Global Journal of Medicine & Public Health

A comparative study of N/L ratio in patients of metabolic vs non-metabolic syndrome attending a tertiary care hospital.

M.Sai Varun[1], Mudipalli Deepthi[2]*

ABSTRACT

Background

Numerous studies have shown an association of metabolic syndrome (MS) and insulin resistance with inflammation. The prevalence of MS 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. Neutrophil-lymphocyte ratio, which is calculated from a routine complete blood count with a widely used marker of inflammation.

Aims and objectives

The aim of the present study was to evaluate the neutrophil-lymphocyte ratio in patients with MS and to correlate the same with the severity of MS based on the categories of MS.

Materials and Methodology

In this cross-sectional study, 210 patients with and without MS were included after detailed history and examination. Patients were considered as cases based on the NCEP, ATP III criteria for MS. Both groups of patients were subjected to routine investigations which included complete blood counts, total white blood counts, neutrophil and lymphocyte levels, HbA1c levels, serum glucose levels, fasting lipid profile, and electrocardiography. Logistic regression analysis was done to look for the association of neutrophil-lymphocyte ratio with MS. $P < 0.05$ was considered as statistically significant.

Results

It was seen that the neutrophil-lymphocyte ratio in participants without MS was found to be 1.57 ± 0.728 and the ratio in participants with MS fulfilling 3 out of the 5 criteria, 4 out of 5 and 5 out of 5 criteria were, respectively, 2.65 ± 1.003, 3.59 ± 1.258, and 4.79 ± 2.143. This association was statistically significant with a $P = 0.00$.

Conclusion

Participants with MS had increased neutrophil-lymphocyte ratio when compared to participants without MS. Participants fulfilling higher criteria of MS had higher neutrophil-lymphocyte ratio suggesting increasing inflammatory state.

Keywords: Blood glucose, body mass index, cholesterol, glycated hemoglobin A, high-density lipoprotein, insulin resistance, metabolic syndrome, triglycerides, waist circumference

GJMEDPH 2024; Vol. 13, issue 4 | OPEN ACCESS

1*Corresponding author: M.Sai Varun, Assistant professor, Department of Medicine, Narayana Medical College, Nellore, Andhra Pradesh 2 Senior Resident, Email id: msaivarun9@gmail.com 2. Mudipalli Deepthi, Department of Gynecology, ACSR Government Medical College, Nellore, Andhra Pradesh

Conflict of Interest—none | Funding—none

INTRODUCTION

The prevalence of the metabolic syndrome (MS) varies from place to place around the world, due to the difference in the age and ethnicity of the populations studied and the diagnostic criteria applied. [1] The prevalence as defined by the National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP) ranges from 11% to 41% in India. [2] Numerous studies have shown an association of MS and insulin resistance (IR) with inflammation. Two hypotheses have been proposed to explain the relationship of MS with inflammation. The first states that low-grade inflammation going on for a long time leads to metabolic disturbances, which in turn leads to IR. [3] The second suggests that change in the glucose and lipid metabolism causes inflammation which results in IR. [4]The relationship of systemic inflammatory markers high-sensitivity C-reactive protein (hs-CRP) with MS and IR has been shown in several studies. [5] Prediabetic participants who were insulin resistant had comparatively higher levels of markers of inflammation (hs-CRP). Therefore, a pro-inflammatory state can contribute to the atherogenic risk profile in prediabetic patients with increased IR. [6] However, most of these markers are time-consuming and expensive. Recently, it has been shown that there is a strong relationship between the ratio of Neutrophil-Lymphocyte ratio (NLR) and several metabolic diseases, such as diabetes and cardiovascular diseases 5 (CVD).[7] NLR has been shown to be a more valuable marker for CVD than white blood cell (WBC), as it is less likely to be influenced by physiological conditions.[8] NLR, which 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 CVD in addition to the traditionally used markers.[9]

Materials and Methodology:

A cross-sectional study was conducted on 210 participants seen on the outpatient basis at Narayana medical college hospitals attached to India. Out of the 210 participants, 105 participants were with MS and 105 age- and gender-matched controls were without MS. The study period was between June 2023 and December 2023.

