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Red Cell Parameters and their Correlation with Level of Glycemic Control among Patients Undergoing Treatment for Diabetes at a Tertiary Care Centre

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Abstract: ***Introduction****: Diabetes mellitus refers to a group of metabolic disorders that share the phenotype of hyperglycemia. Studies have shown that severity of DM is correlated with the HBA1C level. Red cell parameters are simple and inexpensive parameters used in various workup. Red cell parameters (RDW, MCV, MCHC, MCH) can be considered as a marker of glycemic control in diabetic patients.* ***Aim****: To find out whether there is any correlation between Red cell parameters with their glycemic control among patients undergoing treatment for diabetes at a tertiary care centre.* ***Objectives****: 1) To find out proportion of patients with deranged Red cell parameters among diabetes patients. 2) To assess the distribution of HBA1C among diabetes patients. 3) To determine whether there is any correlation between Red cell parameters and HBA1C in diabetic patients.* ***Methods****: It is a cross - sectional study conducted in Amala institute of medical science for a period of 18 months, that evaluated 250 patients diagnosed with Diabetes Mellitus. These patients had their blood parameters recorded. Data was entered in MS Excel and analyzed using coGuide Statistics software, Version 1.* ***Results****: This cross - sectional study was done in 250 diabetic patients, of which 132 were male and 118 were female. Majority of the patients were in the age group of 56 - 75 years. HEMOGRAM and HBA1C levels were compared and a positive correlation was seen between RDW and HBA1C. P value was statistically significant at p<0.001. RDW level increased with increase in HBAIC level. The study indicated that higher the value of HBAIC, higher is the RDW value.* ***Conclusion****: RDW along with HBA1C may be considered as a marker of glycaemic control in diabetic individuals as there appears to be a positive correlation between HBAIC and RDW. Erythrocyte indice (RDW) is associated with HbA (1c), independently of plasma glucose levels, in the population. The study highlighted that RDW has a significant correlation with HbA1c and is an inexpensive and freely available test so it may be used as a marker of glycemic status.*

Keywords: Red Cell Distribution Width (RDW), HBAIC, RBS

1. Introduction

Diabetes mellitus refers to a group of metabolic disorders that share the phenotype of hyperglycemia. The prevalence of Type 2 DM has been increasing throughout the world. Studies have shown that severity of DM is correlated with the HBA1C level.

HBA1C is defined as a series of glycated variants resulting from attachment of various carbohydrates to N terminal of Hb. It is a non enzymatic glycation process. In other words, Hb is a substance inside RBC that carries oxygen to the cells of the body. When there is increased glucose levels in our body, the glucose sticks to Hb. This is called glycation. So, longer the duration of hyperglycemia, more glucose gets attached to RBCs and hence is the glycation. When once glycated, the RBCs remain glycated throughout its lifespan (120 days). Hyperglycemia has multiple effects on RBCs

a) Glycation of Haemoglobin
b) Reduced deformability
c) Reduced lifespan

Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were first introduced by Wintrobe in 1929 to define the size (MCV) and hemoglobin content (MCH, MCHC) of red blood cells. Termed *red cell indices*, these values are useful in elucidating the etiology of anemias. Red cell indices can be calculated if the values of hemoglobin, hematocrit (packed cell volume), and red blood cell count are known. With the general availability of electronic cell counters, red cell indices are now automatically measured in all blood count determinations.

Variation in the size of red cells (anisocytosis) can be quantified and expressed as red cell distribution width (RDW) or as red cell morphology index[1].

MCV defines the size of the red blood cells and is expressed as femtoliters (10^{-15}; fl) or as cubic microns (μm^3). The normal values for MCV are 87 ± 7 fl.

MCH quantifies the amount of hemoglobin per red blood cell. The normal values for MCH are 29 ± 2 picograms (pg) per cell.

MCHC indicates the amount of hemoglobin per unit volume. In contrast to MCH, MCHC correlates the hemoglobin content with the volume of the cell. It is expressed as g/dl of red blood cells or as a percentage value. The normal values for MCHC are 34 ± 2 g/dl.

RDW represents the coefficient of variation of the red blood cell volume distribution (size) and is expressed as a percentage. The normal value for RDW is 13 ± 1.5%.

Aim
To find out whether there is any correlation between Red cell parameters with their glycemic control among patients undergoing treatment for diabetes at a tertiary care centre.

Objectives of the Study:
a) To find out proportion of patients with deranged Red cell parameters among diabetes patients.
b) To assess the distribution of HBA1C among diabetes patients.
c) To determine whether there is any correlation between Red cell parameters and HBA1C in diabetic patients.

