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Research Article

To Study the Correlation of Leucocytosis with Uncontrolled Hyperglycaemia in Diabetic Patients; A Cross-Sectional Study.

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ABSTRACT

Introduction: Dysfunction of immune system may play a significant role in the development of type II DM and higher WBCs have been shown to play an important role in the advancement of diabetic complications. The study was undertaken to assess the total WBC count in patients with Type II diabetes mellitus (T2DM) and correlate with glycated haemoglobin (HbA1C) values.

Materials And Methods:

Data of the study collected from a sample size of 108 and prevalence of 7.3% according to Harivarshan et al, and considering the consent of people and people with T2DM and excluding people with chronic inflammation, age <18 years any autoimmune disorder malignancy and hematological disorders.

Results: In our study with a sample size of 119.Mean duration of diabetes is 8.84 +/- 5.81, mean HBA1c is 8.89 +/- 2.62. Mean FBS and PPBS were 179.4 +/- 96.3 and 252 +/- 136.5 respectively. Levels of TLC is positively correlated with HBA1C and negatively associated with FBS and PPBS with a statistically significant p value less than 0.05 In our study mean neutrophil count has a positive correlation with HBA1C values with significant P value. Levels of monocytes are positively associated with HbA1C with statistically significant p value less than 0.05.

Conclusion: Total leucocyte count and neutrophil count are increased in patient with uncontrolled sugar.We recommend to have a complete hemogram done for all cases of diabetes mellitus as they provide important clues to the presence of complications and comorbidities.

Keywords: Diabetes mellitus, leucocytes, HBa1c, Monocytes

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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic problem caused by an elevated blood sugar usually caused from pathology in insulin. The hyperglycemia of DM is assosciated with many systemic effects over the period of the time. The carbohydrate, fat and protein metabolism are affected diabetes mellitus and hence known as metabolic disorder.(1) As demonstrated by International Diabetes Federation (IDF). In India, the burden of diabetes has been increasing steadily since 1990 and leaps and at a faster pace from the year 2000. The prevalence of diabetes in India has risen from 7.1% in 2009 to 8.9% in 2019. Currently, 25.2 million adults are estimated to have impaired glucose tolerance, which is estimated to increase to 35.7 million in the year 2045.(2)

Inflammatory responses of the immune system can be identified by increasing levels of plasminogen activator inhibitor-1 (PAI-1), white blood cell (WBC) count and concentrations of cytokines. Because of it's statistical association among insulin resistance markers and inflammation, it has been noted that dysfunction of immune

system may play a significant role in the development of type II DM .(3) Higher WBCs have been shown to play an important role in the advancement of diabetic complications .(4) WBCs may also be triggered by the inflammatory responses, angiotensin II and glycaemic end-products, which may in turn results from hyperglycemia, and may trigger factors such as interleukin b1 and tumor necrosis factor-a (TNF-a) associated with severe diabetes pathophysiology and health problems. (5)

This study was undertaken to assess the total WBC count in patients with Type II diabetes mellitus (T2DM) and correlate with glycated haemoglobin (HbA1C) values which are a measure of glycemic control in these patients

Objective of study

1) To assess neutrophils count in T2 DM

2) To correlate neutrophils with T2DM with HbA1C <7 and >7

MATERIAL AND METHODS: (Inclusion Criteria, Exclusion Criteria, Sample Size, Sample Type, Procedure)

Source of data:

Data for the study will be collected from the patients visiting to Medicine OPD and Inpatients

Sample Size –

Sample size:

In a study done by Harivarshan et al, 7.3% of diabetic patients had elevated TLC levels with 5% absolute precision, sample required for the study is 100.

Taking $n=4pq/d^2$

Where in

P=7.3

Q=100-7.3= 92.7

d=5

Hence the sample size on applying values is 108

Method of collection of data

- **Inclusion criteria**
- Patients willing to give written informed consent
- Patients with type 2 diabetes mellitus

- **Exclusion criteria**
- Age <18 yrs
- active or chronic inflammation,
- autoimmune diseases,
- hematological disorder, recent blood transfusion before enrolment,
- malignancy,
- acute or chronic renal/hepatic diseases, or coronary artery disease

Procedure

After obtaining institutional ethics committee clearance and written informed consent (Annexure 1), the patients in OPD or admitted hospital will be taken up for the study.

119 Diabetes patients on opd basis or admitted as inpatients are included in this study. Information is collected and detailed history is taken using pre-formed proforma (Annexure 2) at the time of admission. Venous blood samples were taken after an overnight fast. All biochemical analyses were studied which include Fasting lipid profile, C-reactive protein (CRP) concentrations. Complete blood count was analyzed.

