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ORIGINAL RESEARCH

A study of relationship between the hba1c level and inflammatory markers neutrophil-lymphocyte ratio & monocyte-lymphocyte ratio in controlled & uncontrolled type 2 diabetes mellitus

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion. Inflammation plays a pivotal role in the pathogenesis of T2DM and its complications. Neutrophil-Lymphocyte Ratio (NLR) and Monocyte-Lymphocyte Ratio (MLR) are emerging as novel inflammatory markers. This study aims to evaluate the relationship between HbA1c levels and inflammatory markers NLR and MLR in controlled and uncontrolled T2DM patients. **Methods:** A hospital-based observational cross-sectional study was conducted on 200 T2DM patients aged 18-70 years. Participants were categorized into controlled (HbA1c <7%) and uncontrolled (HbA1c ≥7%) groups based on ADA criteria. Hematological indices including NLR and MLR were measured. Statistical analysis was performed using SPSS Version 22, with a significance level set at $p<0.05$. **Results:** The mean age was comparable between controlled (54.10±9.56 years) and uncontrolled (55.30±9.86 years) groups. NLR >2 was observed in 40.48% of controlled and 63.29% of uncontrolled diabetics ($p=0.013$). Similarly, MLR >2 was found in 35.71% of controlled and 61.39% of uncontrolled diabetics ($p=0.005$). Significant differences were noted in hematocrit values and red cell distribution width between the two groups ($p<0.001$). **Conclusion:** Elevated NLR and MLR are significantly associated with higher HbA1c levels in T2DM patients, indicating poor glycemic control. These inexpensive and readily available markers can aid in early identification of inflammation in uncontrolled diabetics, potentially guiding therapeutic interventions.

Keywords: Type 2 Diabetes Mellitus, HbA1c, Neutrophil-Lymphocyte Ratio, Monocyte-Lymphocyte Ratio, Inflammation

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both. Type 2 Diabetes Mellitus (T2DM) accounts for approximately 90-95% of all diabetes cases worldwide and is a major public health concern [1]. The prevalence of T2DM is increasing globally, reaching epidemic proportions in many countries, particularly in India [2].

Chronic inflammation plays a crucial role in the pathogenesis and progression of T2DM. Inflammatory processes contribute to insulin resistance and β-cell dysfunction, which are hallmark features of T2DM [3]. Hyperglycemia, increased free fatty acids, and altered lipoproteins can induce endothelial dysfunction, leading to vascular complications [4]. Subclinical inflammation is also associated with increased cardiovascular risk in patients with impaired glucose tolerance [5].

The White Blood Cell (WBC) count and its subtypes, particularly the Neutrophil-Lymphocyte Ratio (NLR) and Monocyte-Lymphocyte Ratio (MLR), have emerged as novel markers of systemic inflammation [6]. NLR is calculated by dividing the neutrophil count by the lymphocyte count, and MLR is calculated by dividing the monocyte count by the lymphocyte count from peripheral blood samples. Elevated NLR and MLR have been associated with

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poor glycemic control and increased risk of diabetic complications [7].

Despite the significance of these markers, limited studies have explored their relationship with glycemic control in the Indian population. Therefore, this study aims to assess the relationship between HbA1c levels and inflammatory markers NLR and MLR in controlled and uncontrolled T2DM patients.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based observational cross-sectional study was conducted in the Department of General Medicine at SMS Hospital and its attached group of hospitals from July 2021 onwards for one year, or until the sample size was achieved, with an additional two months for data compilation and analysis.

Sample Size and Sampling Method

A total of 200 T2DM patients aged 18-70 years were included. The sample size was calculated at a 95% confidence interval and an alpha error of 0.05, assuming a prevalence of HbA1c >7.5% in 51.27% of patients, with an absolute allowable error of 7.5%. Participants were randomly selected.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Patients diagnosed with T2DM according to ADA criteria.
- Age between 18 to 70 years.

