Original Research Article

A prospective study of effect of iron deficiency anemia on HbA1c levels in nondiabetics

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Abstract

Background: The traditional role of HbA1c analysis has been for assessing glycemic control in patients with diabetes. The results of semi-final studies demonstrated that early, intensive glycemic control could significantly reduce the risk of a range of diabetes related complications, and permitted the establishment of precise HbA1c target values for treatment goals.

Aim: This study was to determine the effect of IDA on HbA1c levels in non-diabetic patients, so as to consider IDA as an important factor which influenced the HbA1c levels, while monitoring the glycemic status of diabetics.

Materials and methods: Total number of 150 patients attending (both men and women) Medical department of PSIMS & RF, Chinaoutapalli and were enrolled after they provided written consent. This study was conducted over a period of two years (November 2014 to November 2016). **Results:** The mean HbA1c levels in anemic patients were 5.1%, 4.9% and 4.7% at baseline and after 1 and 2 months, respectively while that in the controls was 5.3%. The base line HbA1c levels were significantly lower in patients than controls, however, there was a significant decrease in HbA1c levels in patients after 2 months of treatment for iron deficiency anemia (P<0.01). The mean HbA1c level in patients after 2 months of treatment than in the controls (P<0.01). The mean absolute HbA1c level in patients at baseline and after 1 and 2 months were 0.49g/dL, 0.57g/dL and 0.66g/dL, respectively while in that controls was 0.72g/dL. A significant decrease in absolute HbA1c levels of patients and controls (P<0.01). Additionally there was a significant decrease in absolute HbA1c levels over the 2 month treatment period (P<0.01). However after 2 months of treatment, there was no significant difference between the

absolute HbA1c levels of patients and controls (P>0.05). A significant correlation between hemoglobin and HbA1c levels in patients at baseline (coefficient of correlation) was observed. It was observed that a significant correlation between hemoglobin and HbA1c levels in patients at baseline (coefficient of correlation= -0.1316; p<0.001; and after 1 month of treatment (coefficient of correlation= -0.391; p<0.001. However, there was no positive correlation between hemoglobin and HbA1c levels at the end of the 2-month treatment period (coefficient of correlation= -0.42; p >0.05.

Conclusion: This study concluded that before considering HbA1c as a diagnostic parameter and glycemic control in Diabetes, Iron Deficiency Anemia should be ruled out; as the severity of the anemia has effect on quantity of HbA1c.

Key words

Prospective study, Iron deficiency, Anemia, HbA1c, Non-diabetics.

Introduction

The traditional role of HbA1c analysis has been for assessing glycemic control in patients with diabetes. The results of semi-final studies [1, 2] demonstrated that early, intensive glycemic control could significantly reduce the risk of a range of diabetes related complications, and permitted the establishment of precise HbA1c target values for treatment goals [3]. More recently, there has been a move towards the use of HbA1c for the diagnosis of type 2 diabetes. The WHO and the ADA have both advocated the use of HbA1c for diagnosing type 2 diabetes, at a value of 6.5% (48 mmol/mol) [4]. Further to the recommendations of the WHO, the UK issued an expert position statement on the application of these recommendations in clinical practice in the UK [5]. One key factor thought to be a confounder in the use of HbA1c is an altered erythrocyte lifespan, in particular due to anemia. The WHO defines anemia in adults as 12 g/dl Hb in non-pregnant women and 13 g/dl in men [6]. It is widely purported that hemolytic anemia can lead to decreased HbA1c values due to reduced erythrocyte lifespan, and iron deficiency (IDA) may result in increased anemia HbA1c values due to an elongation of the erythrocyte lifespan. However, it is not known to what degree alterations in erythrocyte indices affect HbA1c values especially around the diagnostic cut point of 6.5% (48 mmol/mol) or the degree of abnormality severity required to

