Section: Internal Medicine

Original Research Article

A STUDY ON THE RELATIONSHIP BETWEEN RBC INDICES AND GLYCEMIC CONTROL AND ITS ASSOCIATION WITH MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES MELLITUS

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Abstract

Background: Diabetes mellitus is a metabolic disorder caused by hyperglycemia, with various types influenced by genetic and environmental factors. Red blood cell indices, which can predict glycemic control and the development of microvascular complications, may be more cost-effective biochemical markers in predicting DM progression. The study investigates the correlation between red blood cell (RBC) indices and glycemic control, focusing on their significance in predicting glycemic control in type 2 diabetes mellitus compared to HbA1c. **Materials and Methods:** The cross-sectional cohort study was conducted on 200 patients admitted in Rajiv Gandhi Government General Hospital & Madras Medical College during the study period from April 2021 to September 2021. Patients with type 2 diabetes mellitus aged 18–65 years without microvascular complications (100 cases) and with microvascular complications (100 cases) were included. The study analysed various demographic data and biochemical parameters. **Result:** There is a significant difference in systemic hypertension, alcohol intake, and urine sugar between groups ($p<0.05$). There was no significant difference in BMI or diabetes duration between groups. Still, patients with microvascular complications had higher mean haemoglobin content and reduced erythrocytes, indicating a correlation between these factors and the development of complications. A slight positive correlation between HbA1c and haemoglobin, a small negative relationship between RBC count, MCV, MCH, MCHC, and HbA1c levels, and a significant positive correlation between RDW-CV and HbA1c levels. **Conclusion:** The study highlights the importance of regular screening for microvascular complications in older individuals, highlighting the link between alcohol intake, high blood pressure, glycemic control, and anaemia and the need for timely treatment.

INTRODUCTION

Diabetes mellitus is a group of common metabolic disorders caused by hyperglycemia. Complex interactions of genetic and environmental factors cause several distinct types of DM. Sex, age, and ethnic background are important factors in determining the risk of developing DM. Type 2 DM is a heterogeneous group of disorders characterised by variable degrees of insulin resistance, impaired insulin secretion, and increased hepatic glucose production.[1,2] The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and the healthcare system.[3,4]

As countries become more industrialised, the prevalence of type 2 DM is rising more rapidly, mainly due to increasing obesity, reduced activity levels, and population ageing. Also, microvascular complications like retinopathy, neuropathy and nephropathy are increasing among patients with type 2 DM. The diagnosis of type 2 DM has been based on blood glucose and HbA1c levels, which also strongly correlate with Diabetic microangiopathy. Thus, HbA1c levels have been used as the major screening and an early diagnostic tool in identifying the complications associated with type 2 diabetes mellitus. Many researches have been carried out to highlight its correlation in predicting glycemic control and long-term complications.[5,6] However, it

is not routinely possible to do HbA1c levels, especially in a primary healthcare setup.

Hyperglycemia leading to persistent elevation of glycosylated haemoglobin is associated with the structural and functional changes in haemoglobin (Hb) molecule, the osmotic disturbance and the cytoplasmic viscosity within each cell.[7] All these changes could significantly affect many red blood cell indices. Since microvascular complications are attributed to increased HbA1c, changes in red cell deformability and other rheological alterations, red cell indices may be used to monitor the disease progression in diabetic patients.[8,9] Hence, the red blood cell indices may prove to be much more cost-effective biochemical markers in predicting glycemic control and the development of microvascular complications in type 2 DM. The aim is to study the relationship between RBC indices and glycemic control and its association and to determine the significance of RBC indices (RDW, MCV, MCH, MCHC) compared to HbA1c in predicting glycemic control in type 2 diabetes mellitus.

MATERIALS AND METHODS

The cross-sectional cohort study was conducted on 200 patients admitted to Rajiv Gandhi Government General Hospital & Madras Medical College during the study period from April 2021 to September 2021.

Inclusion Criteria

Patients with type 2 diabetes mellitus aged 18–65 years without microvascular complications (100 cases) and with microvascular complications (100 cases) were included.

Exclusion Criteria

Patients with known haematological diseases such as hemolytic anaemia, neoplastic diseases, haematological malignancies, polycythemia vera, metastases to the marrow, nutritional anaemia, hypothyroidism, arthritis, congenital heart disease, liver cirrhosis, anaemia of chronic disease, inflammatory bowel disease, pregnant individuals, and drugs such as cephalosporin, dapsone, levodopa, nitrofurantoin, penicillin, and quinidine and patients with acute febrile illnesses like dengue, malaria, leptospirosis, and other acute infections were excluded.