2. Methodology

Study Design
Cross Sectional Study Design

Study Setting
Patients who are diagnosed with diabetes attending the General Medicine Department in Amala Institute of Medical Sciences.

Sampling

Sample Size Calculation
$\mathbf{n = (Z_{1-\beta} + Z_{2-\alpha/2})^2}$
$\mathbf{(r^2/1 - r^2)}$
r = Correlation coefficient 0.193
$Z_{1-\beta}$ = Power (80%)
$Z_{1-\alpha/2}$ = Desired confidence level 95% (1.96)
Mean, n = 203 ≈ 250

Sample Size
n = 250

Study Period
18 months (18 - 2 - 2021 to 18 - 8 - 2022).

Inclusion Criteria
All patients with Diabetes more than the age of 20 yrs.

Exclusion Criteria
a) Anaemia – WHO criteria Hb< 13 in men and < 12 in women
b) Previous history of any Haemoglobinopathies
c) Polycythemia – WHO criteria Hb> 16.5 in men and > 16 in women, PCV > 49 in men and PCV > 48 in women
d) History of any Chronic Renal failure
e) History of any Cardiac failure
f) History of any Connective tissue disorders
g) Recent history of any Malignancy
h) History of any Chronic Liver Disease
i) Patients not willing for the study

Sampling Procedure
The study was started after obtaining approval from Ethical Committee on 18/02/2021 (Ref. No: 11/IEC/21/AIMS - 30). After obtaining informed consent from patients for inclusion in the study, data was collected using structured proforma from patients in the department of General Medicine at Amala Institute of Medical Sciences, Thrissur. Data collection was continued until the sample size was met (Consecutive sampling).

Methods of Data Collection
After obtaining informed consent from the patient, each participant was given complete information regarding the voluntariness, objective and the benefit of the study. Data was collected using a questionnaire at the point when patient was recruited for the study.

The demographic data, type and duration of Diabetes, related complications, medications used, comorbidities along with other parameters like RBS, HBA1C and Haemogram were collected.

Parameters analysed in the study
- Haemogram
- Random blood sugar
- HBA1C

3. Results

A total of 250 subjects were considered into the study.

Table 1: Descriptive analysis of Age in the study population (N=250)

Name	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower CI	Upper CI
Age	56.49±15.31	59.00	17.00	92.00	54.59	58.39

The mean age was 56.49±15.31 in the study population, minimum level was 17.00 and maximum level was 92 in the study population (95% CI 54.59 to 58.39).

Table 2: Descriptive analysis of Age groups in the study population (N=250)

Age groups	Frequency	Percentage
16 - 35	30	12.00%
36 - 55	81	32.40%
56 - 75	115	46.00%
76 - 95	24	9.60%

In the study population, 30 (12.00%) participants were in age group 16 - 35 years, 81 (32.4%) participants were in age group 36 - 55 years, 115 (32.4%) were in age group 56 - 75 and 24 (9.6%) were in age group 76 - 95 years. (Table 2 & Figure 1)

Table 3: Descriptive analysis of Gender in the study population (N=250)

Gender	Frequency	Percentage
Male	132	52.80%
Female	118	47.20%

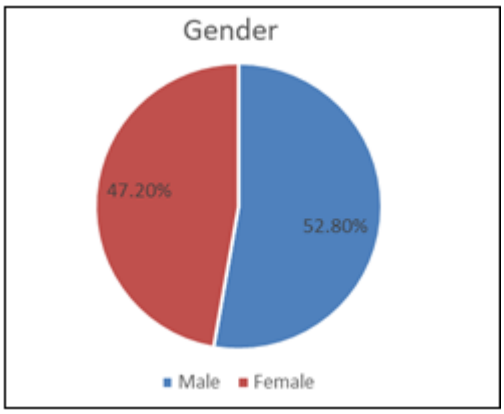

Figure 1: Pie chart of Gender in the study population (N=250)

