serum leptin concentration and leptin-to-adiponectin ratio (LAR) were elevated significantly, while adiponectin level was significantly diminished in all MetS groups when compared to the control.
Conclusion: leukocytes and platelets indices were associated with hyperleptinemia and hypoadiponectinemia as well as MetS components. The study also suggested the necessary role of leukocytes, platelet indices, and LAR as markers in early diagnoses of individuals with MetS components.
© 2018 Diabetes India. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Metabolic syndrome (MetS) is a developing health care concern worldwide as a consequence of urbanization, overnutrition, obesity, and sedentary lifestyles [1]. Since the prevalence of MetS is growing rapidly and it is correlated with an increased risk of insulin resistance, diabetes mellitus, cardiovascular disease (CVD), and total mortality [2], thus, the identification for biomarkers of MetS is of critical significance. Hematological parameters including platelet (PLT) count, hematocrit level (HCT) increased with increasing numbers of MetS components [3]. Also, a number of studies have assessed the relationship between the white blood cell (WBC) count and tissue damage and inflammation [4], with components of MetS. Henceforward, numerous studies had elucidated that leukocytes count was correlated with the severity of type 2 diabetes (T2DM) and MetS [5]. Meanwhile, it is important to report that the elevated number of leukocytes is correlated with MetS and diabetes even in the normal range of WBCs [6]. Along with elevation number of leukocytes, there is a significant relationship between neutrophil–lymphocyte (N/L) ratio and the severity and prognosis of CVD [7].

PLT count is a basic and economic marker of hemostasis in clinical practice. However, elevated PLT count had been correlated with increased prevalence and risk of MetS in both genders [8]. There are numerous evidences reported on the increase in PLT count of patients with MetS and insulin resistance [9]. Moreover, the relation between inflammation and thrombosis can provide a potential mechanism bind PLT count with MetS. Mean platelet volume (MPV), a widely used measure of PLT size, shows a close association with CVD risk factors, such as diabetes mellitus, hypertension, obesity, MetS [10]. Increased WBC and PLT count may serve as markers of a prothrombotic and proinflammatory

* Corresponding author. Molecular Physiology Division, Faculty of Science, Beni-Suef University, Egypt, Salah Salem St., 62511, Beni Suef, Egypt.
E-mail addresses: adel_men2020@yahoo.com, adel.hassan@science.bsu.edu.eg (A. Abdel-Moneim).

https://doi.org/10.1016/j.dsx.2018.12.016
1871-4021/© 2018 Diabetes India. Published by Elsevier Ltd. All rights reserved.

condition that may be leading to MetS and artherothromboembolic complications [11]. It is important to mention that leukocytes play a necessary role in both atherogenesis and thrombus formation.

Leptin and adiponectin have a wide spectrum of functions in the modulation of metabolism and are a central link between obesity and MetS. Adiponectin has been detected as a key modulator with anti-inflammatory action and its deficiency may lead to the event of metabolic disorders [12]. The antiatherogenic adipokine, adiponectin, has been implicated in obesity, insulin resistance, CVD, and the MetS [13]. The relationship between MetS and leptin has been a widely accepted concept in recent years, and numerous studies have been conducted in different populations worldwide [14].

The relationship between hematological parameters with leptin, adiponectin, and LAR in MetS patients remains controversial and has not been discussed extensively. We, therefore, conducted to explore the association between leukocytes, platelet indices with adipocytokines (leptin and adiponectin) as well as components of MetS in Egyptian patients.

2. Patients and methods

2.1. Patients

According to WHO (1999) and NCEP ATP III guidelines [15], the subject is said to have MetS if he/she achieves 3 criteria from the following 5 criteria: waist circumference >102 cm in male and >88 cm in female and/or obesity (body mass index> 30 kg/m^2), serum triglycerides >150 mg/dL (1.7 mmol/l) or patients receiving treatment for hypertriglyceridemia, serum high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL (1.03 mmol/l) in men or < 50 mg/dL (1.29 mmol/l) in women or a previously treated dyslipidemia, arterial blood pressure >130/85 mmHg in two different determinations or if the patients were receiving treatment with drugs, and fasting glucose ≥110 mg/dL. The study protocol was performed as per the announcement of Helsinki and good clinical practice guidelines. After written agreements were obtained from all patients before participation in the experiment, the study was approved by the ethical committee of the Institute of Endocrinology and Diabetes.

A total of 100 healthy subjects and 200 patients diagnosed with MetS components who visited the Institute of Nutrition, Ministry of Health, Cairo, were enrolled in this study from Jul 2016 to March 2018. Eligible MetS patients aged 20–70 years were divided into 4 groups (50 patients). Group1**;** included patients who had 2 criteria (dyslipidemia; hypertriglyceridemia and low HDL); Group 2; included patients with 3 criteria (dyslipidemia + obesity); Group 3; included patients had 4 criteria (dyslipidemia + obesity + hypertension) and Group 4; included patients with 5 criteria (dyslipidemia + obesity + hypertension + hyperglycemia). The patients of group 2–4 are considered as MetS patients because they had 3 criteria of MetS components or more according to the modified NCEP ATP III guidelines. However, patients with hematological disorders, thyroid diseases, infectious diseases, autoimmune disorders, cerebrovascular diseases, allergies, kidney failure, liver dysfunction, and alcohol abuse were excluded from the study.

