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ORIGINAL ARTICLE

Association between Red cells distribution width and glycemic control among people with type 2 diabetes.

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ABSTRACT… Objective: To evaluate Red blood cell distribution width (RDW) in people with type 2 diabetes and its relationship with glycemic control. **Study Design:** Retrospective study. **Setting:** Baqai Institute of Diabetology and Endocrinology, Baqai Medical University. Demographic, Clinical and Biochemical Data were retrieved from hospital management system of BIDE. **Period:** September 2018 to April 2019. **Methods:** Ethical approval was obtained from the Institutional Review Board of BIDE. Based on the HbA1c values, patients were divided into two groups, HbA1c < 7.0% and HbA1c ≥ 7.0%. RDW calculated from RBC histogram in Nihon Kohden fully automated analyzer. **Results:** RDW found 13.9±1.88 and 13.57±1.64 (p-value 0.018) in good and poorly controlled glycemic groups respectively. Poor glycemic group had higher levels of white cell count (9.58±4.34) and Triglycerides (170.12±129.13) (p-value <0.05), whereas controlled glycemic group demonstrated higher levels of BMI (29.03±6.01), MCV (84.36±7.81) and HDL (33.75±12.31). RDW was directly correlated with gender (p-value <0.0001) and duration of diabetes (p-value 0.01), and showed significant and inverse correlation with HbA1c. Age, blood pressure, duration of diabetes, serum LDL cholesterol, and the CBC values demonstrated no significant differences between the both groups. **Conclusion:** We found significant correlation between RDW and glycemic control.

Key words: Glycemic Control, Pakistan, RDW, T2DM.

INTRODUCTION

Red blood cell distribution width (RDW) is mainly used to determine differential diagnosis of anemia.[1] New evidence has emerged that increase in RDW values have been significantly associated with multiple disorders including diabetes, cardiovascular disease, infections and some cancers.[2-6] RDW is a biochemical parameter of heterogeneity in the volume (anisocytosis) of circulating erythrocytes and is easily available from a standard complete blood cell count analyzer.[7-13] An increase in RDW value reflects a profound dysregulation of erythrocyte homeostasis that involves both impaired erythropoiesis and / or abnormal survival of red blood cells, attributable to a variety of underlying biologic / metabolic irregularities such as oxidative stress, shortening of telomere length, inflammation, erythrocyte fragmentation, poor nutritional status, dyslipidemia, hypertension, and alteration in erythropoietin function.[14-17]

Hemorheological alterations (erythrocyte deformability) has been demonstrated to be impaired in diabetes.[18] RDW was found to be independently and positively associated to hemoglobin A1c according to the National Health and Nutrition Examination Study (NHANES).[9] Red blood cells function is affected in DM via an interaction with its membrane and intracellular constituents.[19] Hyperglycemia may affect the RDW value, as it has been shown to increase formation of glycosylated hemoglobin, decrease deformability of RBCs and enhance their osmotic fragility and promote adhesiveness leading to the shortened RBCs life span.[9] Increase in RDW value has also been implicated to diabetic complications. In the NHANES III, people with diabetes in the highest quintile of RDW were more prone to develop diabetes complications

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than those in the lowest quintile.[19]

Even though previous work also proposed that RDW may be used as a prognostic biomarker, with higher RDW even within the normal range independently related to multiple cardiovascular outcomes e.g. myocardial infarction, heart failure, peripheral vascular disease, stroke and atrial fibrillation.[5,9] Nonetheless, the association between RDW and glycemic control has not been well established. So, in this study, we planned to evaluate RDW in people with type 2 diabetes and its relationship with glycemic control.

