

Study of hematological profile and its significance in type 2 diabetes mellitus patients

Bharathi K

Associate Professor, Dept. of Pathology,
Madha Medical College & Research Institute Kovur, Chennai, Tamilnadu

Corresponding Author:

E-mail: bharathi.pathos@gmail.com

Abstract

Introduction: Diabetic patients are more prone to be anemic and it is worsened further by associated chronic kidney disease and metformin treatment. Other hematological features like leukocytosis and platelet abnormalities are also common in type 2 diabetes mellitus patients. We studied the hematological profile of diabetic male patients to know the type of anemia along with the presence of other hematological abnormalities which is often missed clinically.

Objectives: To study the peripheral smear and hematological parameters of type 2 diabetic male patients and to correlate it with disease stage.

Material & Methods: Peripheral smear and hematological parameters of type 2 diabetic male patients were studied and compared with normal healthy males. 100 male patients diagnosed with type 2 diabetes mellitus in our hospital who comes for routine follow up were our study subjects. ADA (American Diabetic Association) criteria was used to select subjects. Statistical analysis was done using SPSS version 18 and Chi square test at p-value of 0.05 and 0.001.

Observation & Results: We observed that 26% of type 2 diabetic males were anemic with hemoglobin <11.5g/dl at P< 0.05. Out of which 10% were mildly anemic, 11% were moderately anemic and 5% were severely anemic. Peripheral Smear picture showed following abnormalities like normocytic normochromic anemia (13%), microcytic hypochromic anemia (8%) and macrocytic anemia with MCV more than 100 fL (5%), thrombocytopenia (5%), neutrophilia (30%), lymphocytosis (05%) eosinophilia (10%), giant platelets (07%) and burr cells (02%). We also observed that diabetic patients with renal disease had more occurrence of anemia and the severity of anemia correlated with severity of renal disease.

Implications: We emphasize that hematological profile should be included as a routine screening investigation to diagnose the type of anemia early in a diabetic patient to treat accordingly. Thus the morbidity of type 2 diabetes can be reduced considerably.

Keywords: Hematological profile, Morphology of anemia, Renal disease, Type 2 diabetes mellitus.

Introduction

India is the diabetic capital of the world. By 2030, about 80 to 87 million people of India will be diabetic and 438 million people (7.8%) of the adult population is expected to have diabetes worldwide⁽¹⁾. Anemia is a common hematological finding in diabetic patients especially in those with chronic kidney disease. Anemia in diabetic male is an added morbidity and it affects the quality of life⁽²⁾. We aim to study the complete hematological profile of type 2 diabetic males who are suffering for more than 5 years and to classify anemia along with other common hematological findings like leukocytosis and platelet abnormalities.

Objectives

Our aim is to study the hematological parameters and peripheral smear of type 2 Diabetes mellitus male patients and to find morphological types of anemia occurring in our study subjects to treat them accordingly.

Material & Methods

A case control study was done to compare the hematological profile of type 2 diabetic males and healthy males. 100 male patients diagnosed with type 2 diabetes mellitus in our hospital who comes for routine

follow up were our study subjects. Our study is a hospital based study done in a tertiary care health center. No other published data is available from our area in this topic. Study duration was 6 months (May 2015 to Oct 2015). Study was conducted in and around Madha Medical College & Research Institute, Kancheepuram district, Tamilnadu. ADA criteria was used to select subjects. Hematological parameters like Hb (haemoglobin), TC (total count), DC (differential count), PCV (packed cell volume), MCV (mean red cell corpuscular volume) done in the automated cell counter and peripheral smear findings were studied and correlated with the renal biochemical parameters. Anemia was graded as mild moderate and severe based on the WHO guidelines [Table 1].

Table 1: WHO criteria for diagnosing anemia and grading it.

S.N.	Grade of anemia	Hemoglobin level (g/dl)
1	Mild	11-12.9g/dl
2	Moderate	8-10.9g/dl
3	severe	<8g/dl

Ethical clearance was obtained from the institutional ethics committee and written informed consent was obtained from the study participants. Statistical analysis was done using SPSS version 18 and Chi square test at p-value of 0.05 and 0.001.

Inclusion criteria: Type 2 diabetic males with the disease for 5 years or more.

Exclusion Criteria: Type I Diabetes mellitus, Cases with hematological disease, females with diabetes mellitus.

We examined the patients along with detailed clinical history. 5 ml of blood was drawn from the patient and it will be analysed in the automated cell counter along with peripheral smear examination. Leishman staining was done in the peripheral smears.