2.2. Laboratory assays

Plasma glucose and serum cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL)-cholesterol and triglycerides concentrations were determined using reagent kits purchased from Bio-Diagnostic. Insulin concentration was determined using reagent kits purchased from Biovendor, while serum leptin and adiponectin levels were estimated by using ELISA Kit purchased from My Bio-source according to the manufacturer's protocol. On the other hand, total WBCs, neutrophils, lymphocytes, monocytes and PLT counts and MPV, PDW values were determined using a MICROS ABX autoanalyzer according to the manufacturer's protocol. In addition, N/L, P/L, M/L, L/M, and dN/L ratios were determined by calculation.

2.3. Statistical analysis

The Statistical Package for the Social Sciences (IBM SPSS for WINDOWS 7, version 20; SPSS Inc, Chicago) was used in our analysis. Comparative analysis was conducted by using the general linear model's procedure (IBM SPSS) and a simple linear correlation analysis was processed by Pearson's method to measure the degree of dependency between variables (IBM SPSS). Values of $P < 0.05$ were considered statistically significant and the data were presented as Mean ± SD.

3. Results

The recorded values in Table 1 showed that the body mass index (BMI) and the atherogenic index were higher significant ($P < 0.001$) in all MetS components groups as compared to the healthy group. However, the systolic blood pressure (SBP) and diastolic blood pressure (DBP) observed significant increases in group 3 and 4 only when compared to the healthy control subjects. Patients of group 4 showed a significant increase in glycated hemoglobin (HbA1c), however, HOMA-IR percentage was significant in MetS patients groups (groups; 2, 3, 4) as compared to the healthy group.

Regarding white cell indices, the data showed that both total WBCs and neutrophils counts were significantly increased in all MetS component groups, however, lymphocytes count was significantly lowered in group 3 and 4 when compared to the control

Table 1
Demographics and characteristics of healthy subjects and different groups of MetS components.

Group Characteristic		*Healthy group 0 criteria*	*Group 1* 2 criteria*	*Group 2* 3 criteria*	*Group 3* 4 criteria*	*Group 4* 5 criteria*	*p*
Age		32.68 ± 7.76^{a}	46.10 ± 8.10^{b}	46.24 ± 10.12^{b}	46.16 ± 10.11^{b}	49.24 ± 5.95^{b}	<0.001
Gendern (%)	F	18 (36)	24 (48)	31 (62)	24 (48)	28 (56)	0.104
	M	32 (64)	26 (52)	19 (38)	26 (52)	22 (44)	
BMI		25.35 ± 3.39^{a}	28.48 ± 4.46^{b}	34.05 ± 4.89^{c}	33.71 ± 4.00^{c}	36.77 ± 6.94^{d}	<0.001
Atherogenic Index		2.09 ± 0.50^{a}	4.86 ± 2.63^{b}	4.70 ± 2.28^{b}	5.10 ± 2.53^{b}	4.93 ± 2.17^{b}	<0.001
SBP		116.80 ± 6.61^{a}	123.60 ± 8.66^{b}	118.44 ± 8.80^{a}	142.06 ± 11.78^{c}	147.42 ± 11.78^{d}	<0.001
DBP		75.70 ± 5.63^{ab}	77.10 ± 10.03^{b}	73.76 ± 6.89^{a}	89.40 ± 5.51^{c}	92.72 ± 6.91^{d}	<0.001
HbA1c		5.42 ± 0.47^{a}	5.69 ± 0.54^{a}	5.58 ± 0.60^{a}	5.71 ± 0.51^{a}	7.85 ± 1.60^{b}	0.001
HOMO-IR		2.47 ± 0.37^{a}	2.72 ± 0.35^{ab}	2.94 ± 0.29^{b}	2.96 ± 0.26^{b}	4.87 ± 1.60^{c}	<0.001

Data are expressed as mean ± SD. Values which share the same superscript symbol are not significantly different. *Group 1: Subjects with dyslipidemia, Group 2: Subjects with dyslipidemia and obesity, Group 3: Subjects with dyslipidemia, obesity and hypertension Group 4: Subjects with dyslipidemia, obesity, hypertension and diabetes. BMI; body mass index, SBP; Systolic blood pressure, DBP; Diastolic blood pressure. HbA1c; Glycosylated hemoglobin. HOMA-IR; Homeostatic model assessment for insulin resistance.

group. The recorded values of monocytes and monocytes/lymphocytes (M/L) ratio showed a significant increase in both group 3 and 4 as compared to the healthy group. In addition, the neutrophil/lymphocyte (N/L) ratio was elevated significantly in MetS patients groups, however, the platelet/lymphocyte (P/L) ratio was significantly increased in all MetS component groups as compared to the control. On the other hand, lymphocyte/monocytes (L/M) ratio showed a significant decrease in group 3 and 4, while the derived neutrophil/lymphocyte (dN/L) ratio revealed a significant increase in all MetS components patients as compared to healthy subjects (Table 2).

Concerning PLT indices, the PLT count was significantly higher in MetS patients groups, while PDW value was significantly increased in all MetS components patients than that of control. Moreover, the MPV value showed a significant increase in groups; 1, 3 and 4 when compared to the control group. On the other hand, the recorded data showed that leptin concentration and leptin/adiponectin ratio (LAR) were elevated significantly in MetS groups, while adiponectin concentration was significantly decreased in all MetS component groups as compared to the healthy subjects (Table 2 and Fig. 1).