METHODS

This retrospective study was conducted at Baqai Institute of Diabetology and Endocrinology (BIDE), Baqai Medical University (BMU), Karachi – Pakistan. Eight hundred and ninety-six (896) people with type 2 diabetes were included (492 males and 404 females). Ethikcal approval was taken from the Institutional Review Board of BIDE (BIDE/IRB-EXEMPT/AFAWWAD/08/10/19/0238b). Demographic, clinical and biochemical data including gender, age, duration of diabetes, systolic and diastolic blood pressure, body mass index (BMI), hemoglobin (Hb), red blood cell (RBC), white blood cell (WBC), hematocrit (HCT), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), RDW, lipid profile [cholesterol, triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL)] and glycated hemoglobin (HbA1c) were retrieved from hospital management system of BIDE from September 2018 to April 2019.

Based on the HbA1c values, people were categories into two group, Group 1: HbA1c < 7.0 % (n = 154) and Group 2: HbA1c ≥ 7.0% (n = 742). The RDW values were divided into 4 categories; category 1 (< 13.75 %), category 2 (13.75–14.65%), category 3 (14.65–16.32 %) and category 4 (>16.32%). RDW calculated from RBC histogram in Nihon Kohden fully automated analyzer.

Statistical Analysis

Student's T-Test or Mann Whitney U Test or Chi-square Test were used to determine distribution of risk factors in relation to glycemic control and correlation of CBC indices. One-way ANOVA or kruskal wallis test were used to identify the risk factors distribution in relation to RDW.

RESULTS

Baseline characteristics and distribution of risk factors in relation to glycemic control are shown in Table-I. RDW was found 13.9±1.88% and 13.57±1.64% (p=0.018) in good controlled and poorly controlled glycemic groups respectively. Poor glycemic control group had higher levels of white cell count 9.58±4.34 p-value <0.0001 and triglycerides 170.12±129.13 p-value 0.004, whereas good glycemic group demonstrated higher levels of BMI 29.03±6.01 p-value 0.009, MCV 84.36±7.81p-value 0.006 and HDL 33.75±12.31 p-value 0.002. Age, systolic and diastolic blood pressure duration of diabetes, serum creatinine, estimated glomerular filtration rate, serum total cholesterol, LDL and CBC values (including Hb, HCT, RBC count, MCH and MCHC) demonstrated no statically significant differences between two groups.

RDW was directly correlated with the gender (p-value 0.0001) and duration of diabetes (p-value 0.01). Furthermore, it showed significant and inverse correlation with HbA1c.

MPV was directly correlated with the gender (p-value 0.003), whereas an inverse correlation of RDW was found with Hb p-value < 0.0001, RBC count p-value < 0.0001, MCH p-value <0.0001 and MCHC p-value <0.0001.

MCV was directly correlated with the age, Hb, MCH and MCHC (p-value < 0.0001) and inversely correlated with gender, RBC count and HbA1c (p-value < 0.0001) shown in Table-II.

Platelets showed inverse correlation with age (p-value < 0.0001), BMI (p-value 0.042), RBC count (p-value <0.0001), Hb (p-value <0.0001), MCH (p-value <0.0001) and MCHC (p-value 0.002), while it was directly correlated with HbA1c (p-value 0.018). Table-II

WBC count was directly correlated with HbA1c (p-value <0.0001) and inversely correlated with RBC count and Hb (both p-value <0.0001), Table-II.

Table-III shows the significant difference in gender and BMI was noted among all 4 categories.

The number of males were lower in the 4th category (42.6%) compared to the rest of 3 categories (65.6%, 60% and 65.1% respectively). There was a higher mean age (54.79±15.16 yrs) in category 3, duration of diabetes was higher in category 4 (12.39±8.43 yrs) and lower BMI was found in category 1 (26.16±5.13 kg/m^2) as compared to other categories.

Hemoglobin (g/dl), RBC count (million/ul), HCT (%), MCV (fl), MCH (pg) and MCHC (g/dl) were found significantly lower in category 4, whereas platelets (x 1000/ul) were within normal range but significantly higher in category 4. eGFR was significantly lower 58.48±22.63 mL/min/1.73m^2 and creatinine (mg/dl) was higher in category 3 and 4. HbA1c was significantly lower in category 4 as compare to other 3 categories. For the distributions of systolic and diastolic blood pressure, WBC count (x1000/ul), triglycerides (mg/dl) and HDL (mg/dl), no statically significant differences were observed among all four categories.

