Original Research Article

Correlation of Iron Deficiency Anemia on HbA1C Levels: Comparison among Patients living with Diabetic and Non-diabetics

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Abstract

Background: Glycated hemoglobin A1c (HbA1c) reflects average plasma glucose for the previous 3 months and is a principal parameter in the diagnosis of diabetes. Multiple non-glycemic parameters affect HbA1c such as iron deficiency anemia (IDA). However, reports on the effects of iron deficiency anemia on HbA1c levels are inconsistent. Objective: To find out the influence of iron deficiency anemia over HbA1c levels. **Methods:** Study was conducted in iron-deficiency anemia and non-anemia patients who were either diabetic or non-diabetic. Basic blood parameters were evaluated long with HbA1c and fasting plasma glucose and population was classified in different grades of anaemia. Correlation of anemia and HbA1c was evaluated using statistical analysis. **Results:**The mean HbA1C in controlled diabetics with and without IDA were 9.53±0.93 & 5.43±0.45 respectively (P<0.05) and in non-diabetics with and without IDA were 5.84±0.71 & 5.12±0.52 respectively (P>0.05). The difference between no, mild, moderate and severe anemia in both diabetics and non-diabetics was statistically significant (p<0.01). Mean HbA1C% was highest in groups with severe anemia (10.2%). Other blood parameters such as Hb, MCV, MCH and MCHC were also significantly different among diabetics who were IDA. **Conclusions:** This study found a positive correlation between iron deficiency anemia and increased HbA1C levels, especially in the controlled diabetic. IDA should be diagnosed and corrected prior to alteration of treatment regimen based on HbA1C for diabetes. Concurrent evaluation for anemia is critical to correctly interpret glycemic status in Indian population with prevalent IDA.

Keywords:diabetes, hemoglobin A1c, anemia.

Introduction

Diabetes is major health problem globally effecting more than 300 million people to be diagnosed with the disease in the next 10 years and 370 million by 2030[1].In 2010, American Diabetes Association (ADA) has considered HbA1C levels as the prime target for glycemic control and as a diagnostic criterion for Diabetes Mellitus (DM). HbA1C ≥ 6.5% has been established for the diagnosis of DM for its high specificity and certified by the World Health Organization (WHO) in 2011[2,3]. It reflects the patient's glycemic status over previous 8 to 12 weeks.Anemia is common among DM and its incidence ranges from 8-66%. Several mechanisms have been discussed about the association of anemia in DM and its complications like nephropathy[4,5].Iron deficiency is one of the most predominant forms of malnutrition affecting is a cause of 50% cases of anemia, globally. An earlier study showed that reduced iron stores have a link with increased glycation of hemoglobin A1C (HbA1c), leading to false-high values of HbA1c in non-diabetic individuals[6]. Its alteration in other conditions, such as hemolytic anemia, hemoglobinopathies, pregnancy, and vitamin B12 deficiency has been explained in a study[7]. Although iron deficiency is the most common nutritional deficiency, reports of the clinical relevance of iron deficiency on HbA1c levels have been inconsistent[6,7].The well-known pathological hostile effects of iron deficiency anaemia (IDA) in the biological system is the glycosylation of proteins[8].

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Previously, attempt has been made to analyze the influence of IDA on HbA1C levels in both non-diabetic and patients living with diabetes individually. However, only very few studies have compared HbA1C variation in both these groups. Due to the variation in the results of multiple studies, in the present study we aimed to investigate and compare the effects of IDA on HbA1C levels in both controlled diabetic and non-diabetic Indian adults.

Materials and methods

Study setting

The present study was designed as a retrospective interventional study conducted in the Department of General Medicine, over a period of 24 months from November 2018 to October 2020 following Institutional ethical committee approval. We consider data from both in and out-patients coming to the medicine department in the study who were willing to participate and provide Informed written consent.

Data collection

We collected the data of 750 diabetic subjects >18 years who already had HbA1c, peripheral smear, hemoglobin, mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), serum ferritin, and plasma glucose levels. Of 750 diabetic subjects, 216 were diagnosed as having iron deficiency anemia (IDA) based on their hemoglobin, red cell indices, and peripheral smear, and 135 patients showed controlled plasma glucose levels (FPG <126 mg/dl) since last 6 months. Of these 135 patients, 15 were excluded based on history of acute blood loss, hemoglobinopathies, haemolytic anaemia, pregnancy, kidney disease criteria and 120 subjects (60 females and 60 males) were considered for the study. Control group consisted of 90 normal (non-diabetics) individuals. Data of HbA1c, peripheral

smear, MCH, MCV, MCHC and plasma glucose levels was also collected from the non-anemic controls (matched for sex and plasma glucose levels) to classify them into different grades of anaemia.On the basis of hemoglobin level, anemic patients were further categorized as Mild anemia (male 12-12.9 gm/dl and female 11-11.9gm/dl), Moderate anemia (male 9-11.9 gm/dl and female 8-10.9 gm/dl) and Severe anemia (male <9 gm/dl and female <8 gm/dl).

Statistical Analysis: The data are presented as mean ±S.D for continuous variables. Group means were compared by student t-test. Pearson's co-efficient of correlation was used to determine the correlation between two variables. p value < 0.05 was considered significant.