Among dyslipidemic and obesity subjects (group 2), WBCs count showed a positive correlation with HOMA-IR (r 0.187; $P < 0.062$), atherogenic index (r 0.290; $P < 0.003$), BMI (r 0.379; $P < 0.001$) and LAR (r 0.418; $P < 0.001$) (Fig. 2). Also, N/L ratio recorded a positive correlation with each of HOMA-IR (r 0.194; P 0.053), atherogenic index (r 0.194; P 0.054), BMI (r 0.363; $P < 0.001$), and LAR (r 0.366; $P < 0.001$) (Fig. 3). Otherwise, regarding patients of group 4 (5 criteria), P/L ratio correlated positively with HOMA-IR (r 0.526; $P < 0.001$), atherogenic index (r 0.551; $P < 0.001$), BMI (r 0.408; $P < 0.001$) and LAR (r 0.582; $P < 0.001$) (Fig. 4).

4. Discussion

Although the etiopathogenesis of MetS has not been actually understood yet, previous studies support the multifactorial properties of the disease, whereas, oxidative stress, insulin resistance, and low-grade inflammation display a central role [16]. In addition, the core mechanism of MetS may be related to increased adiposity and insulin resistance [17], leptin [14], low-grade systemic inflammation [4], and endothelial dysfunction [5]. The current study revealed that leptin concentration and LAR were elevated significantly in all MetS components groups, while adiponectin level was diminished significantly in MetS groups as compared to the control. In consistent with our results, Zhuo et al. mention that elevated leptin concentration and low adiponectin level were associated with a range of variables of MetS [18]. In addition, leptin and adiponectin had opposite actions on subclinical inflammation and insulin resistance, it was found that the combining use of those two adipokines, leptin-to-adiponectin ratio (LAR), may function as a superior biomarker in the identification of MetS. Otherwise, Patel et al. reported that leptin might be a pivotal link in the pathogenesis of hypertension and heart disease induced by obesity and MetS. Furthermore, numerous studies had been speculated that leptin resistance can accelerate insulin resistance and induce abnormal accumulation of lipids in the liver, cardiac and skeletal muscle, reducing fatty acid oxidation that consequently leading to obesity and MetS [19]. Obese subjects observed an increase in leptin level and a decrease in adiponectin level, which suggests leptin resistance and adiponectin deficiency. In such cases, high leptin levels may likewise upregulate proinflammatory cytokines such as TNF-α and IL-6 that contribute to insulin resistance and MetS [20].

Regarding white blood cell indices, our data showed that WBCs and neutrophil counts, dN/L ratio and N/L ratio were increased significantly in all MetS component groups as compared to the control. Additionally, WBCs count showed a positive correlation with HOMA-IR (a marker of insulin resistance), atherogenic index (a marker of dyslipidemia), BMI (a marker of obesity) and LAR (a marker of hyperleptinemia and hypoadiponectinemia). The present findings are in parallel with previous investigations concerning the significant relationship between leukocytes count and platelets indices with MetS and its individual components [7,8]. Several epidemiological studies have suggested the association between some components of MetS and leukocyte subtypes [7]. Furthermore, Jesri et al. [11] reported that subjects with MetS had higher PLT and WBCs counts than control and these two parameters increased linearly with an increase in the number of MetS components. Total and subtype WBCs counts were directly and significantly associated with the incidence of MetS components like, hypertriglyceridemia, low HDL-C and hyperglycemia and the activation of the inflammatory signaling network involved in the pathogenesis of insulin resistance and atherogenic dyslipidemia, the main metabolic disorders underlying MetS [21] which are compatible with our outcome.

Body mass index (BMI) is one of the widely commonly used markers in general practice for adiposity. Hsieh et al. [22] reported that higher level of WBCs count was associated with higher BMI values in both genders. Adipose tissue inflammation causes major events of immune responses, such as the early participation of neutrophils, the following procurement of diverse lymphocyte types, and final procurement of both macrophage and mast cell polarization [23]. Likewise, recent studies have elucidated that elevated neutrophils and total WBCs count are potentially associated with obesity-induced dys-metabolism [24]. In addition, the increased WBCs count, often observed in obese people, would be mediated by the increase in leptin concentration [25]. Moreover, high plasma leptin levels associated with obesity and MetS could

Table 2
Total WBCs count, WBCs subtypes, platelets indices and adipocytokines in healthy subjects and groups of. MetS components.

