Original Article

Association of Neutrophil to Lymphocyte and Platelet To Lymphocyte ratio with Blood Glucose Regulation in Type 2 Diabetes Patients

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Abstract

Introduction: The main characteristic of diabetes is Chronic Hyperglycemia with marked disturbances in fat carbohydrate and protein metabolism. Disorders of lipid metabolism are common in diabetes causing greater cardiovascular risks. Leukocytosis is a major marker of metabolic syndrome

Objective: To investigate the association of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio with blood glucose regulation in patients with type 2 diabetes mellitus.

Materials and Methods: This comparative analytical study was conducted in Shifa International Hospital on diabetic patients. The sample size was calculated as 62 by the WHO sample size calculator. Non-randomized convenient sampling was used. Patients were divided into two groups according to the HbA1c level taking 7% as the cut-off point. Full blood count, lipid profile, and liver profile were carried out. For quantitative normal and dispersed variables, independent student t and Mann Whitney U test were applied respectively.

Results: Out of the total of 93 patients, 33 (35.4%) were males and 60(64.5%) were females. The mean duration of disease was 8.26 ± 5.8 years. Neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR) was elevated in patients having poor glucose control but that difference was not significant. A significant difference between the groups was found with random blood glucose. LDL, triglycerides, cholesterol ratio, ALT, and AST were raised in patients having poor glycemic control.

Conclusion: Patients having poor blood glucose regulation have increased levels of haematological and serological parameters posing greater cardiovascular health risks to patients with type 2 diabetes.

Keywords: Diabetes mellitus, haematological parameters, lipid profile, HbA1c.

Introduction

Diabetes mellitus is a chronic metabolic disorder whose main characteristics are persistent hyperglycemia and certain lipid abnormalities like hypertriglyceridemia, high LDL, and low HDL.[1] It is the commonest metabolic disorder affecting the world population today.[2] Type 2 or maturity-onset diabetes is also linked to metabolic syndrome which comprises elevated triglyceride and uric acid levels, obesity, increased waist circumference with and without hypertension, and impaired fasting glucose.[3] It is often found in patients who eventually develop type 2 or maturity-onset diabetes. The afore-mentioned lipid and other abnormalities have been shown to be linked to increased atherogenic activity leading to increased risk of coronary and cerebral vascular events as compared to normal individuals.[4] This is mostly due to persistent chronic inflammation because of the reduction of certain anti-inflammatory proteins like adiponectin. Glycosylated hemoglobin (HBA1c) is often used to measure long-term glucose control in diabetic patients and is thought to be a predictor of the evolution of diabetic complications.[5] Elevated HBA1C is now considered as an independent risk factor for the development of diabetic complications in diabetic patients[6]. Maintaining an HBA1C level below 7% significantly reduces the risk of developing diabetic complications as shown by the Diabetes complication and control trial (DCCT).[7]

Persistent and chronic inflammation is thought to play a fundamental role in the development and progression of diabetes mellitus and its complications.[8] Leukocytosis is a major marker of metabolic syndrome[9] and is shown to worsen glycaemic control in diabetic patients.[10] Neutrophil to lymphocyte ratio (NLR) is considered a marker of increased risk of cardiac and vascular complications in such patients.[11] Increased NLR values are seen in type DM[12] often along with altered Platelet to lymphocyte ratio (PLR) and are thought to incite subclinical inflammation worsening glycaemic control.[13]

This study was planned to find the association of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio with HbA1c in patients with type 2 diabetes mellitus. The patient's lipid and liver profiles were also taken into consideration.

This study will not only generate useful information regarding blood glucose regulation and complications arising due to poor control, but it will also help in developing new strategies in the treatment plan and patient education for better control of complications in diabetic patients.

Materials and Methods

This comparative analytical study was conducted in Shifa International Hospital, Islamabad from June 2018 to June 2019. Patients having type 2 diabetes mellitus presenting to Falahee OPD of Shifa International Hospital who consented to participate were consecutively recruited in the study. Non-probability convenient sampling was used for the selection of patients. After approval from the Institutional Research Board (IRB) and permission from authorities of Shifa International Hospital, Patients were divided into two groups according to the HbA1c level taking 7% as a cut-off point. Full blood count, lipid profile, and liver profile were done. Patients' duration of disease, body mass index (BMI), Fasting blood sugar, AST, ALT, cholesterol, triglycerides, HDL, LDL, and PLR were assessed in relation to their HbA1c values. All patients diagnosed with type 2 diabetes mellitus regardless of age and gender were included in the study. Patients with serious medical conditions, patients on any medications (except oral antidiabetic agents and insulin), patients with a history of smoking or high levels of triglycerides, and patients taking aspirin or statins were excluded from the study. A structured checklist was used for data collection.

The sample size was calculated using the WHO sample size calculator with a 95 % confidence level and came out to be 62.[9] Data was analyzed by SPSS version 21. Descriptive statistics were calculated for categorical variables. For quantitative normal and dispersed variables, independent student t and Mann Whitney U test were applied respectively. P-Value less than 0.05 was considered significant.

Results

Out of a total of 93, 33 (35.48%)   were males and 60 (64.51%) were females. (Table 1)
Out of a total of 93, 21 have HbA1c up to 7% and 72 have HbA1c above 7%. The mean duration of disease was 8.26 ± 5.8 years. (Table 1) HbA1c was significantly increased in patients having more duration of disease.