Results

Subject characteristics

The mean HbA1C in controlled diabetics with and without IDA were 9.53±0.93 &5.43±0.45 respectively and in non-diabetics with and without IDA were 5.84±0.71 &5.12±0.52 respectively. This result show that the mean HbA1C was higher in those with IDA than in those without IDA in diabetics($p < 0.05$) but such difference was not found in non-diabetics(Table1). Age was comparably similar in all the groups when patents were classified based on IDA and NA features. The mean Hb, MCV, MCH & MCHC in controlled diabetics with and without IDA were statisticallysignificant ($p < 0.05$, Table 2).

Table 1:Comparison of Hba1c% in Study Groups with (IDA) and without Anemia (NA)

Controlled diabetics			
Age		**HbA1c**	
IDA	NA	IDA	NA
52.12 ± 5.88	53.06 ± 4.99	9.53±0.93*	5.43±0.45
Non-diabetics			
Age		**HbA1c**	
IDA	NA	IDA	NA
54.2 ± 6.2	54.5 ± 6.08	5.84±0.71	5.12±0.52
P > 0.05		*P < 0.05	

Table 2: Comparison of Red Cell Indices Between Anemic and Not Anemic in Controlled Diabetics & Nondiabetics

Parameters	Patients group	IDA	NA
Hb (g/dl)	Controlled Diabetics	7.77 ± 0.49*	13.83 ± 1.49
	Non diabetics	11.46±1.10*	15.04±1.50
MCV (fL)	Controlled Diabetics	63.39 ± 5.33*	90.32 ± 9.23
	Non diabetics	73.23 ± 5.23*	98.56 ± 6.22
MCH (pg/cell)	Controlled Diabetics	26.49 ± 2.23*	39.22 ± 3.01
	Non diabetics	28.56 ± 1.97*	38.56 ± 2.22
MCHC	Controlled Diabetics	23.88 ± 2.50*	36.88 ± 4.50
	Non diabetics	27.17 ± 2.33*	27.17 ± 3.33
*P<0.05 vs respective non anaemic group			

HbA1C Variation According to The Degree of Anemia

Among controlled diabetics, 33 had mild anemia with mean HbA1C % of 7.8±0.50, 25 had moderate anemia with mean HbA1C % of 8.79±0.91 and 22 had severe anemia with mean HbA1C % of 10.2±1.12. Similarly, in non-diabetics, 30 had mild anemia with mean HbA1C% of 6.7±0.59%, 15 had moderate anemia with mean HbA1C % of 7.01±0.76 and 12 had severe anemia with mean HbA1C% of 8.05±0.81%. Statistical difference in the HbA1c level was observed when the degree of anaemia was moderate to severe (P<0.01) showing more HbA1c in diabetics than non-diabetics (Figure1).

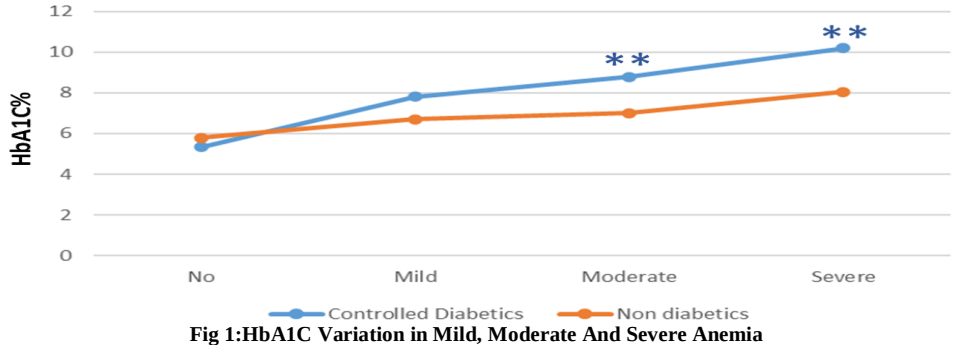

Fig 1:HbA1C Variation in Mild, Moderate And Severe Anemia

Discussion

Glycated hemoglobin is a predictor for the glycemic status when monitored over 8-12 weeks and risk of long-term complications in diabetics can be established. It also identifies individuals who are at high risk for developing diabetes[9].Several studies have demonstrated that anemia is almost twice common in diabetics than non-diabetics[10,11].This factors unrelated to diabetes like IDA affects the HbA1c levels.Increased HbA1C levels in IDA were explained by a) Quaternary structure of hemoglobin is altered leading to rapid glycation of globin chain;[12] b) Increase in the glycated fraction of hemoglobin due to decrease in total hemoglobin at a constant glucose level occurs because HbA1C is measured as a percentage of total Hemoglobin A[13].c) Increased HbA1C levels also due to the higher average age of circulating erythrocytes in IDA due to reduced red cell production[12].Anemia is a major risk factor for cardiovascular complications and diabetic retinopathy in diabetes. But only very few studies have investigated whether IDA alter the value of HbA1C till now inspite being widely used as a diagnostic tool for DM. The results of this study show that HbA1C levels are spuriously elevated in the presence of IDA independent of blood glucose concentration in

both controlled diabetics and non-diabetics. Our finding is similar to previousstudy reporting HbA1C level is elevated in diabetics with IDA than with iron-sufficient controls[14].We also analyzed HbA1c results in different degrees of anemia and found that HbA1C level increases as severityof anemia worsens. Our results are in accordance with the results of previous study[15].This study has few limitations. They are small sample size and the results were obtained from a single center and with a cross-sectional design, we couldn't follow up after iron therapy.

Conclusion

Iron deficiency anemia elevates HbA1c levels in diabetic individuals with controlled plasma glucose levelsin both diabetics and non-diabetics.IDA should be diagnosed and corrected before deciding on the regimens for controlling HbA1C in patients living with diabetes.

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