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Original Research Article

A study of platelet to lymphocyte ratio in patients with metabolic syndrome

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ABSTRACT

Background: The prevalence of the metabolic syndrome varies around the world, in part reflecting the age and ethnicity of the populations studied and the diagnostic criteria applied. Numerous studies have shown an association of Metabolic Syndrome (MS) and insulin resistance (IR) with inflammation. Platelet-lymphocyte ratio (PLR) has recently emerged as a novel inflammatory index that may serve as an important predictor of inflammatory state and overall mortality. Aim of this study is to evaluate the PLR in patients with MS and to correlate the same with the severity of MS based on its categories.
Methods: A cross sectional study was conducted on 210 subjects (105 subjects with Metabolic Syndrome and 105 age and gender matched control participants without Metabolic Syndrome) seen on outpatient basis at hospitals attached to Basaveshwara medical college and research institute, Chitradurga. Detailed history including history of risk factors if any, physical examinations and baseline investigations like complete blood counts, HbA1c levels, serum glucose levels, fasting lipid profile, electrocardiography and the data was analyzed using appropriate statistical methods.
Results: PLR was 6% higher in males (PLR-144.77±34.6) when compared to females (PLR-136.57±30.4) in subjects with metabolic syndrome. There was 95.9% higher PLR in subjects with metabolic syndrome when compared to subjects without metabolic syndrome ($p<0.05$). Furthermore, PLR increased more as severity of metabolic syndrome increased (5/5 PLR-180.55±25.3,4/5 PLR-132.33±23.6, 3/5 PLR- 109.63±22.6 and non-metabolic syndrome (PLR-77.45±19.5).
Conclusions: In this study, PLR above 90 predicted significant inflammation. PLR is calculated from complete blood count with differential, is an inexpensive, easy to obtain, widely available marker of inflammation, which can aid in the risk stratification of patients with various cardiovascular diseases in addition to the traditionally used markers.

Keywords: Insulin resistance, Metabolic syndrome

INTRODUCTION

Prevalence of metabolic syndrome as defined by the National Cholesterol Education Programme, Adult Treatment Panel III (NCEP,ATP) and other criteria indicates ranges from 11% to 41% in India.[1] Numerous studies have shown an association of metabolic syndrome and insulin resistance with inflammation. Two hypotheses have been proposed to explain the relationship of MS with inflammation. The first states that chronic low-grade inflammation leads to metabolic disturbances, which in turn leads to insulin resistance.[2] The second suggests that altered glucose and lipid metabolism trigger inflammation which results in insulin resistance.[3]

The relationship of systemic inflammatory markers high-sensitivity CRP (hs-CRP) with metabolic syndrome and

insulin resistance has been shown in several studies.[4] Prediabetic subjects who were insulin resistant had higher levels of inflammatory markers (hs-CRP). Therefore, a proinflammatory state can contribute to the atherogenic risk profile in prediabetic patients with increased insulin resistance.[5] However, most of these markers are time consuming and expensive.

Platelets and leukocytes are the important components of these processes associated with the development of atherosclerosis. Platelet-to-lymphocyte ratio (PLR) is a new prognostic index that integrates the risk prediction of these 2 parameters. It gives an idea about both the aggregation and inflammation pathways.[6] Authors hypothesized that Platelet-to-lymphocyte levels could predict the severity of inflammation in metabolic syndrome.

METHODS

A cross sectional study was conducted on 210 subjects seen on outpatient basis at hospitals attached to Basaveshwara medical college and research institute, Chitradurga. Out of the 210 subjects, 105 subjects were with Metabolic Syndrome and 105 age and gender matched control participants were without Metabolic Syndrome. The study period was between November 2017 to May 2019.

Inclusion criteria

Patients of age ≥18yrs, subjects fulfilling the National Cholesterol Education Program and Adult Treatment Panel III (NCEP:ATP III) modified criteria of Metabolic Syndrome and patients with normal cardiovascular system, respiratory system, per abdomen and central nervous system examinations.

Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria 3 (NCEP ATP 3).[7] Those criteria require the presence of 3 or more of the following:

- Abdominal obesity (waist circumference [WC] >102 cm in men and >88 cm in women);
- A high triglyceride (TG) level >1.7 mmol/L (>150 mg/ dL);
- A low high-density lipoprotein (HDL) cholesterol level<1.0 mmol/L for men, and <1.3 mmol/L for women (<40 mg/dL for men and <50 mg/dL for women);
- A high blood pressure (BP; systolic, >130 mm Hg; and/or diastolic, >85 mm Hg); and
- A high fasting blood glucose (FBG) concentration >5.6 mmol/L (>110 mg/dL).

