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ORIGINAL RESEARCH

Haematological parameters in type 2 diabetes mellitus, controlled and uncontrolled

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ABSTRACT

Aims: To compare HbA1c levels with inflammatory markers that include a neutrophil-to-lymphocyte ratio (NLR) and monocyteto-lymphocyte ratio (MLR) in controlled and uncontrolled diabetics.

Materials and methods: Two hundred type 2 diabetes mellitus (T2DM) patients were separated into two groups of managed (HbA1c 7%) diabetics. HbA1c (glycated haemoglobin) levels, leukocyte count (WBC), haemoglobin (Hb), hematocrit (Hct), red blood cell distribution width (RDW), neutrophils, lymphocytes, and monocytes were all measured using recent laboratory data. The laboratory results were used to determine the NLR and MLR.

Results:Controlled diabetics had a mean age of 58.30 years, while uncontrolled diabetics had a mean age of 55.62 years. The mean NLR in diabetics with and without diabetes was 2.61 and 4.88, respectively. The distinction was discovered to be statistically significant ($p < 0.05$). The mean MLR in diabetics with and without diabetes was 0.2 and 0.24, respectively, however the difference was not statistically significant ($p > 0.05$). The data showed a modest positive connection between HbA1c levels and the haematological indices, but it was statistically insignificant.

Conclusion: The study found a substantial difference in NLR between diabetics who were well-controlled and those who were not. Although only a slight positive connection was detected between glycated Hb levels and the haematological indices, the results revealed a substantial difference in NLR between the two groups. This demonstrates that these ratios have the potential to be used as inflammatory indicators in T2DM.

Keywords: Diabetes, Diabetes mellitus, Hematological indices, Inflammation, Inflammatory markers, Microvascular complications, Monocyteto-lymphocyte ratio, Neutrophil-to-lymphocyte ratio, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a collection of metabolic illnesses distinguished by chronic hyperglycemia and abnormalities in carbohydrate, lipid, and protein metabolism caused by deficiencies in insulin production, action, or both [1]. The global adult diabetes burden has risen considerably from 108 million in 1980 to 463 million cases and 4.2 million deaths in 2019 [2]. More than three-quarters of the global diabetes burden exists in low and middle-income countries, and the number of diabetics is expected to reach 700 million by 2045 [2].

Diabetes mellitus' global prevalence has risen quickly from 4.7 percent in 1980 to 8.5 percent in 2014, making it the world's sixth biggest cause of death [1]. Diabetes mellitus type 2 (T2DM) is a metabolic condition defined by chronic hyperglycemia caused by insulin

resistance, which can lead to a variety of microvascular and macrovascular problems. Many studies have concluded that an inflammatory response is a likely contribution to insulin resistance, and that prolonged hyperglycemia exacerbates the many consequences of diabetes mellitus [2,3]. Diabetes and uncontrolled hyperglycemia have been linked to the development of cardiovascular disease since the Framingham research. Microvascular problems may result in cardiac events.

Diabetes and hyperglycemia produce a proinflammatory milieu, which leads to microvascular consequences such nephropathy, retinopathy, and neuropathy [4]. Obesity is a key risk factor for diabetes and can cause inflammation by activating TLRs, which recruit proinflammatory cytokines and chemokines [5]. Diabetes has been linked to an increase in the expression of proinflammatory cytokines, C-reactive protein, tumour necrosis factor (TNF)-, and interleukin (IL)-6 [6, 7, 8]. There have only been a few articles that have looked into the association between diabetes and these systemic inflammatory indicators [9, 10, 11, 12]. We hypothesise that comparing uncontrolled diabetes to controlled diabetics will result in an increase in NLR and MLR.

Our study's purpose was to compare the differences in NLR and MLR between controlled and uncontrolled T2DM, as well as to correlate HbA1c with NLR and MLR. Neutrophil-to-lymphocyte ratios and MLR are low-cost, commonly performed, and widely available indicators of inflammation. Establishing a solid relationship between haematological indices and HbA1c would improve the value of these markers in predicting T2DM complications. As a result, the study's necessity is explained.

MATERIALS AND METHODS

SAMPLE AND SAMPLING METHOD

Data were obtained from patients who visited the hospital for a check-up. Only 39 of the 43 individuals served as managed diabetics (HbA1c 7%), and only 39 met the inclusion criteria. Fifty individuals were classified as uncontrolled diabetes (HbA1c >7%). The study excluded subjects over the age of 25 having a history of liver failure, acute sickness, malignancy, or type 1 diabetes mellitus.

To acquire information on HbA1c levels, leukocyte count (WBC), haemoglobin (Hb), hematocrit (Hct), red blood cell distribution width (RDW), neutrophils, lymphocytes, and monocytes, a patient file search was undertaken. The laboratory data was used to determine ratios such as NLR and MLR.