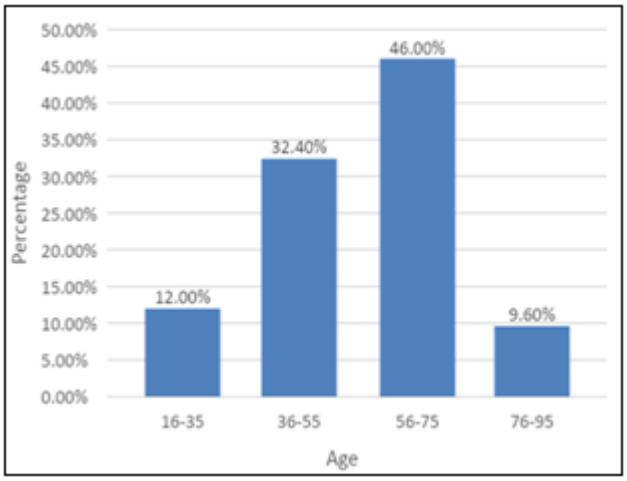

Figure 2: Bar graph of BMI in the study population (N=250)

Table 4: Descriptive analysis of BMI in the study population (N=249)

Name	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower CI	Upper CI
BMI	27.42±4.43	26.70	19.40	37.20	26.87	27.97

Descriptive analysis of BMI in the study population (N=249)

BMI	Frequency	Percentage
18 - 22	23	9.24%
22 - 26	79	31.73%
26 - 30	60	24.10%
30 - 34	72	28.92%
34 - 38	15	6.02%

Table 5: Descriptive analysis of HBA1C in the study population (N=250)

Name	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower CI	Upper CI
HBA1C	8.85±1.86	8.30	6.50	18.20	8.62	9.08

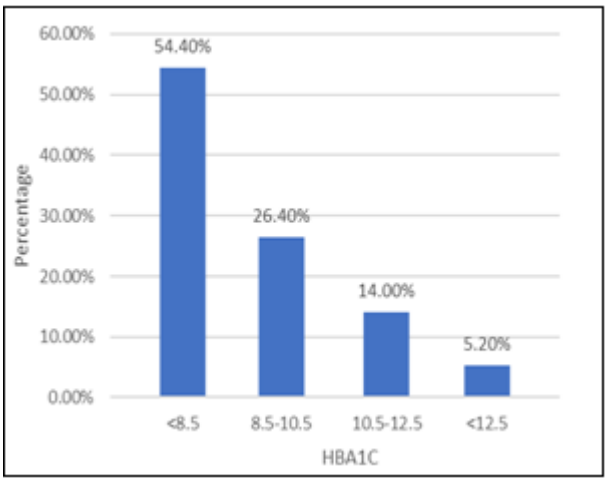

Figure 3: Bar graph of HBA1C in the study population (N=250)

Table 6: Descriptive analysis of Lab Findings in the study population (N=250)

Lab Findings	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower CI	Upper CI
HB	13.51±1.17	13.70	11.00	16.30	13.37	13.66
Platelet	260.61±81.99	246.00	28.00	500.00	250.45	270.78
TC	8.02±2.27	7.90	4.00	20.22	7.74	8.30
MCV	87.80±5.73	87.50	59.90	103.00	87.09	88.51
MCH	29.96±4.90	29.50	18.70	80.80	29.36	30.57
MCHC	34.53±1.35	34.60	30.30	37.00	34.36	34.70
RDW - CV	15.41±2.96	14.15	11.30	24.30	15.04	15.77

Table 7: Descriptive analysis of RBS in the study population (N=250)

Name	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower CI	Upper CI
RBS	181.48±49.76	172.00	109.00	300.00	175.31	187.65

Table 8: Comparison of Gender with HBA1C in the study population (N=250)

Gender	HBA1C				Chi square value	P value
	<8.5 (N=136)	8.5 - 10.5 (N=66)	10.5 - 12.5 (N=35)	>12.5 (N=13)		
Male	67 (49.26%)	42 (63.64%)	16 (45.71%)	7 (53.85%)	4.50	0.2121
Female	69 (50.74%)	24 (36.36%)	19 (54.29%)	6 (46.15%)		

The difference in gender between HBA1C is found to be insignificant with a P - value of 0.2121 with majority of 67 (49.26%) male participants and 69 (50.74%) female participants were reported <8.5 HBA1C. (Table 15 & Figure 7)

