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Jour of Diab and Endo Assoc of Nepal Vol.7, No. 2, July-December 2023
ISSN Print 2594-3367 ISSN Online 2631-2107

Journal of Diabetes and Endocrinology
Association of Nepal

ORIGINAL ARTICLE OPEN ACCESS

# Correlation of Neutrophil Lymphocyte ratio with HbA1c in patients of type 2 Diabetes Mellitus attending Medical Department of a Tertiary Care Centre

Singh R[1], Shrestha JK[2], Chaudhary OP[3],Singh S[4], Agrahari MK[5]

[1]Department of pathology, BP koirala memorial cancer hospital, Bharatpur,[2]Department of Radiology, Bharatpur Hospital, Bharatpur, [3]Bagmati Welfare Society Nepal, Hariwon, [4]Department of Obstetrics and Gynecology, Police Hospital, [5]Department of Medicine, College of medical sciences , Bharatpur

**Abstract**

Type 2 diabetes mellitus is associated with chronic low-grade inflammation. Neutrophil lymphocyte is an indicator of subclinical inflammation. One of the novel inflammatory markers is neutrophil to lymphocyte ratio. We find only less studies that are directly accessing the relation between NLR and HbA1c, in the present study we 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 at Bharatpur Period August 2023 to December 2023. 176 patients with type 2 diabetes mellitus as per ADA criteria aged more than 18 years were included in the study. Microsoft excel and SPSS version 20.0 were used for collection and analysis of the data, $p<0.05$ was considered as significant. **Results:** Out of 176 cases having mean age 55.78±9.111, Mean BMI of all participant was 28.37±4.061, mean absolute Neutrophil count was 7.36±7.123 $10^3/\mu l$ and Mean neutrophil lymphocyte ratio count was 4.03±1.545, in which 147 patients (83.5%) had NLR within normal limit, and remaining 29 patients (16.5%) had NLR within more than 3.53. In our study 123 patients (69.9%) had HbA1C more than 9.0. The association of NLR with HbA1c which was significant association (p=0.047) noted between two parameters indicating higher frequency of 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:** Our study concluded that the association of NLR with HbA1c which was significant association. The Association of HbA1c with absolute neutrophil count was which significant and association of HbA1c with absolute lymphocyte count was which significant. 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.

**Key Words: HbA1c, Glycemic control, Neutrophil lymhphocyte ratio**

## Introduction

Diabetes mellitus a metabolic disorder has multiple etiology. Type 2 diabetes mellitus is heterogeneous group of disorder with variable degree of insulin resistance, impaired insulin secretion and increased hepatic gluconeogenesis, develop with increasing age and obese adolescents.[1] As of IDF, about 425 million people worldwide, 8.8% of adults aged 20-79, are estimated to have diabetes.

In Type 2 DM 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] which produces various pro- inflammatory cytokines, amplified by adipokines like TNF-alpha, IL-1, IL-6, IL-10.[2,3]

Adipose tissue infiltrate by macrophages and immune cells (B cells and T cells) trigger chronic low-grade inflammation, create a pathologic link between obesity, insulin resistance and diabetes. [4,5]

To measure the long-term glycemic control HbA1c is used which plays important role in assessing the adequacy of therapy. However, HbA1c usually does not predict ongoing inflammation and associated

**Corresponding Author**

Dr MahendraK K Agrahari, Department of Medicine, College of medical sciences , Bharatpur, Email -dragrahari@gmail.com, contact -9845045898

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Journal of Diabetes and Endocrinology Association of Nepal
ORIGINAL ARTICLE OPEN ACCESS

complications accurately. NLR is sign of balance between neutrophil lymphocyte levels in body and is an indication of subclinical inflammation. NLR is a simple ratio of absolute neutrophil count and absolute lymphocyte count.[6] 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. The objectives of this studies were to correlate NLR (neutrophil-lymphocyte ratio) with HbA1c in patients of type 2 diabetes mellitus.

## METHODS

Hospital based observational cross-sectional study carried out at department of medicine July 2023 to September 2023. The study was conducted after getting the institutional ethical committee clearance. All the patients gave informed consent for the study. 176 patients with type 2 diabetes mellitus as per ADA criteria for diabetes who were aged more than 18 years were included in the study. Patients were included in the study by simple random sampling.

The exclusion criteria were Cases of type 1 diabetes mellitus, age <18 years, patients with active infection, previously cases of inflammatory disorders, acute and chronic renal failure, chronic liver disease, acute MI, malignancy with leukemia were excluded from the study.

Sample size was calculated to be 176 by correlation calculator, considering significance level ($\alpha$)=0.01, confidence level 99% (0.99), power of test=(1-$\beta$)=0.01 and correlation (r)=0.45.