Parameters	HbA1c (< 7.0%)	HbA1c (≥ 7.0%)	P-value	Overall
Age (year)	56.2±13.56	52.78±15.04	0.021	53.24±14.89
Gender				
Male	63(40.9%)	429(57.8%)	<0.0001	492(54.9%)
Female	91(59.1%)	313(42.2%)		404(45.1%)
Duration of diabetes (year)	10.57±8.75	11.82±8.21	0.13	11.67±8.28
BMI (kg/m^2)	29.03±6.01	27.21±6.28	0.009	27.45±6.27
Systolic blood pressure (mmHg)	122.84±16.25	124.99±18.28	0.119	124.69±18.02
Diastolic blood pressure (mmHg)	78.02±8.46	78.6±8.64	0.524	78.52±8.61
TLC	9.58±4.34	10.81±5.13	<0.0001	10.6±5.02
RBC	4.27±0.84	4.41±0.78	0.126	4.39±0.79
Hb	11.45±2.28	11.62±2.3	0.42	11.59±2.3
HCT	35.72±6.47	36.16±6.22	0.504	36.08±6.26
MCV	84.36±7.81	82.42±7.72	0.006	82.75±7.77
MCH	27.04±3.25	26.45±3.42	0.096	26.56±3.39
MCHC	32.02±2.07	32.03±2.16	0.968	32.03±2.15
Platelets	305.76±120.46	328.11±138.19	0.156	324.27±135.51
RDW	13.9±1.88	13.57±1.64	0.018	13.62±1.69
PCT	0.2±0.07	0.21±0.07	0.334	0.2±0.07
MPV	6.68±1.42	6.51±1.32	0.273	6.54±1.34
PDW	16.75±0.95	16.77±0.89	0.773	16.77±0.9
Serum creatinine (mg/dl)	1.39 ± 0.98	1.36 ± 0.79	0.38	1.37 ± 0.83
Estimated GFR, mL/min	58.35±21.32	61.33±22.06	0.156	60.86±21.96
Cholesterol (mg/dl)	143.01±45.27	148.72±46.44	0.22	147.95±46.29
Triglycerides (mg/dl)	170.12±129.13	198.61±127.78	0.004	194.76±128.24
HDL (mg/dl)	33.75±12.31	30.02±11.54	0.002	30.52±11.71
LDL (mg/dl)	85.89±33.7	92.98±38.7	0.105	91.97±38.09

Table-I. The distribution of risk factors in relation to glycemic control

Data presented as mean ± SD or n (%)
P<0.05 values considered statistically significant.

Parameters	RDW		MCV		MPV		Platelets		TLC	
	R	P-Value	R	P-Value	R	P-Value	R	P-Value	R	P-Value
Age	0.03	0.35	0.154	<0.0001	0.021	0.524	-0.119	<0.0001	0.061	0.058
Gender	0.188	<0.0001	-0.129	<0.0001	0.087	0.003	0.064	0.031	-0.058	0.051
Duration of DM	0.091	0.01	0.018	0.611	-0.028	0.43	-0.033	0.348	0.062	0.081
BMI	0.101	0.005	-0.023	0.524	0.077	0.033	-0.073	0.042	0.002	0.955
Systolic	0.023	0.481	-0.031	0.344	-0.012	0.707	-0.014	0.679	-0.012	0.725
Diastolic	-0.012	0.715	-0.011	0.733	-0.075	0.024	0.034	0.301	0.052	0.117
RBC	-0.12	<0.0001	-0.261	<0.0001	0.174	<0.0001	-0.128	<0.0001	-0.172	<0.0001
Hb	-0.396	<0.0001	0.32	<0.0001	0.177	<0.0001	-0.261	<0.0001	-0.166	<0.0001
MCH	-0.395	<0.0001	0.826	<0.0001	0.022	0.457	-0.211	<0.0001	-0.026	0.375
MCHC	-0.185	<0.0001	0.258	<0.0001	0.014	0.631	-0.092	0.002	0.041	0.165
PCT	0.077	0.009	-0.253	<0.0001	0.057	0.055	0.867	<0.0001	0.397	<0.0001
PDW	-0.153	<0.0001	0.304	<0.0001	-0.125	<0.0001	-0.068	0.021	0.041	0.166
HbA1c	-0.200	<0.0001	-0.085	0.011	0.012	0.712	0.079	0.018	0.145	<0.0001