The inclusion criteria included patients of age ≥18 years, participants fulfilling the NCEP: ATP III modified criteria of MS and patients with normal cardiovascular system, respiratory system, per abdomen and central nervous system examinations. MS was diagnosed according to the NCEP ATP 3. [7] Those criteria require the presence of 3 or more of the following:

1. Abdominal obesity (waist circumference [WC] >102 cm in men and >88 cm in women);
2. A high triglyceride (TG) level >1.7 mmol/L (>150 mg/dL);
3. 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);
4. A high blood pressure (BP) (systolic BP >130 mm Hg; and/or diastolic BP >85 mm Hg) and
5. A high fasting blood glucose concentration >5.6 mmol/L (>110 mg/dL).

While the exclusion criteria included 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 a history of smoking/alcohol, patients on immunosuppressive drugs, and patients with known coronary artery disease.

Detailed history included a history of risk factors, if any, physical examinations and baseline investigations such as complete blood counts, HbA1c levels, serum glucose levels, fasting lipid profile, and electrocardiography. Patients were classified into three groups based on the number of MS criteria: Group 1 (patients with 3 MS criteria), Group 2 (patients with 4 MS criteria), and Group 3 (patients with 5 MS criteria). Height, weight, and WC were measured while fasting and standing up with the standard measuring tools. The narrowest diameter between the costal arch and anterior superior iliac spine was measured for WC. The BP was measured after at least a 10 min rest in the sitting position. The mean of all three measurements with a 2-min interval was considered BP. Data were analyzed using simple statistical methods and represented categorically in Tables 1-4

Results

Our study consisted of 102 females and 108

males. Among the cases, there were 50 females (48.54%) and 53 males (51.46%). While among the controls, there were 50 females (46.73%) and 57 males (53. 27%) details were explained in **table-1.**

Table 1: Gender-wise classification of the participants

Gender	Frequency (%)
Females	102 (48.6)
Males	108 (51.4)
Total	210 (100.0)

The mean age in our study was found to be 57 ± 9.545 years with minimum being 35 years and maximum being 80 years. In our study, the majority of 210 participants, i.e., 146 (69.5%) participants were between the age group of 46–65 years and 32 (15.2%) were of the younger age between 35 and 45 years and 32 (15.2%) participants were above 65 years of age, details about study sample were discussed in **table-2.**

Table 2: Mean age distribution of the participants

	N	Minimum	Maximum	Mean±SD
Age	210	35	80	57.32±9.545

In **table-3** showing results of the study sample, out of the 210 participants in our study, 103 participants had MS and 107 were without MS. The neutrophil-lymphocyte ratio in participants without MS was found to be 1.57 ± 0.728 and the ratio in subjects with MS fulfilling 3 out of the 5 criteria, 4 out of 5 and 5 out of 5 criteria were respectively 2.65 ± 1.003, 3.59 ± 1.258, and 4.79 ± 2.143.

Table 3: Comparison of the mean N/L ratio between the groups using the Mann-Whitney test

	N	Minimum	Maximum	Mean±SD	U	Mean difference	P
Metabolic	103	1	8	3.66±1.769	1401.50	2.09	0.00*
Non-metabolic	107	1	5	1.57±0.728			

The overall neutrophil-lymphocyte ratio in participants with MS was 3. 66 ± 1.769, details were explained in **table-4**

Table 4: Comparison of the mean N/L ration among the groups using Kruskal-Wallis

	N	Minimum	Maximum	Mean±SD	Kruskal-Wallis	P
Non-metabolic	107	1	5	1.57±0.728		
Metabolic 3/5	35	1	7	2.63±1.003	101.72	0.00*
Metabolic 4/5	34	1	6	3.59±1.258		
Metabolic 5/5	34	1	8	4.79±2.143		