а significant change. With result in approximately 29% of non-pregnant women worldwide having anemia in 2011 [7], this translates to a significant number of people where the use of HbA1c for diagnosis of diabetes may be precluded. Since the publication of the recommendations, there has been a demand for clarity on this topic. The key questions asked are: At what level of anemia should I not use HbA1c for diagnosis? and Should I routinely screen patients for anemia when using HbA1c for diagnosis and if so, what test should I use? This systematic review aims to address the above questions by assessing the available evidence on the impact abnormalities of erythrocyte indices and anemia, on HbA1c levels around the diagnostic cut off point of 6.5% (48 mmol/mol). Glycated haemoglobin is produced by a ketoamine reaction between glucose and the N-terminal valine of both β -chains of the haemoglobin molecule. The major form of glycated haemoglobin is haemoglobin A1c (HbA1c) [8]. The measurement of glycated haemoglobin is the standard method for assessing the longterm glycaemic control. When plasma glucose is consistently elevated, the non-enzymatic glycation of haemoglobin increases; this alteration reflects the glycaemic history over the previous 2-3 months, since erythrocytes have an average lifespan of 120 days. The HbA1c fraction is abnormally elevated in patients with chronic hyperglycaemic diabetes

mellitus and it correlates positively with the metabolic control. According to the American Diabetes Association (ADA) guidelines, the value of HbA1c should be kept below 7% in all the diabetics. The values which are greater than 7% indicate an increased chance of progression to the diabetic complications, especially the microvascular ones. HbA1c is majorly affected by the blood glucose levels alone. However, certain studies have proven that the HbA1c levels are altered by various other coexisting factors, along with diabetes, especially that of iron deficiency anaemia, which is a major public health problem in developing countries like India. According to the World Health Organization (WHO), iron deficiency is the commonest of the deficiency diseases worldwide. One of the well-studied pathological ill effects of IDA in the biological system is the glycation of proteins. The nonenzymatic glycation of proteins has pronounced effects on the structure and the The function of proteins. pathological consequences of these alterations depend on the nature of the proteins which are involved, as well as on their functions and concentrations in specific tissue localizations. Thus, the objective of the present study was to determine whether the HbA1c levels were increased among the anaemic patients without diabetes. If so, the iron deficiency had to be corrected before any diagnostic or therapeutic decision was made based on the HbA1c level.

Materials and methods

Total number of 150 patients attending (both men and women) Medical department of PSIMS & RF, Chinaoutapalli and were enrolled after they provided written consent. This study was conducted over a period of two years (November 2014 to November 2016). A total of 75 non-diabetic patients diagnosed with iron deficiency anemia during the study period. Control group consisted of a total of 75 non diabetic, iron sufficient; age and BMI matched subjects were chosen as control group. **Inclusion criteria:** Patients who have been diagnosed to have iron deficiency, age group between 18 and 55 years and both the sex. Hb <12 g/dL in women and Hb <13 g/dL in men.

Exclusion criteria: History of acute blood loss, hemolytic anemia, hemoglobinopathies, kidney disease, pregnancy, established diabetes, impaired fasting glucose, or impaired glucose tolerance.

The investigator met and sought the study and control group with the help of staff and head of the Medicine department for the conduct of the study. Investigator visited the department (both inpatient and outpatients) for Iron Deficiency Anemia cases. All the patients screened during the period of two years were taken as denominator of the study. And for all the patients, meticulous records were maintained regarding clinical features, family history and by performing various investigations like Hemoglobin electrophoresis was performed to rule out hemoglobinopathies. Kidney function tests, including analysis of blood urea and serum creatinine levels, were conducted to determine baseline values by using a chemistry analyzer. All patients were asked to provide a detailed history and were subjected to a physical examination. The levels of hemoglobin, corpuscular hemoglobin mean (MCH), hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), platelet count, total leucocyte count (TLC), and differential leucocyte count (DLC) were measured by an automated counter (SYSMEX) at baseline and then again at 1 week, 1 month, and 2 months following treatment. Peripheral blood smear examinations to define the anemia type, as well as all other investigations, were conducted in our Pathology Department.

On the basis of hemoglobin levels, patients were categorized as having mild, moderate, or severe anemia: mild anemia (male patients, 12-12.9 g/dL and female patients, 11-11.9 g/dL); moderate anemia (male patients, 9-11.9 g/dL

and female patients, 8-10.9); and severe anemia (male patients, less than 9 g/dL and female patients, less than 8 g/dL). Those with predominantly microcytic indices (MCV<80 fL) and hypochromic indices (MCH<26 pg/cell) were considered to have iron deficiency anemia, which was then also confirmed by low serum ferritin levels (<20 ng/mL in female and <29 ng/mL in male patients). Serum ferritin levels were measured by an ELISA test kit (Biochek Inc., India). Serum ferritin was measured again at 1 and 2 months after treatment.

