International Journal of Advances in Medicine
Prabhu S et al. Int J Adv Med. 2019 Aug;6(4):1231-1235
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20193276

Original Research Article

A comparative study of anaemia with the degree of glycaemic control in type 2 diabetes mellitus

Prabhu S., Balakrishna Teli*

Department of Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

Received: 06 June 2019
Revised: 10 June 2019
Accepted: 04 July 2019

***Correspondence:**
Dr. Balakrishna Teli,
E-mail: balakrishnateli27@gmail.com

ABSTRACT

Background: Anaemia is one of the world's most common preventable condition yet it is often overlooked especially in people with Diabetes Mellitus. Anaemia is a common finding in patients with diabetes. Anaemia in patients with diabetes mellitus might contribute to the pathogenesis and progression of cardiovascular disease and aggravate diabetic nephropathy and retinopathy. This aims to study the correlation between HbA1c and blood glucose levels in anaemic diabetics in order to assess the influence of anaemia on HbA1c and the effect of severity and type of anaemia on HbA1c.

Methods: It's a case control study, 200 Diabetic subjects were divided into two groups of 100 each based on their HbA1c levels group A, with good glycaemic control (HbA1c<7) and group B with poor glycaemic control (HbA1c>7), incidence of anaemia was measured and compared among them and also with 100 age and sex matched healthy non Diabetic controls.

Results: In this study, it was found that high incidence of anaemia was found significantly higher in diabetics group with poor glycaemic control. Anemia was detected in 55% of patients among diabetic patients. Anaemia was seen in 71% of patients in group B with poor glycaemic control as compared to group A with good glycaemic control, in which only 39% of patients had anaemia. Mean haemoglobin was significantly lower that is, 10.81±3.0 in group with poor glycaemic control as compared to group with good glycaemic control i.e. 13.04±2.02. There was a statistically significant negative correllation between Haemoglobin percentage and HbA1c.

Conclusion: Anaemia is a common finding in patients with diabetes. Diabetes related chronic hyperglycaemia can lead to a hypoxic environment in the renal interstitium which results in impaired production of erythropoietin by the peritubular fibroblasts and subsequently anaemia occurs. Anaemia in patients with diabetes mellitus might contribute to pathogenesis and progression of cardiovascular disease and aggravate diabetic nephropathy and retinopathy. However, an emphasis on regular screening for anaemia, alongside that for other diabetes related complications, might help to delay the progression of vascular complication in these patients.

Keywords: Anaemia, Diabetes mellitus, Glycaemic control, Haemoglobin, Renal insufficiency

INTRODUCTION

There are currently approximately 40.9 million patients with diabetes mellitus in India and this number is expected to rise to about 69.9 million by the year 2025. This high burden of diabetes is likely to be associated with an increase in associated complications.[1]

Type 2 Diabetes Mellitus is a non-autoimmune, complex, heterogeneous and polygenic metabolic disease condition in which the body fails to produce enough insulin, characterized by abnormal glucose homeostasis. Its pathogenesis appears to involve complex interactions between genetic and environmental factors. Type 2 Diabetes Mellitus occurs when impaired insulin

effectiveness (insulin resistance) is accompanied by the failure to produce sufficient cell insulin.

In type 2 diabetes mellitus patients glycosylated haemoglobin (HbA1c) is an effective tool in monitoring long term blood glucose control. HbA1c gives an accurate estimate of the average of the plasma glucose levels from the past 8 to 12 weeks. Hence glycosylated haemoglobin becomes an important marker of glycemic control in diabetes mellitus. HbA1c testing is a measure of diabetic glycaemic control. Diabetes control is categorized as poor control (HbA1c levels >9%), moderate control (HbA1c levels between 7% and 9%) and good or desired control (HbA1c levels <7%).[2]

Anaemia is one of the world's most common preventable condition yet it is often overlooked especially in people with Diabetes Mellitus.[3]

Anaemia is more common in diabetes and develop earlier than in patients with renal impairment from other causes. However, patients with diabetes may be more vulnerable to the effects of anaemia because many also have significant cardiovascular disease and hypoxia-induced organ damage.

Although anaemia can be considered a marker of kidney damage, reduced hemoglobin levels independently identify diabetic patients with an increased risk of microvascular complications, cardiovascular disease and mortality.[4]

Many factors have been suggested as the reason for the earlier onset of anaemia in patients with diabetes, including severe symptomatic autonomic neuropathy, causing efferent sympathetic denervation of the kidney and loss of appropriate erythropoietin production; damage to the renal interstitium, systemic inflammation; and inhibition of erythropoietin release.[5]

In spite of the plethora of reports on the presence of anaemia in diabetic patients with renal insufficiency, limited study exists on the incidence of anaemia in diabetics prior to the evidence of renal impairment. This may explain why most diabetic patients with normal renal function are rarely tested for anaemia. The need for more studies on incidence of anaemia in diabetic patients prior to renal impairment has therefore become imperative, in order to increase the level of awareness and understanding of anaemia amongst diabetic patients.[6]