Methods

After obtaining clearance and approval from the institutional ethics committee, patients were included in the study as per the inclusion and exclusion criteria. Anticoagulated blood was collected and analysed in an automated blood cell counter. The presence of risk factors for microvascular complications was determined.

Data analysed included age, sex, diabetes duration, smoking status, alcohol consumption, antihypertensive, antilipidemic, and antidiabetic medication, blood pressure, lipid levels (Triglycerides, LDL, HDL), fasting blood glucose, glycated haemoglobin (HbA1c), RBC count, haemoglobin, RBC distribution width (RDW), Mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC).

Diagnosis of DM was established using American Diabetes Association criteria: HbA1c of greater than or equal to 6.5% or fasting blood glucose greater than or equal to 126 mg/dl over 2 hr postprandial glucose following oral glucose tolerance test (OGTT) greater than or equal to 200mg/d. However, patients were examined for microvascular complications like Diabetic retinopathy based on a fundal examination, Diabetic nephropathy based on the urine protein to creatinine ratio and Diabetic neuropathy based on the neurological symptoms.

Statistical Analysis

The data was collected with the help of clinical proforma and was compiled in Microsoft Excel. Statistical analysis was done with the help of statistical software package SPSS v.17 for Windows. This software calculated frequencies, mean, standard deviation, and p-value with the student ‘t-test. Pearson’s correlation coefficient ‘r’ value was calculated. A p-value of < 0.05 was taken as significant.

RESULTS

Among 200 patients, 34.5% were females, and 65.5% were male; most patients were 41 to 50 years old, and most were in the diabetic retinopathy group [Table 1]. The microvascular complications were highest in the age group of >51 years, which is a significant association of the occurrence of microvascular complications with increasing age ($p<0.0001$). There is no significant difference in gender, smoking history, and family history of diabetes between groups ($p>0.05$). 82.6% of the patients with a history of alcohol intake were in the microvascular complications group. 49% of patients with microvascular complications had the presence of urine sugar compared to 36% in the no-complication group. There is a significant difference in systemic hypertension, alcohol intake, and urine sugar between groups ($p<0.05$) [Table 2].

There is no significant difference in BMI and duration of diabetes between groups ($p>0.05$). In patients with microvascular complications, the mean value was 8.95±1.24, which was higher when compared with patients without microvascular complications. The patients with microvascular complications had an overall mean value of 9.77±1.35 g/dL, indicating that low haemoglobin content is a marker of microvascular complications. The patients in the microvascular group had an overall mean value of 3.51±0.75 million cells/µL, indicating a significant reduction of erythrocytes in correlation with the development of microvascular complications. [Table 3]

The patients in the microvascular complications group had low MCH levels with an overall mean

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value of 25.89 ± 3.57 pg. The overall mean value was high in the patients in the microvascular complications group, around 16.40 ± 1.75 %, compared to the group without microvascular complications. There is a significant difference in HbA1c, Hemoglobin, RBC count, MCH, and RDW-CV between groups, but no significant difference in MCV and MCHC [Table 3].

There is a non-significant, slight positive correlation between HbA1c and Hemoglobin. There is a non-significant, very small negative relationship between RBC count, MCV (fL), MCH (pg) and HbA1c levels. A non-significant, very small positive correlation exists between MCHC (%) and HbA1c levels. A significant positive correlation between RDW-CV (%) and HbA1c levels [Table 4 and Figures 1-3].

