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"Evaluation of the Correlation between HbA1c Levels and Inflammatory Markers: Neutrophil-to-Lymphocyte Ratio and Monocyte-to-Lymphocyte Ratio in Controlled and Uncontrolled Type 2 Diabetes Mellitus"

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Abstract

Aim: To assess the relationship between glycated hemoglobin (HbA1c) with inflammatory markers, neutrophil-to-lymphocytes ratio (NLR), and monocyte-to-lymphocytes ratio (MLR) in controlled and uncontrolled type 2 diabetes patients.

Methodology: After obtaining informed consent from patients who met the inclusion and exclusion criteria, 200 diabetic patients were included in the study using the simple randomization method. Following a detailed history and diagnosis, vital demographic information, and blood tests were collected from patients via a predesigned preliminary questionnaire. The following blood tests were collected: white blood cell (WBC), Hb, hematocrit (HCT), red cell distribution width (RDW), neutrophils, lymphocytes, HbA1c, blood glucose, NLR ratio, and MLR ratio. Data were entered and analyzed using Statistical Package for the Social Sciences version 25.0.

Results: The mean age of patients with controlled diabetes mellitus was 54.10 years, while that of patients with uncontrolled diabetes mellitus was 55.3 years. Glycemic control was more in the age group of 51–60 years. Around 54% of males and 46% of females were included in the present study, and no association was found between the two genders with

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poor and good glycemic control. Around 63.29% of participants with uncontrolled diabetes have an increased NLR, and 61.39% of participants with uncontrolled diabetes have an increased MLR. A strong association was found between the NLR and MLR with the glycemic control.

Conclusion: Uncontrolled diabetes mellitus had a positive association with inflammatory markers, that is, NLR and MLR. Statement of significance: Diabetes mellitus is the most common metabolic disorder in Asian countries. It leads to many acute and chronic complications in uncontrolled diabetes. Markers like the NLR ratio and MLR ratio are inexpensive and easily available for blood investigation. Hence, these markers are quite useful in differentiating controlled and uncontrolled diabetes and, therefore, useful in predicting blood sugar control in type 2 diabetes mellitus

Keywords: Diabetes mellitus, NLR, MLR, HbA1C

Introduction

Diabetes mellitus is a condition in which blood sugar is too high for a long time due to deficiency or relative deficiency of the hormone insulin, either due to the inability of the pancreas to produce insulin or insufficient insulin production or insufficient action of insulin action. Type II diabetes is increasing worldwide and has reached epidemic proportions in many countries, especially India.1 Inflammatory processes play an important role before and in the development of type 2 diabetes.

Damage to blood vessels by endothelial cells can be affected by hyperglycemia, increased free fat, altered lipoprotein, and high blood pressure. Subclinical inflammation may be associated with cardiovascular risk in patients with diabetes.2

Leukocytes and their subtypes, neutrophil-to-lymphocyte (NLR) and monocyte-to-lymphocyte ratios (MLRs), are new markers of inflammation. The NLR is a new marker of subclinical disease.3

Many studies have highlighted the increased NLR rate as a result of macrovascular and microvascular complications of diabetes. MLR and NLR are routine investigations, inexpensive, and easy to test. These markers may be quite useful in predicting complications of type 2 diabetes mellitus; hence, the objective of the present study is to find out the relation between glycated hemoglobin (HbA1c) with inflammatory markers, NLR, and MLR in controlled and uncontrolled type 2 diabetes patients.

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Aim and Objectives

Evaluation of hematological indices, NLR, and MLR in controlled and uncontrolled T2DM.

Objectives

To assess the relationship between HbA1c with MLR and NLR.

Materials and Methods

This was a hospital-based cross-sectional study conducted at the Department of Medicine, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, after approval from the Ethics Committee of the institution.

Inclusion Criteria

• Type 2 diabetes mellitus according to ADA criteria. • Age 18–70 years.

Exclusion Criteria

• Acute and chronic liver disease. • Anemic patients. • Hemoglobinopathies (thalassemia and sickle cell anemia) • Patients taking drugs causing alteration in HbA1c, for example, aspirin and vitamins E and C. • Acute infections. • Chronic inflammatory conditions like inflammatory bowel disease, osteoarthritis, rheumatoid arthritis, gout, bronchial asthma, and chronic hepatitis. • Acute myocardial infarction and cerebral infarction. • Acute and chronic kidney disease. • Pregnant. • Patient not willing to participate in the study

A total of 200 patients with diabetes mellitus were included in the study using simple random techniques after written informed consent from the patients who fulfilled the criteria of inclusion and exclusion. Basic demographic details and blood investigations were collected from the patients by means of a predesigned, pretested questionnaire after a detailed history and clinical examination.