Observation & Results

We found in our study that 26% of type 2 diabetic males were anemic with hemoglobin <11.5g/dl. Out of which 10% had mildly anemic, 11% are moderately anemic, 5% are severely anemic. Patients were classified and graded as per WHO criteria. Anemia was also studied in detail and typed based on the morphology seen in the peripheral smear.

Accordingly we found the following findings normocytic normochromic anemia (13%), microcytic hypochromic anemia (8%) and macrocytic anemia with MCV more than 100 fL (5%), thrombocytopenia (5%), giant platelets (7%), Neutrophilia (30%), Lymphocytosis (05%), eosinophilia (10%), burr cells (02%) [Table 2 and Table 3]. Giant platelets are produced due to hyperactive platelets. Diabetic patients with renal disease had more prevalence of anemia with rapid decline of renal function increasing the need for dialysis. They had recurrent respiratory tract infections and non-healing ulcers in the foot. We also observed that most of the findings are reversible with good glycemic control.

Table 2: Shows the percentage of anemia in our study subjects and its grade in type 2 diabetic male patients.

S.N.	Grade of Anemia	Type 2 Diabetic Males	Control Non Diabetic Males
1	Mild	10	6
2	Moderate	11	4
3	Severe	5	2

Table3: Shows the morphological typing of anemia in type 2 diabetic males.

S.N.	Morphological Type of Anemia	Type 2 Diabetic Males	Control Non Diabetic Males
1	Normocytic normochromic anemia	13	4
2	Microcytic hypochromic anemia	8	6
3	Macrocytic anemia	5	2

Discussion

The prevalence of diabetes is increasing globally. Type 2 diabetes mellitus is a complex multifactorial endocrinal disease with progressive deterioration of beta cell function and insulin resistance. The important causes are changes in the dietary pattern and decreased physical activity⁽³⁾. Kokiwar PR et al reported a high prevalence of diabetes 3.67% in a Indian village as compared to WHO report 2.4% for rural India⁽⁴⁾. The prevalence of diabetes among adults in the southern states of India has been reported as being 18.6% in urban populations and approximately 10% in rural populations. The prevalence rate increasing in the younger age groups. The WHO country office for India report on the prevalence of anemia gives the prevalence for males in India as 24% which also relates well with the finding of this study⁽⁵⁾. The International Diabetes Federation (IDF) estimated the total number of diabetic people in India was around 50.8 million in 2010 and it was expected to rise to 87 million by 2030⁽⁶⁾. The global increase in the prevalence of the diabetes is due to population growth, aging, urbanisation, increase of obesity and physical inactivity. Nations health and economy is largely affected by the disease load.

In India prevalence of anemia in diabetic males was found to be 10-12%. WHO has recently acknowledged that India has the maximum number of diabetic patients of around 35 million⁽⁷⁾. India is thus the diabetic capital of the world. AGT was more prevalent among upper socio economic class, obese, inactive sedentary individuals who have high BMI with family h/o diabetes⁽⁸⁾. Life style modification is one of the preventive measure in high risk groups in India.

Many hematologic abnormalities have been defined in diabetic patients but there are no classical hematological findings. Studies of the erythrocyte and the formation of glycosylated hemoglobin have provided a means of documenting long term glycemia control. Oxygen affinity has been noted to be abnormal in diabetic erythrocyte concomitant with decreased concentration of inorganic phosphorus, glycosylation of the^(2,3) diphospho glycerate binding site or pre-existing vascular disease.

RBC membrane viscosity is increased in hyperglycemic state. Abnormalities of leukocyte functions like defects in adherence, phagocytosis, random migration, chemotaxis are observed or described⁽⁹⁾. lymphocytes metabolic properties, mitogenic responses cell surface properties are also altered.

In vitro platelet abnormalities have been studied widely. In vivo behaviour remains controversial. Fluid phase coagulation studies suggested a hypercoagulable state in diabetic patients. Clinical significance of these findings are not defined.

On studying the hematological parameters in diabetes we found that anemia is a common finding

particularly those with albuminuria or reduced renal function [Table 4 and Table 5]. Anaemia in diabetes is seen usually when complicated by infection, cardiac disease, renal failure and enteropathy. Hyperglycemias may lead to shortened red cell life span and decreased erythrocyte deformability. In our study we analyse the haematological profile of type II diabetes mellitus patients in this study incidence and prevalence of anemia among the type 2 diabetes will be focused and studied elaborately.

Table 4: Hematological parameters of type 2 diabetic males.