Group Parameters	*Healthy group 0 criteria*	*Group 1* 2 criteria*	*Group 2* 3 criteria*	*Group 3* 4 criteria*	*Group 4* 5 criteria*	*p*
WBCs	5.63 ± 1.22^{a}	6.75 ± 1.76^{b}	7.07 ± 1.21^{b}	7.92 ± 1.42^{c}	8.20 ± 1.76^{c}	<0.001
Neutrophil	2.88 ± 0.69^{a}	3.66 ± 1.08^{b}	3.97 ± 0.85^{b}	4.46 ± 0.74^{c}	4.83 ± 1.20^{d}	<0.001
Lymphocyte	2.73 ± 0.64^{c}	2.60 ± 0.65^{bc}	2.52 ± 0.57^{abc}	2.35 ± 0.64^{ab}	2.28 ± 3.96^{a}	0.002
Monocyte	0.43 ± 0.13^{a}	0.48 ± 0.24^{a}	0.49 ± 0.17^{a}	0.60 ± 0.17^{b}	0.62 ± 0.18^{b}	<0.001
M/L	0.195 ± 0.04^{a}	0.190 ± 0.08^{a}	0.207 ± 0.08^{a}	0.273 ± 0.10^{b}	0.296 ± 0.14^{b}	<0.001
L/M	5.45 ± 1.55^{b}	5.77 ± 2.51^{b}	5.75 ± 2.57^{b}	4.15 ± 1.56^{a}	4.01 ± 1.63^{a}	<0.001
dN/L	1.05 ± 0.15^{a}	1.19 ± 0.22^{b}	1.31 ± 0.34^{c}	1.34 ± 0.31^{c}	1.45 ± 0.27^{d}	<0.001
PLT	252.02 ± 41.62^{a}	244.12 ± 60.83^{a}	279.12 ± 52.75^{b}	288.18 ± 69.83^{b}	314.46 ± 59.56^{c}	<0.001
MPV	9.13 ± 0.52^{a}	9.80 ± 1.17^{c}	9.37 ± 0.59^{ab}	9.56 ± 0.74^{bc}	10.67 ± 1.26^{d}	<0.001
Leptin	2.86 ± 0.41^{a}	14.59 ± 4.63^{b}	16.11 ± 2.13^{c}	17.45 ± 3.38^{d}	19.04 ± 2.68^{e}	<0.001
Adiponectin	9.98 ± 1.06^{d}	4.92 ± 1.83^{c}	4.77 ± 1.12^{c}	4.13 ± 1.41^{b}	3.29 ± 1.07^{a}	<0.001

Data are expressed as mean ± SD. Values which share the same superscript symbol are not significantly different. WBCs; white blood cell, M/L; Monocyte to lymphocyte ratio, L/M; Lymphocyte to monocyte ratio, dN/L; derived neutrophil to lymphocyte ratio, PLT; Platelets MPV; Mean platelet volume.

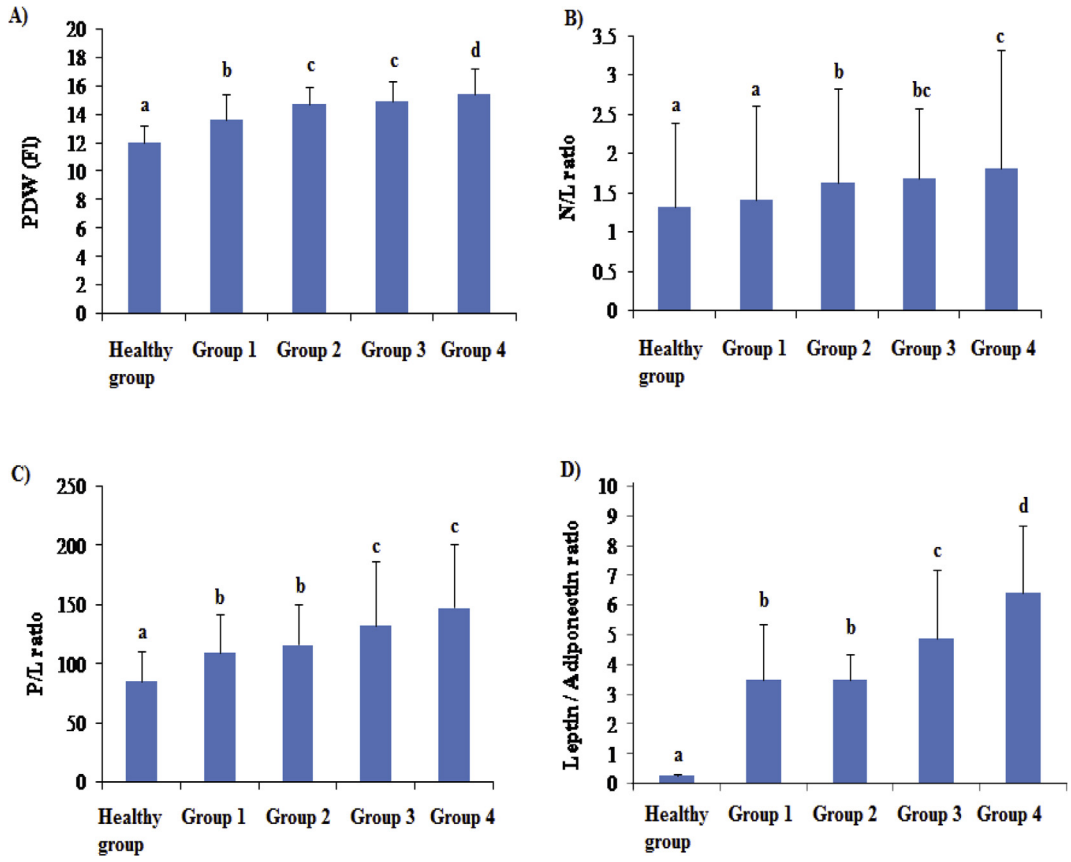

Fig. 1. A) PDW in healthy and metabolic syndrome groups, B) N/L in healthy and metabolic syndrome groups, C) P/L in healthy and metabolic syndrome groups, D) LAR in healthy and metabolic syndrome groups.
PDW; Platelets distribution width, N/L; Neutrophil/lymphocyte ratio, P/L; Platelet/lymphocyte ratio, LAR; Leptin/adiponectin ratio.