Table 1: Characteristics of studied patients

Variable		HbA1c upto 7%	HbA1c above 7%	Significance
Gender	Males	06	27	0.45
	Females	15	45	
Duration since diabetes (years)		6.17 ± 5.88	8.87 ± 5.76	0.019
BMI (kg/m²)		31.17 ± 4.82	30.24 ± 6.14	0.505

White blood cell count and platelet levels were deranged in both groups of diabetic patients. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) was raised in patients having HbA1c above 7% but no significant difference was present between both groups.

Table 2: Comparison of hematological features between two groups

Measure	HbA1c up to 7%	HbA1c above 7%	Significance
White blood cells (No./µL)	9289 ± 2481	9016.81 ± 2474	0.65
Neutrophils (No./µL)	5729.87 ± 2111.47	5642.11 ± 2129.6	0.901
Lymphocytes (No./µL)	3102.98 ± 1923.42	2638.55 ± 870.36	0.339
Platelets (No./µL)	302809.52 ± 80819.9	275104.17 ± 103544.05	0.205
NLR	2.17 ± 1.10	2.47 ± 1.77	0.35
PLR	111.21 ± 38.53	115.44 ± 65.11	0.858

Fasting blood glucose was significantly elevated in the 2nd group of patients. Cholesterol, triglycerides, LDL levels, and cholesterol ratio were elevated in patients having poor glucose control but a significant association was not found. Similarly, AST, ALT, and AST ratios were also elevated in patients having HbA1c above 7%. (Table 3)

Table 3: Comparison of lipid profile between two groups

Variable	HbA1c up to 7%	HbA1c above 7%	Significance
Fasting blood glucose (mg/dl)	171.05 ± 56.4	248 ± 84	<0.001
ALT (IU)	30.95 ± 15.5	48.09 ± 91.2	0.40
AST (IU)	27.95 ± 16.5	43.82 ± 69.07	0.31
AST/ALT	0.93 ± 0.31	1.12 ± 0.9	0.4
Cholesterol (mg/dl)	184.03 ± 39.06	195.5 ± 44	0.30
Triglycerides (mg/dl)	182.2 ± 109.3	232.4 ± 201.62	0.28
HDL (mg/dl)	41.2 ± 8.65	41.87 ± 13.82	0.83
LDL (mg/dl)	114.35 ± 31.84	115.26 ± 36.38	0.91
Cholesterol ratio	4.56 ± 1.04	5.17 ± 2.58	0.30

Discussion

This hospital-based comparative analytical study of 93 diabetic patients showed that lipid profile and hematological parameters are deranged in diabetic patients who have poor glycaemic control as compared to patients with good glycemic control.

Our study showed elevated hematological parameters, i.e. increased NLR and PLR in patients with poor glycemic control. The result is equivocal to a study conducted in Pakistan which concluded that increased NLR Level is associated with increased HbA1c value and poor glycemic control in type 2 diabetics.[14] Similarly, a study has confirmed that increased PLR is present in patients suffering from diabetic ketoacidosis,[15] hence indicating a possibility of complication According to another study, there is a positive correlation between NLR and IGF-1(insulin-like growth factor 1) and between PLR and IGF-1.[16] Therefore, patients having poor glycemic control have deranged levels of NLR and PLR when compared to patients having good glycemic control.

Our research manifested a significantly increased level of fasting blood glucose in patients with increased HbA1c which is consistent with a Turkish study.[9]

The present study showed that triglycerides level and cholesterol ratio were raised in both groups of diabetic patients, more in patients with HbA1c above 7% and comparatively less so in patients with HbA1c of 7%. This result is similar to a study conducted on the correlation of lipid profile and HbA1c in India which showed a significant correlation between HbA1C and lipid profile parameters between the two groups (less than 7% and more than 7% of HbA1C).[17] Similarly, a study by Khan HA, et al, showed the impact of glycemic control on various lipid parameters in which severity of dyslipidemia increase in patients with

higher HbA$_1$C value,[18] which is similar to the results of this study. One African study on type 2 Diabetes Mellitus patients showed that 35% had increased total serum cholesterol levels, and a study in England found that 73% had increased total serum cholesterol levels.[17] This is similar to the results of our study in which both diabetic groups have raised cholesterol levels. However, more raised in patients with more HbA1c value.

The present study shows that increased HbA1C is an indicator of glycation of LDL and subsequent predisposition to atherosclerosis. The present study also demonstrates that the severity of dyslipidemia increases with increased HbA1C values. It is quite evident from the study that poor glycemic control also deranges certain hematological parameters in the body which predisposes the body to several infections. Hence, good glycemic control through adequate anti-diabetic therapy along with lifestyle modifications can reduce the risk of atherosclerosis and related complications. Good glycemic control can prevent the human body from developing cardiovascular complications and infections.

This study can form the basis for future research in this area to determine the effects of increased levels of blood glucose levels on various systems of the human body. It will equally form the basis for the proper education of the patients regarding keeping a strict glycemic control to prevent them from developing serious complications.

Conclusion

Patients having poor blood glucose regulation have increased levels of haematological and serological parameters posing greater cardiovascular health risks to patients with type 2 diabetes.

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