Original Article

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Study of Association of Hematological Parameters with HbA1c and Microvascular Complications in type II Diabetes Mellitus

Tamilselvi Ramachandran[1], Saranya Balasubramanian[2], Bharathi[3], Shankar Radhakrishnan[4]

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Abstract

Background: Studies have proved that complications of diabetes particularly the microvascular complications are strongly associated with HbA1c levels [2,3]. The higher the Hba1c values the higher the chance of developing complications. Hba1c values have thus become a valuable marker in assessing the glycemic control and the risk of developing complications as it is convenient, reproducible and efficient in reflecting chronic hyperglycemia. *Aim:* To assess the association and correlation of haematological parameters with HbA1c levels in type II diabetes mellitus patients. *Methodology:* A cross-sectional study was conducted for a period of one year with 150 patients with diabetes and 150 controls were taken without diabetes. Patients', age, gender, blood pressure, accompanying disease history, medication history and medical history were recorded using pre-tested and semi-structured questionnaire. Five milliliters of fasting blood sample was collected by laboratory technologist for fasting blood glucose (FBG) determination after 10–12 hours of fasting with the exception of water and medication. FBG was estimated by following glucose oxidase method using MINDRAY BS300 fully auto chemistry analyzer, made in china according to manufacturer's instructions. The quantitative urine albumin/ creatinine ratio in morning spot urine samples was used for albuminuria determination in the diagnosis of microalbuminuria. *Results:* The mean values of fasting and postprandial blood glucose along with HbA1c were found to be significantly higher among the diabetes group than the control group, similarly the urine albumin levels also was found to be significantly higher in the diabetes group, whereas the renal parameters (serum urea and creatinine) did not show statistical significant difference between the diabetes and control group. HbA1c and the other hemotological parameters and we found a statistically significant positive correlation with WBC, ploymorphs, lymphocytes and mean platelet volume and a statistically significant negative correlation was observed with platelet count among the diabetic group whereas among the control group there were no statistical significant correlation between HbA1c and the other hemotological parameters. *Conclusion:* The routine hematological profile checking of patients with T2DM may help to prevent complications associated with aberrations in hematological values.

Keywords: Diabetes; Haematological Parameters; Microvascular Complications.

Author's Affiliation: Professor, [1]Professor [2]Assistant Professor, Department of Pathology, [3]2nd year MBBS, [4]Associate Professor, Department of Preventive Medicine, Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu 636 308, India.

Corresponding Author: Tamilselvi Ramachandran, Professor, Department of Pathology, Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu 636 308, India.
E-mail: drselvipatho@yahohoo.com

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Introduction

Diabetes mellitus is one of the most prevalent metabolic disorders that has acquired a global pandemic status. It is characterized by hyperglycemia and its associated protein and lipid disorders that have been shown to be associated with many complications leading to significant morbidity and mortality. Currently, there are 62 million people diagnosed with diabetes in India [1]. The etiology of diabetes is multifactorial with genetic

factors coupled with environmental influences like lifestyle modifications, obesity, urbanization. Many studies have proved that complications of diabetes particularly the microvascular complications are strongly associated with HbA1c levels [2,3]. The higher the Hba1c values the higher the chance of developing complications. Hba1c values have thus become a valuable marker in assessing the glycemic control and the risk of developing complications as it is convenient, reproducible and efficient in reflecting chronic hyperglycemia.

Hematological parameters like white blood cell count (WBC), platelet count, mean platelet volume (MPV), platelet distribution width (PDW), hematocrit (HCT), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) are considered to be predictors of inflammation and endothelial dysfunction [4]. Studies have observed derangements in hematological parameters like white blood cell count, red blood cell count, platelet function, hematocrit, mean platelet volume in patients with insulin resistance [5].

Aim

To assess the association and correlation of haematological parameters with HbA1c levels in type II diabetes mellitus patients.

Materials and Methods

Study Design

Cross-sectional study

Study Population

150 type 2 diabetic patients and a control group of 150 healthy people were enrolled in the study.