DATA COLLECTION AND LABORATORY METHODS

Face-to-face interviews were used to obtain data on socio-demographic and behavioural factors using a pretested structured questionnaire. Using a checklist, clinical characteristics such as diabetes duration, anti-DM medicine type, and fasting blood glucose level for the previous two months were extracted from diabetic patients' medical records. The average blood glucose level was calculated using participants' fasting blood glucose readings for at least three months, including the current value. Clinical nurses measured blood pressure (BP) with an analogue sphygmomanometer and stethoscope. After the patient had been sitting for more than 5 minutes, measurements were collected from the upper arm with the hand at the heart level.

Anthropometric variables such as height (to the nearest centimetre without shoes), weight (to the nearest 0.1 kg), and waist circumference (WC) (measured midway between the lowest rib and the iliac crest) were gathered in accordance with the methodology for anthropometric measurements. Body mass index (BMI) was computed by dividing weight in kilogrammes by height in metres squared. Following an interview, record review, anthropometric, and blood pressure assessment by qualified clinical nurses, study participants were transported to a

laboratory where a blood sample was obtained for evaluation of FBG and haematological parameters.

After an overnight fast, laboratory experts obtained a six-milliliter venous blood sample (2ml in a serum separator tube and 4ml in an EDTA tube) from each T2DM patient. At the moment of donation, four millilitres of venous blood were taken into an EDTA test tube from the control group (blood donor). FBG was determined using serum produced from a serum separator tube. The glucose oxidase method [13] was used to assess fasting blood glucose using a Biosystems A25 (Costa Brava, Spain) automated chemistry analyzer according to the manufacturer's instructions. The coulter counting, spectrophotometry, and VCSn technology were used to examine the complete blood cell count (CBC) using the UniCelDxH 800 (Beckman Coulter, USA) automated haematology analyzer [14].Fasting blood glucose, haematological parameters (RBC, Hgb, Hct, MCV, MCH, MCHC, RDW, WBCs, absolute lymphocytes, monocyte, basophil, eosinophil, neutrophils, platelet count, and MPV) were all measured at the hospital laboratory and recorded on a laboratory result registration form for each study participant.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) 22.0 software package was used for statistical analyses. An independent t-test was performed to compare haematological indicators in managed diabetes against uncontrolled diabetics. Furthermore, the Karl Pearson correlation test was used to compare HbA1c levels to haematological indicators. The t-test results included 95 percent confidence intervals and a p value. The findings of the Karl Pearson correlation test were expressed as a R value and a p value. A p value of 0.05 was regarded as significant.

RESULTS

A total of 89 diabetic patients were classified as managed (HbA1c 7%, n= 50, mean age 55.62 ± 11.14). The groups' mean Hb, Hct, and RDW values were equal. The mean HbA1c levels in controlled T2DM were 6.02 ± 0.50 percent and 11.52 ± 2.31 percent in uncontrolled T2DM. Table 1 shows a comparison of the two groups in terms of demographic and laboratory data using a two-sample t-test. The following variables, such as HbA1c levels, WBC count, neutrophil count, and NLR, showed statistically significant differences ($p < 0.05$) across groups.

There were no statistically significant differences between the groups in the following variables: age, Hb, Hct, RDW, lymphocyte count, monocyte count, and MLR.

A correlation test was performed using the Karl Pearson correlation test between HbA1c values and the haematological markers NLR and MLR in Table 2. When HbA1c was compared to NLR and MLR, a slight positive connection was discovered. These findings were determined to be statistically insignificant.

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Table 1: Demographic and laboratory data of controlled and uncontrolled diabetics

parameters	HbA1c < 7	HbA1c > 7	p-value
Age	58.30 ± 12.02	55.62 ± 11.14	0.28
HbA1c (%)	207	553	<0.01*
WBC	253	507	0.002*
Haemoglobin	12.72 ± 2.85	12.40 ± 2.43	0.58
Haematocrit	42.04 ± 8.73	40.78 ± 7.36	0.47
RDW	14.76 ± 2.02	13.81 ± 2.46	0.051
Neutrophil	5.15 ± 1.85	7.22 ± 4.09	0.002*
Lymphocyte	2.22 ± 0.93	2.33 ± 0.88	0.58

Monocyte	0.44 ± 0.16	0.48 ± 0.20	0.34
NLR	2.61 ± 1.31	4.11 ± 4.64	0.03*
MLR	0.2 ± 0.08	0.24 ± 0.14	0.27

Table 2: Correlation between HbA1c and hematological indices

HbA1c vs parameters	R value	p-value
HbA1c vs NLR	+0.062	0.55
HbA1c vs MLR	+0.031	0.89

FACTORS ASSOCIATED WITH ANEMIA AMONG TYPE 2 DIABETIC ADULT PATIENTS

Categorical variables were constructed from haemoglobin after it was corrected with a factor of 1.9 for an average altitude of 3000 metres, as recommended by the World Health Organization (WHO) [15]. In diabetics, the associations of anaemia with predictor variables were investigated using univariable and multivariable logistic regression analysis. Gender, duration of DM, anti-DM medicine, and milk consumption were all linked with anaemia with a p-value less than 0.2 in the bivariable logistic regression analysis.The multivariable logistic regression model included variables with pvalues less than 0.2; diabetes duration and milk consumption were substantially linked with anaemia. Patients with diabetes for 7 years or more were three times more likely to have anaemia than those with diabetes for less than 7 years (AOR = 3.05, 95 percent CI = 1.12–8.34).