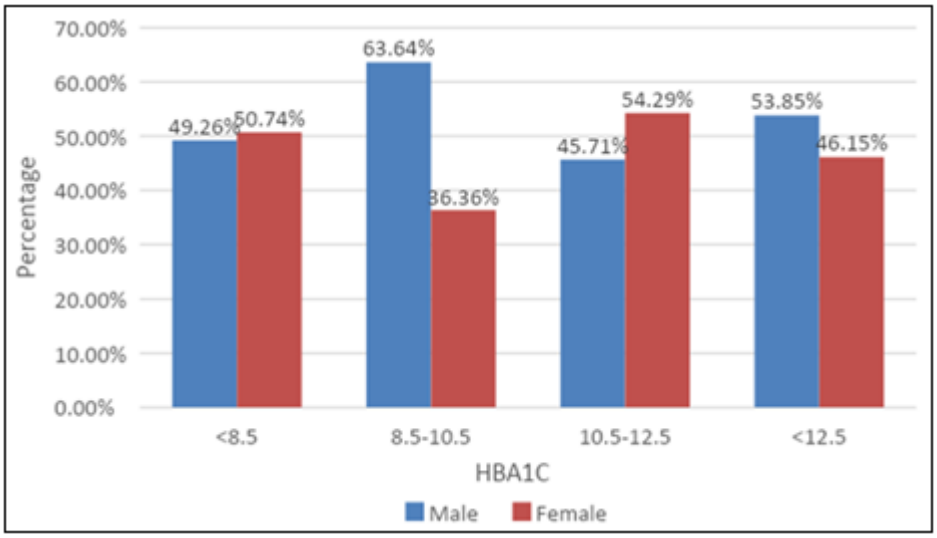

Figure 4: Combined bar graph of comparison of Gender with HBA1C in the study population (N=250)

Table 9: Comparison of Age with HBA1C in the study population (N=250)

Age	HBA1C				Chi square value	P value
	<8.5 (N=136)	8.5 - 10.5 (N=66)	10.5 - 12.5 (N=35)	>12.5 (N=13)		
18 - 22	9 (6.67%)	6 (9.09%)	7 (20.00%)	1 (7.69%)	15.03	0.2396
22 - 26	41 (30.37%)	22 (33.33%)	11 (31.43%)	5 (38.46%)		
26 - 30	35 (25.93%)	12 (18.18%)	10 (28.57%)	3 (23.08%)		
30 - 34	39 (28.89%)	25 (37.88%)	5 (14.29%)	3 (23.08%)		

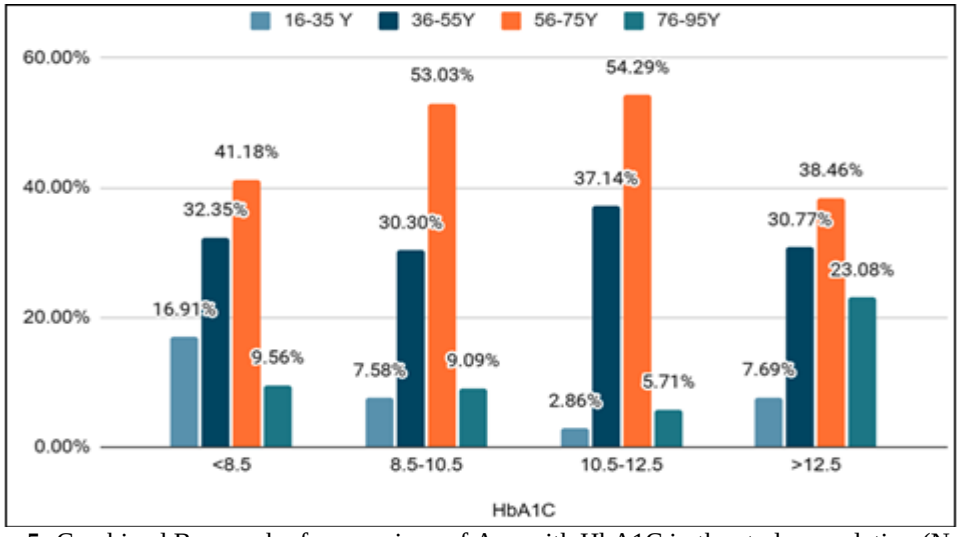

Figure 5: Combined Bar graph of comparison of Age with HbA1C in the study population (N=250)

Table 10: Comparison of BMI with HBA1C in the study population (N=250)

BMI	HBA1C				Chi square value	P value
	<8.5 (N=136)	8.5 - 10.5 (N=66)	10.5 - 12.5 (N=35)	>12.5 (N=13)		
18 - 22	9 (6.67%)	6 (9.09%)	7 (20.00%)	1 (7.69%)	15.03	0.2396
22 - 26	41 (30.37%)	22 (33.33%)	11 (31.43%)	5 (38.46%)		
26 - 30	35 (25.93%)	12 (18.18%)	10 (28.57%)	3 (23.08%)		
30 - 34	39 (28.89%)	25 (37.88%)	5 (14.29%)	3 (23.08%)		
34 - 38	11 (8.15%)	1 (1.52%)	2 (5.71%)	1 (7.69%)		

