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To determine the effects of iron and or B12 deficiency anemia on HBa1C levels in non-diabetics.

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Abstract

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. DM is one of the leading causes of end-stage renal disease (ESRD), non-traumatic lower extremity amputations, and adult blindness. **Material and Methods:** Study–SAIMS Hospital-Indore Sample size -70 patients. **Inclusion criteria:** Non-diabetics with iron and or B12 deficiency anemia. Age>18 years and <70 years, both males and females. **Result:** We analyzed 70 anemic patients who were non- diabetics. They were divided into iron deficiency, B12 deficiency and dual deficiency groups. Each group was analyzed for pre and post treatment HbA1c variation. Each group is further divided into two sub-groups based on increase or decrease in HbA1c levels with treatment of anemia. Significance was assessed (both clinical and statistical) in each subgroup group and group as a whole. Out of total 70 patients, 36 subjects had iron deficiency anemia, 22 subjects had B-12 deficiency anemia and 12 subjects had dual deficiency anemia. Of the 36 participants in iron deficiency anemia group 23 (63%) were females and 13(37%) were males. **Conclusion:** As many as 40% subjects in our study had HbA1c levels in pre- diabetic range (5.7-6.4%) before treatment of anaemia.

Keywords: Iron and or B12 deficiency anemia on HBa1C levels in non-diabetics.

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. DM is one of the leading causes of end-stage renal disease (ESRD), non-traumatic lower extremity amputations, and adult blindness. The prevalence of type 2 DM is raising rapidly in India, presumably because of increasing obesity, reduced activity levels and industrialization. Hence diabetes will be a major health factor in years to come [(1)]

While glucose remains the major determining factor of HbA1c(2) other conditions like hemolytic anemia(3), hemoglobinopathies (4) , acute and chronic blood loss(5,6), pregnancy(8) uremia, iron deficiency anemias and vitamin B 12 deficiency anemia have also been shown to affect HbA1c levels. Among these disorders nutritional anemia is one of the highest prevalent disease in Asian countries like India (8).

Hence we undertook this study to know the relationship of iron or B12 deficiency anemia and HbA1c so as to determine its value in diagnosing patients with anemia and diabetes. HbA1c is widely used as an important marker of glycemic control, and it is of utter importance to exclude factors which could spuriously elevate its levels. Hence, we conducted a study in iron-deficient individuals with FPG levels below 126 mg/dl to assess whether anemia has any effect on A1C levels, and anemia can be considered before making any therapeutic decisions based solely on HbA1c levels.

Aim

To determine the effects of Iron and or B12 deficiency anemia on HbA1c levels in non-diabetics.

Background

Glycated hemoglobin (mainly HbA1c) were discovered in the late 1960s.Implementation of these glycated components in the field of medicine began in late 1970s mainly for the follow-up of patients on anti- diabetic medications which was indeed a milestone in Diabetes.

Allen et al. demonstrated the heterogeneity of hemoglobin(Hb) for the first time in 1958 by utilizing the cation exchange chromatography[16] Other groups confirmed and established the identity between Hb fractions separated by chromatography and by electrophoresis.[17,18]

Almost all of these experiments in the beginning revealed the unexpected elution of minor Hb peaks, the so called —fast hemoglobins, or HbA_1, before the major HbA fraction which was later called as HbA_o. These Hb peaks in the chromatography were designed as HbA_{1a} to HbA_{1e} on the basis of their elution order[9] as a result of differences in physico-chemical properties. These Hb fractions resulted from the binding of various adducts to HbA, allowed their separation based on the changes in physico-chemical properties. In the late 1970s, it was shown that various sugars or sugar phosphates formed these minor hemoglobins, which were incidentally glycated hemoglobins.

Also very few follow up studies are mentioned in the literature which actually describe the variation of HbA1c after treating anemia. Still the controversies exist whether or not the HbA1c raises in anemic states and the cause of it. So we have taken up this study to look into the effect of iron and or B12 deficient anemia on HbA1c levels in non-diabetic Indian population.

Materials and Methods

Study – SAIMS Hospital-Indore

Sample size - 70 patients

Inclusion criteria: Non-diabetics with iron and or B12 deficiency anemia.Age>18 years and <70 years, both males and females.

Exclusion criteria: Diabetics, Anemia of chronic disease/malignancy associated, Hemolytic anemia, Pregnant women, Patients with Chronic alcohol intake, Hb<5gms/dl

Statistical analysis: Data was entered in SPSS package. For comparing pre and post therapy glyco-hb levels, we used Paired t test. Mean hemoglobin and mean HbA1c were calculated in each type of anemia. Standard deviation was calculated and p value obtained using the test (with upper and lower limits and degree of freedom). p value <0.01 was considered as statistically significant change. Statistical analysis was done using SPSS-16.

Results

We analyzed 70 anemic patients who were non-diabetics. They were divided into iron deficiency, B12 deficiency and dual deficiency groups. Each group was analyzed for pre and post treatment HbA1c variation. Each group is further divided into two sub-groups based on increase or decrease in HbA1c levels with treatment of anemia. Significance was assessed (both clinical and statistical) in each subgroup group and group as a whole. Out of total 70 patients, 36 subjects had iron deficiency anemia, 22 subjects had B-12 deficiency anemia and 12 subjects had dual deficiency anemia. Of the 36 participants in iron deficiency anemia group 23 (63%) were females and 13(37%) were males.B12 deficiency anemia had 1:1 ratio of males and females. Dual deficiency anemia population had 67% males and 33% female participants. Both iron deficiency group and Dual deficiency anemia group had a female preponderance.