S.N.	Hematological finding	Type 2 Diabetic Males	Control Non Diabetic Males
1	Normocytic Normochromic Anemia	13	4
2	Microcytic Hypochromic Anemia	8	6
3	Macrocytic Anemia with MCV more than 100 Fl	5	2
4	Thrombocytopenia	05	01
5	Giant platelets	07	01
6	Neutrophilia	30	02
7	Lymphocytosis	05	02
8	Eosinophilia	10	04
8	Burr Cells	02	0
9	Malarial parasite	01	0

Table 5: Diabetic Nephropathy associated with anemia (%)

S.N.	Grade of renal disease	Renal disease in Type 2 diabetic males (%)	Associated Anemia (%)
1	Mild	40	10
2	moderate	25	11
3	severe	15	5

Diabetic males are more prone to be anemic than normal. It was six times more for diabetic females. Anemic diabetic males and females are younger in age than their non-diabetic counterparts suggesting an earlier onset of kidney disease leading them to anemia. Anemia can falsely lead to low HbA1c levels which may result in under treatment of hyperglycemia which in turn will contribute to the progression of both micro and macro vascular complications.

The earliest duration of diabetes which could affect hemoglobin significantly was 4 years in males and 8 years in females⁽¹⁰⁾. So we have enrolled subjects of diabetes with 5 year or more of duration. Anemia occurs in approximately 45-50% of diabetics and the severity significantly increases after 4 years of duration in males. As anemia is a key indicator of renal pathology and occurs early in diabetics all diabetics need to be screened for anemia at least after 4 years of diabetes even if there are no clinical features of renal insufficiency.

The occurrence of anemia in diabetics was earlier attributed to renal pathology but studies have shown that anemia develops earlier in patients with diabetes when compared to patients with renal involvement due to other causes. Observational studies also indicate that low hemoglobin levels in diabetics may increase risk for progression of kidney disease and cardiovascular morbidity and mortality. The Reduced hemoglobin levels independently identify diabetic patients with an increased risk of microvascular complications, cardiovascular disease and mortality.

Many factors have been suggested as the reason for anemia in patients with diabetes, including autonomic neuropathy, systemic inflammation, and changes in the renal tubulointerstitium disrupting the interaction between interstitial fibroblasts, capillaries and tubular cells required for normal hemopoietic function. EPO deficiency is considered to be one of the main cause of anemia. Another review report suggests erythropoietin hyporesponsiveness as a cause for anemia in diabetics. It is believed to represent impaired antiapoptotic action of erythropoietin on proerythroblasts. Other Possible causes of this erythropoietin hypo responsiveness include systemic inflammation and microvascular damage in the bone marrow. There is also a possibility of defect in anemia-sensing mechanism rather than erythropoietin secretory mechanisms as a cause of anaemia in diabetes. Low testosterone levels and hypogonadotropic hypogonadism are common in men with type 2 diabetes. As testosterone stimulates erythropoiesis, low testosterone levels may also contribute to anaemia in them.

Wang ZS, et al studied the association of RBC count with micro vascular complications in type 2 diabetes patients⁽¹¹⁾. They reported that the proportion of patients with microvascular complications increased as the RBC count decreased. The prevalence of anemia was increased in persons with diabetes and diabetes associated with chronic kidney disease compared to persons without diabetes. Anemia was more prevalent in the diabetic patients with creatinine clearance <60 ml/min. In most studies to date, impaired renal function and albuminuria are the predominant risk factors for anemia in diabetic patients. Women with diabetes had increased prevalence of anemia than men. In patients with diabetes, anemia is primarily a risk factor for CKD. Correction of anemia may have a significant role in prevention of other diabetic complications. Nevertheless, these findings require confirmation in other cohorts that have more complete patient-level data, including information on medication exposures.

Anemia is associated with increased risk of diabetic complications including nephropathy and micro vascular disease. Anemia may be significant in determining the outcome of heart failure and hypoxia induced organ damage in diabetes. Diabetics with moderate renal impairment are twice more likely to have anemia than mild renal impairment reported by

another study. Patients at high risk can be identified by the presence of renal impairment or albuminuria. Treatment with recombinant erythropoietin increased the hemoglobin and hematocrit level. Patients had severe autonomic neuropathy, tubulointerstitial damage and microangiopathy. It is unproven whether anemia directly contributes to acceleration of complications of diabetes or to the progression of diabetic nephropathy. However patients with diabetes are more vulnerable to the effects of anemia because they have significant associated cardiovascular disease and hypoxia induced organ damage. Use of ACE inhibitors can also cause anemia in diabetics due to direct blockade of pro erythropoietic effects.

