STUDY OF PLATELET-TO-LYMPHOCYTE RATIO IN PATIENTS WITH METABOLIC SYNDROME

Mohammed Aslam Shaikh[1], Bhanuprakash P[2]

[1]Associate Professor, Department of Medicine, M.S. Ramaiah Medical College, Bangalore.
[2]Junior Resident, Department of Medicine, M.S. Ramaiah Medical College, Bangalore.

ABSTRACT

BACKGROUND

Metabolic Syndrome (MS) is considered as a major public health concern since the prevalence has reached epidemic proportions in the past decade. The Platelet-to-Lymphocyte Ratio (PLR) has recently emerged as a novel inflammatory biomarker, which has been used in many diseases for predicting inflammation and mortality. Hence, the present study was done to study the association between the platelet-to-lymphocyte ratio and presence of metabolic syndrome.

MATERIALS AND METHODS

50 patients with metabolic syndrome were included in the study. 50 age and sex matched healthy individuals were included as the control group. The study was carried out over a period of 1 year from October 2015 to September 2016. The new international diabetic federation (IDF) criteria was used to make a diagnosis of metabolic syndrome. Platelet-to-lymphocyte ratio was calculated from the complete blood count.

RESULTS

The mean age of the patients in the study group was 52.62 ± 15.42 years. The mean hs-CRP was significantly higher in patients with MS (4.0982 ± 2.2971) when compared with patients without MS (1.449 ± 0.9657) ($p<0.005$). Mean PLR was also higher in patients with MS (194.64 ± 72.13) when compared with patients without MS (92.72 ± 35.32) ($p<0.005$).

CONCLUSION

As platelet-to-lymphocyte ratio is an easily available and cheap inflammatory biomarker, it can be used as a marker of metabolic syndrome.

KEYWORDS

Platelet-to-Lymphocyte Ratio, Metabolic Syndrome, High-Sensitive C-Reactive Protein.

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BACKGROUND

The term Metabolic Syndrome (MS) is defined as constellation of physical, biochemical and metabolic parameters that increase the risk of cardiovascular disease, type 2 diabetes mellitus and all-cause mortality.[1] Occurrence of metabolic syndrome in a given individual confers a 5-fold increase in the risk of type 2 diabetes mellitus and 2-fold increase in the risk of development of cardiovascular disease over next 5-10 years.[2,3] The prevalence of metabolic syndrome seem to have progressively increased with time in the past decade. The current dietary practices such as increased consumption of simple sugars, processed food and sedentary lifestyle are to be blamed for increasing incidence of metabolic syndrome.

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Corresponding Author:
Dr. Mohammed Aslam Shaikh,
#22, "Zaheera Mahal" , 3rd Cross,
Akashwani Layout, Vidyaranyapura,
Bangalore-560097.
E-mail: drmdaslam@yahoo.com
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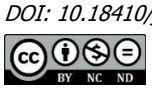

Various Indian studies have reported that the prevalence of metabolic syndrome among Indians vary from 6.5% to 46% and have shown a slightly higher prevalence among women.[4,5] Due to lack of nationwide survey in India, less is known about the magnitude of metabolic syndrome in India. Though different diagnostic criteria are used for diagnosis of metabolic syndrome such as International Diabetic Federation (IDF) and World Health Organization (WHO) criteria, the central obesity, dyslipidaemia, hypertension and glucose intolerance form the main components of metabolic syndrome.

Inflammation plays a pivotal role in the development of insulin resistance and metabolic syndrome. There is increased inflammation in patients with metabolic syndrome, which can be demonstrated by increase in levels of High-Sensitive C-Reactive Protein (hs-CRP). There are suggestions to include hs-CRP as one of the diagnostic criteria for metabolic syndrome.

Studies have shown that high Platelet-to-Lymphocyte Ratio (PLR) reflects inflammation, atherosclerosis and platelet activation. There are no additional costs for measurement of platelet-to-lymphocyte ratio when compared with hs-CRP. PLR can be easily calculated from complete blood count. Hence, the present study was carried out to study the association between PLR and presence of MS.

Aims and Objectives of the Study

To study the association between platelet-to-lymphocyte ratio and presence of metabolic syndrome.