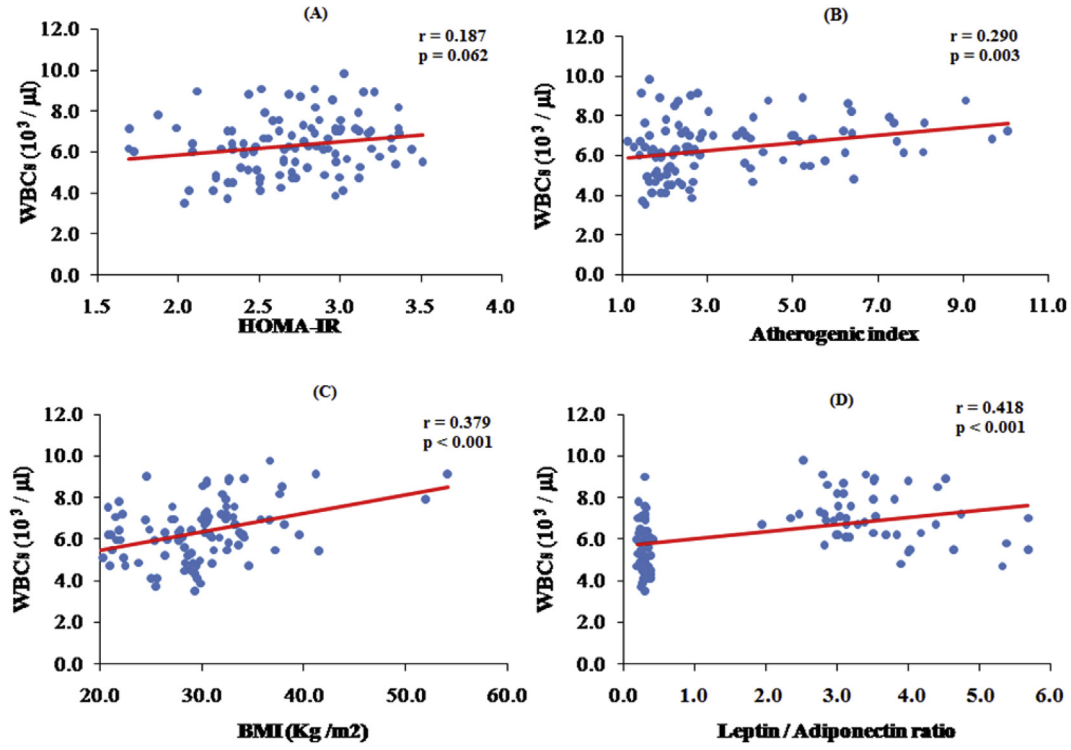

Fig. 2. The correlation between WBCs with HOMA-IR, Atherogenic index, BMI, LAR in group 2.
WBCs; white blood cells, BMI; Body mass index, HOMA-IR; Homeostatic model assessment for insulin resistance, LAR; Leptin/adiponectin ratio.

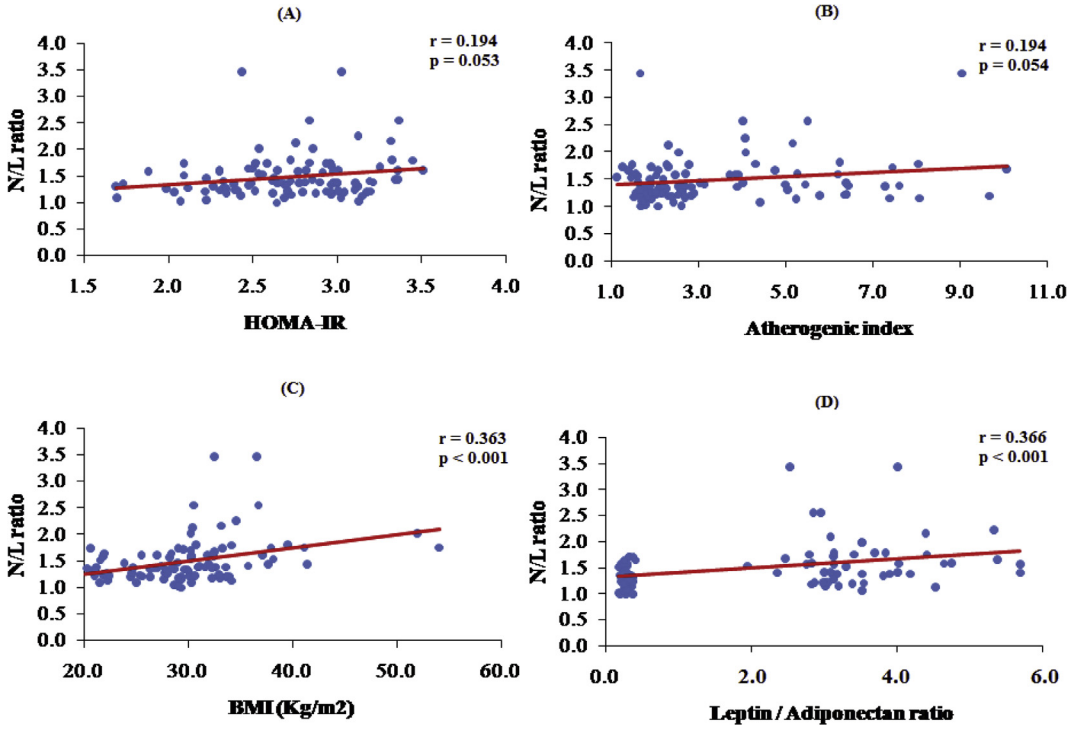

Fig. 3. The correlation between N/L ratio with HOMA-IR, Atherogenic index, BMI, LAR in group 2.