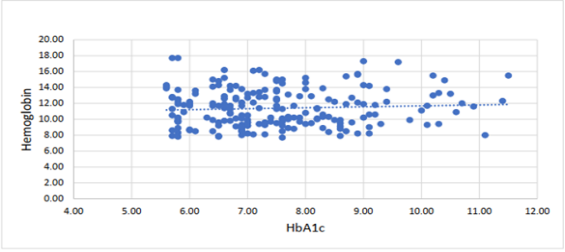

Figure 1: Correlation between Hemoglobin and HbA1c

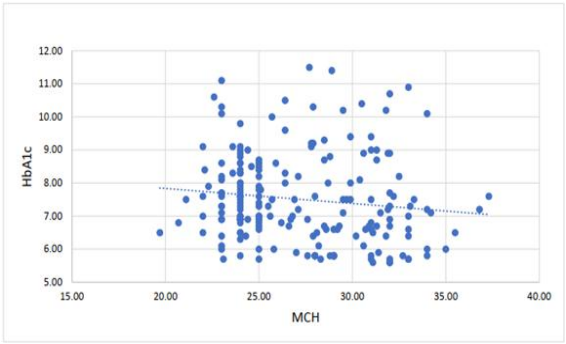

Figure 2: Correlation between MCH and HbA1c

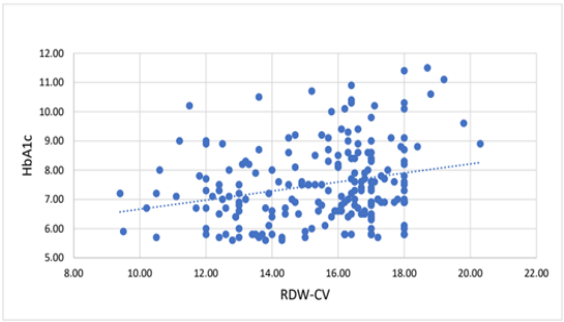

Figure 3: Correlation between RDW-CV and HbA1c

Table 1: Demographic data of the study

		Frequency	Percentage
Gender	Females	69	34.5%
	Males	131	65.5%
Age group	< 40 years	29	14.5%
	41 – 50 years	130	65%
	>51 years	41	20.5%
Microvascular complications (MVC)	Diabetic nephropathy	33	33%
	Diabetic neuropathy	29	29%
	Diabetic retinopathy	38	38%

Table 2: Comparison of parameters between groups

	DM With MVC*	DM Without MVC*	P value
Age group	8	21	<0.0001
	55	75	
	37	4	
Gender	38	31	0.298
	62	69	
Systemic hypertension	33	49	0.021
	67	51	
Alcohol intake	43	64	<0.0001
	19	4	
Smoking history	38	52	0.092
	24	17	
Family history of diabetes	66	74	0.217
	34	26	
Urine sugar	49	64	0.022
	51	36	

Table 3: Comparison of mean biochemical parameters between groups

MEAN ± SD			
	DM With MVC*	DM Without MVC*	P value
BMI	24.32 ± 2.11	24.42 ± 1.89	0.732
Duration of diabetes	9.43 ± 3.32	9.8 ± 3.52	0.445
HbA1c	8.95 ± 1.24	7.56 ± 1.44	<0.0001
Haemoglobin	9.77 ± 1.35	13.01 ± 1.99	<0.0001
RBC count	3.51 ± 0.75	4.59 ± 0.5	<0.0001
MCV	82.99 ± 6.56	82.74 ± 6.88	0.79
MCH	25.89 ± 3.57	28.6 ± 3.39	<0.0001
MCHC	33 ± 2.21	33.05 ± 2.34	0.864
RDW-CV	16.4 ± 1.75	14.46 ± 2.13	<0.0001

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Table 4: Comparison of biochemical parameters with HbA1c using Pearson coefficient.

		HbA1c
Hemoglobin (g/dL)	r value	0.06792
	p-value	0.3392
RBC count	r value	-0.05
	p-value	0.479
MCV	r value	-0.094
	p-value	0.187
MCH	r value	-0.127
	p-value	0.074
MCHC	r value	0.127
	p-value	0.073
RDW-CV	r value	0.251
	p-value	0.000

DISCUSSION

The study involved 131 male and 69 female patients, with a mean age of 46.69 ± 5.78 years. Most patients were 41 to 50 years old, and approximately 92.2% of patients over 51 had microvascular complications. There is a significant statistical association between age and diabetes. Also, increasing age is associated with increasing progression of microvascular complications in type 2 diabetes. Similarly, Cheema et al,[10] discuss the risk factors for microvascular complications in which it was shown that higher age was a significant risk factor. Of 1034 patients, the mean age of diabetic patients with one or more microvascular complications was 55±10 years compared to patients without microvascular complications. Hence, screening diabetic patients for microvascular complications is important, especially in the older age group.

In our study, 200 patients with various conditions found a significant association between systemic hypertension and diabetes mellitus. Of these patients, 59% had coexisting systemic hypertension, with 51 patients in the non-microvascular complications group and 67 in the microvascular complications group. The data showed a p-value of 0.02, indicating a significant association between hypertension and diabetes. A similar comparison was made in the Ramanathan RS,[11] study wherein 500 patients with diabetes mellitus with microvascular complications were compared with hypertension, glycemic control and duration of diabetes in which 90% of diabetic retinopathy patients, 92% of diabetic neuropathy patients and all diabetic nephropathy patients had high blood pressure. This shows that adequate glycemic and blood pressure control are also required to prevent microvascular complications.

