Significance of Hematological Parameters in Uncomplicated Diabetes Mellitus

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Abstract

Background: Diabetes mellitus leads in chronic metabolic syndromes worldwide. The physiochemical changes in the blood bought about by persistent hyperglycemia are reflected in the hematological parameters on complete blood count.

Introduction: Diabetes Mellitus is a smouldering global pandemic destroying mankind slowly and silently. The associated detainable microvascular and macrovascular complications are responsible for much of morbidity and mortality. With ever increasing incidence and prevalence, it is important to device economical method to easily monitor, predict and prevent untoward health outcomes in these patients. Complete blood count being used as a basic and easily available investigation can be utilized for this purpose.

Material and Method: A case control study was carried out at Datta Meghe Medical College and Shalini Tai Meghe Hospital and research center in association with Acharya Vinobha Bhave hospital & research center and Jawaharlal Medical College, both a tertiary care hospital for a duration of 3 months. Study group of 100 diabetic patients and control group of 100 nondiabetic patients were evaluated using questionnaire, clinical findings, case records and hematological findings. Hemogram was analysed on Beckman coulter five part cell counter. Leishman stained peripheral smears were studied. The data thus collected was analysed using test of significance to find out relevance of changes in hematological parameters in diabetic patients.

Results: Anaemia along with higher leucocyte and platelet counts were observed in diabetic group.

Conclusion: Monitoring changes in hematological parameters can be a useful tool in better management of diabetic patients.

Keywords: *Diabetes mellitus, anaemia, erythropoiesis.*

Introduction

Diabetes Mellitus is a global pandemic with associated significant morbidity and mortality. Due to urbanization and adverse lifestyle changes like undesired food habits and sedentary life style, the incidence is constantly increasing with younger population becoming victim[29]. In 2015 International Diabetes Federation reported around 415 million people with diabetes and predicted this number to rise by 642 million by 2040[30]. India is known to be diabetic capital of the world and by 2030, it is estimated that about 80 to 87 million people of India will be diabetic[31,32]. Consistent hyperglycemia can be associated with functional and structural changes in hemoglobin molecule, cytoplasmic

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viscosity and osmotic disturbances within red blood cell and affects cellular metabolism by oxidative stress, which are reflected in various hematological parameters. This is depicted as changes in the various hemogram parameters. Glycation of haemoglobin molecule with resultant physiochemical changes in the red blood cells are reflected in parameters like MCV, MCH, MCHC and RDW[33]. Anemia is a common hematological finding in diabetic patients. Role of renal impairment in etiopathogenesis of anemia is well established, however, research studies have suggested association of anemia with diabetes in patients even prior to development of renal insufficiency[34],[35].Patients with diabetes mellitus show significant derangement in various haematological parameters. In fact, several haematological changes affecting the red blood cells (RBCs), white blood cells(WBCs), platelet and the coagulation factors are shown to be directly associated with DM.RDW is now being considered as an inflammatory marker and an elevated RDW value is shown to be significantly associated with diabetic nephropathy in type2 diabetes patients independent of traditional risk factors including diabetes duration and glycemic control[36]. Elevated WBC count is a basic inflammatory marker which can be used to measure the oxidative stress at cellular level. Endothelial dysfunction can be predicted by parameters like platelet count and platelet to lymphocyte ratio[37]. Complete blood count being a basic routinely advised investigation can be used to predict the glycemic control and in turn various degenerative complications of DM[38]. Hence these haematological parameters can prove to be easily available and economical method to monitor and predict health outcome in these patients. However, limited studies are available on this subject and exact relationship of changes in these parameters in predicting glycemic control and associated morbidity is not well established. Hence to have a better understanding of this, we propose to undertake this study with the objective to determine the hematological profile among type 2 Diabetes mellitus in comparison with non-diabetic controls.

Aims and Objectives:

Aim: To determine utility of hematological parameters in uncomplicated diabetes mellitus.

Objectives of study

1. To collect data on hematological parameters by using Beckman Coulter five part cell counter.
2. To collect further data by clinical history and previous case files.
3. To analyse all data thus collected to find out the differences in the two study groups.
4. To establish the role of hematological parameter as early preventive strategy.

Material and Method

A case control study was carried out at Datta Meghe Medical College and Shalini Tai Meghe Hospital and research center in association with Acharya Vinobha Bhave hospital & research center and Jawaharlal Medical College, a tertiary care hospital under Datta Meghe Institute of Medical Sciences, for duration of 3 months. Hundred subjects were included in each of the groups mentioned below. Subjects were evaluated using detailed history, clinical findings, previous case papers and hematological findings.

Patients were selected from out patients visiting central clinical laboratory. The data was analysed using test of significance to find out relevance of differences in hematological parameters in the two groups.

