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RESEARCH ARTICLE

NEUTROPHIL LYMPHOCYTE RATIO (NLR): A WELL ASSESSMENT TOOL OF GLYCEMIC CONTROL IN TYPE-2 DIABETIC PATIENTS

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ABSTRACT

Aim & Objectives: To investigate the relationship between NLR and blood glucose level in type 2 diabetic patients. **Material and Method:** This observational study was conducted on 100 patients with type 2 diabetes mellitus in INDEX MEDICAL COLLEGE AND HOSPITAL, from June 2018 to July 2019. The study group comprised of males and females of age group 35 to 75 years. Patients were divided into 3 groups according to HbA1c levels: group 1, HbA1c levels <6.5% (excellent control) group 2, HbA1c levels between 6.5% to 8.5% (poor control) & group 3 HbA1c levels >8.5% (worst control). Venous WBC, neutrophil and lymphocyte counts were determined. **Result:** Of 100 patients included, fasting serum glucose, neutrophil count and leucocyte count counts were significantly higher in group 3 compared with group 2 > group 1. NLR had a positive correlation with HbA1c. **Conclusion:** Increasing level of NLR is associated with elevated HbA1c level and poor glycemic control in patients with type 2 diabetes mellitus. Therefore, HbA1c level can be used as a disease monitoring tool for the follow up of diabetic patients.

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INTRODUCTION

Diabetes mellitus is a chronic preventable metabolic disorder which is characterised by hyperglycemia and is considered to be one of the silent killer because most of the patients remain asymptomatic unless they develop complications. The burden of diabetes is rising in middle and lower income countries due to urbanization, sedentary life style, nutritional and epidemiological transition. The increased number of circulating leukocytes not only reflects a presence of acute infection in the body but they also have a dominant inflammatory role in the pathogenesis of different phases of atherosclerosis and various cardiovascular disorders. Studies have shown that increasing leukocyte counts is a reliable marker of systemic inflammation having a good diagnostic and prognostic value in patients with angina, myocardial infarction, stroke, peripheral vascular disease and micro and macro vascular complication. These days there is more concern about NLR, as a potential marker for determining inflammation in various cardiac and non-cardiac disorders because it has got a superior predictive, diagnostic and discriminative ability than total WBC count. Moreover predictive value of NLR is comparable to various other inflammatory markers such as C-reactive protein (CRP), tumor necrosis factor (TNF-) and interleukin (IL-6) in the detection of subclinical inflammation.

Nowadays HbA1c is usually advised by most clinicians to measure the long term glycemic control in diabetic patients for a period of previous 2-3 months. It also gives information about the severity of hyperglycemia and is considered to be a biomarker for diabetes related micro and macro-vascular complications. However, NLR predicts ongoing inflammation and diabetes associated complications which are not predicted by HbA1c precisely.

MATERIALS AND METHODS

The study is cross-sectional and observational in nature consisting of 100 patients attending different OPD at INDEX MEDICAL COLLEGE AND HOSPITAL for a period from July 2018 to July 2019. Only patients with type 2 diabetes mellitus were included. Patients of both gender from 25 to 75 years of age are included in the study. On the basis of HbA1c level, participants were divided into three groups:

- Group 1, HbA1c <6.5% (excellent control/regulated diabetes)
- Group 2, HbA1c between 6.5% to 8.5% (poor control/unregulated diabetes) and
- Group 3, HbA1c >8.5% (worst control).

Method of Collection of Data: After an overnight fast, venous blood samples (2ml) were collected into haemogram tubes containing di-potassium ethylenediaminetetra-acetic acid

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(EDTA) (1.5– 2.2mg/ml). Samples were maintained at room temperature and tested within 1h of collection, to minimize variations due to sample ageing. Total WBC, neutrophil and lymphocyte levels were determined using an automated blood cell counter. (Sysmex XS 800i). NLRs were quantified as total neutrophil counts divided by lymphocyte counts. (in %) HbA1c levels were measured using automated ion exchange high performance liquid chromatography. Hexokinase enzymatic method was used to measure Serum glucose levels.

RESULTS

) In Group I there were 36% patients, in Group II there were 32% patients and in Group III there were 32% patients.

Table 1. Distribution of patients according to age

Age Group	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
25-40 years	4	11.1	5	15.6	5	15.6
41-60 years	22	61.1	18	56.3	17	53.1
61-80 years	10	27.8	7	21.9	9	28.1
>80 years	0	0.0	2	6.3	1	3.1
Total	36	100.0	32	100.0	32	100.0

) The above table shows the distribution of patients according to age in all three groups.

In all the three groups, the majority of the patients were in the age group 41-60 years followed by 61-80 years.

Table 2. Comparison of mean RBS between the three groups

Group	No.	Mean ± SD	F value	P value	Post-hoc Tukey		
					Group I to II	Group I to III	Group II to III
Group I	36	129.69 ± 38.66	25.423	0.001*	0.056, NS	0.001*	0.001*
Group II	32	186.22 ± 65.93					
Group III	32	300.50 ± 158.57					

The above table shows the comparison of mean RBS among the three groups.

) Comparison of pairs was done using Post-hoc Tukey test.

The comparison of mean RBS between Group I and Group II was statistically comparable (p>0.05), while the mean RBS was significantly higher in Group III in comparison to both Group I and Group II (p<0.05).

) As the HbA1c was increasing the mean RBS also showed increase.



