

Original Research Article

Correlation of neutrophil lymphocyte ratio with HbA1c in patients of type 2 diabetes mellitus

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ABSTRACT

Background: Neutrophil lymphocyte is an indicator of subclinical inflammation. Type 2 diabetes mellitus is associated with chronic low-grade inflammation. One of the novel inflammatory markers is hemogram derived neutrophil to lymphocyte ratio. There are very few studies which are directly accessing the relation between NLR and HbA1c, so in the present study our aim to correlate neutrophil lymphocyte ratio with glycemic control in patients having type 2 diabetes.

Methods: Hospital based observational cross section study was carried out at department of medicine, Pt JNMMC and Dr BRAM Hospital, Raipur, between September 2018 to August 2019. 105 patients with type 2 diabetes mellitus according to ADA criteria who were aged more than 18 years were included in the study. Relevant investigation and complete blood count were performed. Microsoft excel and SPSS version 25 were used for collection and analysis of the data, $p < 0.05$ was considered as significant.

Results: Out of 105 patients who were given the consent for the study, the ration of male is to female was 1:0.98, mean age of all the patients was 51.77 ± 10.56 years, mean neutrophil lymphocyte ratio among the patients was 6.30 ± 2.646 , HbA1c count more than ≥ 9 was 54 (51.27%). NLR had a positive correlation with HbA1c and was found to be an independent predictor of poor glycemic control in patients with type 2 diabetes mellitus.

Conclusions: Increased NLR is associated with elevated HbA1c and poor glycemic control. Type NLR should be used as a marker of diabetic control level in addition to HbA1c in type 2 diabetic subjects.

Keywords: NLR, American heart association, HbA1c, Glycemic control

INTRODUCTION

Diabetes mellitus describes a metabolic disorder having multiple etiology. It is characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Symptoms are polyuria, polydipsia, polyphagia. If left untreated, diabetes can cause many complications.¹ Type 2 diabetes mellitus is heterogeneous group of disorders characterized by variable degree of insulin resistance, impaired insulin secretion and increased hepatic gluconeogenesis, typically develop with increasing age and particularly in

obese adolescents.¹ It is predominant form of diabetes worldwide. The incidence of diabetes is increasing day by day. The epidemic of diabetes is under way in both developing and developed countries. According to IDF, some 425 million people worldwide, or 8.8% of adults aged 20-79, are estimated to have diabetes. About 75% live in low and middle income countries. If these trends continue, by 2040 some 642 million people, or one adult in ten, will have diabetes.

In Type 2 diabetes mellitus sub-acute chronic inflammation is a common and at least two major inflammatory pathways, stress-activated Jun N-terminal

kinases (JNK) and the transcription factor NF-kappa B.² This inflammatory state produces various pro-inflammatory cytokines, which amplified by adipokines like TNF-alpha, IL-1, IL-6, IL-10, leptin, adiponectin, monocyte chemoattractant protein, angiotensinogen, resistin, chemokines, serum amyloid protein.^{2,3} Adipose tissue infiltrate by macrophages and immune cells (B cells and T cells) which trigger local and systemic chronic low-grade inflammation, by producing more cytokines and chemokines which create a pathologic link between obesity, insulin resistance and diabetes.³⁻⁶ In patients with diabetes to measure the long-term glycemic control HbA1c is used. It plays important role in assessing the adequacy of therapy and need for intervention in patients with poorly controlled diabetes mellitus. However, HbA1c usually does not predict ongoing inflammation and diabetes associated complications accurately. Neutrophil lymphocyte ratio (NLR) is sign of balance between neutrophil lymphocyte level in body and is an indication of subclinical inflammation. NLR is a simple ratio of absolute neutrophil count and absolute lymphocyte count.⁷ It is also a potential marker to determine inflammation in various cardiac and non-cardiac disorders. It is used to predict the prognosis of diseases such as acute myocardial infarction (MI), stroke, and heart failure. There are very less studies which shows the direct correlation between HbA1c and NLR in patients with type 2 diabetes, so in this study we are going to access the relation between HbA1c and NLR in patients with type 2 diabetes.

Aim and objectives

Aim and objectives of current studies were to correlate NLR (neutrophil-lymphocyte ratio) with HbA1c in patients of type 2 diabetes mellitus and to estimate NLR (neutrophil-lymphocyte ratio).

METHODS

Hospital based observational cross-section study was carried out at department of medicine, Pt JNMMC and Dr BRAM hospital, Raipur, between September 2018-August 2019. The study was conducted after getting the institutional ethical committee clearance. All the patients gave informed written consent for the study. 105 patients with type 2 diabetes mellitus according to ADA criteria who were aged more than 18 years were included in the study. Patients were included in the study by simple random sampling. Patients of type 1 diabetes mellitus, age <18 years, patients having active infection, known cases of inflammatory disorders, acute and chronic renal failure, chronic liver disease, acute MI, malignancy i.e. Leukaemia were excluded from the study.

Sample size

Sample size was calculated to be 105 by correlation calculator, considering significance level (α)=0.01,

confidence level 99% (0.99), power of test=(1- β)=0.01 and correlation (r)=0.45.