Correction of the anaemia not only lessens fatigue, greater exercise tolerance, and an improved quality of life but also to a reduction in outpatient and hospital admissions for congestive heart failure. Data are accumulating that suggestive treatment of anaemia will slow the progression of microvascular and macrovasular complications including postural hypotension from autonomic neuropathy, retinopathy and diabetic nephropathy. Promptly diagnosing and treating anaemia in patients with diabetes may result in improved quality of life and decreased morbidity and mortality.[7]

The aim of the study was:

- To study the correlation between anaemia and the degree of glycaemic control in type 2 diabetic patients
- To study the prevalence and type of anaemia in diabetic patients.

METHOD

About 100 patients of type 2 diabetes mellitus with their glycosylated hemoglobin levels less than 7%, 100 patients of type 2 diabetes mellitus with their glycosylated hemoglobin levels more than 7% attending the Medicine outpatient and inpatient departments of hospitals attached to Bangalore medical college and research institute were selected for the study. 100 age and sex matched controls were selected randomly from in and around Hospitals attached to Bangalore medical college and research institute. The study was conducted between october 2018 to march 2019. The study protocol was approved by the hospital ethical committee.

Inclusion criteria

- Patients willing to give written informed consent
- Age >18 years
- Clinically proven cases of type 2 diabetes mellitus with Anaemia.

Diabetes Diagnosed as per ADA guidelines i.e. symptoms of diabetes with random blood sugar >200 mg/dl or fasting blood sugar >126 mg/dl or HbA1c >6.5% or 2-hour plasma glucose >200 mg/dl during an oral glucose tolerance test. Anaemia is diagnosed as per WHO guidelines i.e. Hb <13 g/dl in male and Hb <12 in non-pregnant females.

Exclusion criteria

- Diabetic patients with chronic kidney disease (GFR <60 mL/min/1.73 m^2 for 3 months)
- Pregnant women
- Age <18 years
- Acute blood loss
- Diabetic patients who are on metformin
- Patient not willing to give consent for the study
- Other causes of anaemia in diabetes mellitus.

All the subjects and control will be generally and systemically examined to rule out the presence of other co-morbid conditions. Anthropometry: Height, Weight, BMI were measured, waist to hip ratio was collected. A questionnaire was provided to the controls and subjects to know about their lifestyle, past history, family history and list of medications.

Blood sample from the study and control group will be drawn under complete aseptic precautions, after obtaining informed consent. Fasting and two hours post prandial blood sample will be collected for analysis in vacuum evacuated tubes as follows:

- Clot activator containing vacuum evacuated tubes for estimation of Complete Haemogram, Peripheral Blood Smear, Renal Function Test and Iron Profile
- Fluorides EDTA vacuum evacuated tubes for estimation of blood glucose and glycosylated hemoglobin.

Statistical analysis

The Continuous data in this study was assessed using repeated measure ANOVA and unpaired 't' test. Categorical data was assessed using chi-square test. Sub-group analysis was done for relevant metabolic parameters.

RESULTS

About 200 diabetic patients are divided into two groups based on their glycaemic control; group A with better glycaemic control (HbA1c <7) and group B with poor glycaemic control (HbA1c >7) and 100 controls were taken-group C. Age distribution of the study participants and mean age in all three groups are comparable as shown table 1 and 2.

Table 1: Age distribution of study participants.

Age	HbA1c<7	HcA1C≥7	Control	Total
18-32 Yrs	39	04	03	46
33-47 Yrs	28	29	34	91
48-62 Yrs	23	43	36	102
63-77 Yrs	10	19	20	49
78-92 Yrs	0	05	07	12
Total	100	100	100	300

Table 2 : Mean ages of all the groups .

Paramets	HbA1c<7	HbA1c≥7	Control
Age	53.44±10.811	53.38±12.75	53.88±13.62

In our study there were 154 males and 146 females. Anemia was detected in 110 (55%) patients among 200 diabetic patients.Anaemia was seen 71 (71%) patients among 100 patients in group B with poor glycaemic control as compared to group A with good glycaemic control , where ony 39 (39%) patients had anaemia.The above findings are tabulated and graphically represented in table 4 and figure 1. Mean haemoglobin was significantly lower i,e 10.81±3.0 in group with poor glycaemic control as compared to group with good glycaemic control i,e 13.04±2.02 as shown in table 3.Hence in a group with good glycaemic control has better haemoglobin percentage as compared to group with poor glycaemic control, which was statistically significant.

Table 3: Mean haemoglobin in three different groups.

Parametes	HbA1c<7	HbA1c≥7	Control
Age	53.44±10.811	53.38±12.5	53.88±13.62

Table 4: Anaemia in different groups.