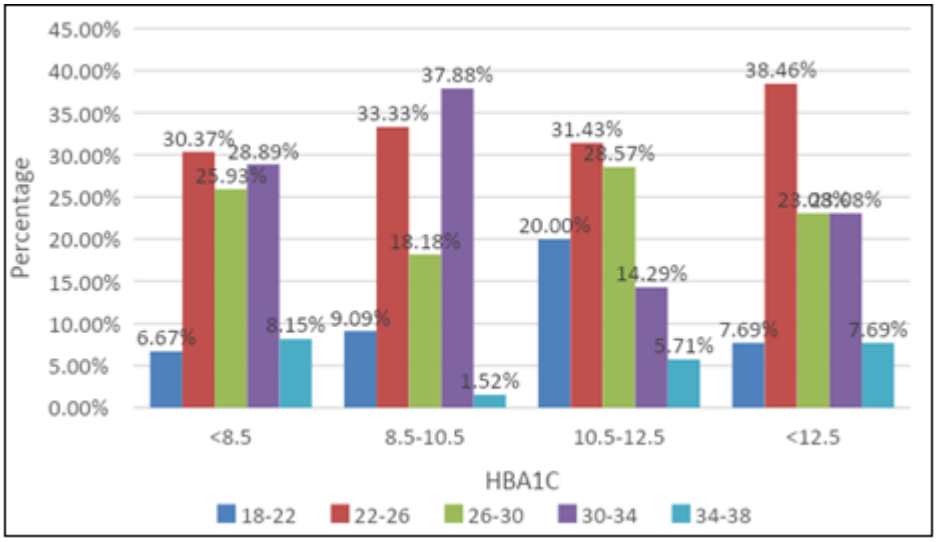

Figure 6: Combined bar graph of comparison of BMI with HBA1C in the study population (N=250)

Table 11: Comparison of Lab Findings with HBA1C in the study population (N=250)

Lab Findings	HBA1C				P Value
	<8.5 (N=136)	8.5 - 10.5 (N=66)	10.5 - 12.5 (N=35)	>12.5 (N=13)	
HB	13.50 ± 1.22	13.63 ± 1.14	13.27 ± 0.96	13.70 ± 1.21	0.4715†
Platelet	244.00 (187.0 to 322.75)	260.00 (216.25 to 321.5)	273.00 (191.5 to 325.0)	226.00 (196.0 to 321.0)	0.5296‡
TC	8.10 (6.7 to 9.3)	7.40 (6.0 to 8.4)	8.10 (6.45 to 9.5)	8.10 (7.3 to 8.9)	0.0813‡
MCV	87.55 (84.2 to 93.45)	87.70 (82.75 to 91.65)	88.40 (83.6 to 92.25)	83.30 (81.4 to 87.4)	0.3430‡
MCH	29.45 (28.3 to 30.8)	29.50 (28.5 to 31.2)	30.00 (27.95 to 31.4)	28.80 (28.4 to 29.8)	0.6182‡
MCHC	34.38 ± 1.42	34.79 ± 1.12	34.63 ± 1.38	34.45 ± 1.57	0.2407†
RDW	13.55 (12.8 to 14.1)	16.80 (13.95 to 17.67)	19.10 (18.2 to 20.75)	22.20 (21.8 to 22.2)	<0.001‡

Note: *† - Independent t test, ‡ - Mann Whitney test*

The difference in Lab Findings (HB, Platelet, TC, MCV, MCH, MCHC) between HBA1C grouping was statistically insignificant (P Value >0.05) and the difference in RDW between HBA1C grouping was statistically significant. (P value <0.001)