MATERIALS AND METHODS

50 patients with metabolic syndrome were included in the study. 50 age and sex matched healthy individuals were included as the control group. The study was carried out over a period of 1 year from October 2015 to September 2016.

Inclusion Criteria

Patients aged above 18 years and diagnosed to have metabolic syndrome according to new International Diabetes Federation (IDF) criterias.[6] MS was defined as presence of central obesity defined as waist circumference ≥90 cm for men and ≥80 cm for women plus any two of the following four factors-

1. Raised triglyceride level (TG) ≥150 mg/dL (1.7 mmol/L) or specific treatment for this lipid abnormality.
2. Reduced HDL cholesterol- <40 mg/dL (1.03 mmol/L) in males, <50 mg/dL (1.29 mmol/L) in females or specific treatment for this lipid abnormality.
3. Raised blood pressure- systolic ≥130 mm of Hg or diastolic >85 mm of Hg or treatment for previously diagnosed hypertension.
4. Raised Fasting Blood Sugar (FBS) ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes mellitus.

Exclusion Criteria

Patients who have acute infection or chronic infection like tuberculosis, patients who have chronic systemic inflammatory disease like rheumatoid arthritis, Systemic Lupus Erythematosus (SLE) etc., pregnant women, patients with acute myocardial infection or acute stroke and patients on steroids were excluded from the study.

Methods of Data Collection

100 patients who attended medicine outpatient and inpatient services at M.S. Ramaiah Hospitals fulfilling inclusion and exclusion criteria were included in the study. It was a hospital-based case-controlled study. Study was carried out over a period of one year from October 2015 to September 2016. Purpose of the study was explained to the patients and informed consent was obtained. Thereafter, patients were assessed, vital parameters measured and anthropometric measurements like height, weight, Body Mass Index (BMI), waist circumference, hip circumference, waist hip ratio and skin fold thickness (triceps) were measured. Blood pressure was measured on the right arm after a 20-minute rest in the sitting position using a mercury sphygmomanometer by the auscultatory method in accordance to the American Heart Association protocol. Waist circumference was measured on bare skin during mid-inspiration at the narrowest indentation between the tenth rib and the iliac crest using a plastic anthropometric tape. BMI was calculated as weight in kilograms divided by height in meter square.

Blood samples for Complete Blood Count (CBC), Platelet-to-Lymphocyte Ratio (PLR), lipid profile and hs-CRP were sent. Blood samples were taken after 12 hours overnight fast. PLR were obtained from complete blood count as ratio of absolute platelet count to the absolute lymphocyte count. PLR was measured as a part of Automated Complete Blood Count using Sysmex XE-2100 and XT-2000i. The data and investigations were entered in clinical proforma. Clinical parameters and laboratory investigations were compared among the study groups and control group.

Statistical Analysis

Minitab version 17 was used for computation of statistics. Continuous variables are presented as mean for parametric data and median if the data is nonparametric or skewed. Student's t-test was applied for calculation of statistical significance whenever the data followed normative distribution. Mann-Whitney test was applied whenever data followed non-normative distribution. Categorical variables are expressed as frequencies and percentages. Nominal categorical data between the groups was compared using Chi-square test or Fisher's exact test as appropriate.

RESULTS

The mean age of the patients was 52.62 ± 15.42 years in the patients with metabolic syndrome (study group) and 50.04 ± 14.87 years in the patients without metabolic syndrome (control group). 56% of the patients in both the groups were males. 66% of the patients in the study group and 20% of the patients in the control group had hypertension. The study group's means of height, weight, BMI, waist circumference, hip circumference, waist-to-hip ratio and skin fold thickness (triceps) were 1.56 ± 0.12 meter, 76.84 ± 10.86 kg, 32.29 ± 6.83 kg/m^2, 91.68 ± 5.14 cm, 94.24 ± 13.28 cm, 0.99 ± 0.13, and 19.08 ± 6.32 cm, respectively. Anthropometric measurements like weight, Body Mass Index (BMI), waist circumference, waist-to-hip ratio and skin fold thickness were significantly higher in patients with metabolic syndrome when compared with patients without metabolic syndrome (Table 1).