Investigation

After overnight fast and after complete aseptic precautions venous blood samples (10ml) were collected in hemogram tubes containing EDTA and biochemistry tubes, samples were maintained at room temperature and tested within 1 hour of collection to minimize variations due to sample ageing and neutrophil and lymphocyte count were measured by automated hematology analyzer. Neutrophil lymphocyte ratios (NLR) were estimated by dividing the absolute neutrophil count to absolute lymphocyte count. HbA1c was estimated by HPLC on Bio-Rad HPLC analyzer using manufacturer's protocol. The fully automated HPLC variant II (Bio-Rad laboratories, Munich, Germany) was used.

Statistical analysis

Collected data were expressed as percentage and mean±standard deviation (SD). SPSS software was used for statistical analysis. Chi square test was used for categorical variables. Pearson correlation coefficient (r) was calculated to know the relation between HbA1c and NLR, $p < 0.05$ was considered statistically significant.

RESULTS

The present study was conducted in the department of medicine, Dr. B. R. A. M. hospital Raipur on 105 patients of Type 2 Diabetes Mellitus and baseline demographic characteristic of population of study shown in (Table 1). The study comprises of 105 patients. Out of 105 cases having mean age 51.77 ± 10.56 , out of 53 were males having mean age was 51.32 ± 10.05 years and rest 52 were females having mean age was 52.37 ± 11.34 . Mean BMI of all participant was 24.76 ± 2.40 . 30(28.57%) of the participants had systolic blood pressure more than 140mmhg while 71.43% of the patient had SBP lower than 140mmhg, whereas Diastolic Blood Pressure in 48 (45.71%) of the participants had more than 90mmhg as shown in above (Table 1). For all 105 participants had mean absolute Neutrophil count was $8.31 \pm 4.19910^3/\mu\text{l}$, among 105 study subjects 63 patients (60%) their absolute Neutrophil count was more than 7.0 and 42 patients (40%) their absolute neutrophil count was within normal limit. 81 patients (77.14%) had normal absolute lymphocyte count, 20 patients had absolute lymphocyte count less than 0.9, remaining 4 patients (3.82%) had absolute lymphocyte count more than 2.9. Mean neutrophil lymphocyte ratio count was 6.30 ± 2.646 , in which 79 patients (75.23%) had NLR more than 3.53, and remaining 26 patients (24.77%) had NLR within normal limit. In our study 54 patients (51.42%) had HbA1C more than 9%, 39 patients (37.14%) had HbA1C in between 7.1-9%, rest 12 patients (11.44%) had HbA1c less than 7.0%. Among 105 patients, 72 patients (68.6%) were not fulfilling the ADA treatment goal of FBS. Out

of which 33(31.4%) were female patients and 39(68.6%) were male patients. That of for PPBS, 72 patients (68.6%) were not fulfilling the ADA treatment goal of PPBS. Out of which 32 (61.5%) were female patients and 40 (75.5%) were male patients as shown in above (Table 2).

Table 1: Demographic data of study population.

Parameters	Mean±SD/N (%)
Age	51.77±10.56
Gender	
Male	53 (50.47)
Female	52 (49.53)
BMI (Kg/m²)	24.76 ± 2.40
SBP (mmHg)	
<140	75 (71.43)
≥140	30 (28.57)
DBP (mmHg)	
<90	57 (54.28)
≥90	48 (45.71)

The association of NLR with HbA1c which was significant association (p<0.001) noted between two parameters indicating higher frequency of NLR with higher HbA1c% is shown in table, also NLR and HbA1c was positive moderately correlated was observed. Association of HbA1c with absolute neutrophil count was assessed and found significant association between two parameters indicating higher frequency of increased neutrophil count in subjects with High HbA1c levels. Association of HbA1c with absolute lymphocyte count was assessed and found significant association between two parameters indicating higher frequency of increased lymphocyte count in subjects with High HbA1c levels.

Table 2: Hematological distribution of study population.

Parameters	Mean±SD/N (%)	Max.	Min.
Absolute neutrophil count 10³/μl	8.31±4.199		
<1.7	0 (0)	24.73	1.76
1.7-7.0	42 (40)		
>7.0	63 (60)		
Absolute lymphocyte count (10³/ul)			
<0.9	20 (19.04)		
0.9-2.9	81 (77.14)		
>2.9	4 (3.82)		
Neutrophil lymphocyte ratio	6.30±2.646		
<0.78	0 (0)	11.28	1.36
0.78-3.53	26 (24.77)		
> 3.53	79 (75.23)		
HbA1c			
<7.0	12 (11.44)		
7.0-9.0	39 (37.14)		
>9.0	54 (51.42)		
FBS (mg/dl)			
<130	33 (31.40)		
≥130	72 (68.80)		
PPBS (mg/dl)			
<180	33 (31.40)		
≥180	72 (68.80)		
WBC 10³/μl			
<04	1 (0.95)		
04-11	77 (73.33)		
>11	27 (25.72)		

Table 3: Association and correlation of NLR with HbA1c among study subjects.