Discussion

MS refers to a group of metabolic abnormalities related to a state of IR which is frequently associated with a high-risk overweight/obesity phenotype. The major characteristics of MS include IR, abdominal obesity, high BP, and lipid abnormality (i.e., increased levels of TGs and low levels of HDL cholesterol). [2] The co-occurrence of these disorders seems to be more frequent than would be expected by chance, and their collection seems to add essential cardiovascular risk above and beyond that of the individual risk factors. Moreover, there are several inklings in favor of a common pathophysiological background for the syndrome, at the center of which lies IR. [10] In obese conditions in humans and animals, inflammation contributes to the pathogenesis of diabetes through IR. Therefore, anti-inflammation therapy may be proposed as a strategy for the improvement of IR. High-dose salicylates directly suppress inflammation by targeting nuclear factor kappa B, which improves insulin sensitivity and reduces blood glucose in patients with diabetes. [11] Consistent with the literature, the present study showed that the number of neutrophils increased in MS. The study also showed that the participants with all the five criteria of MS had higher neutrophil-to-lymphocyte ratio when compared to participants with 4 or 3 criteria signifying that as severity of MS increases, neutrophil-to-lymphocyte ratio also increases. Leukocyte activation occurs during an inflammatory reaction. Leukocytes were detected to have a role in atherogenesis. Along with a high number of leukocytes, there is a significant relationship between neutrophil–lymphocyte ratio (NLR) and severity and prognosis of CVD. Previous studies demonstrated that WBC, leukocyte subtype, and NLR predicted systemic inflammation. Number of neutrophils is considered to be associated with the formation, complexity, and activation of atheromatous plaque. [12] In a study by Buyukkaya et al. who performed a neutrophil-to-lymphocyte ratio on participants attending the cardiology outpatient clinic in Turkey found similar results with neutrophil-to-lymphocyte ratio. Participants meeting 5 MS criteria had higher NLR than those meeting 3 and 4 criteria, whereas there was no difference between the patients meeting 3 and 4 MS criteria. Participants with NLR above 1.84 had higher hs-CRP levels which in turn predicted inflammation. [12] There are some limitations that should be noted meanwhile. First, the number of observed events is to some extent small which limits the statistical power of this explorative study. However, the sample size of this research is sufficient to draw a conclusion. Second, the neutrophil-lymphocyte ratio was not compared with a known inflammatory marker.

Conclusion

In our study, NLR above approximately 1.57 predicted significant inflammation. Neutrophil-to-lymphocyte ratio is calculated from complete blood count with differential, is an economical, easy to obtain, affordable, accessible marker of inflammation, which can help in the risk stratification of patients with various CVD in addition to the traditionally used markers.

Future implications

Further prospective studies of larger numbers are required to confirm the findings of the present study and the optimal cutoff value of NLR in inflammation.

REFERENCES

1. Eckel RH. The metabolic syndrome. In: Kasper D, Hauser S, Jameson L, Fauci A, Longo D, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 19th ed. Vol. 2. New York: McGraw-Hill Professional Publishing; 2015. p. 2450.
2. Misra A. in Metabolic Syndrome. API Textbook of Medicine. Munjal YP, Sharma SK, Agarwal AK, Singal R.K, Gupta P, Sundar S, et al. editors. 9th edition, New Delhi, India. Jaypee Brothers Medical Publishers Ltd, 2012;2.
3. Fernández-Real JM, Ricart W. Insulin resistance and chronic cardiovascular inflammatory syndrome. Endocr Rev 2003; 24:278-301.
4. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest 2006; 116:1793-801.
5. Prakash K, Mamatha TR, Nirgude D, Prakash B. High sensitivity C-reactive protein in metabolic syndrome. Int J Adv Med 2016; 3:607-10.
6. Brownlee M, Aiello L, Cooper M, Vinik A, Nesto R, Boulton A, et al. Complications of diabetes mellitus. In: Melmed S, Polonsky K, Larsen R, Kronenberg H, editors. Williams Textbook of Endocrinology. 12th ed. Philadelphia: Saunders, Elsevier; 2011. p. 1523.
7. Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khoueiry G, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases. Expert Rev Cardiovasc Ther 2013; 11:55-9.
8. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005; 45:1638-43.
9. Surendar J, Indulekha K, Mohan V, Pradeepa R. Association of neutrophil-lymphocyte ratio with metabolic syndrome and its components in Asian Indians (CURES-143). J Diabetes Complications 2016; 30:1525-9.
10. Sarafidisa PA, Nilsson PM. The metabolic syndrome: A glance at its history. J Hypertens 2006; 24:621-6.
11. Sun Q, Li J, Gao F. New insights into insulin: The anti-inflammatory effect and its clinical relevance. World J Diabetes 2014; 5:89-96.
12. Buyukkaya E, Karakas MF, Karakas E, Akçay 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