The means of biochemical parameters like fasting blood glucose, postprandial blood glucose, total cholesterol, triglyceride and Low-Density Lipoprotein (LDL) in study group were 127.58 ± 36.7 mg/dL, 183.32 ± 41.94 mg/dL, 231.27 ± 29.08 mg/dL, 192.86 ± 43.15 mg/dL and 155.56 ± 24.98 mg/dL, respectively and were significantly higher when compared with patients without metabolic syndrome (Table 2).

Mean platelet count in study group was 3,68,900 ± 72,693.16 cells/mm^3 and 2,26,280 ± 79,256.5 cells/mm^3 in the control group ($p<0.005$) (Figure 1), mean lymphocyte count in study group was 2,055 ± 573.47cells/mm^3 and 2,485.4 ± 393.53 cells/mm^3 in the control group ($p=0.002$) (Figure 2). Platelet-to-lymphocyte ratio was significantly higher in study group when compared with the control group (194.64 ± 72.13 and 92.72 ± 35.32, respectively) ($p<0.005$)

(Figure 3). Optimal sensitivity and specificity of PLR was calculated by Area Under the Curve (AUC) = 0.594 (0.542-0.641), p<0.001). PLR had a sensitivity of 86% and specificity of 84% with a cut-off value of 120 in predicting presence of metabolic syndrome (Figure 4).

Hs-CRP was significantly higher in study group when compared with the control group. Mean hs-CRP was 4.0982 ± 2.2971 mg/L in patients with metabolic syndrome and 1.449 ± 0.9657 mg/L in patients without metabolic syndrome (p<0.005) (Table 3).

Anthropometric Measurement	Cases (n=50)	Controls (n=50)	p value
Height (in meters)	1.56 ± 0.12	1.53 ± 0.12	0.289
Weight (in kg)	76.84 ± 10.86	62.14 ± 9.24	<0.05
BMI (kg/m2)	32.29 ± 6.83	27.04 ± 6.03	<0.05
Waist circumference (in centimetres)	91.68 ± 5.14	84.54 ± 4.9	<0.05
Hip circumference (in centimetres)	94.24 ± 13.28	93.48 ± 13.47	0.777
Waist hip ratio	0.99 ± 0.13	0.92 ± 0.13	0.01
Skin fold thickness (triceps) (in centimetres)	19.08 ± 6.32	7.68 ± 2.59	<0.05

Table 1. Anthropometric Measurements

Laboratory Parameter	Cases (n=50) Mean ± SD	Controls (n=50) Mean ± SD	p value
FBS (mg/dL)	127.58 ± 36.7	95.76 ± 21.94	<0.005
PPBS (mg/dL)	183.32 ± 41.94	159.08 ± 34.29	0.002
Total cholesterol (mg/dL)	231.27 ± 29.08	143.56 ± 20.71	<0.005
Triglyceride (mg/dL)	192.86 ± 43.15	103.38 ± 26.94	<0.005
HDL (mg/dL)	37.14 ± 3.87	39.22 ± 4.11	0.011
LDL (mg/dL)	155.56 ± 24.98	83.56 ± 19.03	<0.005

Table 2 Biochemical Parameters

Laboratory Parameter	Cases (n=50) Mean ± SD	Controls (n=50) Mean ± SD	p value
Total leukocyte count (cells/mm^3)	8182 ± 1384.56	8164 ± 1388.84	0.948
Platelet count (cells/mm^3)	368900 ± 72693.16	226280 ± 79256.5	<0.005
Lymphocyte count (cells/ mm^3)	2055 ± 573.47	2485.4 ± 393.53	0.002
PLR	194.64 ± 72.13	92.72 ± 35.32	<0.005
hs-CRP	4.0982 ± 2.2971	1.449 ± 0.9657	<0.005

