HEMATOLOGICAL PARAMETERS IN ADULT TYPE 2 DIABETES MELLITUS PATIENTS VISITING A TERTIARY CARE CENTER OF WESTERN NEPAL

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ABSTRACT

INTRODUCTION

Various mechanisms suggest changes in hematological profiles of Type 2 Diabetes Mellitus (T2DM) patients. Similarly, alterations in hematological profiles have been linked with pathogenic mechanisms in Diabetes. We aim to determine hematological profiles of adult T2DM patients.

MATERIAL AND METHODS

This hospital-based cross-sectional study was conducted from March 2020 to December 2020 at the department of Pathology and Biochemistry of Universal College of Medical Sciences. After ethical clearance (UCMS/IRC/016/20), 90 adult patients diagnosed with T2DM were considered. Both verbal and written consent was taken. Type 1 diabetics, patients with history of hemoglobinopathies, recent blood transfusion, chronic illnesses and acute infections, and whose peripheral smear showed dimorphic pictures were excluded.

The glycemic and hematological parameters were estimated. The data were analyzed using SPSS (version 20). Categorical data were expressed in frequency and percentage. Numerical data were expressed as median (interquartile range). Mann-Whitney U test was used to compare the hematological parameters between patients with good and poor glycemic control.

RESULTS

Among the total 90 participants, 34.4% had anemia. Mean Corpuscular Hemoglobin Concentration (MCHC) correlated positively with both Random Blood Sugar (RBS) and HbA1C. RBC count and Packed Cell Volume (PCV) were significantly higher in patients with good glycemic control, whereas MCHC was significantly lower in that group.

CONCLUSION

High prevalence of anemia was noted in T2DM patients. RBC and PCV levels were significantly lower in patients with poor glycemic control and MCHC levels were significantly lower in patients with good glycemic control.

KEYWORDS

Diabetes, Hematological Parameters, Type 2 Diabetes Mellitus

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM), characterized by resistance to insulin action and suboptimal insulin secretory response, is a common endocrine disorder affectng approximaely 462 millions worldwide.[1] Osmotic disturbances, cytoplasmic visocosity asociated with persistant elevation of glycated hemoglobin (HbA1C), free redical generation, and formaton of advanced glycation end-products (AGEs) in DM is associated with structural and functional changes in hemoglobin molecule. These changes greatly influence the hematological parameters including red blood cell count, Hematocrit(Hct), Mean Corpuscular Volume(MCV), Mean Corpuscular Hemoglobin (MCH), and Mean Corpuscular Hemoglobin Concentration (MCHC). Hemoglobin concentration has been closely linked to diabetic patients with diabetic profiles. Furthermore, DM is also asscoaitated with platelet and WBC dysfunctions. Inflammatory conditions have been hypothesized to play an important role in DM pathogenesis as well.[2,3]

While there have been renewed interests in scientific community regarding associations between DM and hematological alterations, no current guidelines recommend the periodic monitoring of hematological parameters in DM patients.[4] Further insights demonstrating their association is of immense clinical benefit including the understanding and prevention of diabetic complications. However, data regarding these are scarce, especially from Nepal. This study was aimed to determine hematological indices among type-2 DM patients.

MATERIAL AND METHODS

This hospital-based cross-sectional study was conducted at the department of pathology and biochemistry of Universal College of Medical Sciences and Teaching Hospital (UCMS TH) from March 2020 to December 2020. Ethical clearance for the study was taken from institutional review committee (IRC) of UCMS TH (UCMS/IRC/016/20). Physician diagnosed type 2 DM adults (both new and old) of more than 35 years of age were included for the study. Both written and verbal consent was taken. Type 1 DM patients, patients with history of hemoglobinopathies and anemia of any causes, patients with history of recent blood transfusion, patients with chronic illnesses and acute infections, and patients whose peripheral blood smear showed dimorphic pictures were excluded. Minimum sample size was calculated by using Cochran's formula, $n = z^2PQ/e^2$, where $z = 1.96$, $p = 6.1\%$ (prevalence of type 2 DM in South Western Nepal);[5] $Q = 100- P = 93.9\%$; e = allowable error = 5%. Finally, a total of 90 patiets were included for the study. The convenience sampling technique was used for the selection of the participants.

Each participant required to fill a detailed study proforma that included socio-demographic details; glycemic parameters; and hematological profiles. The glycemic parameters included random blood sugar (RBS), HbA1C, and estimated average glucose (eAG). The hematological profile included Hemoglobin (Hb) levels, Red blood cell (RBC) count, Packed cell volume (PCV), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular Hemoglobin concentration (MCHC), and Red cell distribution width (RDW).

