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Elevation of Glycated Hemoglobin (Hba1c) In Non-Diabetic Individuals, By Effect of Microcytic Hypochromic Anemia

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ABSTRACT

Background: The affecting the erythrocyte normality will affect the concentration of HbA1c in the blood. Although many forms of anemia are associated with lowering of HbA1c, iron deficiency tends to increase HbA1c.

Objective: The aim of this study is to analyze the effects of iron deficiency anemia on HbA1c levels.

Materials and Methods: The study included 120 cases of non-diabetic patients who were diagnosed as having iron deficiency anemia and comparison to 180 cases of healthy individuals. Estimation the HbA1c and absolute levels of HbA1c, for all cases in this study after confirmation that all cases have normal level of fasting blood sugar and don't have any history for diabetes. The data of the individuals attending Shree Krishna Hospital Karamsad, Anand between August 2015 to July 2017 was collected. The study was approved by an institutional ethics committee.

Results: The mean HbA1c level (6.5 ± 0.5%) in the iron deficiency anemia was higher than that the mean HbA1c level (5.4 ± 0.7%) in the control group. There were no significant differences in the levels of fasting and postprandial glucose between the IDA and the control groups ($p > 0.05$).

Conclusion: The microcytic hypochromic anaemia has an effect on the increased level of glycosylated hemoglobin (HbA1c), especially iron deficiency anemia. That the necessary intervention can be done by administration of iron. This helps to avoid misdiagnosis of diabetics, based on elevated the level of HBA1C, in patients with iron deficiency anemia.

Keywords: Iron deficiency anemia, ferritin, Hemoglobin A1c and non-diabetic patients.

I. INTRODUCTION

Microcytic hypochromic anaemia is highly prevalent in a tropical country like India. Iron deficiency is the most common cause of microcytic and hypochromic anemia(1), The operational definition of microcytic hypochromic anaemia is a decrease in hemoglobin (< 11 gm/dl), MCV (< 80 fl), MCH (< 27 pg)(2). HbA1C is widely used for the assessment of glycemic status of the diabetic patients and the American Diabetes Association (ADA) recommended its use for diagnosing diabetes .The microcytic hypochromic anemia is important factor which influences the HbA1c levels. There have been a paucity of studies showing that iron deficiency may be associated with elevated levels of HbA1c,(3) which in turn can cause problems in the diagnosis of diabetes mellitus in iron-deficient patients. Iron deficiency anemia is the most common form of anemia in India(4). previous studies by Sluiter et al. (5), Brooks et al. (6), and Mitchell et al. (7) detected the relationship between iron deficiency anemia and HbA1c levels and tried to explain the alteration in HbA1c levels in iron deficiency anemia on the basis of both modifications to the structure of

hemoglobin and levels of HbA1c in all stage of age red blood cells. Later, Heyningen et al. (8)and Hansen et al. (9)reported that there were no differences between the HbA1c levels of anemic patients and controls. These observations were strikingly different from those of previous studies.

Therefore, both because of this contradiction in corresponding evidence and since no such studies have been conducted on the Gujarati population, we were prompted to conduct the current study to investigate the effects of iron deficiency anemia on HbA1c levels in Indian patients.

II. METHODOLOGY

The data of 300 participants attending Shree Krishna hospital Karamsad, Anand between August 2015 to July 2017 was collected and classified into groups. Group 1, non-diabetic who were diagnosed as having iron deficiency anemia. The diagnosis confirms by hemoglobin, Hb index and ferritin levels and peripheral blood. It was made sure that the patients were nondiabetic (Fasting Plasma Glucose <100 mg/dl). Group 2, 180 subjects of healthy individuals (non-anemic - nondiabetic). Patients with a history of acute blood loss, hemolytic anemia, hemoglobinopathies, kidney disease, pregnancy, confirm diabetes were excluded. Those with no history of glucose intolerance, but with fasting blood glucose levels greater than 100 mg/dL at the time of enrollment were also excluded. The case control study was approved by the Human Research Ethics Committee (HREC) in Pramukhswami Medical College (PSMC), Karamsad.

Biochemical testing included Plasma Fasting Blood Glucose, Random Blood Glucose, Past Prandial Blood Glucose and Glycated hemoglobin HbA1c % were used Automated Chemistry Analyzer (Siemens-Dimension-RXL-and X pand). Serum ferritin Analysis was done by using (ADVIA Centaur® XP Immunoassay analyser) Method: Immunometric Assay (sandwich principle). Glycated Hemoglobin Hb (HbA1c) was determined by Turbidimetric Inhibition Immunoassay Method. 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.

Statistical analysis:

The results were presented as sample size (n), mean ± standard deviation (SD). The statistical significance between the groups was analyzed by studying t-test and compare between results in various groups in considering P-value < 0.05 as significant. All statistical significances were done using The Statistical Packages for Social Science (SPSS 20). Endnote x7 program was used for references management.

III. RESULTS

In 300 cases in this study, distribution into 120 cases of iron deficiency anemia with fasting and postprandial blood sugar were normal and 180 healthy individuals as a control.

The decrease of serum ferritin levels (index of the iron deficiency status) and the hypochromic microcytic picture of the peripheral blood smears confirmed the diagnosis of the iron deficient anemia.

In our study of 300 participants, we found 139 males out of a total of 300 cases, 91 of the healthy individuals while 48 of them have iron deficiency anemia. In total 161 females, 89 of the healthy individuals while 72 of them have iron deficiency anemia. (See table 1).