Table 3. Basic Laboratory Parameters

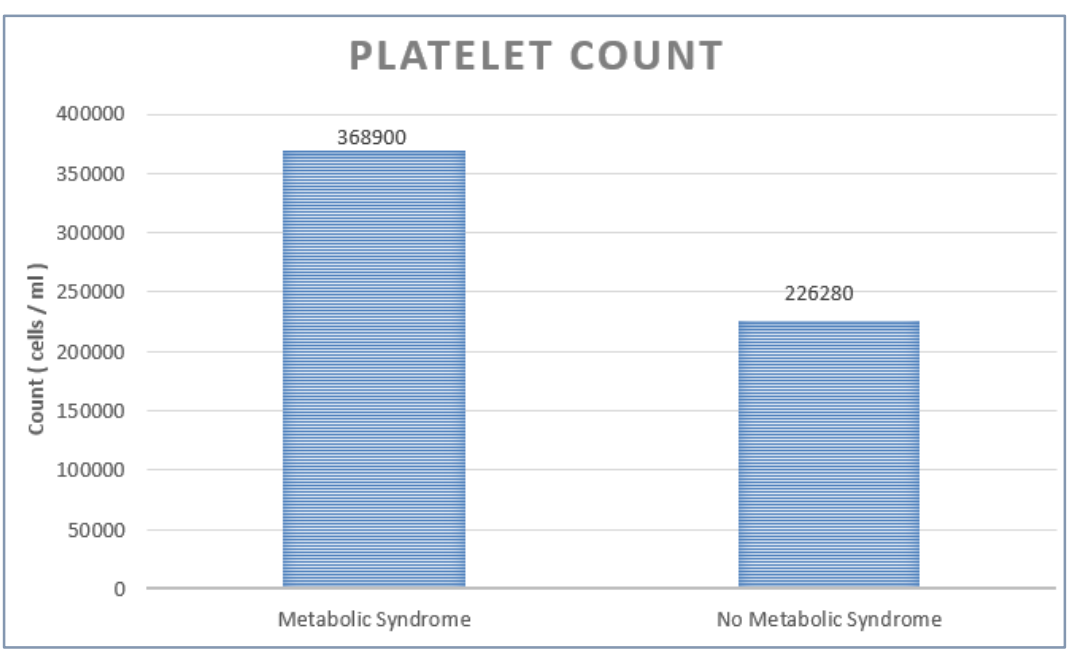

Figure 1. Platelet Count

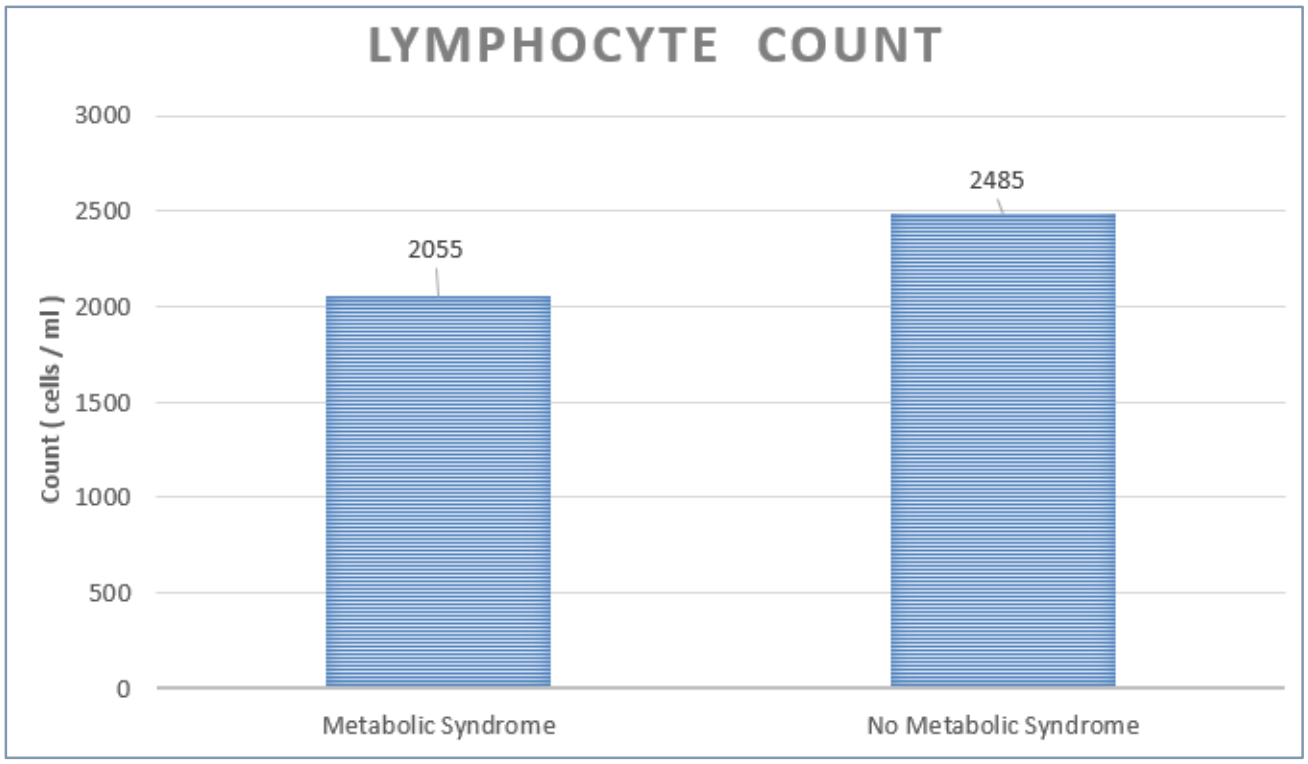

Figure 2. Lymphocyte Count

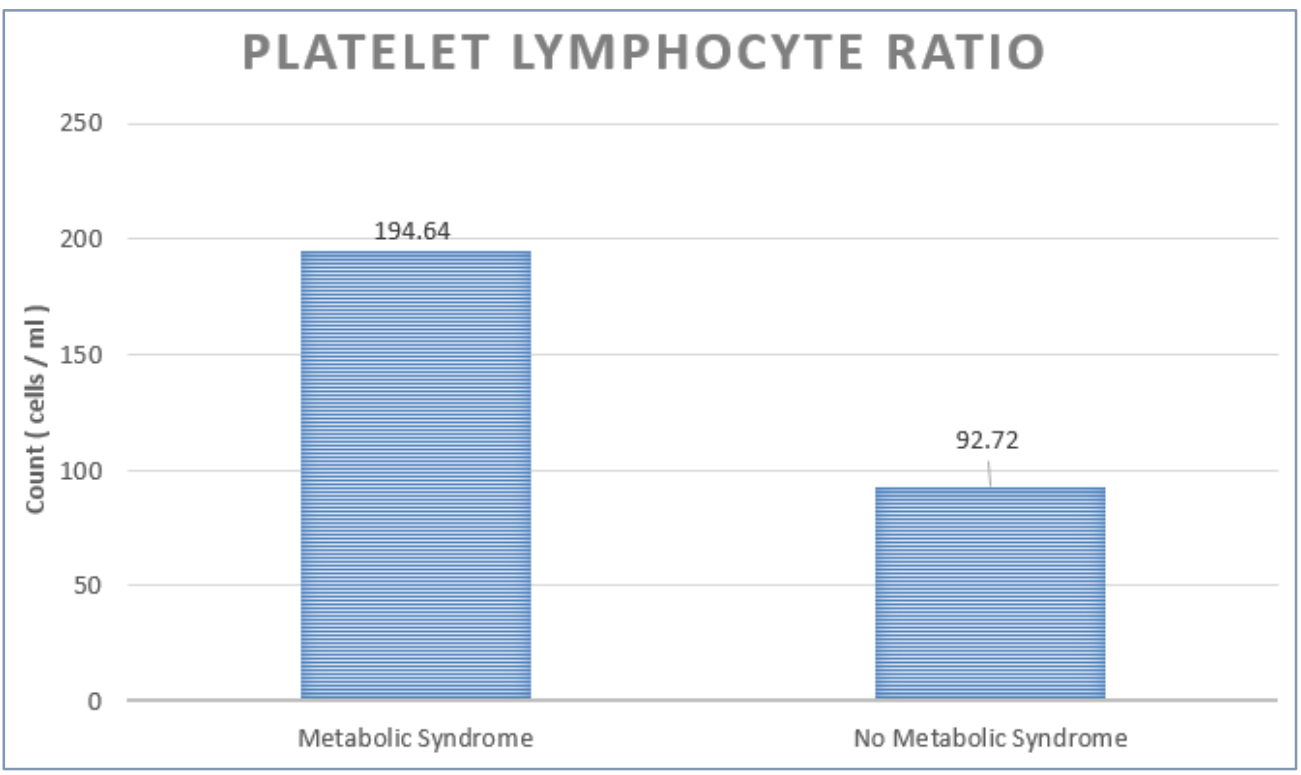

Figure 3. Platelet-to-Lymphocyte Ratio