Inclusion Criteria

Known type II diabetic patients with a duration of 3–5 years were included in the study. Age and sex matched controls without any chronic morbidities were also included in the study.

Exclusion Criteria

Patients with acute illness, hepatic failure, heart failure, renal failure, hematologic diseases, chronic diseases, alcohol abuse, those on medication altering the platelet function, and atherosclerotic diseases were excluded from the study.

Method of data collection

Patients', age, gender, blood pressure, accompanying disease history, medication history and medical history were recorded using pre-tested and semi-structured questionnaire. Five milliliters of fasting blood sample was collected by laboratory technologist for fasting blood glucose (FBG) determination after 10–12 hours of fasting with the exception of water and medication. FBG was estimated by following glucose oxidase method using MINDRAY BS300 fully auto chemistry analyzer, made in china according to manufacturer's instructions. Creatinine levels was analysed using Jaffe method. HbA1c was estimated using HPLC method. Three milliliters venous blood samples were collected in test tubes, containing EDTA anticoagulant, for hematological tests and were analyzed using Merilyzer Cel Quant 3 hematologyanalyzer. The results of the evaluation of other parameters such as Hgb, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), MPV, platelet distribution width (PDW), red cell distribution width (RDW), and the count of RBCs, WBCs, platelets, absolute lymphocytes, mixed cells (monocyte, basophil, and eosinophil [MID]), and neutrophils were recorded.

The quantitative urine albumin/creatinine ratio in morning spot urine samples was used for albuminuria determination in the diagnosis of microalbuminuria.

Statistical Analysis

Statistical analyses will be carried out using the Statistical Package for Social Sciences software, Windows version 21 (SPSS, Chicago, IL, USA). Mean and standard deviation was derived for all parametric variables, student T test was applied to test the statistical significance between diabetes and control group. Pearson's correlation test was applied to assess the correlation between HbA1c and haematological parameter.

Results

Table 1 shows the age and gender wise distribution of the study population. It is seen from the table that majority of the study subjects were in the age group between 40 and 50 years in both diabetes group and the control group. The minimum age in both the groups was 24 years and the maximum age was 78

years. The mean age among the diabetes group was 52.4 years and in the control group it was 49.9 years and there was no statistically significant difference between the two groups (p>.05). The comparison of various hemotological parameters between the two groups shows that the mean total WBC count, polymorphs and lymphocytes were found to be higher among the diabetes group than the control group and the difference was found to be statistically significant (p<.05), similarly the red cell distribution width (RDW) and the platelet distribution width (PDW) was also high among the diabetes group in comparison with the control group, whereas the platelet count was found to be significantly low in the diabetes group when compared to the control group and the difference was found to be statistically significant (p<.05) (Table 2). Biochemical parameters related to renal function test alone was performed on all subjects along with fasting blood glucose, postprandial blood glucose and HbA1c. For assessing the microvascular complications we performed urine examination for assessing microlbuminuria. The mean values of fasting and postprandial blood glucose along with HbA1c were found to be significantly higher among the diabetes group than the control group, similarly the urine albumin levels also was found to be significantly higher in the diabetes group, whereas the renal parameters (serum urea and creatinine) did not show statistical significant difference between the diabetes and control group (Table 3). Pearson's correlation test was applied to find the correlation between

Table 1: Age and gender wise distribution of the study population

Age group	Diabetes group		Controls (Non-diabetes)		P value
	Male (n=84)	Female (n=68)	Male (n=78)	Female (n=72)	
20- 30	5 (5.9%)	2 (2.9%)	6 (7.6%)	4 (5.5%)	0.516
31 – 40	18 (21.4%)	13 (19.1%)	21 (26.9%)	15 (20.8%)	0.391
41 – 50	26 (30.9%)	23 (33.8%)	22 (28.2%)	24 (33.3%)	0.681
51 – 60	19 (22.6%)	10 (14.7%)	13 (16.6%)	9 (12.5%)	0.715
61 – 70	10 (11.9%)	11 (16%)	13 (16.6%)	11 (15.2%)	0.492
71 – 80	6 (7.1%)	9 (13.2%)	3 (3.8%)	9 (12.5%)	0.296
Mean ± SD	52.45 ± 5.43		49.96 ± 6.21		0.729

p value derived by applying Chi-square test

Table 2: Comparison of the various haematological parameters between the diabetes and the control group