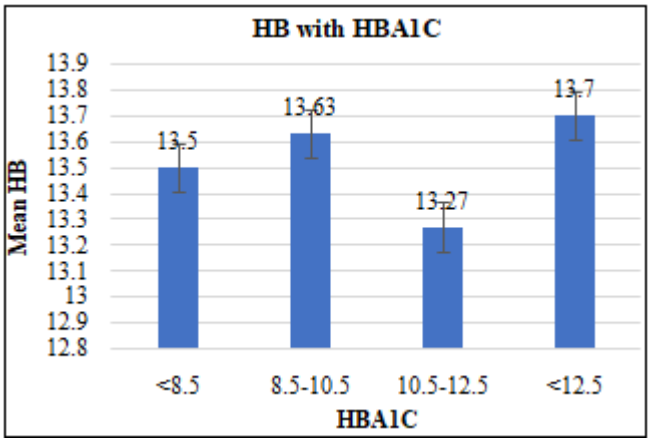

Figure 7: Bar graph of Comparison of HB with HBA1C

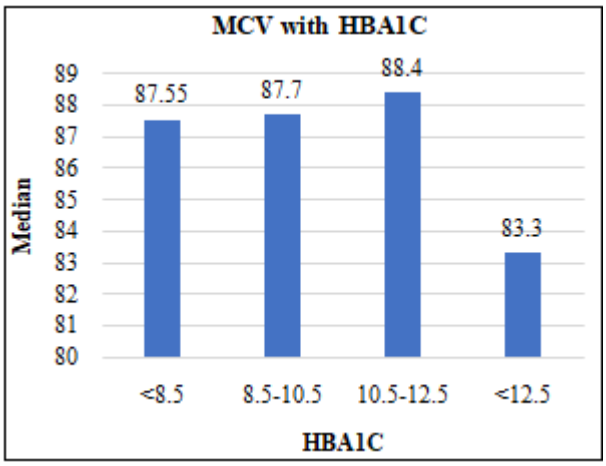

Figure 8: Bar graph of Comparison of MCV with HBA1C

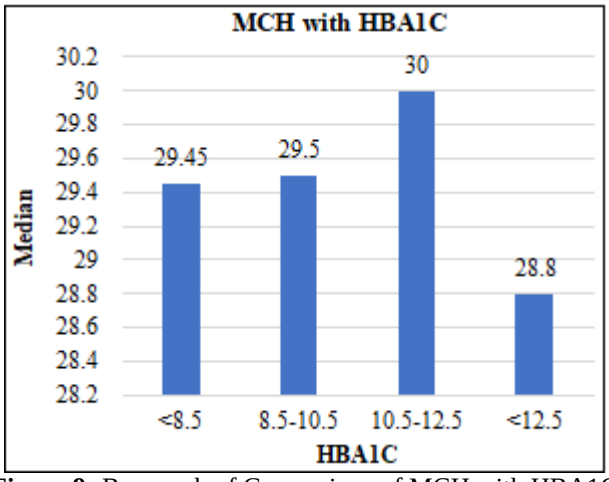

Figure 9: Bar graph of Comparison of MCH with HBA1C

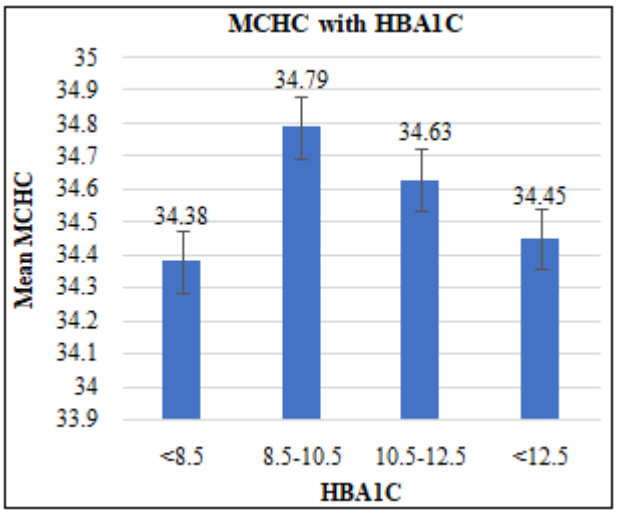

Figure 10: Bar graph of Comparison of MCHC with HBA1C

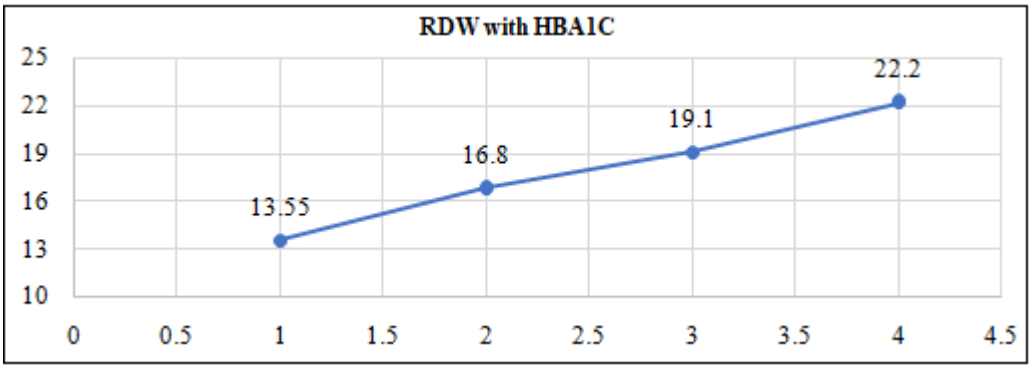

Figure 11: Linear curve of RDW with HBA1C

Table 12: Comparison of RDW with HBA1C among male population (N=250)