Table: 1. Iron deficiency anemia-change with treatment

Decrease in HbA1C levels(sub group 1,n=25)			Increase in HbA1C levels (group 2,n=11)		
	Before treatment	After treatment		Before treatment	After treatment
Mean Hb	9.11	12.34	Mean Hb	9.58	12.59
% Increase in Hb	26%			23.91%	
Mean HbA1c	5.76	5.12	Mean HbA1c	5.12	5.79
% Decrease in HbA1c	11.1%		% increase in HbA1c	11.57%	

The percentage increase in Hemoglobin was 26% and 23.91% in sub-group 1 and sub-group 2 respectively. The percentage decrease in HbA1c in sub-group 1 was 11.1% and percentage increase in HbA1c in sub-group 2 was 11.57%. (study group showing increase in HbA1c with treatment of anemia).

The patients in this subgroup had Hb levels ranging from 6 to 10.5 with a mean of 9.58 before treatment and the final Hb levels ranging from 11.3 to 13.4 with a mean of 12.59.The initial HbA1c levels in this group ranged from 4.7 to 5.7 with a mean of 5.12 and the final HbA1c levels after treatment ranged from 5.2 to 6.3 with a mean of 5.79.

The mean increase in the HbA1c in this sub-group is also clinically significant.

So when we analyzed this data statistically with mean difference of 0.68, standard deviation of 0.197, we found that the mean variation of HbA1c post treatment in this group is significant ($p<0.01$).

These patients had Hb levels ranging from 6.8 to 10.8 with a mean of 9.12 before treatment and the final Hb levels ranging from 10.8 to 13.5 with a mean of 12.2.The initial HbA1c levels in this group ranged from 5.2 to 6.1 with a mean of 5.71 and the final HbA1c levels after treatment ranged from 4.3 to 6 with a mean of 5.03. This subgroup had only 3 subjects of which all were males.

All the three patients showed a clinically significant increase in HbA1c with a mean increase of 0.65.

Statistical analysis revealed that the change of HbA1c was not significant (p=0.019).

Table: 2. Number of patients with HbA1c levels in pre-diabetic range.

	Number of patients whose initial HbA1c was in pre-diabetic range
Iron deficiency anemia	**13**
B12 deficiency anemia	**10**
Dual deficiency anemia	**4**

Discussion

With the dramatic increase in worldwide prevalence of diabetes mellitus over the past two decades and in view of the projection by International Diabetes Federation that 438 million individuals will have diabetes by the year 2030 diabetes mellitus is one of the major health risk concerns (1) in world health. The prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries are becoming more industrialized, and due to the aging of the population(1).

Anemia and HbA1c: Hemoglobin A1c which has been included as a diagnostic tool for the diagnosis of diabetes in American Diabetes Association criteria 2010, will now play an important role in diagnosis and treatment of diabetes mellitus. However several factors (10) other than blood sugar which can alter the HbA1c levels like blood loss, hemolytic anemia, blood urea, pregnancy, Iron deficiency anemia and vitamin B 12 deficiency anemias must be taken into account.

Sex distribution: Out of total 70 subjects in our study, 38 were female and 32 were male individuals. The number of females in Iron deficiency anemia were 23 which is 32.8% of total and 63.9% of iron deficient individuals. In the study conducted by Nitin Sinha and et.al (98), out of 50 individuals, 34 (68%) were female and 16 (32%) were male. All the other studies conducted by Balasubramanian.S (99), Earl.S (105) etc also had female population as the majority of study group. This emphasizes the burden of iron deficiency in female population of developing countries like India(91). This may be due to fact that nutritional deficiency, along with the menstrual blood loss, pregnancy state etc. may contribute to the worsening iron deficiency state.

Age distribution: In our study the mean age of all the groups together is 50.6 years, of which dual deficiency anaemia group had the highest mean age (58years).

Effect of iron deficiency anemia on HbA1c levels: One of the earliest path breaking studies which put forward the interactions between anemia and HbA1c was by (11). They observed that HbA1c levels were significantly higher in iron deficiency anemia patients and decreased after treatment with iron. The mechanisms leading to increased glycated HbA1 levels were not clear. It was proposed that, in iron deficiency, the quaternary structure of the hemoglobin molecule was altered, and that glycation of the globin chain occurred more readily in the relative absence of iron. Most of the subjects in our study (n=50) had a similar fall in HbA1c with the treatment of anemia.

This study has a significant relevance because anemia is very highly prevalent in a tropical country like India. IDA and B12 deficiency anemia, being common variables, influence the HbA1c levels when they are estimated by the most commonly employed methods like immunoturbidometry and so, the anemia must be corrected before making any diagnostic or therapeutic decision based on the HbA1c levels. HbA1c is commonly used to assess the long-term blood glucose control in the patients with diabetes mellitus, because the HbA1c value has been shown to predict the risk for the development of many of the chronic complications in diabetes.

Conclusion

As many as 40% subjects in our study had HbA1c levels in pre- diabetic range (5.7-6.4%) before treatment of anaemia. HbA1c levels of majority of subjects in the study had a significant reduction on treatment of anaemia with appropriate therapy. This significant change in HbA1c in anaemia patients might result in misclassification of diabetic status of these individuals. Hence anaemia should be treated before using HbA1c as a diagnostic tool in normal populations as well as prognostic tool in diabetic patients

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