



ORIGINAL ARTICLE

The pattern of hematological parameters in type 2 diabetes.

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ABSTRACT... Objective: To study the pattern of hematological parameters in Type 2 diabetic patients. **Study Design:** Observational Cross Sectional. **Setting:** Creek General Hospital, Karachi. **Period:** June to December 2021. **Material & Methods:** Two hundred and five diabetic patients were selected by convenient sampling technique. Inclusion Criteria was individuals more than 30 years old, diagnosed with Type 2 DM greater than 3 months. Exclusion Criteria was patients with other chronic diseases including renal, cardiac, respiratory, hepatic or autoimmune disease, with Type 1 DM or less than 30 years old or diagnosed less than 3 months ago. Complete blood count parameters were recorded and analyzed. **Results:** Mean hemoglobin value was 11.5gm/dl. Hemoglobin was decreased in 121(59%). Out of 65 males the hemoglobin was decreased in 38(58.5%) and in 140 females decreased in 83(59.3%). ($p=0.339$). The TLC was increased in 50(24.4%), normal in 148(72.2%) and decreased in 7(3.4%). Among 65 males 11(16.9%), had increased TLC and in females in 39(27.9%). ($p=.213$). The platelet count is increased in 15(7.4%), normal in 173(84.8%) and decreased in 16(7.8%). In males the platelet count was increased in 2(3%), and in females in 13(9.4) ($p=.180$). Decreased hemoglobin and increased white cell count was highest in middle aged group. Microcytic anemia was common. There was a significant decrease in hemoglobin, an increase in white blood cell and platelet count in those on oral hypoglycemic in contrast to those on insulin or mixed therapy. **Conclusion:** Adult diabetics have a higher probability of having decreased hemoglobin and increased leucocyte count.

Key words: Diabetes, Hemoglobin, Platelets.

INTRODUCTION

Diabetes Mellitus is still a continuing challenge for clinicians and the global community despite its worldwide awareness. It is a disorder that has far reaching consequences for the quality of life of the patient. Lack of proper glycemic control and associated metabolic abnormalities can lead to complications that may vary from renal, neurological, and other microvascular and macrovascular complications.¹ The current prevalence of type 2 diabetes mellitus in Pakistan is 11.77%. In males the prevalence is 11.20% and in females 9.19%.² World Health Organization had predicted a rise in the prevalence of diabetes mellitus to 592 million people worldwide by the year 2035.³

Research has shown that diabetes affects hematological parameters such as red blood cells

(RBCs), white blood cells (WBCs) and platelets (PLT), etc.⁴ Microvascular and macrovascular diabetic complications have been associated with increased platelet activity and changes in platelet morphology.^{5,6} Multiple microvascular syndromes have been proven to be associated with Type 2 diabetes due to the markedly increased blood viscosity. Former studies demonstrated that poor glycemic control leads to hematological and biochemical changes increasing the generation of oxygen-derived free radicals causing vascular inflammation.⁷

The lack of awareness, education and a proper approach to the healthcare system in the community in Pakistan leads to a late diagnosis of diabetes and hence development of complications at an earlier stage. This leads to an increase in morbidity and mortality being a

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financial and economic liability. Multiple studies have shown conflicting results regarding the relationship between glycemic control in Type 2 Diabetes Mellitus patients and their hematological parameters. The establishment of a connection between hyperglycemia and changes in hematological parameters can prove to be a sign of the need for greater glycemic control that can further help prevent complications associated with diabetes mellitus. This study aims to analyze the changes in hematological parameters in diabetes mellitus within a lower socioeconomic community.

Rationale; To establish a correlation, if any, between the hematological parameters in type 2 diabetics and their significance. Expected changes in hematological markers are a significant aspect of managing this systemic disease for a clinician.

MATERIAL & METHODS

A cross sectional study was conducted on 200 diabetic patients presenting at Creek General Hospital, Karachi between June to December 2021, selected by random convenient sampling technique. Ethical approval was taken by IRB committee (ref # UMDC/Ethics/2021/22/12/299). Inclusion Criteria is Individuals more than 30 years old and diagnosed with Type 2 DM greater than 3 months. Exclusion Criteria is Patients with other chronic diagnosed diseases including renal, cardiac, respiratory, hepatic, and autoimmune disease, with Type 1 DM or less than 30 years old and patients diagnosed with Type 2 DM less than 3 months ago.