HbA1c levels (%) were measured at the time of enrolment and then again at 1 and 2 months following the start of treatment. HbA1c levels were measured using the Glycohemoglobin Reagent Kit (TECO Diagnostics, India) on the basis of the principle that glycohemoglobin (HbA1a, HbA1c) moves as a fast fraction and thus elutes first during cation exchange column chromatography. After separation of glycohemoglobin from nonglycosylated hemoglobin by cation exchange, the absorbance values for glycohemoglobin and total hemoglobin were measured at 415 nm. These values, along with values of standards provided in the kit, were used for calculating the percent glycohemoglobin and HbA1c according to instructions provided by the manufacturer. Absolute HbA1c levels were calculated from the measured HbA1c levels by using the following formula;

Absolute HbA1c (g/dL)= [Glycated hemoglobin (%)×Hemoglobin (g/dL)]/100;

All the laboratory parameters analysed for patients were analysed for the control group as well. However, in the case of the control group, the readings were recorded just once, at the time of enrolment. The exclusion criteria for the control group were the same as for patients. The data are presented as mean±SD for continuous variables. A Student's t-test was applied for comparison of group means. Pearson's coefficient of correlation was calculated to determine the correlation between 2 variables. *P* value of less than 0.05 was considered statistically significant.

Results

This study presented here has revealed results which are as follows. Overall 400 cases were screened for Iron Deficiency Anemia during the study period (two years) in medical department, out of which 75 cases have been diagnosed to have Iron Deficiency Anemia.

Mean age of the control participants was 29.98 years (range:-18-55 years) and the mean age of the patients was 31.64 years (range:- 18-48 years). Out of 75 patients in the control group, 36 (48%) were male and 39 (52%) were female, in the study group 33 (44%) were male and 42(56%) were females.

Study group 48%% (36) had out door occupation, 52% (39) had indoor occupation. BMI and Waist: Hip Ratio in control and study groups was observed to be similar (**Table – 1**).

<u>**Table - 1**</u>: Demographics distribution in the study.

Variable	Control	Study group			
	group	(n=75)			
	(n=75)				
Age distribution	Age range	Mean			
		age±SD			
Study group	18-48 years	31.64±8.52			
Control group	18-55 years	29.98±8.71			
Sex distribution					
Male	36	33			
Female	39	42			
Occupation					
Outdoor	33	36			
Indoor	42	39			
Mean BMI, waist hip ratio					
BMI	22.68±3.35	22.67±2.06			
Waist hip ratio	0.874	0.812			

Severe anemia was seen in 12% (9) of patients and moderate anemia was in 88% (66) patients. None of the patients in our study group had mild anemia. Majority of patients had moderate

anemia. Majority of patients complained of generalized weakness 82%. Patients had Mild Splenomegaly 48% (<2cms) on palpation of abdomen and 12% patients have ejection systolic murmur on auscultation (**Table – 2**).

<u>**Table - 2:**</u> Variables on examination.

Severity of anemia	No of	%	
	patients		
Severe	9	12%	
Moderate	66	88%	
Mild	0	0%	
Symptoms			
Generalized Weakness	62	82%	
Malaise	52	69%	
Lack of interest in work	43	57%	
Dyspnea	9	12%	
Pica	4	5.3%	
Presence of worms in stool	7	9.3%	
Clinical Signs			
Pallor	75	100%	
Nail changes	18	24%	
Koilonychias	4	5.3%	
Mild Splenomegaly	36	48%	
Ejection systolic murmurs	9	12%	