STATISTICAL TOOL FOR ANALYSIS:

All the data will be compiled in Microsoft excel and Descriptive statistics will be calculated. To compare the quantitative variables t-test or Mann-Whitney U test will be used. To compare the qualitative attributes Chi-square test or Fisher's exact test will be used. To find the correlation between variables Karl Pearson correlation coefficient or spearman's rank correlation will be used. The data will be analyzed using statistical software'

DEMOGRAPHIC REPRESENTATION

Table 1; BASIC CHARACTERISTICS

VARIABLES	VALUES
sample size	**119**
age, mean (SD)	**56.65 (9.67)**
gender	**female - 36,** **Male - 83**
duration of diabetes(years), mean(SD)	**8.84(5.81)**
HB1ac, mean(SD)	**8.89(2.65)**
FBS, mean (SD)	**179.44(96.35)**
PPBS, mean(SD)	**252.07(136.59)**

Figure 1

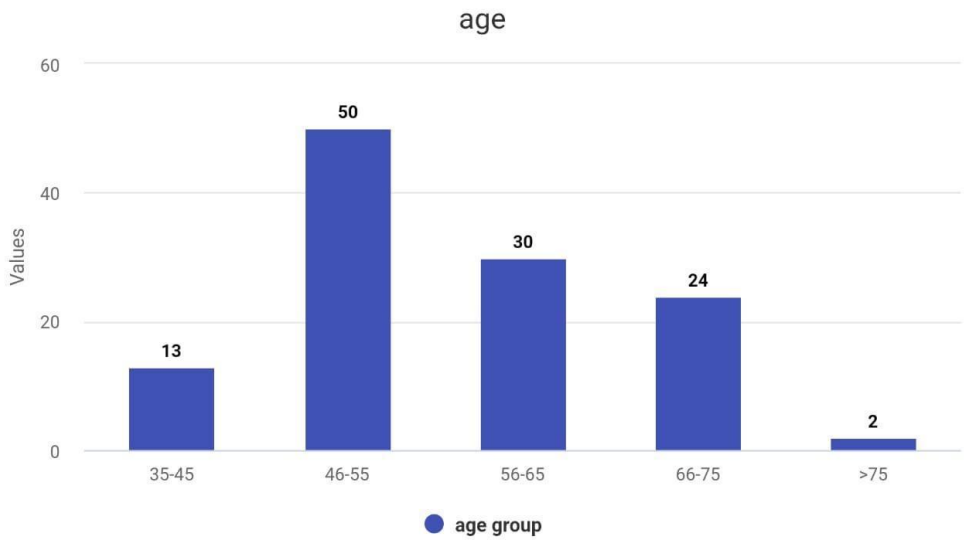
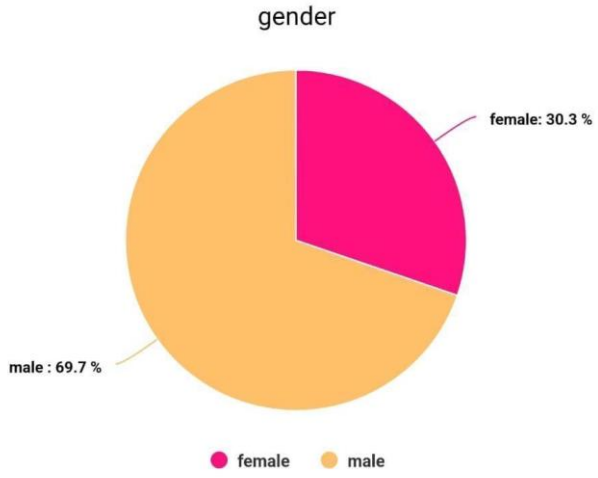


Figure 2



Among 119 patients, the mean age is 56.65. Maximum age of >75 years and minimum of age 35 years. (Table -1)

83(69.7%) were male and 36(30.3%) were female. Fig(1)

Table 2; Correlation of patients with diabetic nephropathy and diabetic patients without nephropathy

Variables	Type 2 DM with nephropathy	Type 2 DM without nephropathy	p value
Albumin(mean)	**0.695**	**1.923**	**0.035**
total protein,mean(SD)	**6.58(0.86)**	**6.75(1.35)**	**0.51**
ALT,median (IQR)	**17 (12, 32)**	**18.35(12, 28)**	**0.92**
AST median(IQR)	**19 (14, 30)**	**19.05 (12.5, 30)**	**0.84**
TLC median(IQR)	**8540 (7880, 9970)**	**7615 (6080, 9560)**	**0.023**
platelet, median (IQR)	**2.68 (1.94, 3.12)**	**2.62(1.98, 3.25)**	**0.81**
Creatinine, median (IQR)	**1.6 (1.2, 2.4)**	**0.7(0.6, 1.1)**	**<0.001**
urine PCR, median (IQR)	**0.5(0.38, 0.8)**	**0.4(0.27, 0.55)**	**0.014**
GGT, median (IQR)	**65(36, 120.5)**	**37(19.1, 66)**	**0.002**