Haematological	Diabetes group		Control group		P value
parameter	Mean	SD	Mean	SD	
Total WBC count (103 / µL)	6.21	1.38	5.13	1.26	<.001
Polymorphs (103 / µL)	3.51	1.28	3.11	1.12	<.001
Lymphocytes (103 / µL)	3.64	1.41	3.25	1.33	<.001
Eosinophils	3.67	1.36	3.52	1.41	0.718
Haemoglobin (gm%)	11.1	1.09	11.34	1.16	0.0914
Haematocrit (%)	31.04	2.52	30.21	2.26	0.518
MCV (fl)	82.5	4.3	81.7	4.8	0.614
MCH (pg)	27.8	3.1	27.8	3.6	0.513
MCHC (g/dl)	33.9	2.8	33.8	2.1	0.725
RDW.SD (fl)	43.8	4.8	42.1	5.1	<.0001
RDW.CV (fl)	13.1	1.7	13.0	1.3	0.638
RBC (103 / µL)	3.64	1.1	3.55	0.9	0.755
MPV (fl)	9.48	1.08	9.47	1.12	0.518
PCT (fl)	0.24	0.08	0.21	0.04	0.429
PDW (fl)	14.8	1.12	13.1	1.21	<.0001
Platelet count (103 / µL)	2.33	1.08	4.47	1.65	<.0001

p value derived by applying student T

HbA1c and the other hemotological parameters and we found a statistically significant positive correlation with WBC, ploymorphs, lymphocytes and mean platelet volume and a statistically significant negative correlation was observed with platelet count among the diabetic group whereas among the control group there were no statistical significant correlation between HbA1c and the other hemotological parameters (Table 4).

Discussions

Research evidences suggest that hematological indices are altered in patients with T2DM. In patients with DM, persistent hyperglycemia exposes RBCs to elevated glucose concentrations, thus resulting in glycation of hemoglobin, prothrombin, fibrinogen, and other proteins involved in clotting mechanisms [6]. In this study, RBC indices had shown increment in diabetic patients as compared to control group, although the difference was not statistically significant. This finding is in agreement with that reported by several previous studies [7,8]. This might be the indirect features of IR syndrome, since it is associated with increased WBC and RBC counts, and increased levels of Hgb and Hct. Significant elevations of Hct and MCV might be due to the variety of morphological changes exhibited by RBCs and compositional changes in plasma associated with T2DM [9].

In contrast to this study, a study conducted on Chinese patients with T2DM reported that a decreased RBC count is associated with microvascular complications [10]. Likewise, a study performed in Tobago (Caribbean) reported that RBC

Table 3: Comparison of the various biochemical parameters and HbA1c level between the diabetes and the control group

Biochemical	Diabetes group		Control group		P value
parameter	Mean	SD	Mean	SD	
Fasting blood sugar (mg/dl)	161.8	6.8	99.3	5.8	<.001
Postprandial blood sugar (mg/dl)	222.7	10.6	113.9	9.5	<.0001
HbA1c (gm%)	6.78	1.13	5.29	1.08	<.0001
Urea (mg/dl)	33.7	2.5	29.3	1.8	0.0241
Creatinine (mg/dl)	0.95	0.06	0.88	0.02	0.615
Urine albumin (microgm/gm	255.8	18.2	205.8	20.6	<.001

Table 4: Pearson's correlation between HbA1c levels and other hemotological parameters