Table-II. Correlations of complete blood count indices with various variables

Parameters	RDW ≤ 12.4	RDW 12.5 - 12.9	RDW 13.0 - 13.4	RDW ≥ 13.5	P-value	Overall
Age	52.18±15.1	52.1±15.5	54.79±15.16	54.22±13.82	0.157	53.43±14.67
Gender						
Male	177(65.6%)	117(60%)	98(55.1%)	216(42.6%)	<0.0001	608(52.9%)
Female	93(34.4%)	78(40%)	80(44.9%)	291(57.4%)		542(47.1%)
Duration of DM	10.67±8.38	11.47±8.4	11.11±8.09	12.39±8.43	0.089	11.62±8.38
BMI	26.16±5.13	27.07±6.62	28.47±6.41	27.94±6.48	0.009	27.4±6.22
Systolic BP	123.33±19.29	125.06±16.88	127.45±17.62	124.94±17.72	0.21	124.93±18
Diastolic BP	78.35±8.7	78.98±8.63	79.03±8.36	78.51±8.75	0.903	78.63±8.65
TLC	10.18±3.84	11.04±6.01	10.29±4.94	10.44±4.73	0.607	10.46±4.82
RBC	4.52±0.64	4.45±0.72	4.44±0.67	4.32±0.88	0.001	4.41±0.78
Hb	12.54±1.96	12.42±2.23	12.12±1.97	10.69±2.11	<0.0001	11.64±2.24
HCT	38.75±5.51	37.98±5.93	37.37±5.17	33.79±5.89	<0.0001	36.22±6.1
MCV	85.96±5.26	85.58±5.01	84.54±6.23	79.2±9.3	<0.0001	82.7±8.04
MCH	27.82±2.47	27.96±2.62	27.39±2.78	25.08±3.82	<0.0001	26.57±3.46
MCHC	32.35±1.92	32.63±1.98	32.38±2.01	31.58±2.21	<0.0001	32.06±2.12
Platelets	318.5±125.21	322.3±136.69	307.05±107.67	345.46±143.86	0.003	329.26±133.99
L	22.9±9.62	23.66±9.93	24.23±8.62	22.82±9.06	0.187	23.2±9.28
M	3.49±1.32	3.63±1.44	3.55±1.34	3.65±1.58	0.634	3.59±1.46
N	72.13±13.1	71.17±13.3	71.66±10.39	72.35±12.11	0.337	71.99±12.31
PCT	0.2±0.07	0.2±0.07	0.2±0.07	0.21±0.08	0.062	0.21±0.07
MPV	6.48±1.18	6.55±1.44	6.68±1.27	6.41±1.35	0.014	6.49±1.32
PDW	16.85±0.67	17.01±0.84	16.83±0.77	16.62±1.02	<0.0001	16.77±0.89
EGFR	67.26±20.21	64.67±22.01	58.97±21.58	58.48±22.63	<0.0001	61.69±22.11
Cholesterol	152.98±47.09	157.32±49.5	141.98±42.89	142.17±45	0.003	147.54±46.44
Triglyceride	188.93±115.1	224.61±163.93	197.24±120.09	183.45±117.82	0.059	194.32±127.93
HDL	29.51±10.49	29.88±11.81	31.31±11.8	30.64±12.25	0.597	30.32±11.69
LDL	97.55±38.72	97.86±38.74	87.64±36.62	87.17±37.04	0.001	91.68±37.98
Creatinine	1.19±0.4	1.28±0.62	1.43±0.9	1.45±1.04	0.025	1.36±0.84
HbA1c	10.5±2.94	9.78±2.57	9.31±2.44	9.1±2.45	<0.0001	9.58±2.65