Exclusion criteria

Patients on any medications (except oral hypoglycemic agents and lipid lowering agents) that may have affected the results of the study and inflammation parameters, patients with history of smoking/alcohol, patients on immunosuppressive drugs, and patients with known coronary artery disease.

Detailed history including history of risk factors, if any, physical examinations and baseline investigations like complete blood counts, HbA1c levels, serum glucose levels, fasting lipid profile, electrocardiography. Patients were classified into 3 groups based on the number of metabolic syndrome criteria: Group 1 (patients with 3 metabolic syndrome criteria), group 2 (patients with 4 metabolic syndrome criteria), and group 3 (patients with 5 metabolic syndrome criteria).

Height, weight, and waist circumference were measured while fasting and standing up with standard measuring tools. The narrowest diameter between costal arch and anterior superior iliac spine was measured for waist circumference. The blood pressure was measured after at least a 10-minute rest in sitting position. The mean of all 3 measurements with a 2-minute interval was considered as blood pressure.[8] Data was analyzed using simple statistical methods and represented categorically in tables and figures.

RESULTS

Out of the 210 subjects, 93 were females and 113 were males (Figure 1).

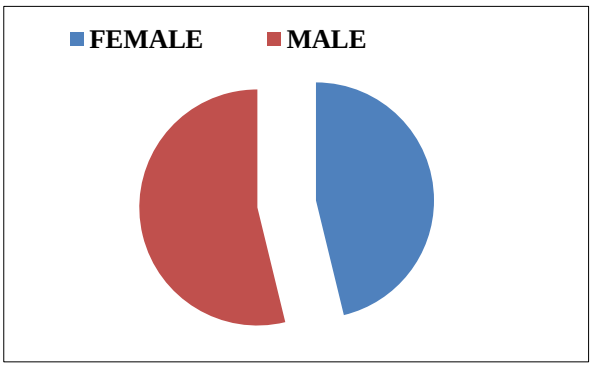

Figure 1: Gender wise classification of the subjects.

Out of the 93 females, 45 had MS and 51 subjects did not qualify for MS. Similarly out of the 113 male subjects, 58 were metabolic syndrome and 55 were non metabolic syndrome. Mean age group of the study population was 45-65 years.

The PLR ratio in the subjects with MS was higher than those without MS. Furthermore, platelet to lymphocyte ratio increased more as severity of MS increased (Figure 2). In participants without metabolic syndrome, platelet to lymphocyte ratio was detected to be significantly lower compared to those with metabolic syndrome meeting 3, 4, and 5 criteria.

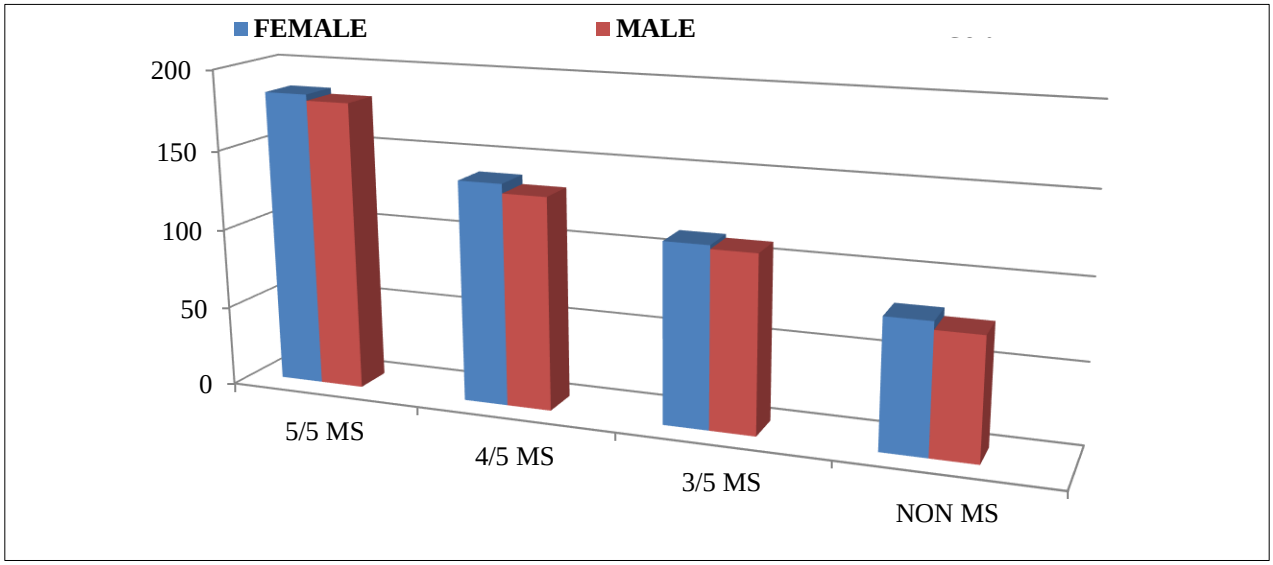

Figure 2: Comparision of the mean PLR between the groups.