The glycemic Control Criteria was that if the HbA1c is less than 7.5% it is a good glycemic control while HbA1c > 7.5% indicated poor glycemic control (uncontrolled T2DM). If HbA1c was not available, controlled T2DM was RBS < 180mg/dl or FBS 70-120mg/dl in last two weeks and vice versa for poor control. The questionnaire's first part includes demographical data, duration of diabetes, medications (only those on Metformin, Sulphonylurea or conventional insulin were included), presence of other comorbid (like hypertension, coronary artery disease, cerebrovascular disease, chronic

liver disease, and chronic kidney disease), smoking status and glycemic control status. The second part was a record of the hematological or Complete blood counts (CBC) parameters; RBC parameters included Hb (hemoglobin), MCV (mean corpuscular volume), MCH (mean corpuscular hemoglobin), Hct (hematocrit) and RBC (red blood cell) Count. WBC parameters included TLC (total leukocyte count), Neutrophil, Lymphocyte, Eosinophil, Basophil and Monocyte differential. Platelet count was noted. Tests that assessed the functionality of these platelets was beyond the scope of this study.

Laboratory Sample Collection and Evaluations: Four milligram of blood samples for CBC were collected in specialized tubes containing ethylene di-amino tetra acetic acid (EDTA) and calculated by an automatic counting machine at the Laboratory and Diagnostics Centre of Creek General Hospital. The data was analyzed using Statistical Package for Social Sciences IBM version 22. The normal reference ranges considered for this research are as mentioned below:⁸

1. Range of hemoglobin: Males: 13.1-17 g/dl, Females: 12.1-15 g/dl
2. Anemia Reference Range: Males: Hb <13g/dl, Females: Hb <12g/dl
3. MCV range: 80-95 fL
4. MCH range: 27-31 pg
5. Hematocrit: Adult males: 42%-54%, Adult women: 38%-46%
6. RBC count: 4.52-5.90 x10¹²/L in adult male, 4.10-5.10 x10¹²/L in adult female
7. Total leukocytes: 4.00-11.0 x 10⁹/L
8. WBC differential ranges:
 - Neutrophils - 2500-8000 per mm³ (55-70%)
 - Lymphocytes - 1000-4000 per mm³ (20-40%)
 - Monocytes - 100-700 per mm³ (2-8%)
 - Eosinophil - 50-500 per mm³ (1-4%)
 - Basophils - 25-100 per mm³ (0.5-1%)
9. Platelet count: 150,000 - 400,000 per mm³

RESULTS

Among the 205 patients 65 (31.7%) were male while 140 (68.3%) were female. According to the 3 age groups, 18 (8.8%) patients were between 18 and 39 years, 124 (60.5%) being between 40

and 59 years old and 63 (30.7%) above 60 years.

Means

Mean hemoglobin value was 11.5gm/dl (\pm 2.12, Range 12.2)

Mean MCV value was 79.9 fl (\pm 8.8, Range 54)

Mean MCH value was found to be 26.49 (\pm 3.7, Range 22)

Mean hematocrit was 34.4 (\pm 6.4, Range 43)

Mean RBC count was 4.5 (\pm 2.7, Range 40.7)

Mean TLC count was 13,489

Mean platelet count was 281000

Among the 205 adults, increased hemoglobin was found in 1(0.5%), normal in 83(40.5%) and decreased in 121(59%). Out of 65 males the hemoglobin was increased in 1(1.5%), normal in 26(40%) and decreased in 38(58.5%). Among the 140 females there was only normal hemoglobin in 57(40.7%) and decreased in 83(59.3%). ($p=0.339$). The TLC was increased in 50(24.4%), normal in 148(72.2%) and decreased in 7(3.4%) from the 205 subjects. In the 65 males 11(16.9%), 51(78.5%), 3(4.6%) is the count of TLC increased, normal and decreased respectively. In females the TLC is increased, normal, decreased in 39(27.9%), 97(69.3), 4(2.9%), respectively ($p=.213$).