Five ml of blood samples were collected under aseptic conditions and distributed to plain vial for glucose estimation (2 ml) and EDTA vial for hematological parameters and HbA1C estimation (3 ml). Plain vial was centrifuged and serum samples were used for glucose estimation. Blood glucose was measured by enzymatic method using automated analyzer (Humalyzer 600). HbA1C was measured using quantitative nephelometric assay (GPP-100 HbA1C kit).

The hematological parameters were analyzed using electronic cell coulter counter (Beckman Coulter DxH 520). The eAG values were obtained using the following formula: eAG = HbA_{1C} X 28.7 - 46.7. The following reference ranges were used as per manufacturer's instructions: RBS = 70-100 mg/dl, HbA1C < 5.4%, eAG = 70 -126 mg/dl, RBC count = 3.8-4.8 millions/mm3 (females) & 4.5 – 5.5 millions/mm^3 (male), Hb ≥ 12 g/dl (female) & ≥ 13 g/dl (male), MCV = 80 - 100 fl MCH = 27 – 32 pg/cell, MCHC = 31.5 – 34.5 grams/-deciliter (g/dl), RDW = 12-14%. Furthermore, patients were further categorized as having good glycemic control (HbA1C <7%) and poor/inadequate glycemic control (HbA1C ≥ 7%).[6] Finally, a peripheral blood smear (PBS) was done for morphological study of RBCs.

The collected data were entered into Microsoft Excel (2016) and analyzed using statistical package for social sciences (SPSS version 20). Numerical data were expressed in their median and interquartile ranges as they were deviated significantly from normality. Both frequency and percentage were used to express categorical data using tabulated form. Mann-Whitney U test was employed to compare the hematological parameters between good glycemic control and poor glycemic control groups. A *p*-value of <0.05 was considered statistically significant.

RESULTS

Among total 90 participants, 46 (51.1%) were females. The median age of the participants was 50 years (IQR: 43.5 years -62 years). The median RBS, HbA1C%, and eAG were 230 mg/dl (IQR: 155 mg/dl – 363.3 mg/dl), 7.31% (IQR: 6.7%-9.6%), and 163.2 mg/dl (IQR: 145.5 mg/dl- 229 mg/dl) respectively. Out of 90 patients, 41 had poor glycemic control (HbA1C < 7%).

The average values and prevalence of hematological parameter categories are presented in table 1 and 2 respectively. Anemia was found in 34.4% of the participants, of which 3.3% had severe anemia. Table 3 shows the prevalence of RBC morphology as estimated by peripheral blood smear. Majority of the participants had normocytic normochromic blood picture (83; 92.22%).

Table 4 presents the correlation of RBS and HbA1C levels with hematological parameters. MCHC lelvels correlated significantly with both RBS ($p = 0.002$; $\rho = 0.332$) and HbA1C ($p = 0.002$; $\rho = 0.322$) levels. Comparision of hematological parameters between poor and good glycemic control showed significant differences with RBC count, PCV, and MCHC (Table 5). PCV and RBC counts were significantly higher in patients with good glycemic control, whereas MCHC was significantly higher in patients with poor glycemic control ($P < 0.001$), albeit within reference limits in both groups. Although RBC count was higher in patients with poor glycemic control, the average values in both groups were within the reference range.

Table 1. Median and IQR values of hematological parameters

Hematological Parameters	Median Values	25th Percentile	75th Percentile
RBC count (millions/mm3)	4.8	4.1	5.3
Hb (g/dl)	13.3	11.5	14.6
PCV (%)	39.8	35.8	45.4
MCV (fl)	85.2	79.9	87.9
MCH (pg)	27.8	26.3	29.9
MCHC (g/dl)	32.6	31.7	35
RDW (%)	14.8	14.3	15.8

Table 2. Prevalence of hematological parameters

Hematological Parameters	Category	Frequency (Percentage)
RBC Count	Normal	48 (53.3%)
	Decreased	17 (18.9%)
	Increased	25 (27.8%)
Hemoglobin	Normal	59 (65.6%)
	Mild anemia	13 (14.4%)
	Moderate anemia	15 (16.7%)
	Severe anemia	3 (3.3%)
PCV	Normal	45 (50%)
	Decreased	33 (35.7%)
	Increased	12 (13.3%)
MCV	Normal	59 (65.6%)
	Decreased	29 (32.2%)
	Increased	2 (2.2%)
MCH	Normal	52(57.8%)
	Increased	30 (33.3%)
	Decreased	8 (8.9%)
MCHC	Normal	46 (51.1%)
	Decreased	17(18.9%)
	Increased	27 (30%)
RDW	Normal	77 (85.6%)
	Low	0 (0%)
	High	13 (14.4%)

Table 3. Distribution of study cases according to morphology of RBCs in PBS (N=90)