We found the HbA1c levels were significantly increased in the iron deficiency anemia patients as compared to those in the controls. The mean HbA1c (6.5 ± 0.5%) level in the iron deficiency anemia was

higher than that the mean HbA1c (5.4 ± 0.7%) level in the control group (P-value = 0.001). There were no significant differences in the levels of fasting and postprandial glucose between the IDA and the control groups (p > 0.05). (See table 2).

Table 1: Gender distribution of the study population

Groups	Male (count & %)	Female (count %)	Total (count & %)
IDA group (n=120)	48 (60.0%)	72 (40.0%)	120 (40.0%)
Control group (n=180)	91 (49.4%)	89 (50.6%)	180 (60.0%)
Total	139 (53.7%)	161 (46.3%)	300 (100%)

Table 2: comparison between the mean levels of HbA1c in cases and control.

Parameters	Case (IDA)	Control (Healthy)
Fasting glucose, mg/dl	93.6±9.4	91.7±10.2
Postprandial glucose, mg/d	108.6±5.8	104.9±5.7
HbA1c, %	6.5 ± 0.5%	5.4 ± 0.7%
Absolute HbA1c	0.63	0.734

In this table, the both fasting and the postprandial blood sugar levels confirmed the nondiabetic condition in all participants. But the level of HbA1c (6.5 ± 0.5%) was higher in the patients who have iron deficiency anemia compared in the healthy individuals, the level of HbA1c was (5.4 ± 0.7%).

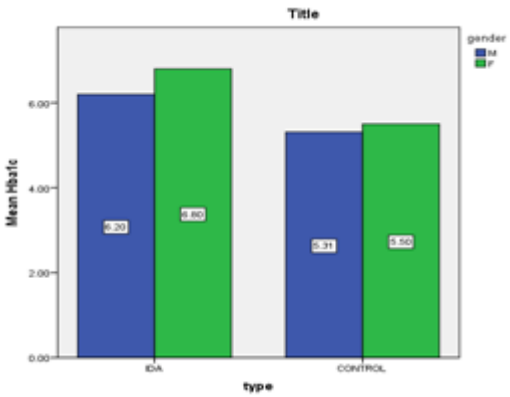

Figure 1. Distribution of the mean HbA1c (%) gender in subjects with iron deficiency anemia and control.

The figure shows the comparison between the mean level of HbA1c in males and females in both groups, which showed an increase in females compared to males in both groups. In Iron deficiency anemia, the mean level of HbA1c was 6.2% in males while 6.8% in females. Also in control group, the mean level of HbA1c was 5.3% in males while 5.5% in females.

Table 3. The mean level of Hemoglobin, Red Blood Cells Index and Ferritin in cases and control groups

Parameters	IDA group (n=120)	Control group (n=180)
Hb (g/dl)	9.7 ±1.3	13.6±0.97
Hct (%)	29.6.2±2.9	42.1±2.5
MCV (fl)	70.4±4.1	85.9±4.4
MCH (pg)	23.09 ±2.1	27.8±1.9
Ferritin (ng/ml)	5.38±1.9	82.3±9.3

In this table, showing the difference between the mean level of Hb, Hct, MCV, MCH and Ferritin in cases with IDA group and control. Which increased in control group more than in case group (IDA). This confirms the diagnosis of anemia due to iron deficiency.

IV. DISCUSSION

Hemoglobin A1c (HbA1c) is a glycated hemoglobin that can be used as an indicator of a patient's glycemic status over the previous 3 months. The American Diabetes Association (ADA) and World Health Organization (WHO) have recently approved the use of HbA1c for screening and diagnosis of diabetes.(10-13). Also the American Diabetes Association (ADA) guidelines and World Health Organization (WHO), have suggested that concentrations of 6.5% or more be considered diabetes, and the ADA has suggested 5.7–6.4% as diagnostic of pre diabetes(12, 14). Many studies reported that besides blood sugar. Other conditions such as hemolytic anemia, hemoglobinopathies, acute and chronic blood loss, pregnancy, and uremia have affected on HbA1c levels (15-17). Iron deficiency anemia is the most common form of anemia. Brooks et al. studied the effects of iron deficiency anemia on HbA1c levels. 14 That study was conducted on non-diabetic patients having iron deficiency anemia, before and after treatment with iron. They observed that HbA1 levels were significantly higher in iron deficiency anemia patients and decreased after treatment with iron.(6). Alap L. Christy et al observed that the mean HbA1c of nondiabetic with iron deficiency anemia was 6.87 ± 1.4%, but it was 5.65 ± 0.69% in the healthy individuals($p<0.01$)(18). Similarly, our results suggested that IDA was associated with higher concentrations of HbA1c compared to the results of healthy individuals. The mean level in IDA was (6.5 ± 0.5%) while it was (5.4 ± 0.7%) in healthy individuals as a control. In another study, using a different method for estimating of HbA1c by cation exchange column chromatography, concluded that HbA1c elevation synchronous with an increase ferritin level, unlike the other studies(4). Increased HbA1c in iron deficiency anemia. The mechanisms leading to increased HbA1c 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. IDA affects HbA1c levels when they are assessed by the most common methods such as immunoturbidometry, and therefore the IDA should be corrected before any diagnostic or therapeutic decision is made based on HbA1c levels.

V. CONCLUSION

The microcytic hypochromic anaemia has an effect on the increased level of glycosylated hemoglobin (HbA1c), especially iron deficiency anemia. That the necessary intervention can be done by administration of iron. This helps to avoid misdiagnosis of diabetics, based on elevated the level of HBA1C, in patients with iron deficiency anemia.

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