RBW	HBA1C				P Value [Kruskal Wallis Test]
	<8.5 (N=67)	8.5 - 10.5 (N=42)	10.5 - 12.5 (N=16)	>12.5 (N=7)	
	13.60 (12.8 to 14.1)	17.00 (14.1 to 18.05)	18.95 (18.3 to 20.1)	22.20 (21.9 to 22.45)	<0.001

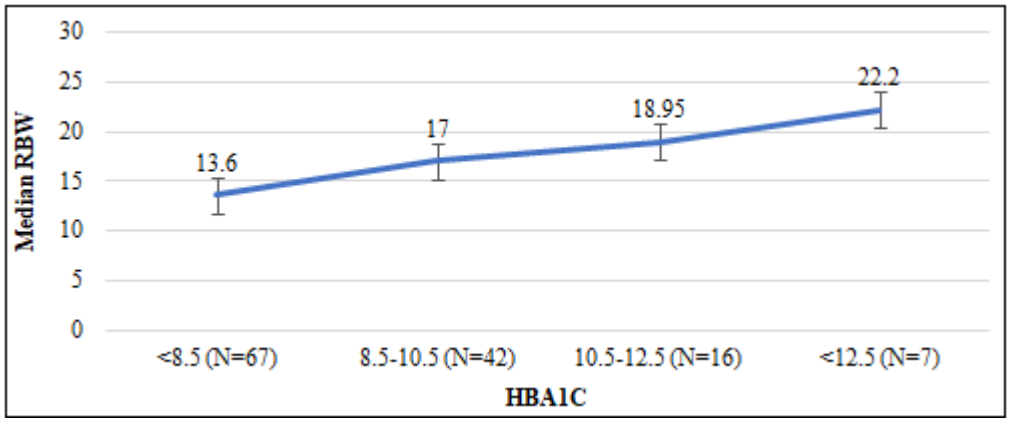

Figure 12: Line chart of comparison of RDW with HBA1C among male population (N=250)

Table 13: Comparison of RDW with HBA1C among female population (N=250)

RBW	HBA1C				P Value [Kruskal Wallis Test]
	<8.5 (N=69)	8.5 - 10.5 (N=24)	10.5 - 12.5 (N=19)	>12.5 (N=6)	
	13.50 (12.7 to 14.1)	14.85 (13.58 to 17.22)	19.20 (18.05 to 21.05)	22.05 (21.83 to 22.2)	<0.001

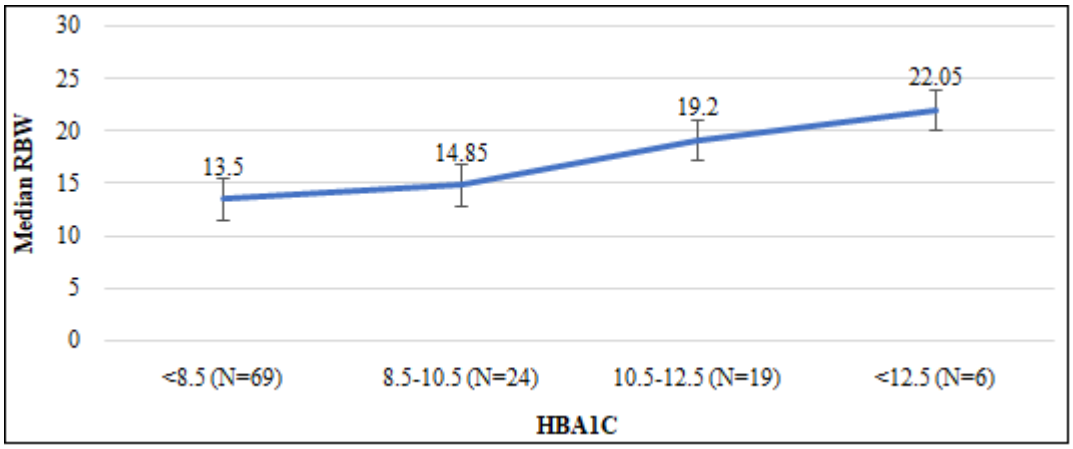

Figure 13: Line chart of comparison of RBW with HBA1C among female population (N=250)