RBC Morphology	Frequency (n)	Percentage (%)
Normocytic normochromic cells	83	92.22%
Normocytic hypochromic with mild microcytes	6	6.67%
Microcytic hypochromic cells	1	1.11
Total	**90**	**100**

Table 4. Correlation of hematological parameters with RBS and HbA1C

Hematological Parameters	Correlation	HbA1c	RBS
Hb	ρ	-0.91	-0.084
	P value	0.411	0.450
PCV	ρ	-0.168	-0.150
	P value	0.128	0.177
MCV	ρ	-0.170	-0.122
	P value	0.125	0.271
MCH	ρ	0.062	0.118
	P value	0.577	0.290
MCHC	ρ	0.332	0.322
	P value	0.002	0.003
RDW	ρ	0.024	-0.068
	P value	0.826	0.540
RBC	ρ	-0.104	-0.107
	P value	0.351	0.338

P-values obtained by Spearmann correlation analysis. ρ (rho)=Spearman coefficient. P statistically significant at the level <0.05.

Table 5. Comparison of hematological paramters based on glycemic control

	Comparison group Good glycemic (n=41)	Poor glycemic control (n=49)	*P*-values[a]
RBC count (millions/mm3)	4.8 (4.5-5.5)	4.7 (4 – 5.1)	0.039
Hb (g.dl)	13.5 (11.5 – 15.1)	13.1(11.5 – 14.3)	0.371
PCV (%)	41.4 (37.3 – 48.2)	39.1 (35.1 – 42.8)	0.048
MCV (fl)	85.2 (80.6 – 88.4)	85.2 (79.6 – 87.3)	0.865
MCH (pg/cell)	27.4 (26.2 – 28.5)	27.9 (26.3 – 31.1)	0.051
MCHC (g/dl)	32 (31.3 -32.8)	33.6 (32.1 – 35.6)	<0.001
RDW (%)	14.8 (14.3 - 16)	14.9 (14.2 – 15.8)	0.958

Data expressed in their median values with their inter-quartile ranges in parenthesis. [a]P values obtained from Mann-Whitney test. P <0.05 considered statistially significant.

DISCUSSION

In our study, anemia was found among 34.4% of the diabetic patients. MCHC was significantly and positively correlated with both RBS and HbA1C levels. MCHC levels were significantly higher in patients with poor glycemic control as compared to the patients with good glycemic control. RBC count and PCV were significantly higher in patients with good glycemic control. Rest of the hematological parameters were not significantly different between the two groups. The average values of all hematological parameters were within the reference range.

Asmamaw M et al[7] reported significantly reduced RBC and Hb count in patients with good glycemic control. RBC count also correlated negatively with HbA1C levels, which is similar to our finding but it was not statistically significant in our case. We also found significantly reduced Hb levels in such patients. MCV, RDW, and MCH levels positively correlated with HbA1C levels with MCV and MCH levels being significantly higher in patients with poor glycemic controls.[7] Jamal MS et al reported increased MCHC in patients with poor glycemic control.[8] In a comparative study by Rashed ER et al, MCV, MCH, and MCHC correlated negatively with HbA1C levels.[9] Other comparative studies showed varied results including MCHC levels in, increased RDW, and decreased MCH in diabetic patients as compared to healthy controls.[10-13]

These results, while diverse, suggest hematological parameters, especially RBC count, Hb levels, MCV, MCH, and MCHC to be altered in diabetic individuals, especially when the glycemic control is poor. The cause and effect relations were however not explored, although many articles suggest both. That is, DM can lead to alteration in hematological parameters and altered hematological parameters might also play a role in pathogenesis and complications of DM. Various alterations in diabetic patients like AGE formation, free radical generations, altered osmotic environment and cytoplasmic viscosity, etc. are suggested to be important factors in altering the hematological indices. Simialrly, altered WBC functions, increased inflammatory milieu could play a crucial role in diabetic pathology.[2,3] However, these associations are speculative at best in the current scenario. Further large-scale studies, including prospective and community-based studies, molecular studies are worth pursuing owing to the dual relation between DM and hematological abnormalities suggested by the studies so far.

CONCLUSION

There was high prevalence of anemia in T2DM patients, with RBC counts and PCV being significantly lower on patients with poor glycemic control. Higher MCHC levels was associated with poor glycemic control.

LIMITATIONS OF STUDY

There are few limitations to our study. Firstly, we did not measure all the hematological parameters. Furthermore, newer parameters that are worth pursuing like neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR) were also not evaluated.[14,15] However, from our study it is clear that certain hematological abnormalities are seen in diabetic patients, especially those have poor glycemic control, and hence warrants further research.

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CONFLICT OF INTEREST

None

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