There was an increase in platelet-lymphocyte ratio in males with metabolic syndrome as age progressed whereas a decline in platelet-lymphocyte ratio in females as age progressed (Table 2).

Table 1: Comparision of the mean PLR between the groups.

Criteria	Female	Male
5/5	184.31±26.5	180.55±24.7
4/5	138.11±18.6	132.33±17.6
3/5	111.89±16.8	109.63±14.4
NON MS	79.95±12.5	74.95±12.1

Table 2: Comparision of the mean PLR between males and females.

Age (years)	Female	Male
<45	126.46±23.5	90±19.4
45-65	113.32±21.4	105.13±20.6
>65	91.45±20.8	110.92±24.6

DISCUSSION

Metabolic syndrome consists of multiple and interrelated risk factors of metabolic origin that appear to directly promote the development of atherosclerosis. The metabolic risk factors consist of atherogenic dyslipidemia (elevated TGs, low HDL cholesterol concentrations), elevated BP, elevated plasma glucose, prothrombotic state, and inflammatory state.[6]

Although both hereditary and environmental factors contribute to the development of metabolic syndrome, little is known about the underlying pathogenic mechanisms. All the components comprising metabolic syndrome were demonstrated to be associated with systemic inflammation.[9]

Moreover, inflammation has been recently identified as an independent risk factor for cardiovascular disease and is associated with atherosclerosis. Leukocyte activation occurs during an inflammatory reaction. Leukocytes were detected to have a role in atherogenesis and thrombus formation. As inflammation and leukocyte subtypes have effect on every stage of atherosclerosis, it is important to be able to easily study parameters that can demonstrate the progression of atheromatous plaque.[9]

In atherosclerosis, the presence of inflammation inhibits the anti-adhesion properties of platelets, which tends to increase the interaction of platelets with the endothelium. This circumstance sets off a series of inflammatory effects in cascade, analogous to the phenomena that occur in thrombosis and haemostasis. Greater platelet activation triggers the secretion of cytokines and, in turn, creates a "chemotaxis" effect that some authors have termed "inflamed endothelium". There is also an important interaction between platelets and leukocytes in the context of atherogenesis, promoting cell recruitment to the area of the lesion through selectins and integrins.[10]

In this study authors found that in subjects with metabolic syndrome there was significantly higher platelet to lymphocyte ratio when compared to subjects without metabolic syndrome. The study also showed that the subjects with all the 5 criteria of metabolic syndrome had higher platelet to lymphocyte ratio when compared to subjects with 4 or 3 criteria signifying that as severity of metabolic syndrome increases platelet to lymphocyte ratio also increases. Authors also found that younger females have higher levels of inflammation (higher platelet to lymphocyte ratio) and decreased as age

progressed and in males, the platelet to lymphocyte ratio increased as age progressed.

Unlike neutrophil to lymphocyte ratio, the platelet to lymphocyte ratio is less investigated. There is also a sex difference in platelet to lymphocyte ratio, with higher in women than in men. The difference may be associated with the higher platelet counts in women. Many studies have found that females have higher platelet count than males. The mechanisms of sex-related difference in platelet count are also not well known. One explanation is that there is lower serum iron in menstruating and elder women, which stimulates platelet production. Additionally, sex hormonal difference such as estrogen level may be also play a role. It was reported that estrogens favour platelets formation in mouse. Apart from sex, platelet count varies by age, being higher in youth than in old age, which may be associated with hematopoietic stem cell. In elderly people a reduction in hematopoietic stem cell reserve would lead to a reduction of the platelets formation.[11]

In a study by Lishan Wu et al who performed a platelet to lymphocyte ratio on Chinese Han population from Chaoshan region in South China found similar results with neutrophil to lymphocyte ratio. The females had a higher NLR at age 30~49 than the males while the NLR at age 60~69 was higher in males than in females. The PLR was higher in female than in male.[11]

This study has been the first of its kind to do a platelet to lymphocyte ratio in subjects with metabolic syndrome to signify platelet to lymphocyte ratio as a marker of inflammation.

CONCLUSION

In this study, Platelet-lymphocyte ratio above 90 predicted significant inflammation. Platelet to lymphocyte ratio is calculated from complete blood count with differential, is an inexpensive, easy to obtain, widely available marker of inflammation, which can aid in the risk stratification of patients with various cardiovascular diseases in addition to the traditionally used markers. Further prospective studies are required to confirm the findings of the present study and the optimal cut-off value of PLR in inflammation.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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