These data provided evidence that hemoglobin was indeed lower in anemic patients than in healthy controls, and the observed difference was statistically significant (p < 0.01). After 2 months of treatment for iron deficiency anemia, there was a significant increase in the hemoglobin levels of anemic patients (p < 0.01). However, the mean hemoglobin levels of patients after 2 months of treatment was still lower than that of the control group at baseline, and this difference was still statistically significant (p < 0.01). The mean baseline serum ferritin levels were significantly lower in patients than in controls (p < 0.01). However, at 2 months after treatment, the mean serum ferritin levels were significantly higher in patients than in the control group (p < 0.01). The mean baseline serum iron levels were significantly lower in patients than in controls (p < 0.01). However, at 2 months after treatment, the mean serum iron levels were significantly higher in

patients than in the control group (p<0.01). There was a significant decrease in HbA1c levels in patients after 2 months of treatment for iron deficiency anaemia (P<0.001). The mean HbA1c levels were significantly lower in patients after 2 months of treatment than in the controls (P<0.001). There was a significant decrease in absolute HbA1c levels over the 2 month treatment period (P<0.01). However after 2 months of treatment, there was no significant difference between the absolute HbA1c levels of patients and controls (P>0.05) as per **Table - 3**.

There was a significant decrease in absolute HbA1c levels over the 2 month treatment period (P<0.01). However after 2 months of treatment, there was no significant difference between the absolute HbA1c levels of patients and controls (P>0.05). A significant correlation between hemoglobin and HbA1c levels in patients at baseline (coefficient of correlation) was observed. It was observed that significant correlation between hemoglobin and HbA1c levels in patients at baseline (coefficient of correlation= -0.1316; p < 0.001; and after 1 treatment (coefficient month of of correlation= -0.391; p < 0.001. However, there was no positive correlation between hemoglobin and HbA1c levels at the end of the 2month treatment period (coefficient of correlation= -0.42; *p* >0.05 (**Table – 4**).

Discussion

Iron deficiency anemia is the most common form of anemia. HbA1c is glycated hemoglobin that can be used to assess the glycemic status of diabetic patient for the previous 3 months. Besides blood sugar, other conditions such as hemolytic anemias, hemoglobinopathies, acute and chronic blood loss, pregnancy, and uremia have been shown to affect HbA1c levels. Recently, researchers have become interested in studying HbA1c levels in more commonly encountered anemias like iron deficiency anemia. Iron deficiency is defined as decreased total iron body content. Iron

deficiency anemia occurs when iron deficiency is severe enough to diminish erythropoiesis and cause the development of anemia. Iron deficiency is the most prevalent single deficiency state on a worldwide basis. Iron deficiency anemia develops when body stores of iron drop too low to support normal red blood cell (RBC) production. Inadequate dietary iron, impaired iron absorption, bleeding, or loss of body iron in the urine may be the cause. Iron equilibrium in the body normally is regulated carefully to ensure that sufficient iron is absorbed in order to compensate for body losses of iron.

Variables	Control group (n=75)	Study group (n=75)	P value			
Mean Fe levels (g/dl)						
At baseline	234.44	41.8	<0.001			
1Month		171.03	<0.001			
2 Months		279.53	<0.001			
Mean Serum Iron levels (µg/dl)						
At baseline	120.27	59.32	< 0.001			
1 Month		79.46	< 0.001			
2 Months		110.54	< 0.05			
Mean HbA1c levels (%)						
At baseline	5.3	5.13	<0.001			
1Month		4.99	< 0.001			
2 Months		4.72	< 0.001			
Mean Absolute HbA1c levels (g/dl)						
At baseline	0.72	0.49	<0.01			
1Month		0.57	<0.01			
2 Months		0.70	>0.05			

Table - 3: Hematological Parameters.

<u>Table – 4</u>: Comparison of hemoglobin and HbA1c levels in patients and controls.

	Patients (at	Patients	Patients (at 2	Controls
	baseline)	(at 1	months)	
	Mean ± SD	month)	Mean ± SD	
Age	31.64±8.52	-	-	29.98±8.71
BMI	22.67±2.06	-	-	22.68±3.35
Hemoglobin (g/dL)	9.57±1.07	11.48±1.22	13.55±0.83	13.52±1.36
Serum Iron (g/dL)	59.32±19.51	79.46±19.89	110.54±28.29	120.27±35.77
Serum Ferritin (ng/dL)	41.8±20.46	171.03±27.47	279.53±65.33	234.44±58.44
TIBC (mcg/dL)	451.32±25.15	396.18±17.91	349.82±21.6	293.58±66.67
MCV (fL/red cell in adult)	70.56±8.21	77.95±7.4	84.66±6.6	88.07±6.38
MCH (pg / cell in adult)	24.87±3.76	28.07±3.87	32.79±4.2	29.02±4.01
MCHC (g/dL)	29.07±2.97	31.96±2.18	38.23±2.44	33.35±1.54
FBS (mg/dl)	88.58±11.53	88.82±10.84	91.18±9.27	86.88±8.7
PPBS (mg/dl)	111.2±12.01	112.42±10.76	111.68±9.68	119.26±17.57
HbA1c (%)	5.11±0.41	4.9±0.41	4.7±0.44	5.0±0.27
Absolute HbA1c (g/dl)	0.49±0.06	0.57±0.06	0.70±0.06	0.72±0.07