DISCUSSION

The NLR and MLR are laboratory markers that are comparatively newer, simpler, and less expensive. The link between these haematological characteristics and a variety of medical diseases has been well established [16, 17, 18]. The purpose of our study was to examine NLR and MLR ratios in managed and uncontrolled diabetics, and then to link these ratios with HbA1c values. When compared to controlled diabetics, uncontrolled diabetics had higher mean WBC and neutrophil counts, with the difference being statistically significant. Higher NLR values (4.11 ± 4.64 vs 2.61 ± 1.31) were detected in uncontrolled diabetes compared to controlled diabetics.

The distinction was discovered to be statistically significant. Higher MLR values (0.24 ± 0.14 vs 0.2 ± 0.08) were discovered when comparing uncontrolled diabetes (HbA1c >7%) to controlled diabetics (HbA1c <7%). This distinction was shown to be statistically negligible. A Karl Pearson correlation test was used to compare HbA1c levels to NLR and MLR. A slight positive connection was discovered between HbA1c levels and haematological markers. The results, however, were statistically insignificant.

T2DM patients are at increased risk for microvascular problems, which are caused in part by inflammation. Inflammation is significantly linked to both beta cell secretory function and insulin resistance [12]. Inflammatory chemicals in the bloodstream can reduce beta cell activity directly through secretory malfunction or uncontrolled apoptosis [12, 19]. As a result, glucotoxicity and lipotoxicity occur, resulting in an accelerated inflammatory response [12, 20, 21]. It is widely understood that inflammation is linked to an increase in WBC count. Diabetes and diabetic nephropathy have been linked to raised NLR levels, whereas diabetic retinopathy has been linked to elevated MLR levels.

In the current investigation, we discovered that Hgb, as an indicator of anaemia, was considerably lower in T2DM patients than in controls. Previous studies conducted in Bangladesh, India [22], Libya [23], and Nigeriahave found considerably lower Hgb in T2DM patients than the control group. Anemia was found in 17.9 percent of the population (95

percent CI: 11.5–24.5), which is comparable to studies undertaken in Saudi Arabia (22% [6], Australia (17.8 percent [7], and Sudan (18.3 percent [21]).

In contrast, our prevalence estimate was lower than those reported by studies in India (71.4 percent [32]), Nigeria (45.2 percent [41]), and Dessie, northeast Ethiopia (26% [42]). This disparity could be attributed to differences in the study population's characteristics as well as sample size variation. The participants in our study were all adults, with the majority of them being men.

Yazici et al.'s [18] study to evaluate the application of the MLR to predict diabetic retinopathy discovered that the MLR was elevated in diabetic retinopathy patients [17]. The study, however, did not compare MLR in controlled and uncontrolled T2DM. The difference in MLR between controlled and uncontrolled T2DM was determined to be statistically negligible in our investigation. A modest positive connection was discovered between glycated haemoglobin levels and MLR values, however this result was also statistically insignificant. Demirtas et al. conducted a study to investigate the relationship of haematological indices with diabetes, poor glucose regulation, and microvascular consequences of diabetes [24, 25].

The study discovered a statistically significant difference in NLR between the healthy, control, and diabetic groups. T2DM is associated with an increase in inflammatory markers, according to one study. Another study on NLR: a good assessment tool of glycemic control in T2DM patients found that increasing NLR values were linked with raised HbA1c levels and poor glycemic control in T2DM patients [26]. Although there is only a slight positive link between glycated haemoglobin levels and the ratios, our findings revealed a substantial difference in NLR when comparing controlled and uncontrolled diabetics.Studies combining HbA1c with inflammatory markers in managed and uncontrolled diabetics have yielded positive results, which could broaden the use of these ratios in the diagnosis of T2DM [27].

CONCLUSION AND RECOMMENDATIONS

There was a statistically significant difference in the haematological parameters (total WBC count, absolute count of neutrophil, lymphocyte, eosinophil, and basophil, platelet count, Hgb, RDW, and MPV) of T2DM patients compared to controls in the current study. This study also found that anaemia was a common haematological change in T2DM patients, and it was a minor public health issue in our clinical practise. Nearly one out of every five diabetic patients studied was anaemic. Diabetes duration and milk consumption enhanced the probability of anaemia. Anthropometric measures were substantially linked with platelet count and MPV.

The number of red blood cells and RDW were found to be associated to the duration of diabetes. Thus, assessing haematological alterations in T2DM patients will be critical to establishing an effective and early therapeutic response to prevent the emergence of significant problems. For optimal care of type 2 diabetes patients, regular monitoring of haematological markers should be considered. In terms of haematological abnormalities, the duration of diabetes and dietary practises should be closely monitored. A longitudinal study with a bigger sample size would be preferable for accurately assessing the problem. Furthermore, for T2DM patients, morphological and coagulation profile studies should be considered.

LIMITATIONS

Our research has some limitations. For starters, a limited sample size from a single institution may not accurately represent the general community. Second, because our study is cross-sectional, we cannot establish a cause-and-effect link.

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