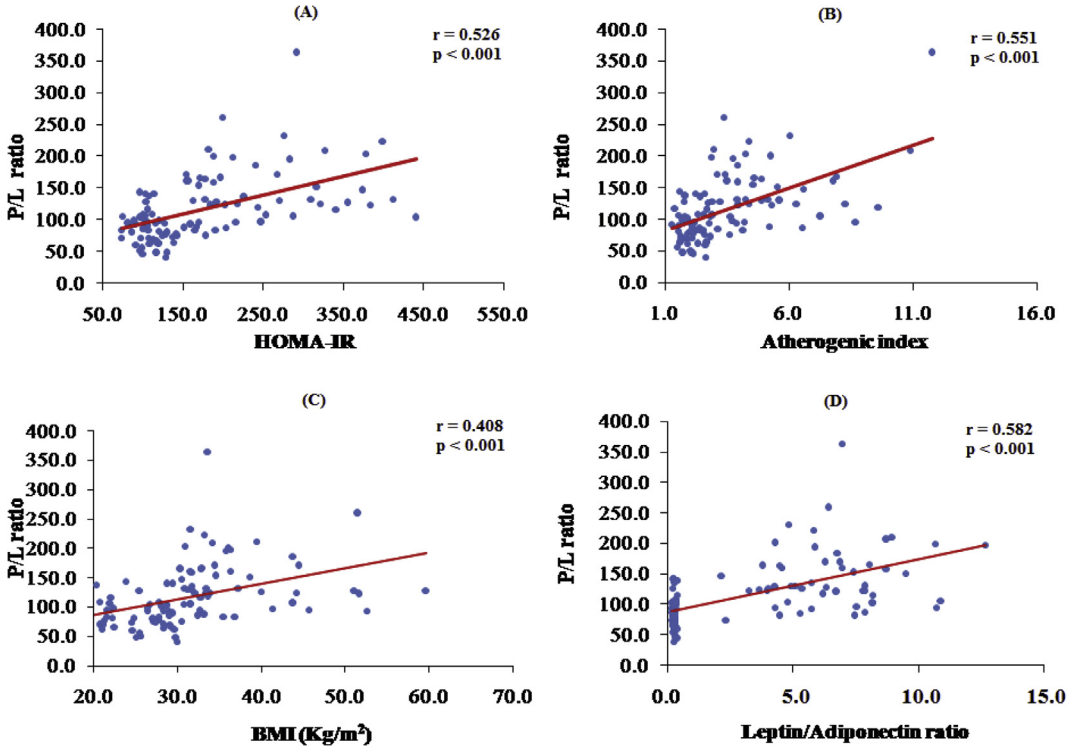

Fig. 4. The correlation between P/L ratio with HOMA-IR, Atherogenic index, BMI, LAR in group 4.

participate in the differentiation of granulocytes from hemopoietic progenitors [26]. Moreover, leptin increments with body fat mass, has mainly pro-inflammatory effects, and was shown to influence neutrophil functions such as chemotaxis, apoptosis, and seems to be a survival cytokine for neutrophils [27].

However, some systemic investigations have studied the association between MetS and differential leukocyte counts. In the present study, a positive correlation was observed between N/L

ratio and each of HOMA-IR, atherogenic index, BMI, and LAR. A study in the urban Chinese population demonstrated an association between total leukocytes, neutrophil, and lymphocyte counts with the prevalence of MetS [28]. Also, this relationship has also been reported for total leukocyte counts and neutrophils, lymphocytes, monocytes, basophils and eosinophil's counts in a cross-sectional study of Korean individuals [29]. Recently, neutrophil to lymphocyte ratio (N/L), derived neutrophil to lymphocyte ratio (dN/L), platelet to lymphocyte ratio (P/L) and lymphocyte to monocyte ratio (L/M) were promising biomarkers used to predict diagnosis and prognosis in various inflammatory responses diseases [30]. The N/L, starting to find a place in the literature, was found to be correlated with the occurrence and the severity MetS and also considered a powerful indicator of some diseases, including obesity [31], and MetS [32],

Metabolic syndrome (MetS), as an enormously growing global public health problem, is comprised of heterogeneous cardiometabolic risk factors and all-cause mortality [33]. Our data revealed that PLT count, PDW and MPV levels, and P/L ratio were significantly higher in MetS patients as compared to the control. In accordance with the current results, Jesri et al. demonstrated that PLT was positively correlated to the number of MetS risk factors [11]. Additionally, Lim et al. reported that higher PLT counts were associated with insulin resistance and increased prevalence and risk of MetS [34]. Otherwise, some investigators have noted that vascular endothelial cells are activated by the presence of atherosclerotic risk factors, such as hypertension, hyperlipidemia, and hyperglycemia, thus, accelerated the increased production and release of pro-inflammatory cytokines that could lead to chronic low-grade inflammation which influence in PLT counts [35]. An increased pro-inflammatory state is then thought to further enhance activation of WBCs and endothelial cells, thereby promoting PLT aggregation and thrombus formation [36]. Adipokines regulate glucose homeostasis, insulin sensitivity, lipids metabolism, as well as endothelial and PLT function. Elbatarny and Maurice, mention that leptin accelerates PLT activation by induced PLT aggregation and adhesion and provides a mechanistic basis for the prothrombotic effect of this adipocytokine [37]. However, Shoji et al. stated that hypoadiponectinemia could be a potential regulator of PLT activation [38]. Moreover, adiponectin has anti-atherosclerotic, anti-inflammatory, and anti-oxidative properties beyond its insulin-sensitizing effects [39]. Thus, Leptin/adiponectin ratio (LAR) has been considered as a novel marker for atherosclerotic plaque formation as well as tissue insulin sensitivity in obese patients [40].