After overnight fast and after complete aseptic precautions venous blood samples (10ml) were collected in tubes containing EDTA and biochemistry tubes, samples were 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.

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.

The study was conducted after the ethical approval from Institutional Review Committee, Bhartapur hospital (Ref:079/80-001). Participants were explained about the research detail, its significance, the benefit and harm in Nepali language before obtaining the consent, their queries were answered. A statement indicating that the participants has understood all the information in the consent form and is willing to participate voluntarily was obtained. Participants were able to withdraw from the study at any time without giving any reason during the study period. The confidentiality of participants was assured and code number was used in each interview schedule and name of the participants was not mentioned anywhere.

| Parameters | N (%) | Mean ± SD |
|---|---|---|
| **Age** | | 55.78±9.111 |
| <40 Years | 11 (6.3%) | |
| 40-49 Years | 29(16.5%) | |
| 50-59 Years | 71(40.4%) | |

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| | | |
|---|---|---|
| > 60 Years | 65(36.9%) | |
| **Gender** | | |
| Female | 100(56.8%) | |
| Male | 76(43.2%) | |
| **BMI** | | 28.37±4.061 |
| Underweight | 2(1.1%) | |
| Normal | 34(19.3%) | |
| Over weight | 94(79.5%) | |

The study comprises of 176 patients. Out of 176 cases having mean age 55.78±9.111, out of 100 (56.8%) were female and 76 (43.2%) were males. Mean BMI of all participant was 28.37±4.061, out of 94 (79.5%) were overweight and only 2 (1.1%) were underweight. 90(51.1%) of the participants had systolic blood pressure more than 140mmhg while 86(48.9%) of the patient had SBP lower than 140mmhg, whereas Diastolic Blood Pressure in 112 (63.6%) of the participants had more than 90mmhg and 64 (36.4%) of the participants had less than 90 mmHg.

**Table 2: Hematological Distribution of Study population**

| **Parameters** | **N (%)** | **Mean ± SD** |
|---|---|---|
| **Absolute neutrophil count $10^3$/µl** | | 73.68±7.123 |
| <1.7 | 0 (0.0%) | |
| 1.7-7.0 | 71(40.4%) | |
| >7.0 | 105(59.7%) | |
| **Absolute lymphocyte count ($10^3$/ul)** | | 17.48±1.545 |
| <0.9 | 9(5.1%) | |
| 0.9-2.9 | 167 (94.9%) | |
| >2.9 | 0(0%) | |
| **Neutrophil Lymphocyte ratio** | | 4.03±0.495 |
| <0.78 | 0(0.0%) | |

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| | | |
|---|---|---|
| 0.78-3.53 | 29(16.5%) | |
| >3.53 | 147(83.5%) | |
| **HbA1c** | | 8.63±0.956 |
| <7.0 | 10(5.7%) | |
| 7.0-9.0 | 43(24.4%) | |
| >9.0 | 123(69.9%) | |
| **FBS (mg/dl)** | | 139.42±24.571 |
| <130 | 36(20.5%) | |
| >130 | 140(79.5%) | |
| **PPBS (mg/dl)** | | 237.55±45.326 |
| <180 | 36(20.5%) | |
| ≥180 | 140(79.5%) | |
| **WBC $10^3$/µl** | | 9.96±2.587 |
| <4 | 7(4.0%) | |
| 4-11 | 64(36.4%) | |
| >11 | 105(59.7%) | |

The study comprises of 176 participants had mean absolute Neutrophil count 7.36±7.123 $10^3$/µl, among 176 study subjects 105 patients (59.7%) had their absolute Neutrophil count more than 7.0 and 71 patients (40.4%) their absolute neutrophil count was within normal limit. 167 patients (94.9%) had normal absolute lymphocyte count, 9 patients (5.1%) had absolute lymphocyte count less than 0.9. Mean neutrophil lymphocyte ratio count was 4.03±1.545, in which 147 patients (83.5%) had NLR within normal limit, and remaining 29 patients (16.5%) had NLR more than 3.53. In our study 123 patients (69.9%) had HbA1C more than 9%, 43 patients (24.4%) had HbA1C in between 7-9%, rest 10 patients (5.7%) had HbA1c less than 7.0. Among 176 patients, 140 patients (79.5%) were not fulfilling the ADA treatment goal of FBS. That of for PPBS, 140 patients (79.5%) were not fulfilling the ADA treatment goal of PPBS. Mean WBC was 9.96±2.587 $10^3$/µl, among 176 study subjects 105 patients (59.7%) their WBC was more than 11 and 64 patients (36.4%) their WBC was within normal limit.