Vitamin B12 deficiency anemia is highly prevalent in type 2 diabetes mellitus and type 1 diabetes mellitus⁽¹²⁾. The probable mechanism is the use of metformin. It causes pancytopenia, megaloblastic anemia, peripheral neuropathy and subacute combined degeneration of the spinal cord. So a routine screening and supplementation of Vit B12 injection is needed for those patients. Symptomatic improvement is observed in such cases.

Leukocytosis presents as neutrophilia, eosinophilia and lymphocytosis. Chronic inflammation as indicated by higher WBC count is associated with micro vascular complications in type 2 diabetes patients. Elevated WBC count even within normal range is associated with micro & macro vascular complications. Impaired white cell (poly morph) function is also noted in diabetes mellitus⁽¹³⁾. Other changes of neutrophils or macrophages are defective chemotaxis. Patients with diabetes are more prone for recurrent infections. It is mainly due to defect in leucocyte function and defective chemotaxis.

Abnormal platelet function (increased platelet aggregability) leading to thrombotic predisposition is also observed. Platelet hyperactivity accelerated platelet turnover and giant platelets has been observed in our study. It favours accelerated athero thrombotic events⁽¹⁴⁾. The primary goal in management of diabetes is the attainment of normal glycemia. In India more than half of patients have poor glycemic control and have vascular Complications. Therefore there is an urgent need to develop novel therapeutic agents.

Conclusions

We conclude from our study 26% of type 2 diabetic males were anemic with hemoglobin <11.5g/dl mainly of normocytic normochromic type. We also observed that diabetic patients with renal disease had more prevalence of anemia and the severity of anemia

correlated well with severity of renal disease. We emphasize that hematological profile should be included as a routine screening investigation to diagnose the type of anemia in a diabetic patient and treat accordingly. Treating anemia in type 2 diabetic males definitely improve the quality of life and decrease the speed of progression of renal disease. In future therapeutic prevention of anemia in diabetes can retard the progress of diabetic nephropathy and its complications.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27(5):1047-53.
2. Ramachandran A, Snehalatha C. Current scenario of diabetes in India. *J Diabetes*. 2009; 1(1):18-28.
3. IDF Diabetes atlas, 4th edition. International diabetes federation, 2009.
4. Kokiwar PR, Sunil Gupta, Durge PM. Prevalence of diabetes in a rural area of Central India. *Int J Diab Dev Ctries* 2007; 27(1):8-10.
5. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and mineral information system. Geneva, world health organisation, 2011.(WHO/NMH/NHD/11.1)(<https://www.who.int/vmnis/indicators/hemoglobin.pdf>).
6. Mohan V, Deepa R. Prevalence of diabetes and metabolic syndrome among Asians. *International Journal of Diabetes in Developing Countries*. 2010; 30(4):173.
7. Premalatha G, Shanthi, Rani CS, Deepa E, Rema M, Mohan V. Prevalence of diabetic complication in south Indians-The Chennai urban population study. *NOVO Nordisk Diabetic Update*. 2000; 59-64.
8. Cristoph H. Anaemia in Patients with Diabetic Nephropathy-Prevalence, Causes and Clinical Consequences. *European Cardiovascular Disease* 2007.
9. Jones RL, Peterson CM. Hematologic alterations in diabetes mellitus. *Am J Med* 1981; 70(2):339-52.
10. Lingaraj Jayalakshmi, Komala Sampath Damodar, Shankarappa Chikkannna. Anaemia in Type 2 diabetes- Its occurrence and relationship with duration of diabetes: A pilot study. *Electronic Physician*, 2012; 4(2):497-501.
11. Wang ZS, Song ZC, Bai JH, Li F, Wu T, Qi J et al. Red blood cell count as an indicator of microvascular complications in Chinese patients with type 2 diabetes mellitus patients. *Vacs health risk manag* 2013; 9:237-43.
12. De-Jager J, Kooy A, Leher P, et al: Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial. *BMJ* 2010, 340:c2181.
13. Tong PC, Lee KF, So WY, NgMH, Chan WB, LoMK et al. White blood cell count is associated with macro and micro vascular complications in Chinese patients with type 2 diabetes. *Diabetes care* 2004; 27(1):216-22.
14. Ferreiro JL, Angiolillo DJ. Platelet abnormalities in diabetes. *Diabetes and vascular disease research*. 2010;7(4):251-9.