Group	Anaemia		P value
	Present	Absent	
HbA1c<7	39	61	0.0001
HbA1c≥7	71	29	
Control	16	84	
Total	126	174	

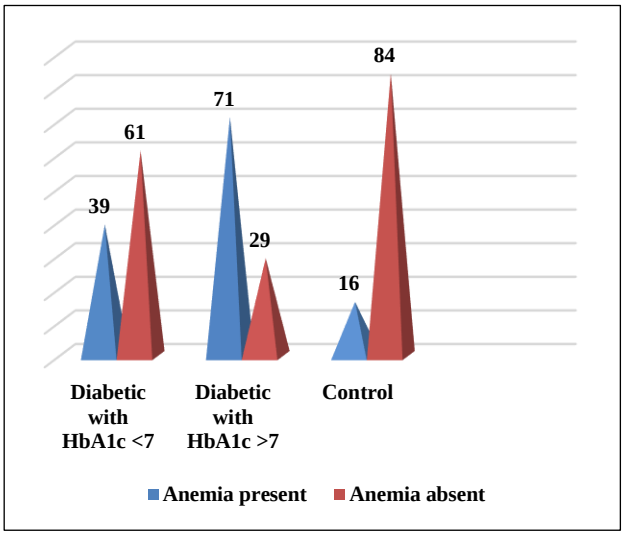

Figure 1 : Anaemia in different groups.

In group with poor glycaemic control, mean FBS was high i,e 257.67±68.48 as compared to group with good glycaemic control i,e 244.93±98.23 and also PPBS was high in group with poor glycaemic control compared to group with good glycaemic control as shown in table 5.There was statistically significant difference between group A and group B, and also between group A and group C (P <0.01).

Table 5 : Mean FBS and PPBS in different groups.

Parameters	HBA1C<7	HBA1C≥7	Control
FBS	244.93±98.23	257.67±68.48	114.71±80.99
PPBS	305.41±53.139	350.94±74.389	148.01±97.83

Relationship between HbA1c and Haemoglobin in different groups shown in table 6. There was a statistically significant negative correlation between Haemoglobin percentage and HbA1c.

Table 6 : Correlation between Hb and HbA1c.

	Group A	Group B	Group C
HbA1c (%)	6.845±1.1755	10.716±2.8374	5.519±1.6424
Hb (%)	13.085±2.029	10.809±3.0005	13.174± 2.008

In group with good glycaemic control; 82% had normocytic anaemia, 13% had iron defiency anaemia and 5% had VIT B 12 deficiency anaemia as shown in Figure 2.

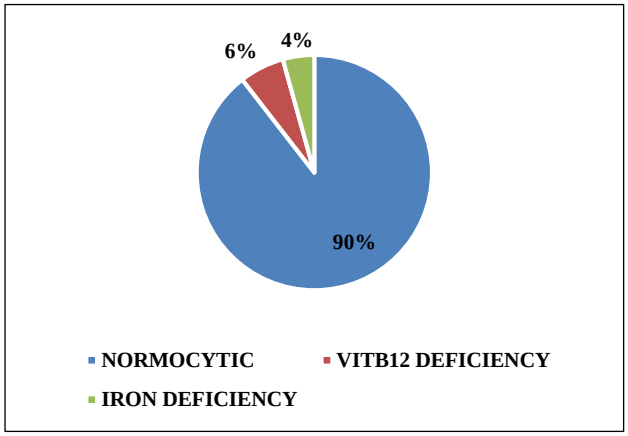

Figure 2: Incidence and type of anaemia in group with HbA1c< 7.

In group with poor glycaemic control 71% had normocytic anaemia, 18% had iron deficiency anaemia and 11% had Vit B 12 as shown in Figure 3.

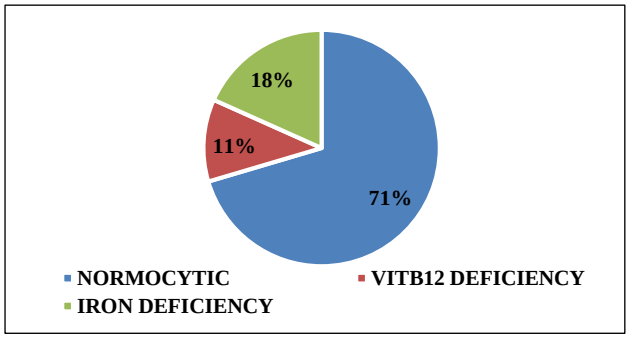

Figure 3: Incidence and type of anaemia in group with HbA1c ≥7.

Table 7 : Different parameters in the study.