Table 14: Comparison of RBS with HBA1C in the study population (N=250)

RBS	HBA1C				P Value [Kruskal Wallis Test]
	<8.5 (N=136)	8.5 - 10.5 (N=66)	10.5 - 12.5 (N=35)	>12.5 (N=13)	
	172.00 (140.0 to 200.25)	175.00 (144.75 to 210.0)	170.00 (154.5 to 202.0)	156.00 (132.0 to 185.0)	0.7012

4. Discussion

This study was done to see the correlation between Red cell parameters with their glycemic control among patients undergoing treatment for diabetes at a tertiary care centre in central Kerala. This study was conducted among 250 patients visiting a teritiary care centre over a span of 18 months (18 - 2 - 2021 to 18 - 8 - 2022).

Among the 250 patients, 52.80% were males and 47.20% were females. Most of the patients were between 56 - 75 years. HBAIC comparison was done with several variables like HB, Platelet, TC, MCV, MCH, MCHC and RDW. In the study population, 136 (54.4%) participants were reported in <8.5 HBA1C, 66 (26.4%) participants were reported in 8.5 - 10.5 HBA1C, 35 (14.00%) were reported in 10.5 - 12.5 HBA1C and 13 (5.2%) were reported in <12.5 HBA1C.

The difference in Lab Findings (HB, Platelet, TC, MCV, MCH, MCHC) between HBA1C grouping was statistically insignificant (P Value >0.05) and the difference in RDW between HBA1C grouping was statistically significant. (P value <0.001). Subjects whose HBAIC level higher than the normal level had higher RDW values. The Comparison of RDW with HBA1C in the study population<8.5 (N=136) 13.55, 8.5 - 10.5 (N=66) 16.80, 10.5 - 12.5 (N=35) 19.10, <12.5 (N=13) 22.20. Positive correlation between RDW and HBAIC was observed. Pearson value was statistically significant at p<0.001. RDW level increased with increase in HBAIC level.

The present study showed that RDW has a linear correlation with HBAIC, This was in line with a previous study of Malandrino et al. However, the study done by Engstrom et al showed that high RDW was associated with markedly increased risk of developing DM.

There is diversity in the results of previous studies regarding the correlation of these parameters and HbA1c; a study by Hardikar et al. on non - diabetic subjects observed an inverse correlation between HbA1c and MCV ($r = - 0.22$, $p < 0.05$), MCH ($r = - 0.30$, $p < 0.05$), and MCHC ($r = - 0.32$, $p < 0.05$) [19] while another study by Koga et al. found HbA1c was inversely associated with MCV ($r = - 0.368$, $p < 0.0001$) and MCH ($r = - 0.320$, $p < 0.0001$) in premenopausal women but postmenopausal women have shown no such relation between HbA1c and MCV ($r = - 0.019$, $p = 0.771$) and MCH ($r = - 0.104$, $p = 0.107$).

The study also showed that subjects whose HBA1c values higher than the normal values had higher RDW values. This was contrary to the report published by Cakir et al who did not find such a difference. Although it has not been clearly established that an increased level of RDW is an indicator of an underlying biological and metabolic imbalance, it is reasonable suggest that this parameter should be broadened far beyond the differential diagnosis of anaemia.

5. Limitations

1) The study was conducted in a single institution and consists of a small population which may not be representative.
2) Majority of the patients in Asian population have anaemia and some have polycythemia such patients cannot be taken up for the study.
3) Further studies on a larger scale is required.

6. Conclusion

As it is a well - known fact that diabetes mellitus is a life - long metabolic disease, patients with DM keep asking for cost - effective and easily available means of monitoring their glycemic status.

This study was conducted among 250 diabetic patients visiting a tertiary care centre over a span of 18 months (18 - 2 - 2021 to 18 - 8 - 2022). Among the 250 patients, 52.80% were males and 47.20% were females. Most of the patients were between 56 - 75 years.

From the study, RDW along with HBA1C may be considered as a marker of glycaemic control in diabetic individuals as there appears to be a positive correlation between HBAIC and RDW. Erythrocyte indice (RDW) is associated with HbA (1c), independently of plasma glucose levels, in the population. The study highlighted that RDW has a significant correlation with HbA1c and is an inexpensive and freely available test so it may be used as a marker of glycemic status.

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