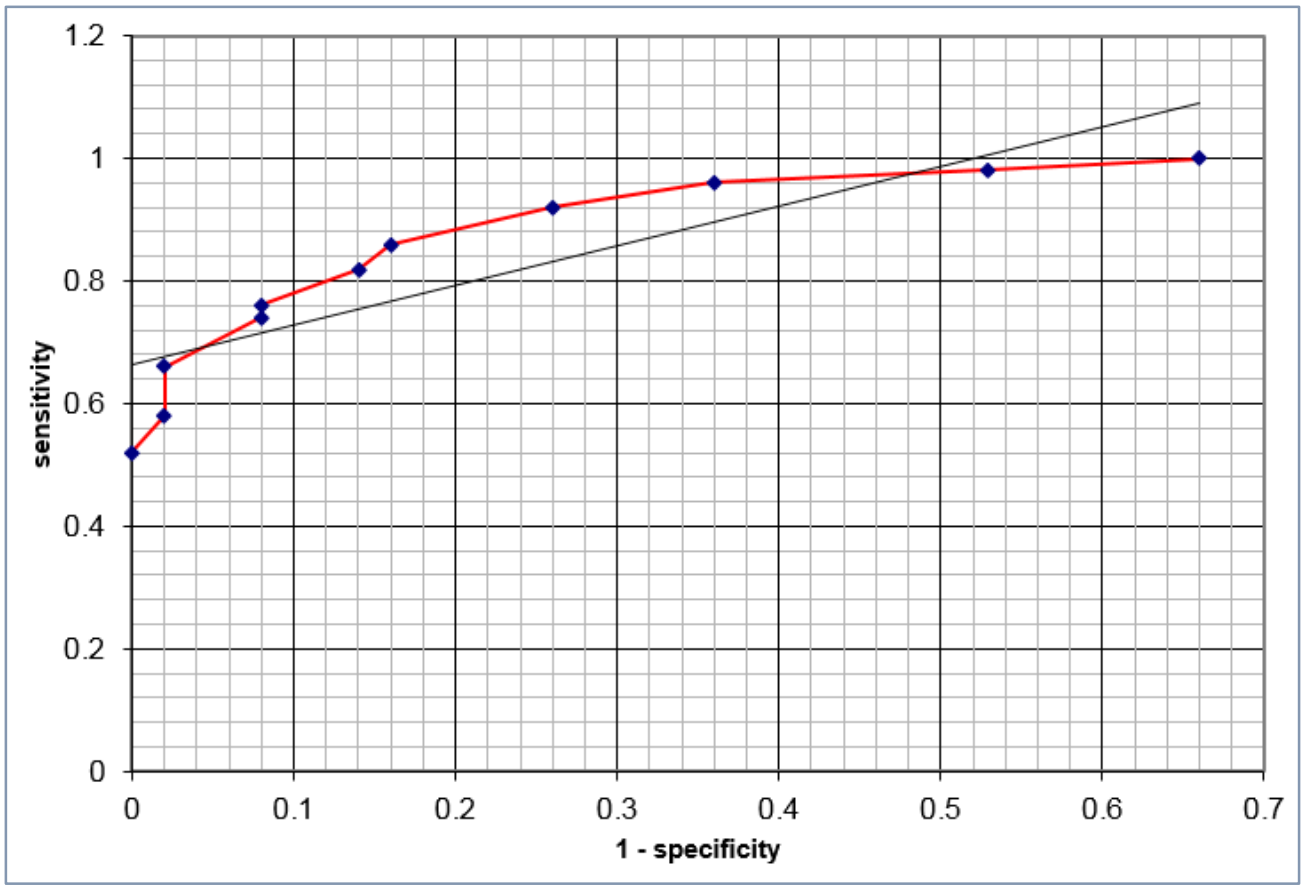

Figure 4. Area under Curve for PLR

DISCUSSION

Metabolic syndrome is clustering of cardiovascular risk factors in an individual, which includes abdominal obesity, hypertension, glucose intolerance, dyslipidaemia and insulin resistance. MS has an increased propensity for development of diabetes mellitus and cardiovascular disease. The increasing burden of obesity is the driving force behind the rising prevalence of the metabolic syndrome. About one third of Indians especially from urban areas have metabolic syndrome.