Following blood investigation, data were collected: white blood cell (WBC), Hb, hematocrit (HCT), RDW, neutrophils, lymphocytes, HbA1c, blood sugar, NLR ratio, and MLR ratio.

Data were analyzed and summarized as percentage correlation between HbA1c and NLR and MLR in controlled and uncontrolled type 2 diabetes mellitus, analyzed by the Chi-squared test and student's t-test. A value of $p < 0.05$ was considered to be statistically significant.

Results

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A total of 200 diabetic patients participated in this study. In the present study, the majority, that is, 19 participants with controlled diabetes, belonged to the age group between 51 and 60 years, while only four participants belonged to the 24–40 years of age group. The mean age group of participants with controlled diabetes was 54.10 years, with a standard deviation of 9.56 years. Similarly, 60 participants in the age group of 51–60 years had uncontrolled diabetes, while only 16 participants belonged to the age group of 24–40 years. The mean age group of participants with uncontrolled diabetes was 55.3 years, with a standard deviation of 9.86 years.

A total of 24 males had controlled diabetes, while the majority of them, that is 91 males, had uncontrolled diabetes, and 18 females had controlled diabetes, while the majority of females, that is, 67, had uncontrolled diabetes. There has been no substantial difference in terms of age and sex distribution between the individuals with controlled and uncontrolled diabetes mellitus.

Study shows that only a few participants, that is, 17 with controlled diabetes mellitus ratio of <2. Likewise, among 158 participants with uncontrolled diabetes mellitus, 100 patients had an NLR of >2, while only 58 of them had a ratio of <2. Therefore, the results were determined to be statistically significant ($p = 0.013$) according to the NLR.

Study shows that, among 42 participants with controlled diabetes mellitus, 64.29% of them had an MLR of <2, while the remaining had a value of >2. Similarly, in participants with uncontrolled diabetes mellitus, the majority, that is, 61.39% of them, had an MLR of >2, whereas only 38.61% had a ratio of <2. So, the results were determined to be statistically significant in terms of MLR ($p = 0.005$).

Discussion

Glycated hemoglobin (HBA1c) is used to measure the long-term glycemic control in diabetic patients but does not predict the ongoing inflammation of diabetic-associated complications accurately.

The NLR is a sign of balance between neutrophil and lymphocyte levels in the body and is an indication of subclinical inflammation. The NLR is a potential marker to determine inflammation in various cardiac and noncardiac disorders.

The present study was thereby conducted to find the relationship between the HbA1c level and inflammatory markers like NLR and MLR in controlled and uncontrolled type 2 diabetes mellitus. In the present study, it was found that the mean age of patients with controlled

diabetes mellitus was 54.10 years, while that of patients with uncontrolled diabetes mellitus was 55.3 years. Glycemic control was more in the age group of 51–60 years.

Selvin et al.4 published an article stating that people diagnosed with diabetes between the ages of 30 and 65 have poorer glycemic control than people diagnosed at ages 65 and older. Similar results were observed in the study of Shamshirgaran et al.,5 which concluded that compared with the ≤49 age group, the middle-aged group (50–59 years) and the elderly group (60 years and above) were less likely to have poor blood sugar control. Nanayakkara et al.6 also published in their article that younger age is associated with poor glycemic control and poor cardiovascular outcomes. Kakade et al.7 found in their study that there was no difference between the ages of patients with poor and good glycemic control.

In our study, we found that 54% of men and 46% of women were included in the study, and there was no study that did not find a relationship between poor control and glycemic control in both genders. A 2002 UK cross-sectional study8 involving 10,663 people aged 17–98 with type 2 diabetes and another Canadian study9 involving 5,569 patients also found no association between gender and HbA1c level.

In our study, a very significant increase in the NLR was observed in patients with uncontrolled diabetes compared to patients with controlled diabetes. These results are based on Devamsh et al. It is supported by research conducted by Devamsh et al.,10 who found that the neutrophil ratio was positively correlated with HbA1c and was indicative of poor glycemic control in patients with type 2 diabetes. Increased neutrophil levels were associated with increased HbA1c and poor glycemic control.

Conclusion

Diabetes mellitus is the most common metabolic disorder in Asian countries. It leads to many acute and chronic complications in uncontrolled diabetes. Uncontrolled diabetes mellitus had a positive association with inflammatory markers, that is, NLR and MLR. Moreover, markers like NLR and MLR are inexpensive and easily available for blood investigation.

Hence, these markers are quite useful in differentiating controlled and uncontrolled diabetes and, therefore, useful in predicting blood sugar control in diabetes mellitus. Our study has limitations because the small size of a single institution may not represent the general population.

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