Graph 1. Bar diagram showing comparison of mean RBS according to groups

Table 3. Comparison of mean Total Count between the three groups

Group	No.	Mean ± SD	F value	P value	Post-hoc Tukey		
					Group I to II	Group I to III	Group II to III
Group I	36	7.95 ± 3.82	23.481	0.001*	0.001*	0.001*	0.044*
Group II	32	12.32 ± 4.67					
Group III	32	14.89 ± 4.22					

The above table shows the comparison of mean total count among the three groups. The comparison of mean total count among the three groups was found to be statistically significant (p=0.001), showing that there is a variation in the total count among the three groups. The mean total count was highest in Group III and lowest in Group I. Comparison of pairs was done using Post-hoc Tukey test.

Table 4. Comparison of mean Neutrophil Count between the three groups

Group	No.	Mean ± SD	F value	P value	Post-hoc Tukey		
					Group I to II	Group I to III	Group II to III
Group I	36	68.53 ± 13.57	3.320	0.040*	0.300, NS	0.032*	0.556, NS
Group II	32	73.44 ± 14.24					
Group III	32	76.95 ± 12.85					

The above table shows the comparison of mean neutrophil count among the three groups. The comparison of mean neutrophil count among the three groups was found to be statistically significant (p=0.040), showing that there is a variation in the total neutrophil count among the three groups. The mean neutrophil count was highest in Group III and lowest in Group I.

Comparison of pairs was done using Post-hoc Tukey test.

Table 5. Comparison of mean Lymphocyte Count between the three groups

Group	No.	Mean ± SD	F value	P value	Post-hoc Tukey		
					Group I to II	Group I to III	Group II to III
Group I	36	26.84 ± 12.23	3.767	0.027*	0.386, NS	0.020*	0.324, NS
Group II	32	23.09 ± 12.48					
Group III	32	19.05 ± 10.09					

The above table shows the comparison of mean lymphocyte count among the three groups. The comparison of mean lymphocyte count among the three groups was found to be statistically significant (p=0.027), showing that there is a variation in the total lymphocyte count among the three groups. The mean lymphocyte count was highest in Group I and lowest in Group III. Comparison of pairs was done using Post-hoc Tukey test. The above table shows the comparison of mean N/L Ratio among the three groups. The comparison of mean N/L Ratio among the three groups was found to be statistically significant (p=0.024), showing that there is a variation in the total N/L Ratio among the three groups. The mean N/L Ratio was highest in Group III and lowest in Group I.

Table 6. Comparison of mean N/L Ratio between the three groups

Group	No.	Mean \pm SD	F value	P value	Post-hoc Tukey		
					Group I to II	Group I to III	Group II to III
Group I	36	3.43 \pm 2.36	3.894	0.024*	0.244, NS	0.018*	0.504, NS
Group II	32	5.47 \pm 3.64					
Group III	32	6.92 \pm 5.83					

DISCUSSION

HbA1c levels are an indicator of blood glucose regulation, and increased HbA1c levels may be associated with increased risk of cardiovascular complications in patients with type 2 diabetes mellitus. We found a positive correlation between HbA1c levels and NLR in the current study. WBC count is an essential marker of inflammation, and increased WBC levels are associated with vascular complications in patients with type 2 diabetes mellitus and metabolic syndrome. Findings from the present study are consistent with previous publications, in that WBC count and NLR were found to be higher in patients with HbA1c levels $>8.5\%$ (unregulated diabetes), compared with those <6.5 and between 6.5 to 8.5% (regulated diabetes). Our data suggests the relation between hyperglycaemia and increased NLR. Patients with type 2 diabetes mellitus also show insufficient proliferation of lymphocytes due to low expression of interleukin-2 receptors.

The NLR may be a more effective predictor of cardiovascular events compared with WBC or neutrophil count. There is a positive correlation reported between NLR and C-reactive protein (CRP; a marker of inflammation) in patients with coronary artery disease. It is suggested that the role of CRP in insulin resistance might be more significant than that of WBC.

In the present study, patients with type 2 diabetes mellitus were grouped according to HbA1c levels and, consistent with published studies, a significant positive correlation was found between NLR and HbA1c.

Lee et al.¹ investigated the relation of NLR with long-term complications following myocardial infarction in 2,559 consecutive acute myocardial infarction patients and found that NLR was an independent risk factor for long-term complications in diabetic patients. Yilmaz et al.², who investigated the benefit of NLR in the diagnosis of gestational DM, found a higher NLR value in pregnant women with gestational DM when compared to pregnant women without gestational DM, and found that a NLR value >2.93 had a sensitivity of 76% and a specificity of 94% for gestational DM. Shiny et al.³ studied the relationship between glucose intolerance and NLR and concluded that NLR value was higher in patients with DM compared to the patients with impaired fasting glucose, and in patients with impaired fasting glucose compared to normal individuals. The NLR was significantly higher in the poorly controlled DM group compared to the well controlled DM group in the study

performed by Sefil et al.⁴, which reported results that were similar to those found in this present study. Comparing the result of this study with the study performed by Sefil et al. showed that the mean NLR value was reduced in the patients in whom glycaemic parameters improved 3 months later. Hussain et al.⁵ reported similar results between NLR and glycaemic regulation. They found a significant association between NLR and HbA1c among the groups divided into three according to the glycaemic control status. In this study, NLR values after treatment were not investigated. In a prospective study conducted by Guo X et al.⁶ on a nondiabetic cohort of 38,074 candidates, NLR was associated with the incidence and prevalence of T2DM. This result suggests that the NLR is a better predictor for diabetes.

Conclusion

In diabetic patients, NLR deterioration is associated with glycaemic disorder, which increases the importance of haemogram in diabetic patients. Cases in which HbA1c cannot be measured, and if the glycaemic condition is not evaluated earlier, NLR can be a useful parameter. Improvement of NLR after glycaemic regulation has suggested that this parameter may be more useful in demonstrating glycaemic regulation rather than complications. NLR is now considered as an easily measurable, noninvasive, and cost-effective parameter for the follow-up of diabetic patients.

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