Study groups are outlined below:

- Known Diabetic Patients with history of diabetes mellitus for at least 2 yrs.
- Non diabetic healthy individuals.

Inclusion Criteria:

Group 1: All uncomplicated type 2 diabetic patients visiting out patient department.

Group 2: Healthy individuals visiting out patient department for routine health check up or for minor ailments and hospital staff.

Exclusion Criteria:

Group 1: Diabetic patients with micro or macrovascular complications, patients on insulin/aspirin or any antiplatelet drugs and patients with any other acute unrelated illness were not included in the study.

Group 2: Individuals with history of any chronic illness or any acute infective illness were not included in the study.

Sample Collection Process: 2 ml of venous blood was collected under aseptic conditions in EDTA bulbs

and hemogram was analysed on Beckman coulter five part cell counter. Peripheral smear stained with leishman stain were studied.

Results

In our study we included 100 subjects in each group. The mean age of patients in group 1 was 48.7 years with youngest subject being 38 yrs and oldest 59 yrs. There were 64 males and 36 females. The mean age of subjects in control group was 46.9 yrs, with youngest being 35 yrs and oldest 60 yrs. There were 58 males and 42 females (Table 1). There was no significant difference between age and sex distribution of the two groups. In group 1, patients had history of diabetes from 2 to 10 yrs duration, with average duration being 5.3 years.

Among the diabetics 48% of subjects were anaemic, with 33%, 12% and 3% having mild, moderate and severe anaemia respectively, whereas among non diabetics 25% were anaemic, with 15%, 09% and 1% having mild, moderate and severe anaemia respectively. Haemoglobin was significantly low in patients with diabetes (9.8±2.5g/dl) compared to controls (12.1±1.5 g/dl). Among other RBC parameters PCV and RBC count, were significantly lower in diabetic patients, whereas, RDW-CV, MCHC and MCV were significantly higher. MCH did not show any significant difference.

Mean WBC count with mean lymphocyte count was significantly higher in diabetic patients compared to non diabetics.

Mean Platelet count and MPV were significantly higher in diabetic patients compared to non diabetics.

Table 1 Age and Gender distribution of study population

	Diabetics	Non Diabetics	p value
Males	64%	58%	0.385
Females	36%	42%	0.385
Mean Age	48.7±7.5 yrs	46.9±8.2 yrs	0.106

Table 2 Comparision of various haematological parameters in the two groups

Parameter	Diabetics	Non Diabetics	p value
Haemoglobin (g/dl)	9.8±2.5	12.1±1.5	<0.0001
RBC count (10^6/µl)	4.01±1.52	4.82±1.14	<0.0001
PCV (%)	29.4±5.28	36.3±4.82	<0.0001
MCV (fl)	98.53±15.33	82±14.82	<0.0001
MCH (pg)	29.7±5.8	28.3±4.9	0.066
MCHC (g/dl)	37.1±5.3	34.1±6.2	0.0003
RDW (%)	18.8±5.3	16.4±4.2	0.0005
WBC count ($X10^3$/µl)	8.5±3.3	7.3±2.8	0.0061
ALC (/cmm)	4200±502	3400±600	<0.0001
ANC (/cmm)	6000±840	5800±750	0.077
AMC (/cmm)	650±150	600±250	0.087
AEC (/cmm)	450±270	390±180	0.065
Platelet count ($X10^3$/µl)	270±150	210±150	0.005
MPV (fl)	13.5±2.3	11.5±2.2	<0.0001

*ALC- Absolute lymphocyte count, ANC- Absolute neutrophil count, AMC-Absolute monocyte count, AEC- Absolute eosinophil count

Table 3 Comparision of grades of Anemia in the two groups

Grade of Anemia	Diabetic	Non Diabetic	p value
Mild	33	15	0.0008
Moderate	12	09	
Severe	03	01	

Table 4 Peripheral Smear findings in the two groups

PS finding	Diabetic	Non Diabetic	p value
Normocytic Normochromic	18	05	0.004
Microcytic Hypochromic	10	13	0.507
Macrocytic	20	07	0.007
Giant platelets	12	01	0.001
Neutrophilia	02	00	0.156
Lymphocytosis	50	02	<0.0001
Eosinophilia	07	01	0.030
Monocytosis	01	00	0.3
Polychromasia	17	02	0.0003
Fragmented RBCs	24	05	0.0001
Burr cells	01	00	0.3

Discussion

Diabetes Mellitus is a complex metabolic multisystemic disorder with steadily increasing prevalence. Persistent hyperglycaemia results in non enzymatic glycation of various proteins in blood such as haemoglobin, prothrombin and fibrinogen, which in turn changes viscosity, flow, red cell deformability, surface charge, erythrocyte aggregation and other physiochemical properties of blood[39]. Also the pro inflammatory milieu associated with diabetes brings about various changes in haematological parameters. The resultant RBC, WBC and platelet dysfunction is reflected in the hemogram[8].