Mean platelet volume (MPV), the most ordinarily used measure of PLT size, is a potential marker of PLT reactivity. Larger PLT consist of more granules and produce large amounts of vasoactive and prothrombotic factors. PLT aggregate more rapidly under the stimulus of agonists and finally, they express a greater number of adhesion molecules [41], leading to greater hemostatic efficiency. Although several studies have concluded that there is a close relationship between MPV and obesity, MetS, and body fat [42], the interaction between MPV, obesity and MetS had not been affirmed. Meanwhile, MPV was increased in the presence of MetS and it was significantly correlated with a number of components of MetS (blood pressure, BMI, and fasting plasma glucose) that in parallel with the data of our outcome. Recently, P/L ratio has been introduced as a novel indirect inflammatory marker. In accordance with our finding, P/L ratio was significantly higher among patients with MetS and also there was a close relationship between P/L and the MetS components [43]. The authors added that several reports claimed that higher P/L ratio can be used as a predictive marker for both the presence and severity of MetS.

5. Conclusions

The overall outcome showed significant increases in leukocytes, platelet indices and leptin in the patients with different MetS components, while it showed a significant decrease in adiponectin level. There were significant correlations between leukocytes, platelet indices, with leptin–to-adiponectin ratio and the MetS markers. Therefore, our study provides additional evidence for the use of leukocytes and platelet indices as well as LAR as new markers for early detection of MetS components.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.12.016.

References

[1] Kaur J. A Comprehensive review on metabolic syndrome. Cardiol Res Pract 2014;2014:943162.
[2] Dajani R, Khader YS, Hakooz N, Fatahalla R, Quadan F. Metabolic syndrome between two ethnic minority groups (Circassians and Chechens) and the original inhabitants of Jordan. Endocrine 2013;43(1):112–9.
[3] Kawamoto R, Tabara Y, Kohara K, Miki T, Kusunoki T, Abe M, Katoh T. Hematological parameters are associated with metabolic syndrome in Japanese community-dwelling persons. Endocrine 2013;43(2):334–41.
[4] Jung CH, Lee WY, Kim BY, Park SE, Rhee EJ, Park CY, et al. The risk of metabolic syndrome according to the white blood cell count in apparently healthy Korean adults. Yonsei Med J 2013;54:615–20.
[5] Kim JA, Choi YS, Hong JI, Kim SH, Jung HH, Kim SM. Association of metabolic syndrome with white blood cell subtype and red blood cells. Endocr J 2006;53:133–9.
[6] Oda E, Kawai R. Comparison between high-sensitivity C-reactive protein (hs-CRP) and white blood cell count (WBC) as an inflammatory component of metabolic syndrome in Japanese. Intern Med 2010;49:117–24.
[7] Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005;45(10):1638–43.
[8] Lim HJ, Seo MS, Shim JY, Kim KE, Shin YH, Lee YJ. The association between platelet count and metabolic syndrome in children and adolescents. Platelets 2015;26:758–63.
[9] Kotani K, Sakane N, Saiga K, Mu H, Kurozawa Y. Clustered components of the metabolic syndrome and platelet counts in Japanese females. Clin Chem Lab Med 2007;45:376–9.
[10] Kutlucan A, Bulur S, Kr S, Bulur S, Önder E, Aslantaş Y, et al. The relationship between mean platelet volume with metabolic syndrome in obese individuals. Blood Coagul Fibrinolysis 2012;23(5):388–90.
[11] Jesri A, Okonofua EC, Egan BM. Platelet and white blood cell counts are elevated in patients with the metabolic syndrome. J Clin Hypertens 2005;7. 705–11; quiz 712–3.
[12] Okamoto Y, Kihara S, Funahashi T, Matsuzawa Y, Libby P. Adiponectin: a key adipocytokine in metabolic syndrome. Clin Sci (Lond) 2006;110(3):267–78.
[13] Ghadge AA, Khaire AA, Kuvalekar AA. Adiponectin: a potential therapeutic target for metabolic syndrome. Cytokine Growth Factor Rev 2018;39:151–8.
[14] Mantzoros CS, Magkos F, Brinkoetter M, Sienkiewicz E, Dardeno TA, Kim SY, et al. Leptin in human physiology and pathophysiology. Am J Physiol Endocrinol Metab 2011;301:E567–84.
[15] Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. "Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III)". J Am Med Assoc 2001;285(19):2486–97.
[16] Wang Y, Yu Q, Chen Y, Cao F. Pathophysiology and therapeutics of cardiovascular disease in metabolic syndrome. Curr Pharmaceut Des 2013;19: 4799–805.
[17] Alberti KG, Zimmet P, Shaw J. Metabolic syndrome–a new world-wide definition. A consensus statement from the international diabetes federation. Diabet Med 23:469–480.
[18] Zhuo Q, Wang Z, Fu P, Piao J, Tian Y, Xu J, et al. Comparison of adiponectin, leptin and leptin to adiponectin ratio as diagnostic marker for metabolic syndrome in older adults of Chinese major cities. Diabetes Res Clin Pract 2009;84(1):27–33.
[19] Patel SB, Reams GP, Spear RM, Freeman RH, Villarreal D. Leptin: linking obesity, the metabolic syndrome, and cardiovascular disease. Curr Hypertens Rep 2008;10:131–7.
[20] Lopez-Jaramillo P, Gomez-Arbelaez D, Lopez-Lopez J, Lopez-Lopez C, Martinez-Ortega J, Gomez-Rodriguez A, et al. The role of leptin/adiponectin ratio in metabolic syndrome and diabetes. Horm Mol Biol Clin Invest 2014;18(1): 37–45.