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**Table 3: Association and correlation of NLR with HbA1c among study subject**

| NLR | HbA1c N (%) | | | Total | Chi-Square | P Value |
|---|---|---|---|---|---|---|
| | <7 | 7-9 | >9 | | | |
| 0.780-3.53 | 4(2.3%) | 9(5.1%) | 16(9.1%) | 29(16.5%) | 18.716 | 0.022 |
| >3.53 | 6(3.4%) | 34(19.3%) | 107(60.8%) | 147(83.5%) | | |
| Total | 10(5.7%) | 43(24.4%) | 123(69.9%) | 176(100.0%) | | |

The association of NLR with HbA1c was significant (p=0.047) noted between two parameters indicating higher frequency of NLR with higher HbA1c% as shown in table, also NLR and HbA1c was positive correlated moderately was observed.

The Association of HbA1c with absolute neutrophil count was significant (p<0.0001) noted between two parameters indicating higher frequency of increased neutrophil count in subjects with High HbA1c levels.

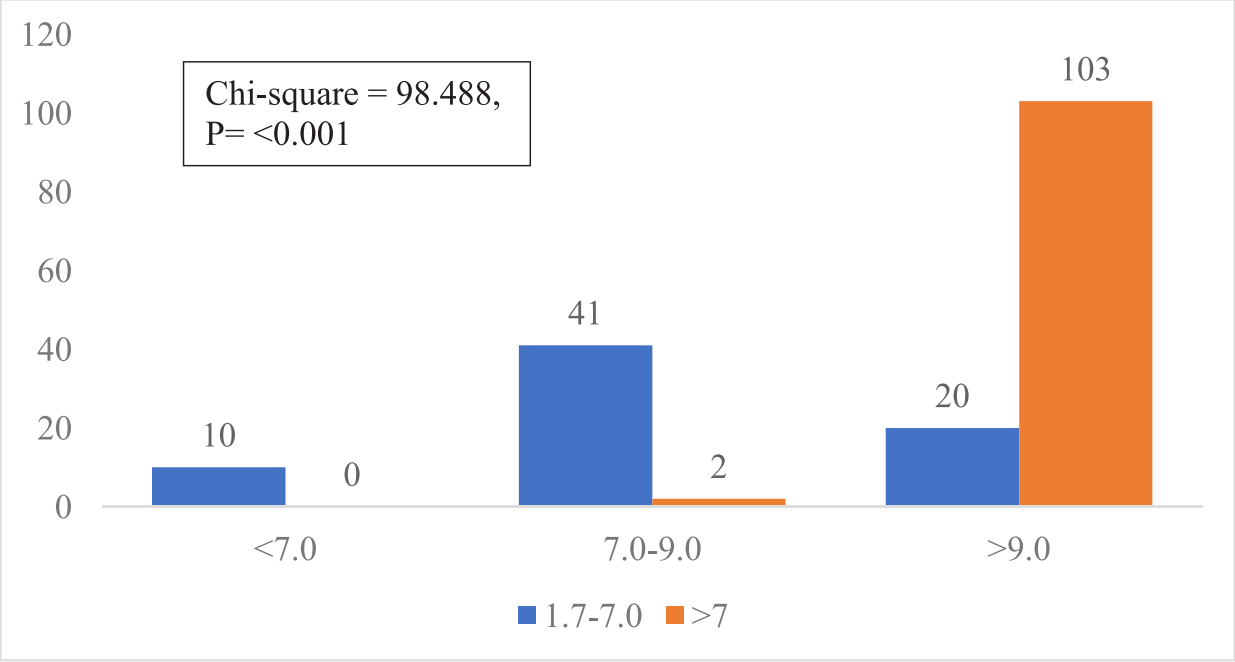


**Figure 1: Association of HbA1c with absolute neutrophil count**

The Association of HbA1c with absolute lymphocyte count was which significant association (p<0.0001) between two parameters indicating higher frequency of increased lymphocyte count in subjects with high HbA1c levels.