The present study was a prospective study done at PSIMS & RF, Chinaoutapalli among 75 patients from the Medical department who met the inclusion criteria over a period of two years from November 2014 to November 2016 who were diagnosed of Iron Deficiency Anemia. This study presented here has revealed results which are as follows. Overall 400 cases were screened for Iron Deficiency Anemia during the study period (two years) in medical department, out of which 75 cases have been diagnosed to have Iron Deficiency Anemia. In the present study, the mean hemoglobin levels of patients at baseline and after 1 and 2 months were 9.57 g/dL, 11.48 g/dL, and 12.58 g/dL, respectively. The mean hemoglobin level of the control group was 13.52 g/dL. These data provided evidence that hemoglobin was indeed lower in anemic patients than in healthy controls, and the observed difference was statistically significant (p < 0.01). After 2 months of treatment for iron deficiency anemia, there was a significant increase in the hemoglobin levels of anemic patients (p < 0.01). However, the mean hemoglobin levels of patients after 2 months of treatment was still lower than that of the control group at baseline, and this difference was still statistically significant (p < 0.01). The mean serum ferritin levels of anemic patients at baseline and after 1 and 2 months were 41.8 ng/mL, 171.03 ng/mL, and 279.53 ng/mL, respectively, and that of controls was 234.44 ng/mL. The mean baseline serum ferritin levels were significantly lower in patients than in controls (p < 0.01). However, at 2 months after treatment, the mean serum ferritin levels were significantly higher in patients than in the control group (p < 0.01). The mean serum iron levels of anemic patients at baseline and after 1 and 2 months were 59.32 µg/dL, 79.46 µg/dL, and 110.54 µg/dL, respectively, and that of controls was 120.27 µg/dL.

The mean baseline serum iron levels were significantly lower in patients than in controls (p<0.01). However, at 2 months after treatment, the mean serum iron levels were significantly

higher in patients than in the control group (p < 0.01). The mean HbA1c levels in anaemic patients were 5.1%, 4.9% and 4.7% at baseline and after 1 and 2 months, respectively while that in the controls was 5.3%. The base line HbA1c levels were significantly lower in patients than controls, however, there was a significant decrease in HbA1c levels in patients after 2 months of treatment for iron deficiency anaemia (P<0.001). The mean HbA1c levels were significantly lower in patients after 2 months of treatment than in the controls (P<0.001). The mean absolute HbA1c level in patients at baseline and after 1 and 2 months were 0.49g/dL, 0.57g/dL and 0.70 g/dL, respectively while in that controls was 0.72g/dL. A significant difference was observed between the baseline values of patients and controls (P<0.01). Additionally there was a significant decrease in absolute HbA1c levels over the 2 month treatment period (P<0.01). However after 2 months of treatment, there was no significant difference between the absolute HbA1c levels of patients and controls (P>0.05). All studies were reviewed for data on erythrocyte indices and markers of iron status as these provide further insight into which adjunct tests may support the use of HbA1c for diagnosis. Combinations of the following indices were measured: Hb, packed cell volume (PCV), MCV, MCH, MCH concentration (MCHC), ferritin, transferrin saturation (TSAT), reticulocytes, redcelldistribution width (RDW) and erythrocyte protoporphyrin. Some studies only used the values to identify or exclude patients with iron deficiency or anaemia whereas others correlated changes in erythrocyte indices with changes in HbA1c value. Of the studies that focused on IDA, three studies compared values pre and post treatment with iron replacement and two compared values in patients with anemia against control participants. All studies demonstrated an increase in MCV and MCH with treatment or higher levels in controls compared with anaemia patients. Two studies [9, 10] demonstrated an inverse correlation between