Among the 205 patients, the platelet count is increased in 16(8%), normal in 173(84.8%) and decreased in 16(7.8%). In 65 males the platelet count was increased in 2(3%), normal in 56 (86.2 %) and decreased in 7(10.8%). In 140 females the

platelet count was increased in 14(10%), normal in 117(84%) and decreased in 9(6.5%). ($p=.180$) The hematological parameters in age groups are mentioned in Table-I.

Anemia was found in 121(59%) patients. According to MCV, the type of anemia was microcytic in 66(54.5%), normocytic in 53(43.8%) and macrocytic in 2(1.7%). Among the total 38 anemic males the MCV value was increased in 2(5.3%), normal in 19(50%) and decreased in 17(44.7%). Out of the 83 females who were anemic, 34(41%) was normocytic and 49(59%) was microcytic. ($P=.054$).The MCH value among the 121 anemic was increased in 5(4%), normal in 45(37.2%) and decreased in 71(58.7%). ($p= .139$). The hematological parameters based on diabetic duration are shown in Table-II. The hematological parameters in relation to medication are displayed in Table-III. The CBC in control and uncontrolled groups are shown in Figure-1 and 2 respectively.

Percentages shown in brackets are the frequency of hematological parameter in that age group from the total hematological parameter.

Percentages shown in brackets are the frequency of hematological parameter in that duration group from the total hematological parameter.

Percentages shown in brackets are the frequency of hematological parameter in that medication group from the total hematological parameter.

Parameter		Young (18-39 years) n=18	Middle-aged (40-59 years) n= 124	Elderly (>60 years) n=63	Total
Hemoglobin p= .830	Hemoglobin increased	0 (0%)	1(100%)	0(0%)	1(100%)
	Hb normal	9(10.8%)	50(60.2%)	24(28.9%)	83(100%)
	Hb decreased	9(7.4%)	73(60.3%)	39(32.2%)	121(100%)
TLC p= .571	Increased	5(10%)	27(54%)	18(36%)	50(100%)
	Normal	13(8.8%)	91(61.5%)	44(29.7%)	148(100%)
	Decreased	0(0%)	6(85.7%)	1(14.3%)	7(100%)
Platelets p= .279	Increased	1(6.7%)	8(53.3%)	6(40%)	15(100%)
	Normal	17(9.8%)	108 (62.4%)	48 (27.7%)	173(100%)
	Decreased	0(0%)	8 (50%)	8 (50%)	16(100%)

Table-I. Hematological parameters in age groups

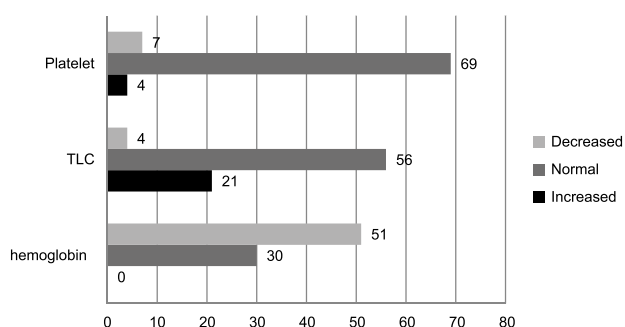
		<1 year	1-5 years	6-10 years	10-20 years	>20 years	Total
Hemoglobin (p=.079)	Hemoglobin increased	1(100%)	0(0%)	0(0%)	0(0%)	0(0%)	1(100%)
	Hb normal	9 (10.8%)	45 (54.2%)	14 (16.9%)	10 (12%)	5 (6%)	83(100%)
	Hb decreased	16 (13.2%)	43 (35.5%)	29 (24%)	22 (18.2%)	11 (9.1%)	121(100%)
MCV (p=.819)	Increased	1 (50%)	1 (50%)	0(0%)	0(0%)	0(0%)	2(100%)
	Normal	6 (11.3%)	19 (35.8%)	15 (23.8%)	9 (17%)	4 (7.5%)	53(100%)
	Decreased	9 (13.8%)	23 (34.8%)	14 (21.2%)	13 (19.7%)	7 (10.6%)	66(100%)
TLC (p=.153)	Increased	7 (14%)	20 (40%)	9 (18%)	11 (22%)	3 (6%)	50(100%)
	Normal	19 (12.8%)	61 (41.2%)	34 (23%)	21 (14.2%)	13 (8.8%)	148(100%)
	Decreased	0(0%)	7 (100%)	0(0%)	0(0%)	0(0%)	7(100%)
Platelets (p=.844)	Increased	3 (20%)	6 (40%)	2 (13.3%)	3 (20%)	1 (6.7%)	15(100%)
	Normal	22 (12.7%)	75 (43.4%)	36 (20.8%)	28 (16.2%)	12 (6.9%)	173(100%)
	Decreased	1 (6.2%)	7 (43.8%)	5 (31.2%)	1 (6.2%)	2 (12.5%)	16(100%)

