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Original Research Article

Significance of Neutrophil Lymphocyte Ratio and High Sensitivity C-Reactive Protein in Type 2 Diabetic Patients

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ABSTRACT

Introduction: Low-grade inflammation is the basic pathophysiology in metabolic syndrome and the development of T2DM. Previous studies have demonstrated that increased neutrophil-lymphocyte ratio (NLR) is a marker of cardiovascular disease and cancer. Apart from many inflammatory markers, NLR is believed to be the balance between innate (neutrophils) and adaptive (lymphocytes) immune system responses to the low-grade inflammation.

Methods: The present study was to find the relationship between NLR and hsCRP (High sensitive C reactive protein) in patients with T2DM in a tertiary care centre. Age and sex-matched 60 T2DM patients (males 32, female 28) were included in this study. After getting the written informed consent 5ml of fasting blood sample was collected for the analysis of fasting blood glucose, Total, differential WBC count and High sensitive Creative protein.

Results: Our study showed that there is a strong positive correlation between increased NLR and hsCRP.357 (p≤ 0.005). Here, it is important to note that, males have low levels of hsCRP (2.63±3.23) than females (4.82±4.16) and these changes are also statistically significant (p≤ 0.026).

Conclusion: The White blood cell count is one of the markers of subclinical inflammation. In diabetes, due to the presence of low-grade inflammation, the white cell count, NLR and hsCRP were increased. Hence, by assessing NLR, which is a simple clinical investigation will be useful in T2DM patients to control future vascular risk events.

Key Words: White blood cell (WBC) count, Neutrophil lymphocyte ratio (NLR), Type 2 diabetes mellitus (T2DM), High sensitive C-reactive protein (hsCRP)

INTRODUCTION

Diabetes mellitus is one among the chronic metabolic disorder with increasing prevalence all over the world, in particular, South-East Asia. It has been reported by the IDF, 2017 that the prevalence of Diabetes in India is around 8.79 and projected that to be 11.4 during the year 2045 in the adult population (72.9 million to 134.3 million – age of 20 to79 years). Diabetes and its complications not only affect the health and wealth of the population but also affect the economics and growth of the country because of the increase in financial burden. If we aware of novel markers of inflammation to find out the disease early, we can postpone the complications or even can reduce the complications with proper intervention.

Many studies have proven that Neutrophil Lymphocyte ratio (NLR) which is nothing but the subtraction of absolute neutrophil count to absolute lymphocyte count is a simple investigation, but with lots of information regarding the disease status in diabetes mellitus.[1] There was a significant association between NLR with Insulin resistance (IR) and high NLR values may be considered as a potential predictive marker of IR.[2]

Low-grade inflammation is the basic Pathophysiology in metabolic syndrome and the development of T2DM. Apart from many inflammatory markers, NLR is believed to be the balance between innate (neutrophils) and adaptive (lymphocytes) immune system responses to the low-grade inflammation.[3,4]

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Previous researches have been proved that elevated NLR is associated with increased concentration of various pro-inflammatory cytokines which may cause cellular DNA damage.[5-7]

Cardiovascular disease, which is an inflammatory disease, the use of hs-CRP appears to represent a valid tool to identify people at risk of cardiovascular disease.[8] Many studies have proven that hs-CRP is an important inflammatory marker of cardiovascular disease risk and is relating to the pathophysiology of atherosclerosis, providing additional importance in the prevention of future events.[9]

The present study was to find the relationship between Neutrophil Lymphocyte Ratio (NLR) and inflammatory marker high sensitive C-reactive protein (hsCRP) in patients with T2DM in a tertiary care teaching centre.

MATERIALS AND METHODS

Age and sex-matched 60 T2DM patients (males 32, female 28) were included in this study. Patients who are on chemotherapy, steroids, antibiotics, immunomodulators, haematological disorders, T1DM, GDM were excluded from this study. Also the patients who were on statin therapy and Non-steroidal anti-inflammatory drugs (NSAIDs).

After getting the written informed consent 5ml of fasting blood sample was collected for the analysis of Fasting blood glucose, Lipid profile, Total & Differential WBC count and High sensitive Creative protein (hsCRP). Biochemical parameters were done on Cobas e311 auto analyzer and Cell count was done in Mindray BS5300, CBC analyzer. Results were analyzed by using SPSS 16.0 version. Student *t*-test and Pearson Correlation have been used for statistical analysis.

Results were analyzed in the SPSS 16.0 version. Student t-test and Pearson correlation were used for the statistical analysis of parameters.