HbA1c and Hb, MCV and MCH levels. Overall, the data indicate that iron deficiency, demonstrated by low Hb, low MCV and low MCH, is associated with increased HbA1c levels both with and without overt anaemia. In addition, normal MCV and MCH with low Hb would not be associated with increased HbA1c levels but rather a decrease in values. Ferritin was measured in nine studies. Of these, most showed an increase in ferritin levels. Post treatment for anaemia and also showed that ferritin levels were lower in iron deficient participants compared with controls. Similar studies were conducted by Juliana Frezza Silva, et al. [11] (2015) conducted a study on Effect of iron deficiency anemia on HbA1c levels is dependent on the degree of anemia with 122 patients. They concluded that IDA affects HbA1c results and this effect is dependent on anemia degree. These upward changes are statistically significant but they may not clinically relevant when the overall variability of the HbA1c test is considered.

The presence of slight anemia is likely to have a minor effect on HbA1c levels favouring its use to diagnose diabetes in patients with mild anemia. SM Attard, et al. [12] (2015) conducted an analysis from the China Health and Nutrition Survey, longitudinal a population based study. This analysis included 7308 adults. And they found potential misclassification of diabetes using HbA1c in areas of endemic Iron Deficiency anemia. Estimating diabetes prevalence using HbA1c may result in under diagnosis in women with ID and over diagnosis in men with anemia. Nitin S, et al. [13] (2010) studied on HbA1c and factors other than diabetes mellitus affecting it. They concluded that HbA1c is not affected by blood sugar levels alone, and there are various confounding factors when measuring HbA1c. It is hence prudent to rule out all other confounding before factors making a therapeutic decision based on the HbA1c levels. Also, the effects of iron deficiency and Vitamin B12 deficiency on HbA1c should be studied in

greater detail. Nitin Sinha, et al. [14] (2012) conducted a study on Effect of Iron deficiency anemia on Haemoglobin A1C Levels in 75 patients. In contrast to the observations of previous studies, they concuded that HbA1c levels and absolute HbA1c levels increased with treatment of iron deficiency anemia. This could be attributable to nutritional deficiency and/ or certain unknown variables. Further studies to confirm and elucidate the roles of these factors are warranted. Tae Hyuk Kim, et al. [15] (2013) studied on Diagnosing Diabetes with Haemoglobin A1c: Current debates and considerations for anaemic patients. They concluded that HbA1c is a convenient new measure for diagnosing diabetes. Clinicians should determine the suitability of HbA1c for diagnostic purposes and their specific setting with consideration of the various epidemiologic factors and conditions that can affect its measurement.

Bala Subramanian Shanthi, et al. [16] (2013) conducted a study on Effect of Iron Deficiency on Glycation of Haemoglobin in Non diabetics in 75 patients. They concluded that HbA1c is not affected by the blood sugar levels alone, and there are various confounding factors when HbA1c is measured, especially that of iron deficiency, which is the commonest of the deficiency diseases worldwide. It is hence prudent to rule out IDA before making a therapeutic decision, based on the HbA1c levels. Alap L. Christy, et al. (2014) conducted a study on Influence of Iron deficiency Anemia on Hemoglobin A1c levels in Diabetic individuals with controlled Plasma Glucose Levels and they found a positive correlation between iron deficiency anemia and increased especially in the controlled A1c levels, diabetic women and individuals having FPG between 100-126 mg /dl. Hence, before altering the treatment regimen for diabetic patient, presence of iron deficiency anemia should be considered. Vishal Kalasker, et al. [17] (2014) conducted a study on Effect of Iron deficiency Anemia on Glycosylated Hemoglobin levels in Non Diabetic Indian

Adults. They concluded that the trend for HbA1c to increase with iron deficiency does not appear to require screening for iron deficiency in ascertaining the reliability of HbA1c in the diagnosis of diabetes/ prediabetes. Lynn Bry, et al. [18] (2001) conducted a review of the literature describing the effects of variant Hemoglobins on gHb assay methods commonly used in clinical laboratories. A variety of patient and laboratory related factors can adversely affect the measurement of gHb in patients harbouring Hb variants or derivatives. Identification of the variant or derivative Hb before or during testing may allow accurate measurement of gHb by the selection of a method unaffected by the given variant or derivative. However, laboratories should make available alternative, non Hb based methods for assessing long term glycemic control in individuals with HbCC, HbSS or HbSC disease, or with other underlying disorders where the concentration of gHb does not accurately reflect long term glycemic control.