Central obesity is a key feature of the syndrome, being both a symptom and a cause of it. The increasing adiposity often reflected in high waist circumference often results from and often contributes to insulin resistance. However, despite the importance of obesity, patients who are of normal weight may also be insulin-resistant and have the syndrome.

The pathogenesis of metabolic syndrome is multifactorial. However, insulin resistance is considered as a cornerstone in the pathogenesis. The exact mechanisms of the complex pathways of metabolic syndrome are under investigation. The pathophysiology is very complex and has been only partially elucidated. A number of markers of systemic inflammation, including C-reactive protein are often increased as are fibrinogen, interleukin-6, Tumour Necrosis Factor Alpha (TNF-α) and others.[7]

High-sensitive CRP is an acute phase reactant and a sensitive marker of systemic inflammation. It has been found to be raised in conditions like diabetes mellitus and coronary artery disease.[8] High concentration of hs-CRP, a proinflammatory cytokine is associated with insulin resistance and metabolic syndrome.[9] Measurement of hs-CRP is the simplest way to identify a proinflammatory state in clinical practice. Levels of hs-CRP less than 1, 1 to 3 and greater than 3 mg/L (milligrams per litre) discriminate between individuals with low, moderate and high risk for future coronary artery disease events and stroke.

Platelet-to-Lymphocyte Ratio (PLR)

People with the metabolic syndrome typically manifest prothrombotic state with elevations of fibrinogen, plasminogen activator inhibitor-1 and other coagulation factors. These abnormalities, however, are not routinely detected in clinical practice. Platelet-to-Lymphocyte Ratio (PLR) is a novel indicator of systemic inflammation that combines prognostic values of an individual's platelet and lymphocyte count. Platelet-to-Lymphocyte Ratio (PLR) has recently been identified as a biological indicator of the balance between inflammation and thrombosis. The PLR ratio is an independent predictor of mortality in patients with acute myocardial infarction, ovarian cancer, hepatocellular carcinoma and oesophageal carcinoma.[10,11,12,13] Prior studies have demonstrated the association between the major adverse cardiovascular outcomes and both higher platelet and lower lymphocyte counts.

In the present study, hs-CRP was significantly higher in patients with metabolic syndrome (4.0982 ± 2.2971) when compared with patients without metabolic syndrome (1.449 ± 0.9657) ($p<0.005$). Similar findings were noted by Maleki et al in Iran (6.96 ± 8.79 and 6.16 ± 7.74) and it was statistically significant. In a study done by Akboga MK et al,

patients with metabolic syndrome had significantly higher PLR level compared to those without metabolic syndrome.[14] Similar findings were noted in our study. Since the sample size in our study was small, further studies with larger population are required to establish PLR as a marker of MS.

Inflammation plays a key role in most of the chronic diseases. Increased platelet activity correlates with an increase in severity of inflammation. Higher PLR in absence of absolute thrombocytosis is associated with increased thrombosis and inflammation. PLR not only shows the state of coagulation, but also reflects the inflammatory status. Higher platelet counts may reflect underlying inflammation and lower lymphocyte counts may represent an uncontrolled inflammatory pathway. Thus, a higher PLR maybe a useful inflammatory marker. Elevated PLR has been demonstrated to be associated with end-stage renal disease, SLE, psoriatic arthritis and subclinical inflammation in atherosclerosis.[15,16,17] Increased platelet activation plays a major role in the initiation and progression of atherosclerosis. Recent studies have shown Platelet-to-Lymphocyte Ratio (PLR) to be a new inflammatory marker and predictor of adverse outcomes in various cardiovascular diseases.

CONCLUSION

Complete blood count is a routine, inexpensive test done routinely and PLR can be easily calculated from the complete blood count. In the present study, PLR was significantly higher in patients with metabolic syndrome when compared with patients without metabolic syndrome. Hence, in developing country like India, PLR can be used as a marker of metabolic syndrome.

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