Exclusion Criteria:

- Patients with acute or chronic liver disease.
- Anemic patients or those with hemoglobinopathies (thalassemia, sickle cell anemia).
- Patients taking medications affecting HbA1c levels (e.g., aspirin, vitamin E, vitamin C).
- Patients on statins, aspirin, or thiazolidinediones.
- Patients with acute infections or chronic inflammatory conditions.
- Patients with acute myocardial infarction or cerebral infarction.
- Patients with acute or chronic kidney disease.
- Pregnant women.
- Patients unwilling to participate.

Data Collection and Measurements

After obtaining informed written consent, participants underwent detailed history taking, clinical examination, and relevant laboratory investigations. Hematological indices measured included WBC count, hemoglobin (Hb), hematocrit (Hct), Red Cell Distribution Width (RDW), neutrophil count, lymphocyte count, HbA1c, fasting blood sugar (FBS), postprandial blood sugar (PPBS), NLR, and MLR.

Operational Definitions

- Controlled Diabetes: HbA1c <7% according to ADA criteria.
- Uncontrolled Diabetes: HbA1c ≥7%.
- Neutrophil-Lymphocyte Ratio (NLR): Neutrophil count divided by lymphocyte count; normal NLR is <2.0.
- Monocyte-*Lymphocyte Ratio (MLR):* Monocyte count divided by lymphocyte count; normal MLR is <2.0.

Statistical Analysis

Data were analyzed using SPSS Version 22. Quantitative variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Student's t-test was used for quantitative data comparisons, and the Chi-square test for categorical data. A p-value <0.05 was considered statistically significant.

RESULTS

Participant Characteristics

A total of 200 T2DM patients were enrolled, with 42 in the controlled group (HbA1c <7%) and 158 in the uncontrolled group (HbA1c ≥7%). The mean age was 54.10±9.56 years for controlled diabetics and 55.30±9.86 years for uncontrolled diabetics, with no significant difference between the groups (p=0.478). Males constituted 57.14% of the controlled group and 57.59% of the uncontrolled group (p=0.902).

Duration of Diabetes

In the controlled group, 69.05% had diabetes for 1-5 years, whereas in the uncontrolled group, 58.86% had diabetes for 6-10 years. The mean duration of diabetes was 4.79±2.89 years in the controlled group and 7.89±3.53 years in the uncontrolled group (p=0.478).

Glycemic Control

Significant differences were observed in FBS and PPBS levels between the groups. The controlled group had a mean FBS of 124.48±25.97 mg/dL, while the uncontrolled group had a mean FBS of 159.46±33.92 mg/dL (p<0.001). The mean PPBS was 165.52±49.00 mg/dL in the controlled group and 230.01±56.20 mg/dL in the uncontrolled group (p<0.001).

Hematological Indices

- **Hemoglobin:** No significant difference was observed between the controlled (12.38±1.53 g/dL) and uncontrolled groups (12.66±1.39 g/dL) (p=0.096).
- **WBC Count:** The mean WBC count was 7.04±1.75 x10^3/µL in the controlled group and 7.89±2.28 x10^3/µL in the uncontrolled group (p=0.171).
- **Hematocrit:** A significant difference was noted, with the controlled group having a mean Hct of

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46.00±4.00% and the uncontrolled group 52.97±3.34% (p<0.001).

- **RDW:** The controlled group had a mean RDW of 14.36±1.87%, while the uncontrolled group had a significantly higher mean RDW of 19.34±4.96% (p<0.001).
- **Inflammatory Markers**
- **Neutrophil-Lymphocyte Ratio (NLR):** NLR >2 was observed in 40.48% of controlled diabetics and 63.29% of uncontrolled diabetics (p=0.013).
- **Monocyte-Lymphocyte Ratio (MLR):** MLR >2 was found in 35.71% of controlled diabetics and 61.39% of uncontrolled diabetics (p=0.005).

Tables and Figures

Table 1: A total of 200 T2DM patients were enrolled, with 42 in the controlled group (HbA1c <7%) and 158 in the uncontrolled group (HbA1c ≥7%). The mean age was 54.10±9.56 years for controlled diabetics and 55.30±9.86 years for uncontrolled diabetics, with no significant difference between the groups (p=0.478). Males constituted 57.14% of the controlled group and 57.59% of the uncontrolled group (p=0.902).