Table-II. Hematological parameters based on diabetic duration

		Oral Hypoglycemic	Oral and Insulin	Insulin Only	No Medication	Total
Hemoglobin p=.351	Hemoglobin increased	1(100%)	0(0%)	0(0%)	0(0%)	1 (100%)
	Hb normal	68 (81.9%)	9 (10.8%)	6 (7.2%)	0(0%)	83 (100%)
	Hb decreased	80 (66.1%)	15 (12.4%)	24 (19.8%)	1 (0.8%)	121 (100%)
TLC p=.898	Increased	33 (66%)	8 (16%)	9 (18%)	0(0%)	50 (100%)
	Normal	110 (74.3%)	16 (10.8%)	20 (13.5%)	1 (0.7%)	147 (100%)
	Decreased	6 (85.7%)	0(0%)	1 (14.3%)	0(0%)	7 (100%)
Platelets p=.615	Increased	13 (86.7%)	2 (13.3%)	0(0%)	0(0%)	15 (100%)
	Normal	124 (71.7%)	22 (12.7%)	25 (14.5%)	1 (0.6%)	172 (100%)
	Decreased	12 (75%)	0(0%)	4 (25%)	0(0%)	16 (100%)

Table-III. Hematological parameters in relation to medication

Hematological parameters in controlled diabetes(559)



Hematological parameters in uncontrolled diabetes(559)

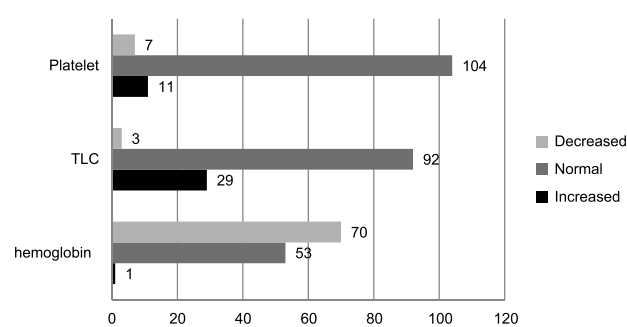


Figure-1 and 2. Hematological markers in controlled and uncontrolled diabetes.

DISCUSSION

In the recent decade, there has been renewed curiosity in hematological parameters as a prognosticator of endothelial dysfunction and inflammation. Our study reflected that anemia prevails in a diabetic patient. The mean hemoglobin and mean RBC count was suboptimal in our study which ascertains Farooqi's findings.⁹

Arkew¹⁰ confirmed a higher tendency to low mean hemoglobin, a higher white blood cell and increased platelet count in diabetics similar to our results.

A decrease in hemoglobin, an index of anemia, was higher than predicted in our results inspite of excluding obvious co morbid or complications.