Parameters	HbA1c≥7	HbA1c<7
S. Iron	40.00±15.82	46.34±17.71
S. Ferritin	89.81±208.69	90.08±204.02
TR Saturation	13.03±7.62	14.01±7.58
TIBC	379.77±92.40	392.72±95.14
Vit B12	328.99±258.27	337.20±213.48
S Folic acid	12.35±4.05	13.09±4.0

The different parameters in study like serum iron, serum ferritin, transferin saturation, TIBC, Vit B12 and serum folic acid were as in Table 7.

DISCUSSION

In the present study, there was significant prevalence of unrecognised anaemia was found among diabetics as compared to non-diabetics, which was significantly higher among uncontrolled diabetes than controlled diabetes, even in the patients with normal renal function.

A study done by Bhargav K et al, demonstrated that there is significant negative correlation between haemoglobin and HbA1c. Anaemia was present in 40% of diabetics and majority was in the age group between 50-60 years and majority of anaemia was normocytic (66%) as compared to microcytic (29%).[5] Another study done by Adejumo et al in 2012 showed that incidence of anaemia was 15.3% in participants with diabetes without renal insufficiency. The study added that patients who have poorly controlled diabetes were at higher risk of anaemia than those with controlled diabetes.[6]

Several studies have reported factors that increase the risk of anaemia, which include damage to renal interstitium due to chronic hyperglycaemia and consequent formation of advanced glycation end products by increased reactive oxygen species, and systemic inflammation as well as reduced androgen levels induced by diabetes as shown by Adejumo et al, and Fetch et al in 2016.[6,8-9]

Andrews and Arredono determined that the presence of anaemia in type 2 diabetes as well as evaluating the expression of genes related to inflammation and immune response. The results found by the authors demonstrate that diabetic patients with anaemia exhibit increased expression of proinflammatory cytokines as compared to diabetic patients only.

In anaemic patients increase in IL-6 production as well as B cell activity, was confirmed which reinforces the association between IL-6 and antierythropoetic action.[10]

Hence there is a need of studies about anaemia in diabetes without renal dysfunction.

CONCLUSION

Anaemia is common finding in type 2 diabetes mellites patients when compared with the general population. Anaemia in patients with poor glycaemic control might contribute to pathogenesis and progression of morbid conditions related to cardiovascular disease and aggravate diabetic nephropathy and retinopathy. However, emphasis on regular screening for anaemia in diabetics along with that of other diabetes related complications, might help to delay the progression of micro and macrovascular complications in these patients.

In patient with diabetes, it would be desirable to evaluate for anaemia often, even when the renal parameters are within normal limits for better quality of life.

ACKNOWLEDGEMENTS

Authors would like to thank all patients who participated in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sucharita S, Bantwal G, Idiculla J, Ayyar V, Vaz M. Autonomic nervous system function in type 2 diabetes using conventional clinical autonomic tests, heart rate and blood pressure variability measures. Indian J Endocrinol Metab. 2011;15(3):198.
2. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomarker Insights. 2016;11:BMI-S38440.
3. Singh DK, Winocour P, Farrington K. Erythropoietic stress and anemia in diabetes mellitus. Nature Rev Endocrinol. 2009;5(4):204.
4. Thomas MC, MacIsaac RJ, Tsalamandris C, Power D, Jerums G. Unrecognized anemia in patients with diabetes: a cross-sectional survey. Diab Care. 2003;26(4):1164-9.
5. Bhargav K, Baruah K, Agrawal P, Alam F, Sonal S, Kumar A, et al. Study of Anaemia in Type II Diabetes Mellitus in Relation to Glycemic Control. Int Arch Bio Medical Clin Res. 2016;2(4).
6. Adejumo BI, Dimkpa U, Ewenighi CO, Onifade AA, Mokogwu AT, Erhabor TA, et al. Incidence and risk of anemia in type-2 diabetic patients in the absence of renal impairment Health. 2012;4(6):304-8.
7. McGill JB, Bell DS. Anemia and the role of erythropoietin in diabetes. J Diabetes Complications. 2006;20(4):262-72.
8. Feteh VF, Choukem SP, Kengne AP, Nebongo DN, Ngowe-Ngowe M. Anemia in type 2 diabetic patients and correlation with kidney function in a tertiary care sub-Saharan African hospital: a cross-sectional study. BMC Nephrol. 2016;17(1):29.
9. Aljohani AH, Alrubyyi MA, Alharbi AB, Alomair AM, Alomair AA, Aldossari NA et al. The Relation Between Diabetes Type II and Anemia. Egyp J Hospital Med. 2018;70(4).
10. Andrews M, Arredondo M. Ferritin levels and hepcidin mRNA expression in peripheral mononuclear cells from anemic type 2 diabetic patients. Biological trace element research. 2012;149(1):1-4.

Cite this article as: Prabhu S, Teli Balakrishna. A comparative study of anaemia with the degree of glycaemic control in type 2 diabetes mellitus. Int J Adv Med 2019;6:1231-5.