RESULTS

In this study, 32 males and 28 females study parameter were analyzed with a mean age group of 46.75 (Males, SD 11.08) and 52.17 (Females, SD 12.53). The total WBC count has been increased in females than Males which is statistically significant ($p \leq 0.039$). And it has been found that there is a strong positive correlation between increased NLR and hsCRP → .357 ($p \leq 0.005$). Here, an interesting point to note that, males have low levels of hsCRP (2.63±3.23) than females (4.82±4.16). These changes are also statistically significant ($p \leq 0.026$).

As for as Diabetic parameters are concerned, there is no correlation between Fasting blood glucose (FBG) and NLR, hsCRP but correlated with the total WBC count. But as for as Glycated haemoglobin (HbA1c%) is concerned not cor-

related and statistically also not significant. Using widely available high-sensitivity assays, CRP levels of <1, 1 to 3, and >3 mg/L corresponds to low-, moderate-, and high-risk groups for future cardiovascular events.

DISCUSSION

The neutrophil-to-lymphocyte ratio (NLR) can be obtained by dividing absolute neutrophil to absolute lymphocyte count is a novel simple and inexpensive test for assessing inflammation.[10] There are many strong pieces of evidence suggested that increased NLR has been stated as a potential marker of poor prognosis in multiple tumours [11-13] and cardiovascular diseases[14-16] in the general population. Isaac et al. reported that increased NLR has been associated with mortality among multiple chronic medical disorders.[17]

Our study has proved that diabetic patients have a significantly elevated NLR compared with non-diabetic subjects which are consistent with earlier studies which have stated that increased HbA1c might be associated with increased NLR in patients with type 2 diabetes mellitus.[18,19] Many studies have shown total white blood cell (WBC) counts as an independent risk marker for diabetes cases, impaired insulin sensitivity, Metabolic Syndrome, or coronary artery disease (CAD) White blood cell (WBC) count and high sensitivity C-Reactive Protein (hs-CRP) were more useful biomarkers to indicate inflammation in the obesity and Metabolic syndrome (MetS) severity.[20]

Many numbers of studies revealed that NLR is a useful marker of diabetes-related to not only macrovascular but also microvascular complications, increased NLR levels may be associated with microvascular complications of DM in the elderly population.[21] Inflammatory marker NLR significantly increases in prediabetic and diabetic patients. NLR and Platelet lymphocyte ratio (PLR) values may be reliable predictive markers in prediabetes and diabetes mellitus.[22] NLR is inexpensive, easy to use, a reliable predictor of nephropathy, retinopathy, and CAD in Indian T2DM.[23] The results of our study show that there was a significant relation between NLR and diabetic nephropathy. Therefore, NLR may be considered as a novel surrogate marker of diabetic nephropathy in the early stages.[24] The NLR available also as a marker of inflammation which is cheaper and an important predictor of complications especially microvascular in type 2 diabetes patients.[25] It has been stated that increased NLR level is associated with elevated HbA1c and poor glycemic control in patients with type 2 diabetes mellitus and it can be used as a monitoring tool during the follow up of diabetic patients.[26]

CONCLUSION

Total White blood cell count, which has been proven that as one of the markers of subclinical inflammation and because

of the low-grade inflammation in diabetes, the White blood cell count, NLR and hsCRP were increased**.** By assessing NLR, which is a simple clinical investigation will be useful in T2DM patients to control future cardiovascular risk events, microvascular complications. It can also be a useful marker even to predict the presence of Cardiovascular disease in type 2 diabetic patients along with hsCRP measurement and our study supports the use of NLR as a cost-effective biomarker to predict the future cardiovascular risk and a large scale study is needed for the further establishment of it.

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Table 1: Group statistics analysis and its significance

	Group Statistics				95% confidence interval of the difference	
Parameters	**Sex**	**Number**	**Mean (SD)**	**p -value**	**Lower**	**Upper**
Age	M	32	46.75 (11.08)	0.8	-11.533	0.67549
	F	28	52.17 (12.53)			
WBC	M	31	7770.32 (1592.84)	0.039*	-1831.7448	-47.6100
	F	28	8710 (1828.84)			
NLR	M	32	1.87 (0.67)	0.25	-0.51646	0.13699
	F	28	2.06 (0.57)			
hsCRP	M	32	2.63 (3.23)	0.026*	-4.10203	-0.26948
	F	28	4.81 (4.16)			

*Correlation is significant at the 0.05 level

Table 2: Correlation hsCRP with WBC and NLR

Correlation of hsCRP with	Correlation Coefficient	p-Value
WBC	0.287	0.027*
NLR	0.356	0.005*

* statistically significant <0.05)

Table 3: Correlation of NLR & hsCRP with FBS and HbA1c%

		WBC	NLR	hsCRP
FBS	Correlation Coefficient	0.253	0.167	0.114
	p-Value (2-tailed)	0.053	0.201	0.386
HbA1c%	Correlation Coefficient	0.164	0.223	0.189
	p-Value (2-tailed)	0.214	0.087	0.147