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THE EFFECT OF IRON DEFICIENCY ANEMIA ON GLYCATED HEMOGLOBIN (HBA1C) IN NON DIABETIC ADULTS

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Abstract
Background: Iron deficiency anemia is the most common form of anemia in India. Hemoglobin A1c (HbA1c) is used in diabetic patients as an index of glycemic control reflecting glucose levels of the previous 3 months. Like blood sugar levels, HbA1c levels are also affected by the presence of variant hemoglobins, hemolytic anemias, nutritional anemias, uremia, pregnancy, and acute blood loss. Previous studies suggest that iron deficiency anemia (IDA) affects the levels of HbA1c.
Methods: A prospective observational study on 50 iron deficiency patient cases and 50 healthy control. Exclusion and inclusion criteria were used to recruit cases from the wards and OPDs of the hospital. Appropriate descriptive statistics was used to analyse the data.
Results: The HbA1C was significantly higher in the iron deficiency patients as compare to the control (5.88 ± 0.41 vs 5.03 ± 0.17, respectively, $P < .05$).
Conclusion: Our results showed that iron deficiency was associated with higher proportions of HbA1c, which could cause problems in the diagnosis of uncontrolled diabetes mellitus in iron-deficient patients.
Keywords: Non-Diabetic Patient, Glycosylated Haemoglobin, Iron Deficiency Anaemia.

Introduction:

HbA1c is used as the gold standard for monitoring glycaemic control and used as a foresee of diabetic complications. [1] Throughout the circulatory life of the red blood cell, HbA1c is formed continuously by adjoining of glucose to the Nterminal of the haemoglobin beta chain.

This process is non-enzymatic and reflects the average exposure of haemoglobin to glucose over a period of nearly 70 - 90 days. HbA1c has been defined as the fast fraction haemoglobin (HbA1a, A1c), which elute first during column chromatography with cation-exchange resin. HbA1c levels are not influenced by only blood glucose levels. They are also altered in hemolytic anemias ,hemoglobinopathies , acute and chronic blood loss , pregnancy , and uremia , Vitamin B12, folate, and iron deficiency anemias have also been shown to affect HbA1c levels[2].The two known factors which can modulate the glycation of proteins are the prevailing concentration of glucose and the half life of the protein[3]. But evidences in the literature have documented increased glycated protein levels in some nondiabetic pathological states, like iron deficiency anemia. Some authors have also found that on supplementation with iron therapy, there was a significant decrease in the levels of glycated haemoglobin[4]. Evidence has accumulated, which supports the hypothesis that the glycation reaction, apart from the traditional chronic hyperglycaemia, can be modulated by the iron status of the patient. If the degree of glycation of other proteins in anemic patients was similar to that of the glycated haemoglobin, it would have important clinical implications. Some studies show that HbA1c levels are increased in iron deficiency anemia and attempted to explain on the basis of both modifications to the structure of haemoglobin and level of HbA1c in old and new red blood cells[5]. Some Study showed that HbA1c levels were higher in patients of iron deficiency anemia and decreased significantly upon treatment with iron[6].With this background, the objective of the present study was to study the effect of iron deficiency anemia on glycated hemoglobin (HbA1c) in non diabetic Indian subjects. 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

Type of Study- Prospective observational study

The iron deficiency anaemic patients were recruited on their haemoglobin levels (Hb < 12 in non-pregnant female and 13 in male), ferritin levels (< 9 ng/ mL for women, < 15 ng/ mL for men) and on their peripheral blood smears which indicate iron deficiency anaemia.

The levels of haemoglobin, mean corpuscular haemoglobin (MCH), haematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), platelet count, total leucocyte count (TLC) and differential leucocyte count (DLC) were measured by an automated analyser.

On the basis of haemoglobin level patients were categorised as having mild, moderate or severe anaemia. Mild anaemia (male patients 12 - 12.9 gm/ dL and female patients 11 - 11.9 gm/ dL).

Moderate anaemia (male patients 9 - 11.9 gm/ dL and female patients 8 - 10.9 gm/ dL) and severe anaemia (male patients < 9 gm/ dL and female patients < 8 gm/ dL). Those with predominantly microcytic indices (MCV < 80 fL), hypochromic indices (MCH < 26 pg/ cell) were considered to have iron deficiency anaemia.

Normal HbA1c in nondiabetic individuals is < 5.6%.

Inclusion Criteria

1. Patient without diabetes.

2. Patient belonging to rural and urban area.

3. > 18 yrs. of age.

4. Giving consent for study.

Exclusion Criteria

Patients with history of acute or chronic blood loss, haemolytic anaemia, haemoglobinopathies, kidney diseases, diabetics, pregnancy, chronic alcohol ingestion and impaired glucose tolerance are excluded.

The blood specimens were drawn after an 8-hourly fasting period. A Sysmex automated haematology analyser (MINDRAY) was used for the whole blood counts [haemoglobin (Hb), mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH)]. The serum ferritin levels were measured by using a Diatek kit in a Labowind semiautomated analyser and the peripheral blood smears were examined in all the patients. The HbA1c levels were determined by turbidimetric immunoinhibition.

RESULTS

The present study was conducted among 50 cases having Iron deficiency anemia and 50 apparently healthy controls without iron deficiency anemia. All cases and controls are non diabetic.

Table 1: Demographic variable

Variable	Case group	Control group	p-value
Age (Yrs)	48.23±4.6	47.23±4.92	>0.05
Male : Female	12:38	13:37	>0.05

There were no significant differences between the two groups with regard to age and gender.

Table 2: Comparison of blood parameter

Variable	Case group	Control group	p-value
HB (Gm/dl)	6.01±1.9	12.4±1.2	<0.001
S. Ferritin (ng/mL)	8.71±1.68	90.21±12.54	<0.001
HbA1C	5.88±0.41	5.03±0.17	<0.05

The HbA1C was significantly higher in the iron deficiency patients as compare to the control (5.88 ± 0.41 vs 5.03 ± 0.17, respectively, *P* < .05).

DISCUSSION

Our results suggested that IDA was associated with higher concentrations of HbA1c.The mean HbA1c of cases was 5.88% while it was 5.03% in healthy control. Application of statistical test shows that the difference of HbA1c between case and control group was statistically significant.

In the study conducted by Vishal Kalasker et al , the mean HbA1c of cases was 5.91±0.47 % while it was 6.54±0.39 % in healthy control. Application of statistical test shows that the difference of HbA1c between case and control group was statistically significant indicating statistically higher HbA1c in control group. [7]

In the study conducted by Balasubramanian Shanthi et al , the mean HbA1c of cases was 7.6 ± 0.5 % while it was 5.5 ± 0.8 % in healthy control. Application of statistical test shows that the difference of HbA1c between case and control group was statistically significant indicating statistically higher HbA1c in cases group. [8]

In the study conducted by Alap L. Christy et al , the mean HbA1c of cases was 6.87 ± 1.4% while it was 5.65 ± 0.69% in healthy control. Application of statistical test shows that the difference of HbA1c

between case and control group was statistically significant indicating statistically higher HbA1c in cases group.[8]

CONCLUSION

Our results showed that iron deficiency was associated with higher proportions of HbA1c, which could cause problems in the diagnosis of uncontrolled diabetes mellitus in iron-deficient patients.

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