NLR	HbA1c N (%)			Total	Chi-square	P value	R value
	< 7	7 - 9	> 9				
0.78-3.53	10 (9.52)	14 (13.33)	2 (1.90)	26 (24.76)	37.54	<0.001	0.57
>3.53	2 (1.90)	25 (49.52)	52 (49.52)	79 (75.24)			
Total	12 (11.43)	39 (37.14)	54 (51.43)	105 (100)			

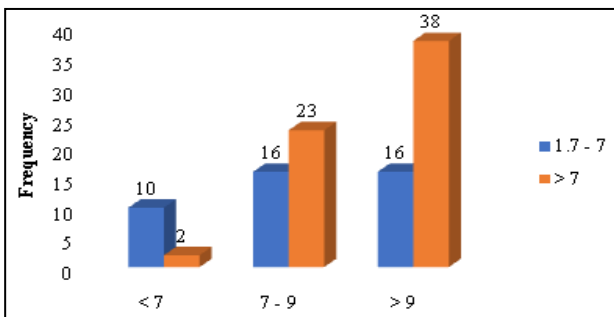


Figure 1: Association of HbA1c with absolute neutrophil count.

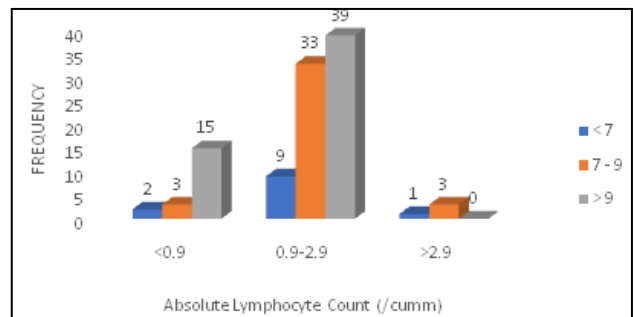


Figure 2: Association of HbA1c with absolute lymphocyte count.

DISCUSSION

Current study depicts moderately positive correlation between NLR and HbA1c. Several studies have observed a link between NLR and insulin resistance, metabolic syndrome and atherosclerosis. To our knowledge, there are only few studies directly correlating NLR and glycemic control. Gender comparison in current study showed that males are more prevalent than females. In ICMR Indian study conducted by Vishwanathan et al the prevalence of type 2 diabetes mellitus was higher in males (46.7%) as compared to females.⁸ But in study conducted by Singh et al found that prevalence of type 2 diabetes mellitus were higher in females (9.91%) as compared to males (6.79%), which is contrary to our study.⁹

In order to determine inflammation in various cardiac and non-cardiac disorders, neutrophil lymphocyte ratio NLR is a potential marker because of its superior predictive, diagnostic and differentiating ability compared to total WBC count or neutrophil. NLR is a dynamic parameter and appears to possess a superior predictive value over total leukocyte count.¹⁰ Compare to the other inflammatory markers NLR has various advantages like easy lab detection, low cost, wide availability, and reliability. Though HbA1c tells about the severity of hyperglycemia and commonly advised to measure the long term glycemic control but usually it does not predict ongoing inflammation and diabetes associated complications accurately. In current study, significant positive correlation was found between NLR and HbA1c, and also they are significantly associated with each other. In studies conducted by Shiny et al revealed that increased NLR has strong association with glucose intolerance and insulin resistance in type 2 diabetic patients.¹¹ In another study conducted by Mazhar et al conducted a study in Pakistan in 2016-17 and concluded that increased NLR is associated with elevated HbA1c and poor glycemic control in type 2 diabetes patients.¹² In turkey study conducted by Sefil et al found that increased NLR may be associated with elevated HbA1c in type 2 diabetes patients.¹³ Devamsh et al October 2019 NLR had a positive correlation with HbA1c and this study found a significant positive correlation between NLR and glycemic control. In studies conducted by Duman et al, Akin et al, Gubbala et al, Mertoglu et al and many more studies found that increased NLR is associated with elevated HbA1c and poor glycemic control.¹⁶⁻¹⁸ In current study we also concluded that there is positive correlation HbA1C and NLR.¹⁴ So there are many study which tells that increased in the NLR is associated with elevated HbA1c.

CONCLUSION

Neutrophil-lymphocyte ratio is a novel indicator of subclinical inflammation. In diabetic patients, NLR deterioration is associated with uncontrolled glycemic status, thereby increasing the importance of hemogram in

diabetic patients. In our study we found a significant positive correlation between NLR and glycemic control. Increased NLR is associated with elevated HbA1c and poor glycemic control. Type 2 DM patients with raised NLR should be evaluated for cardiovascular, renal and ocular complications of diabetes. NLR may be useful as an easily measurable, noninvasive, widely available and cost-effective parameter for the disease monitoring tool

during follow up of diabetic patients. Moreover, NLR can be used as a population screening, disease and drug monitoring tool on large scale basis. NLR can be used as marker of diabetic control in addition to HbA1C in type 2 diabetic subjects.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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