Table-III. Distribution of risk factors in relation to red blood cell distribution width

Data presented as mean ± SD or n (%)

P<0.05 value considered statistically significant

DISCUSSION

This study, found statistically significant association of glycemic control with RDW. RDW was also directly correlated with the gender and duration of diabetes. Furthermore, RDW showed significant and inverse correlation with HbA1c, RBC count, Hb, MCH and MCHC. Moreover, eGFR was significantly lower in relation to increase in RDW. Poor glycemic control group had higher levels of white cell count and triglycerides, whereas controlled glycemic group demonstrated higher levels of BMI, MCV and HDL. Similar to our study higher RDW was found in diabetic patients more than healthy controls in Nada AM study.[12] Association of diabetes with the changes in RDW were found in Xiong XF et al study.[7] Arif MA et al study results showed that increased levels of HbA1c were associated with a rise in RDW.[20] In Blaslov K, study RDW correlated positively with HbA1c.[21] In contrast to our finding, Kizilgul M.et al found RDW levels similar between diabetic and non-diabetic groups.[22]

Comparable to our study finding, there was a strong and significant correlation noted between BMI and RDW in Nada AM, study.[12] Nam JS, et al., study results showed that elevated BMI was associated with RDW in people with diabetes.[23] Lower BMI were found in category 1 as compared to other categories in our study. However, in Xiong XF et al., study changes of RDW value were not statically significant associated with the BMI levels in people with diabetes.[7]

Our study shows RDW was associated with the duration of diabetes. Similarly, Xiong XF et al., study showed positive association of RDW with the longer duration of diabetes.[7] In the same manner Zhang J et al., study showing that RDW values was associated with duration of diabetes.[24] In contrast to our finding there was no correlation observed between RDW and duration of diabetes in Nada AM, study.[12]

RDW was significantly correlated with HbA1c in our study. Similarly, the RDW was associated with HbA1c in Gang L et al., study.[25] In Bhutto AR et al,. study a significant correlation of HbA1c with RDW was found.[27] Significant and positive relationship between HbA1c and RDW was also observed in Engström G et al,. study.[26] However, in Akdoğan M et al., study shows HbA1c was weakly correlated with RDW.[27]

Furthermore, RDW showed significant and inverse correlation with MCH, and MCHC in our study. In contradiction to our study results, Bhutto AR et al. study showed no significant correlation with MCV, MCH, MCHC and HbA1c.[28]

Nada AM study revealed a positive correlation between duration of diabetes and WBC count.[12] However, no significant correlation between WBC count and duration of diabetes was observed in our study. HbA1c was significantly lower in group 4, same observation was found in Xiong XF et al., study.[7] Yin Y et al., study results showed descending tendency of HbA1c similar to our results but no statistically significant difference was found with the increase of RDW.[9] In contrast to this finding, Zhang J et al., study showed that RDW values was not associated with HbA1c status.[24]

Hemoglobin (g/dl) was significantly lower in group 4 of our study. Similar to this observation, Hb was negatively associated with the Q4 group of RDW in Xiong XF et al., study.[7] In the same manner, Zhang J et al., study shows higher RDW values were significantly associated with decreased hemoglobin.[24]

In this study eGFR was significantly lower and serum creatinine was higher in relation to increase in RDW level. Similarly, in Zhang J et al., study higher RDW values were statically significant associated with decreasing eGFR.[24] Single centered with retrospectively collected data are the major limitations of the present study.

CONCLUSION

Found significant correlation between RDW a parameter of routine complete blood count in clinical practice and glycemic control. Furthermore, RDW may be used to identify people with type 2 diabetes having risk of poor glycemic control.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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