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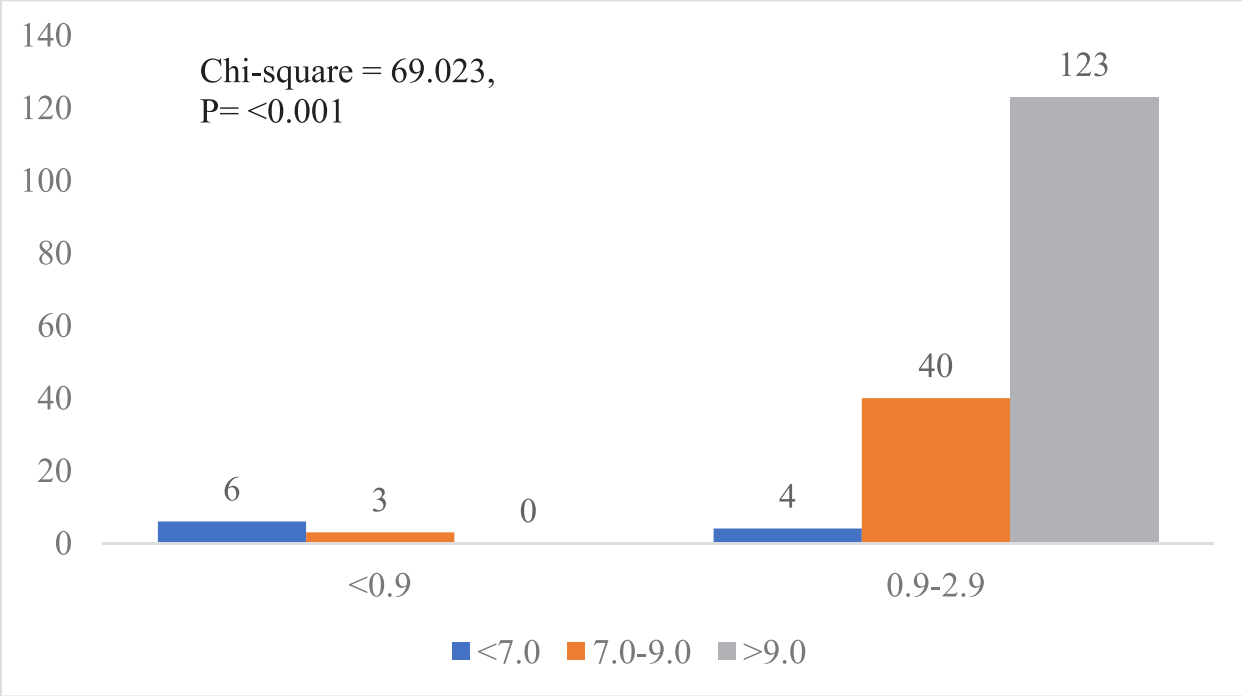


**Figure 2: Association of HbA1c with absolute lymphocyte count**

## Discussion

This study shows a more positive correlation between NLR and HbA1c. Several studies have observed a link between NLR and insulin resistance, metabolic syndrome and atherosclerosis. As there are only few studies directly correlating NLR and glycemic control. This study show that, Out of 176 cases having mean age 55.78±9.111, out of 100 (56.8%) were female and 76 (43.2%) were males. Comparison in current study by Varma S et al. showed that, Out of 105 cases having mean age 51.77±10.56, out of 53 were males having mean age was and 52 were females.[7] 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]

This study show that, in our study absolute Neutrophil count was 105 patients (59.7%) their absolute Neutrophil count was more than 7.0 and 167 patients (94.9%) had normal absolute lymphocyte count. Mean neutrophil lymphocyte ratio was 4.03±1.545, in which 147 patients (83.5%) had NLR within normal limit. Comparison in current study by Varma S et al. showed that, for all 105 study subjects 63 patients (60%) their absolute Neutrophil count was more than 7.0 and 81 patients (77.14%) had normal absolute lymphocyte count. Neutrophil lymphocyte ratio count was in which 79 patients (75.23%) had NLR more than 3.53, and remaining 26 patients (24.77%) had NLR within normal limit.[7]

This study shows that, in our study 69.9% had HbA1C more than 9.0 and 79.5% were not fulfilling the ADA treatment goal of FBS.

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That of for PPBS, 79.5% were not fulfilling the ADA treatment goal of PPBS and 59.7% their WBC was more than 11000 count. Comparison in current study by Varma S et al. showed that, 51.42% had HbA1C more than 9% and 68.6% were not fulfilling the ADA treatment goal of FBS. That of for PPBS, 68.6% were not fulfilling the ADA treatment goal of PPBS.[7] Similar Study by Andersson C, et al, 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]

This study show that, association of NLR with HbA1c which was significant association (p=0.047) 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. 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 concluded that increased NLR is associated with elevated HbA1c and poor glycemic control in type 2 diabetes patients.[12]

This study show that, Association of HbA1c with absolute neutrophil count was which significant association (p<0.0001) noted between two parameters indicating higher frequency of increased neutrophil count in subjects with High HbA1c levels. Comparison in current study by Varma S et al. showed that, 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.[7]

This study show that, association of HbA1c with absolute lymphocyte count was which significant association (p<0.0001) between two parameters indicating higher frequency of increased lymphocyte count in subjects with High HbA1c levels. Comparison in current study by Varma S et al. showed that, 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.[7]

## CONCLUSION

Our study concluded that the association of NLR with HbA1c which was significant association (p=0.047) noted between two parameters indicating higher frequency of NLR with higher HbA1c, also NLR and HbA1c was positive moderately correlated was observed. The Association of HbA1c with absolute neutrophil count was which significant and association of HbA1c with absolute lymphocyte count was which significant. 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.

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