Sharif¹¹ reported a higher incidence in Pakistan. Arkew¹⁰ and an Ethiopian study¹² quoted a lesser incidence compared to our region. Sharif's study showed the anemic count was higher in females compared to males¹¹ while a pilot study drove by Panda¹³ showed anemia to be more common in males (66.7%) compared to female (57%) diabetic population. We saw an equal ratio in both genders nullifying the old general fact that females are more anemic attributed to physiological phenomenon. The diabetic males are equally prone to a decrease in hemoglobin and have to be evaluated effectively. A Nigerian study¹⁴ reported a higher incidence of anemia in older group while we found the middle group to be more affected. Nutritional deficiency of vitamins especially iron is the most common cause of anemia with diabetes but chronic inflammation also reduces hemoglobin synthesis, red blood cell production, or red blood cell survival. Inflammatory cytokines leads to sequestration of iron and its ineffective utilization causing anemia of chronic disease and hence the high incidence of microcytic anemia in ours and Shaheen's study.¹⁵

Diabetes with its inflammatory progression causes higher percentage of white blood cell numerals despite excluding any obvious source of infection. Biadgo¹⁶ saw an increase in leucocyte count in diabetics compared with control. An elevated leukocyte count is a predictor of chronic inflammatory process and can be used to predict advancement of micro and macro vascular complications in diabetics.¹⁷ A Korean study conducted a ten year prospective study and observed that a higher leucocyte count predicted a higher risk of diabetes.¹⁸

The role of platelets in the integrity of homeostasis and vascular wellbeing is established. Platelet hyperactivity can cause vascular complications in chronic metabolic disorders such as accelerated atherosclerosis and arterial thrombosis in diabetics.¹⁹ Biadgo¹⁶ and Arkew¹⁰ found an increase in platelet count in diabetics as compared to non-diabetics while Asrat²⁰ found a decrease in platelet count in diabetics.

The glycemic control plays a vital role in

the variation in the pattern of hematological parameters in diabetics. Sharif¹¹ found a higher incidence and risk of anemia in poorly controlled diabetes. A Nigerian study by Adejumo BI¹⁴, a Kuwaiti study by Aldallal²¹ and a case control study by Antwi-Bafour²² found that the odds of developing anemia were higher in patients with poorly controlled diabetes.

Multiple studies have testified a correlation between TLC and impaired glucose control. This is because the chronic inflammatory state induced in diabetes due to the action of insulin on adipose tissue, muscles and liver promote the differentiation and maturation of WBCs through proinflammatory cytokines resulting in a raise in TLC. Demirtas²³ conducted a case control study showing that in the diabetic group, mean platelet volume and white blood cell count, platelet count, platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) were significantly higher than those in the control group. Arkew¹⁰ found that anemia was higher in patients with longer duration of diabetes but we found no such association.

An eye opener was the finding that there was a significant decrease in hemoglobin, an increase in white blood cell and platelet count in those who were on oral hypoglycemic in contrast to those who are on insulin or on a mixed therapy. Donnelly²⁴ associated Metformin with anemia based on randomized trials and real world study. The mechanism is not certain but could not be based totally on Cobalamin deficiency. In contrast studies have shown that oral hypoglycemics like Metformin, Sulphonylurea and Glitazone exert a beneficial effect on platelet function²⁵ and a decrease in platelet aggregation.²⁶ Scarce studies were found on the impact of insulin on hematological parameters.

Anemia and leukocytosis is an avertable complication of diabetes which is less focused upon by clinicians and hence infrequent screening of their hematologic conditions. This exposes diabetic patients to unwanted complications which are difficult to treat as it advances. This study will help clinicians and health planners

in conducting further studies and designing feasible solutions for hematology screening and corrective strategies.

LIMITATIONS

Our study was a considerably small and monocentric but is a pathway to further studies on a larger community based scale. There were occult confounders that could have impacted the CBC results. Advanced investigations, which were beyond the scope of our hospital laboratory, will help open up a spectrum of changes occurring in the blood plasma of a diabetic person.

CONCLUSION

Adult type 2 diabetics have a higher probability of having decreased hemoglobin and increased leucocyte count.



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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Adina Aslam	Data collection.	
2	Ayesha Shahid	Data collection.	
3	Ayesha Nageen	Corresponding author, Manuscript writing.	