Glycemic Control and Hematological Indices

Significant differences were observed in fasting blood sugar (FBS) and postprandial blood sugar (PPBS) levels between the groups. The controlled group had a mean FBS of 124.48±25.97 mg/dL, while the uncontrolled group had a mean FBS of 159.46±33.92 mg/dL (p<0.001). The mean PPBS was 165.52±49.00 mg/dL in the controlled group and 230.01±56.20 mg/dL in the uncontrolled group (p<0.001).

Key Findings

1. Neutrophil-Lymphocyte Ratio (NLR)

A significant difference was observed in NLR between controlled and uncontrolled diabetics.

TABLE 1: COMPARISON OF NLR BETWEEN CONTROLLED AND UNCONTROLLED DIABETICS

NLR > 2	Controlled Diabetics (HbA1c <7%)	Uncontrolled Diabetics (HbA1c ≥7%)	P-value
Yes	17 (40.48%)	100 (63.29%)	0.013*
No	25 (59.52%)	58 (36.71%)	
Total	**42 (100%)**	**158 (100%)**	

*Significant at p<0.05

2. Monocyte-Lymphocyte Ratio (MLR)

MLR was also significantly higher in uncontrolled diabetics.

TABLE 2: COMPARISON OF MLR BETWEEN CONTROLLED AND UNCONTROLLED DIABETICS

MLR > 2	Controlled Diabetics (HbA1c <7%)	Uncontrolled Diabetics (HbA1c ≥7%)	P-value
Yes	15 (35.71%)	97 (61.39%)	0.005*
No	27 (64.29%)	61 (38.61%)	
Total	**42 (100%)**	**158 (100%)**	

*Significant at p<0.05

3. Hematocrit and Red Cell Distribution Width (RDW)

Significant differences were noted in hematocrit and RDW values.

TABLE 3: HEMATOCRIT AND RDW IN CONTROLLED AND UNCONTROLLED DIABETICS

Parameter	Controlled Diabetics (Mean ± SD)	Uncontrolled Diabetics (Mean ± SD)	P-value
Hematocrit (%)	46.00 ± 4.00	52.97 ± 3.34	<0.001*
RDW (%)	14.36 ± 1.87	19.34 ± 4.96	<0.001*

*Significant at p<0.05

DISCUSSION

The present study investigated the relationship between HbA1c levels and inflammatory markers NLR and MLR in T2DM patients. Our findings indicate that higher NLR and MLR are significantly associated with uncontrolled diabetes (HbA1c ≥7%).

The role of inflammation in T2DM has been well-documented [8]. Chronic hyperglycemia induces oxidative stress and inflammatory responses, contributing to insulin resistance and β-cell dysfunction [9]. NLR and MLR are readily available markers that reflect systemic inflammation and have been associated with cardiovascular risks and diabetic complications [10].

In our study, a significant proportion of uncontrolled diabetics had NLR >2 (63.29%) and MLR >2 (61.39%), compared to the controlled group. These findings are consistent with previous studies that reported elevated NLR and MLR in patients with poor glycemic control [11]. For instance, a study by Liu et

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al. demonstrated that higher NLR values are associated with increased risk of microvascular complications in T2DM [12].

The significant difference in hematocrit and RDW between the groups further supports the presence of inflammation and altered erythropoiesis in uncontrolled diabetics. Elevated RDW has been associated with increased cardiovascular mortality and is considered a marker of anisocytosis due to chronic inflammation [13].

Our study highlights the utility of NLR and MLR as inexpensive and accessible markers for assessing inflammation in T2DM patients. Incorporating these markers into routine clinical practice could aid in early identification of patients at higher risk of complications, allowing for timely interventions.

Limitations

This study is limited by its cross-sectional design, which does not allow for causal inferences. Additionally, being a single-center study, the findings may not be generalizable to all populations. Further multicenter longitudinal studies are warranted to validate these results.

CONCLUSION

Elevated Neutrophil-Lymphocyte Ratio and Monocyte-Lymphocyte Ratio are significantly associated with poor glycemic control in Type 2 Diabetes Mellitus patients. These markers serve as simple, cost-effective tools for detecting subclinical inflammation and may help identify patients at risk of complications, facilitating early intervention strategies.

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