[21] Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation 2005;111:1448–54.
[22] Hsieh CH, Pei D, Kuo SW, Chen CY, Tsai SL, Lai CL. Correlation between white blood cell count and metabolic syndrome in adolescence. Pediatr Int 2007;49:827–32.
[23] Chatzigeorgiou A, Karalis KP, Bornstein SR, Chavakis T. Lymphocytes in obesity-related adipose tissue inflammation. Diabetologia 2012;55:2583–92.
[24] Huang ZS, Chien KL, Yang CY, Tsai KS, Wang CH. Peripheral differential leukocyte counts in humans vary with hyperlipidemia, smoking, and body mass index. Lipids 2001;36:237–45.
[25] Mabuchi T, Yatsuya H, Tamakoshi K, Otsuka R, Nagasawa N, Zhang H, et al. Association between serum leptin concentration and white blood cell count in middle-aged Japanese men and women. Diabetes Metab Res Rev 2005;21(5):441–7.
[26] Laharrague P, Oppert JM, Brousset P, Charlet JP, Campfield A, Fontanilles AM, et al. High concentration of leptin stimulates myeloid differentiation from human bone marrow CD34+ progenitors: potential involvement in leukocytosis of obese subjects. Int J Obes Relat Metab Disord 2000;24(9):1212–6.
[27] Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. Nat Rev Immunol 2011;11:85–97.
[28] Meng W, Zhang C, Zhang Q, Song X, Lin H, Zhang D, et al. Association between leukocyte and metabolic syndrome in urban han Chinese: a longitudinal cohort study. PLoS One 2012;7(11):e49875.
[29] Kim DJ, Noh JH, Lee BW, Choi YH, Chung JH, et al. The associations of total and differential white blood cell counts with obesity, hypertension, dyslipidemia and glucose intolerance in a Korean population. J Kor Med Sci 2008;23:193–8.
[30] Tang K, Liu H, Jiang K, Ye T, Yan L, Liu P, et al. Predictive value of preoperative inflammatory response biomarkers for metabolic syndrome and post-PCNL systemic inflammatory response syndrome in patients with nephrolithiasis. Oncotarget 2017 18;8(49):85612–27.
[31] Bahadir A, Baltaci D, Turker Y, Turker Y, Iliev D, Ozturk S, et al. Is the neutrophil-to-lymphocyte ratio indicative of inflammatory state in patients with obesity and metabolic syndrome? Anatol J Cardiol 2015;15:816–22.
[32] Buyukkaya E, Karakas MF, Karakas E, Akcay AB, Tanboga IH, Kurt M, et al. Correlation of neutrophil to lymphocyte ratio with the presence and severity of metabolic syndrome. Clin Appl Thromb Hemost 2014;20:159–63.
[33] Arbel Y, Havakuk O, Halkin A, Revivo M, Berliner S, Herz I, et al. Relation of metabolic syndrome with long-term mortality in acute and stable coronary disease. Am J Cardiol 2015;115:283–7.
[34] Lim HJ, Seo MS, Shim JY, Kim KE, Shin YH, Lee YJ. The association between platelet count and metabolic syndrome in children and adolescents. Platelets 2015;26(8):758–63.
[35] Park BJ, Shim JY, Lee HR, Jung DH, Lee JH, Lee YJ. The relationship of platelet count, mean platelet volume with metabolic syndrome according to the criteria of the American Association of Clinical Endocrinologists: a focus on gender differences. Platelets 2012;23(1):45–50.
[36] Ross R. Atherosclerosis–an inflammatory disease. N Engl J Med 1999;340:115–26.
[37] Elbatarny HS, Maurice DH. Leptin-mediated activation of human platelets: involvement of a leptin receptor and phosphodiesterase 3A-containing cellular signaling complex. Am J Physiol Endocrinol Metab 2005;289(4):E695–702.
[38] Shoji T, Koyama H, Fukumoto S, Maeno T, Yokoyama H, Shinohara K, Emoto M, Shoji T, Yamane T, Hino M, Shioi A, Nishizawa Y. Platelet activation is associated with hypoadiponectinemia and carotid atherosclerosis. Atherosclerosis 2006;188(1):190–5.
[39] Fuentes E, Fuentes F, Vilahur G, Badimon L, Palomo I. Mechanisms of chronic state of inflammation as mediators that link obese adipose tissue and metabolic syndrome. Mediat Inflamm 2013;2013:136584. https://doi.org/10.1155/2013/136584.
[40] Kotani K, Sakane N. Leptin: adiponectin ratio and metabolic syndrome in the general Japanese population. Korean J Lab Med 2011;31:162–6.
[41] Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996;7:157–61.
[42] Tavil Y, Sen N, Yazici HU, Hizal F, Abaci A, Cengel A. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. Thromb Res 2007;120:245–50.
[43] Akboga MK, Canpolat U, Yuksel M, Yayla C, Yilmaz S, Turak O. Platelet to lymphocyte ratio as a novel indicator of inflammation is correlated with the severity of metabolic syndrome: a single center large-scale study. Platelets 2016;27(2):178–83.