In our study 100 subjects were included in each of the two groups. Mean age of diabetics was 48.7 yrs and of non diabetics 46.9 yrs, which was lower as compared to studies by Ravi Patel[40] and Harish Kumar[3].

Hemoglobin along with RBC parameters like RBC count, PCV and MCHC were significantly lower in diabetic group, whereas MCV and RDW CV showed significant increase. Diabetes with its associated hyperglycemia induced changes in the body's metabolic and physiochemical composition has been shown to be independent risk factor for Anaemia in previous studies[41,42,43]. The etiopathogenesis of anaemia is complex and multifactorial in diabetes. The assosiation of renal failure and development of secondary anaemia through erythropoietin pathway is well known, however, it has been observed that diabetics develop anaemia much earlier in the course of disease and also the severity of anemia when linked to stage of renal impairment was much more compared to non diabetic patients with renal impairment due to various other causes[44]. These findings point towards the complex multifactorial etiopathogenesis of anaemia in diabetes. Other pathways contributing to development of anaemia in these patients are inflammatory meliu with asssosiated increase in cytokines like IL 6 having detrimental effect on erythropoiesis, decreased responsiveness to erythropoietin, direct toxic effect on hematopoiesis, defect in feedback loop of peripheral blood cells and bone marrow and accelerated ageing and destruction of RBCs due to membrane protein glycation, rigidity and increased viscosity[45,46,47,48,49]. Drugs like metformin and ACE inhibitors also contribute to anaemia in diabetic population[18,50]. Decreased hemoglobin concentration along with accelerated ageing of RBCs interfere with HbA1C estimation, thus creating conflict in effective pharmacotherapeutic control of hyperglycemia[51]

.Anaemia in turn hastens the development and progress of micro- and macrovascular complications of diabetes, adding to the morbidity caused by these. Hence, correction of anaemia in diabetic patients can act as a preventive measure, avoiding much of morbidity and in turn improving quality of life[52,53].

MCV was found to be significantly higher in diabetic patients. This reflected megaloblastic anemia in 20 patients, which could be due to use of metformin and/ or alcoholism[54]. Also polychromasia seen in 17 patients contributed to the increased MCV on the whole[55].

RDW showed significant increase in diabetic patients reflecting impaired erythropoiesis and inflammatory mileu[7,56,57]. RDW is being considered as an independant inflammatory marker by some[1,7,58]. Barbieri M et al found RDW to be elevated in patients with macro and microvascular complications in diabetes[27].

Although normal in value, total count along with absolute lymphocyte count showed positive corelation with diabetes. Absolute neutrophil, eosinophil and monocyte count were higher in diabetic patients but they didnot show any significant corelation. Proinflammatory mileu along with oxidative stress present in diabetes is linked to the higher WBC count along with lymphocytosis in these patients, which in turn is linked to development and progress of various angiopathic complications assosiated with diabetes[59,60,61]. Epidemiological workers have suggested role of inflammation in inducing diabetes[4,62,63]. Leucocyte function is derranged in diabetics, making them prone to recurrent infection[64]. Even though absolute eosinophil count did not show any significant corelation, the number of diabetic subjects with eosinophilia was higher than non diabetics. This could be due to asymptomatic/subclinical fungal infections they are prone to[65,66].

Platelet count along with MPV was higher in diabetic subjects compared to control group. Due to microhemorrhages in the atheromatous plaques, the bone marrow is signalled to release reserve and immature giant platelets[67]. Swelling of platelets due to hyperosmalirity of plasma and degranulation of platelets contribute to increase MPV and increased variation in size of platelets reflected in PDW[68]. Platelet function is also affected in diabetes contributing to thrombotic complications[69,70]. Reduced effectiveness of antiplatelet drugs in diabetes has been studied by Mortensen SB et al[71]. Development and progression of atherosclerosis is reflected in platelet parameters, particularly raised MPV[72]. Karthikeyan et al suggested a possible relation between MPV and pathophysiology of cardiovascular disease[73]. Further platelet parameters are shown to be associated with HbA1C levels and cholesterol levels, which in turn is a major determinant of cardiovascular morbidity[9,74,47,48].

Conclusion

To conclude periodic monitoring and careful assessment of haematological parameters can prove to be of utmost help in foreseeing, preventing and delaying many diabetes associated complications.

Ethical Clearance: Taken from institutional ethics committee.

Source of Funding: Self.

Conflict of Interest: Nil.

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