In our study, mean duration of diabetes is 8.84 +/- 5.81, mean HBA1c is 8.89 +/- 2.62. Mean FBS and PPBS were 179.4 +/- 96.3 and 252 +/- 136.5 respectively(table 2))

Table 2- Correlation of heamatological parameters with Hba1c

In our study, mean duration of diabetes is 8.84 +/- 5.81, mean HBA1c is 8.89 +/- 2.62. Mean FBS and PPBS were 179.4 +/- 96.3 and 252 +/- 136.5 respectively (table 1).
In our study mean total leukocyte count with HbA1c <7 is 7464.82 (SD - 2816.1) and HbA1c > 7 is 8550.22 (SD- 3031.90) has no significant correlation with p value 0.077(table 2)

In our study mean neutrophil count with HbA1c <7 is 4362.37 with (SD -1643.7) and HbA1c > 7 is 5524.37 (SD - 2833.2) has significant correlation with a p value 0.029 (table 2)
In our study mean lymphocytes count with HbA1c <7 is 2016.98 with standard deviation of 789.03 and HbA1c > 7 is 7.72 (SD - 3.09) has no significant correlation with a p value 0.884(table 2)
In our study mean monocyte count with HbA1c <7 is 2057.98 with standard deviation of 1435.83 and HbA1c > 7 is 25.66 (SD - 9.75) has no significant correlation with a p value 0.244(table 2)
According to Mehak et al study that lymphocytes were abnormally low in most diabetics, although few patientshad elevated lymphocyte levels Almost all patients had perfectly natural monocyte and eosinophilic value
According to Effrossyni Gkrania-Klotsas et al study Total WBC count was significantly associated with T2D, after adjustment for age, sex, smoking, BMI, waist circumference. Total granulocyte (and subset neutrophil) as well as lymphocyte but not monocyte count were also significantly associated with T2D, after adjustment for age, sex, smoking, BMI, waist circumference The findings were similar for incident T2D in the EPIC-Norfolk cohort analysis.(7)

Table-(3) Association of hematological parameters

In our study levels of neutrophil count is positively correlated with HbA1c and negatively associated with FBS and PPBS (table 3)
Levels of TLC is positively correlated with HBA1C and negatively associated with FBS and PPBS with a statistically significant p value less than 0.05 (table 3)
Levels of monocytes is positively associated with HbA1C with statistically significant p value less than 0.05. (Table 3)

Discussion
In our study with a sample size of 108 , 119 people were considered 83 were men and 36 were women.
Levels of TLC is positively correlated with HBA1C and negatively associated with FBS and PPBS with a statistically significant p value less than 0.05
According to Dr Sonti Sulochana et al. it has been demonstrated that the total and differential leukocyte counts were significantly altered in patients with hyperglycaemia. Patients with Uncontrolled type II Diabetes had higher counts of total WBCs or leucocytes and neutrophils
According to Yan Borné et al the concentrations of total leukocytes, neutrophils and lymphocytes are associated with incidence of diabetes. However, the lack of association with the R262W polymorphism suggests that the associations may not be causal,
In our study mean neutrophil count has a positive correlation with HBA1C values with significant P value. Sefil F,. et al States that there may be a significant relationship between NLR and blood glucose regulation. The authors propose that increased NLR may be associated with elevated HbA1c in patients with type 2 diabetes mellitus(8)
Sanjay Varma et al concluded that Increased neutrophil count is associated with elevated HbA1c and poor glycemic control. Neutrophil should be used as a marker of diabetic control level in addition to HbA1c in type 2 diabetic subjects(9)
Levels of monocytes are positively associated with HbA1C with statistically significant p value less than 0.05.
According to Nathella P kumar et al identified a positive correlation of monocyte activation with HbA1c, suggesting that chronic hyperglycemia drives this complication of DM as is the case for microvascular and macrovascular complications
According to Danqing Min et al results suggest that the circulating monocyte phenotype is altered by diabetic complications status. These changes may be causally related to and could potentially be used to predict susceptibility to diabetic complications.

Conclusion-
Total leucocyte count and neutrophil count are increased in patient with uncontrolled sugar.We recommend to have a complete hemogram done for all cases of diabetes mellitus as they provide important clues to the presence of complications and comorbidities. Study on large scale with more number of patients would definitely provide more information on this problem.

Limitation –
-Single centre study
-Small sample size

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