Our study found a significant association between alcohol intake and diabetes mellitus, with 19 out of 23 patients with a history of alcohol having microvascular complications. This suggests that abstinence from alcohol is crucial to reducing the risk of developing these complications despite other risk factors like smoking, family history, and diabetes duration. A strong correlation between HbA1c levels and the development of microvascular complications in diabetes patients. Around 54 patients with microvascular complications had HbA1c levels >7%, indicating poor glycemic control. Zoungas et al,[12] study shows the association of HbA1c levels with the development of microvascular complications at a threshold value of > 7%. Hence, HbA1c has a strong association with microvascular complications in diabetes.

In our study, haemoglobin concentration has a strong statistical association in predicting the presence of microvascular. There was a significant decrease in haemoglobin in patients with microvascular complications. Thereby suggesting that anaemia can be a marker of microvascular complications. A similar comparison was made by Ranil et al,[13] where Hemoglobin levels were correlated with diabetic retinopathy. The median levels of haemoglobin were between 11 to 12 g/dL in women and 12 to 13g/dL in men. Men were at 2.09 times more risk of developing anaemia. Al Khoury et al,[14] show an early association of anaemia in diabetic individuals developing nephropathy.

In our study, among the 62 males in the microvascular complications group, 32 patients had haemoglobin less than 13g/dL with HbA1c > 7%. Among the 38 females, 13 patients had less than 12g/dL haemoglobin with HbA1c > 7%. The mean corpuscular haemoglobin concentration in patients without microvascular complications was 33.05%, while in patients with microvascular complications, it was 33%, with a standard deviation of 2.21. There is a non-significant, slight positive correlation between HbA1c and Hemoglobin. There is no significant statistical association of mean corpuscular volume. Still, there is a strong statistical association of mean corpuscular haemoglobin in predicting microvascular complications in type 2 diabetes. Afsar et al,[15] showed similar low mean MCH and MCV results. The mean MCV was 82.3 in HbA1c >7 and 84.3 in HbA1c <7; the mean MCH was 27.1 with HbbA1c >7 and 27.3 in HbA1c <7, comparable to our study.

The study found a strong statistical association between red blood cell count and microvascular complications in type 2 diabetes patients. Patients without microvascular complications had a mean red blood cell count of 4.59 million cells/µL. In comparison, those with microvascular complications had a mean red blood cell count of 3.51 million cells/µL. Wang ZS et al,[16] show similar results

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indicating that RBC is a potential marker of microvascular complications in type 2 diabetes. The study classified the patients into four quartiles in which the lower RBC quartiles were increasingly associated with microvascular complications.

Our study found a strong statistical association between red cell distribution width (RDW) and microvascular complications in type 2 diabetes. The mean RDW-CV value was 14.46% in patients without complications and 16.40% in those with complications. A small positive correlation was found between red cell distribution width and HbA1c levels, indicating that higher RDW values are associated with microvascular complications. Renukha P et al,[17] demonstrated a significant negative correlation between RDW and HbA1c. The study included people with diabetes without microvascular complications with a mean value of RDW of 14.36%, comparable to ours. Hence, RDW-CV can be used as a cost-effective potential marker in predicting glycemic control and identifying the risk of progression of microvascular complications.

CONCLUSION

Our study has shown that older individuals are at a higher risk of developing microvascular complications, making frequent screening necessary. Alcohol intake and high blood pressure are closely linked to microvascular complications, so it is important to abstain from alcohol and maintain strict blood pressure control. Glycemic control is also crucial, and HbA1c is a reliable marker for predicting microvascular complications. Certain haematological indices, such as RBC count, haemoglobin concentration, MCH, and RDW-CV, can also serve as markers for detecting the presence of microvascular complications. RDW-CV has a statistically significant positive correlation with HbA1C, making it a potential marker for assessing glycemic control. A simple blood test that includes these parameters can be an effective and cost-efficient tool for predicting microvascular complications and assessing glycemic control. Our study has also found that diabetes may increase the risk of anaemia, which can worsen cardiovascular complications. Therefore, treating anaemia promptly in diabetic individuals is crucial.

Limitations

The study had limitations, including not being a multicentric trial, having a small sample size of 200 patients, not comparing and analysing individual complications, and not following up with the patients involved. Future studies should consider larger sample sizes.

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