Variables	Diabetes group (rho value)	Control group (rho value)
Total WBC count (103 / µL)	0.224*	0.031
Polymorphs (103 / µL)	0.312*	0.0912
Lymphocytes (103 / µL)	0.382*	0.152
Eosinophils	0.06	0.04
Haemoglobin (gm%)	0.149	0.026
Haematocrit (%)	0.106	0.010
MCV (fl)	0.036	- 0.081
MCH (pg)	0.083	- 0.045
MCHC (g/dl)	0.159	- 0.051
RDW.SD (fl)	-0.120	-0.0913
RDW.CV (fl)	0.091	-0.089
RBC (103 / µL)	0.129	0.0958
MPV (fl)	0.614*	0.007
PCT (fl)	0.127	0.118
PDW (fl)	0.038	0.008
Platelet count (103 / µL)	-0.319*	0.081

p<.05 statistically significant

count, Hgb concentration, and Hct levels in T2DM patients are lower than in the control group [11]. The possible hypothesis for this difference might be that chronic hyperglycemia causes nonenzymatic glycosylation of RBC membrane proteins leading to accelerated aging of RBCs [12]. Similar study on middle-aged and elderly Chinese population in Taiwan also contradicts our finding as it is reported a reduced RBC count in patients with IR. But similar to the results obtained in our study, there was no statistically significant difference in Hgb levels between T2DM patients and control group. Another study observed that diabetics are prone to anemia due to reduced kidney functions and decreased production of erythropoietin hormone, which ultimately leads to decreased RBC count in the body [13]. Among the RBC indices, only RDW values achieved statistically significant difference between T2DM and control groups. This finding is in accordance with the previous findings [14-16]. This is due to the fact that high RDW indicates impairment of erythropoiesis, reflecting chronic inflammation and increased levels of oxidative stress, both of which are significant signs of T2DM that result in the RBC size variation [17].

In the present study, WBC indices increased significantly in the T2DM group compared with the control group. The reason for this variation might be due to the fact that the high WBC count in the T2DM group is in keeping with the increased oxidative stress triggered by the high levels of hyperglycemia. Thus, polymorphonuclear and mononuclear WBCs can be activated by AGEs and cytokines in a state of hyperglycemia [18]. This study also included the comparison of the platelet indices between the control and the diabetic patients. We observed a significantly lower platelet count and a significantly higher platelet distribution width (PDW) among diabetic subjects in comparison with the control group, which is in accordance with several studies that have shown an increased number of large circulating platelets compared with controls [19-23]. The reason might be related to the vascular complications in DM patients. There might be small vascular bleeds due the rupture of athrothrombotic plagues leading to bone marrow stimulation to recruit larger hyperactive platelets [24].

In our study we found a statistically significant positive correlation between HbA1c and the few other hemotological parameters like WBC, ploymorphs, lymphocytes and mean platelet volume and a statistically significant negative correlation was observed with platelet count among the diabetic group This is in harmony with a previous study conducted in Toronto and London, Ontario, Canada [25]. A similar study in Brazil demonstrated an association between the hematological indices and body adiposity [26]. A study on middle-aged and elderly Chinese people with T2DM found that WBC count was positively correlated with WHR and BMI [27]. In contrast to our study, a study in North-East Italy cohort reported that no associations were found between hematological indices and BMI in lean, overweight, or obese subgroups [28].

In the current study we found urine albumin was high among diabetic group in comparison with the control group, which is an early indicator for renal diseases and few other studies done in the past had also suggested that increase levels of albumin in urine among the diabetic patients is the early biomarker for renal impairment [29-31].

Conclusion

Mean total WBC count, polymorphs, lymphocytes, red cell distribution width (RDW) and the platelet distribution width (PDW) were found to be higher among the diabetes group than the control group, whereas the platelet count was found to be significantly low in the diabetes group when compared to the control group. WBC, ploymorphs, lymphocytes and mean platelet volume showed a significant positive correlation with HbA1c among the diabetes group and the platelet count showed a significant negative correlation with HbA1c. The routine hematological profile checking of patients with T2DM may help to prevent complications associated with aberrations in hematological values. The limitation of this study is it does not evaluate a cause–effect relationship between variables and diabetes because of cross-sectional nature of the study design.

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