Conclusion

IDA affects HbA1c results and this effect is dependent on anemia degree. These upward changes are statistically significant but they may be not clinically relevant when the overall variability of the HbA1c test is considered. The presence of slight anemia is likely to have a minor effect on HbA1c levels favoring its use to diagnose diabetes in with mild anemia. This study patients concluded that before considering HbA1c as a diagnostic parameter and glycemic control in Diabetes, Iron Deficiency Anemia should be ruled out; as the severity of the anemia has effect on quantity of HbA1c.

References

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. NEJM, 1993; 329: 977–986.

- UK Prospective Diabetes Study (UKPDS) Group. Intensive bloodglucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet, 1998; 352: 837– 853.
- 3. Inzucchi SE, Bergenstal RM, Buse JB. et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, 2012; 35: 1364-1379.
- 4. World Health Organization (2011) Use of glycated hemoglobin (HbA1c) in the diagnosis of diabetes mellitus (abbreviated report of a WHO consultation).
- American Diabetes Association (2013) Standards of medical care in diabetes– 2013. Diabetes Care, 2013; 36(Suppl 1): S11–S66.
- John WG. Use of HbA1c in the diagnosis of diabetes mellitus in the UK. The implementation of World Health Organization guidance 2011. Diabet Med., 2012; 29: 1350–1357.
- 7. United Nations Children's Fund, United Nations University, World Health Organization (2001)Iron deficiency assessment, anaemia prevention, and control: a guide for programme managers. Available from www.who.int/nutrition/publications/en/i da assessment prevention control. pdf
- 8. Stevens GA, Finucane MM, De-Regil LM, et al. (2013) Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women

for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Health, 2013; 1: e16–25.

- Hardikar PS, Joshi SM, Bhat DS, et al. Spuriously high prevalence of prediabetes diagnosed by HbA(1c) in young Indians part-ly explained by hematological factors and iron deficiency anemia. Diabetes Care, 2012; 35: 797–802.
- Koga M, Morita S, Saito H, Mukai M, Kasayama S. Association of erythrocyte indices with glycated haemoglobin in premenopausal women. Diabet Med., 2007 Aug; 24(8): 843-847.
- 11. J.F. Silva, et al. Effect of iron deficiency anaemia on HbA1c levels is dependent on the degree of anaemia, Clin Biochem., 2015. http://dx.doi.org/10.1016/j.clinbiochem. 2015.09.004.
- Samantha M. Attard, Annie Green Howard, Amy H. Herring, Bing Zhang, Shuf a Du, Allison E. Aiello, Barry M. Popkin, Penny Gordon-Larsen. Differential associations of urbanicity and income with physical activity in adults in urbanizing China: findings from the population based China Health and Nutrion Survey, 1991-2009. International Journal of Behavioral

Nutrition and Physical Activity, 2015; 12: 152.

- 13. Nitin S. HbA1c and factors other than diabetes mellitus affecting it. Singapore Med J., 2010 Aug; 51(8): 616-22.
- 14. Sinha N, Mishra TK, Sinha T, Gupta N. Effect of iron deficiency anemia on hemoglobin A1c levels. Ann Lab Med., 2012 Jan; 32(1): 17–22.
- 15. Kim TH, Choi SH. Diagnosing Diabetes with Hemoglobin A1c: Current Debates and Considerations for Anemic Patients. Diabetes & Metabolism Journal, 2013; 37(5): 340-342.
- Shanthi B, Revathy C, Manjula Devi AJ, Subhashree. Effect of Iron Deficiency on Glycation of Haemoglobin in Nondiabetics. Journal of Clinical and Dignostic Research: JCDR, 2013; 7(1): 15-17.
- Vishal Kalasker, Sudhamadhuri, M V Kodliwadmath, Harish Bhat. Effect of Iron Deficiency Anemia on Glycosylated Hemoglobin Levels in Non Diabetic Indian Adults. Int J Med Health Sci., Jan 2014; 3(1): 40-43.
- Bry L, Chen PC, Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin. Clin Chem., 2001; 47(2): 153-63.