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Effect of iron deficiency Anemia on glycated haemoglobin levels in normoglycemic subjects

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Abstract
Background: *Glycated Haemoglobin (HbA1C) is a reliable diagnostic marker to measure the blood glucose control among the diabetes patients and it also reveals the glucose levels for the past three months. Worldwide, Iron deficiency anaemia (IDA) is most prevalent anaemic type and contrasting report exists on HbA1C levels in anaemic patients. In this backdrop, the present study was conducted to evaluate the pattern of HbAIC level in IDA subjects with normal blood glucose level.*
Methods: *A 100 IDA patients with normal blood glucose levels and 100 healthy controls was selected based on the inclusion and exclusion criteria. The patient's demographics details were collected and biochemical measurements such as HbA1C, red blood cell indices, serum ferritin, serum iron, total iron binding capacity was estimated using standard methods. The comparison between the control and anaemic cases was done using student t test. Pearson's correlation was done to study the assicaition between the variables. Results: Mean Hb is decreased in anaemic patients as compared to the controls. Further, HbA1C level was increased in anaemic cases as compared to the controls and it was found to be significant ($p<0.001$). Further, the serum iron and ferritin was decreased and TIBC level was increased in anaemic cases as compared to the controls ($p<0.001$). Pearson's correlation analysis reveals the significant association between Hb and HbA1C levels in anaemic cases ($R=0.632$; $P=0.000$).*
Conclusion: *Increased HbAIC levels in iron deficiency anaemia patients was not depend on the blood sugar levels and proper interpretation is required in these patients.*
Keywords: *Iron deficiency anaemia, glycated haemoglobin, ferritin, Normoglycemic.*

Introduction

Glycated haemoglobin (HbA1C) is formed as a result of glycation of haemoglobin at amino acid terminal of β chain of globin [(1)]. HbA1C is altered form of Hb detected in diabetic patients and mounting studies have studied the association between HbA1C and blood glucose levels. The HbA1C gives an idea about the past 3 months blood glucose level and it is mainly used as a reliable marker to assess the glycaemic control in

diabetic [2]. Further, HbA1C is also employed in the screening of high risk diabetic patients. The American diabetes association (ADA) framed a guidelines and it recommends that HbA1clevel must be maintained <6.5% to overt any diabetic related complications[3]. Apart from elevated blood glucose levels, the HbA1c levels is altered by various factors such as age, haemoglobin traits and the clinical conditions which reduces the RBC level such as anemia, hemoglobinopathies and uraemia. According to the Global Burden of Disease Study 2016, iron deficiency anemia (IDA) is 1 of the 5 leading causes of years lived with disability burden and is the first cause in women [4]. Various clinical studies show that IDA causes an increase of HbA1c, irrespective of plasma glucose levels [5-7]. However, a study done by Sinha et al has shown that HbA1c levels and absolute HbA1c levels are significantly increased during the treatment of iron deficiency anemia[8]. Thus, the level of HbA1C in IDA had displayed conflicting results, so in this backdrop the present study was carried out to evaluate the HbA1C level in iron deficiency anaemia patient with normal blood glucose profiles.

Materials and Methods

This was cross-sectional study conducted during the period from October2018 to September 2020 among the 100 non-diabetic IDA patients attending the General Medicine, outpatient department of Rajah Muthiah Medical College and Hospital. The 100 healthy non anaemic patients were considered as control.

Inclusion Criteria

Age more than and equal to 18 years, patients already diagnosed as iron deficiency anemiawith normal blood sugar levels were included in the study.

Exclusion Criteria

Patients with age less than 18 years, patients diagnosed with type 2 diabetes mellitus with uncontrolled blood sugar levels, patient with known case of any malignancy were excluded from the study.

Based on haemoglobin values, patients were termed as anaemic with cut off of <13 gm/dl in men and <12 mg/dl in women according to WHO criteria (9). Patients with microcytic indices (MCV <80 fl) and hypochromic indices (MCH<26 pg/cell) with peripheral smear of microcytic hypochromic picture were considered to have iron deficiency anaemia.

HbA1C was measured by capillary electrophoresis procedure which separates HbA1c from other Hb fraction based on the difference in the charge and measured using high voltage electro-osmotic flow. The HbA1C values were usually represented as percentage (%).

The other haematological parameter was measure using the auto analyser.

Data Analysis

The values were represented as mean±SD. Students t test was used for the comparison between cases and controls. Pearson's coefficient correlation was done to find the association between the variables. P <0.05 was considered as statistically significant.

Results

The present study was conducted to determine the HbA1C levels in iron deficiency anaemia patients with normal glucose levels and compare with the healthy controls. In this study, 100 patients each in cases and control were selected.

The mean age in the control and anaemic subjects were 40.57± 18.38 and 44.85± 18.38 years respectively. Female preponderance was observed in both the control and anaemic subjects.In control, 75% were females and in anaemic cases 81% were females. The blood glucose level were found to be non-significant and its was in normal range among the controls and anaemic cases.

The mean Hb level was significantly decreased in anaemic cases as compared to controls (7.56± 0.98 vs 14.12± 2.56g/dl; p<0.001). The levels of various red blood indices were shown in Table 1. Further there was a significant increase in HbA1C level among the anaemic cases as compared to the controls

Table 1: Red blood cell indices among the control and anaemic cases

Red blood cell indices	Control (n=100)	Anaemic cases (n=100)	P value
Haemoglobin (g/dl)	14.12± 2.56	7.56± 0.98	<0.001
Mean corpuscular volume (fl)	94.35 ±6.65	67.89 ±4.12	<0.001
Mean corpuscular Haemoglobin (pg)	31.26± 4.12	24.35±2.76	<0.001
Mean Corpuscular Haemoglobin concentration (g/dl)	35.40± 1.94	30.12± 4.45	<0.001
RBC count (millions/cu.mm)	4.96±0.87	2.96± 0.76	<0.001

The data were represented mean ±SD, n=100. P<0.001 was found to be significant. In this study, there was a significant increase in HbA1C level among the anaemic cases as compared to the controls (6.45±0.76 vs 5.25±0.56g/dl; p<0.005). The various parameters related to study the anaemic status were shown in table 2. The serum iron , serum ferritin were significantly reduced in anaemic cases, while the total iron binding capacity (TIBC) was significantly increased in anaemic cases as compared to the control.

Table 2: Anaemic indices among the control and anaemic cases

Anaemic Indices	Control (n=100)	Anaemic cases (n=100)	P value
HbA1C (%)	5.25±0.56	6.45±0.76	<0.001
Serum Ferritin (ng/ml)	224.98 ±72.86	7.76±2.24	<0.001
Serum Iron (µg/dl)	119.12 ±12.05	21.257± 2.76	<0.001
Total iron binding capacity (µg/dl)	295.3±25.12	415.35±31.65	<0.001

The data were represented mean ±SD, n=100. P<0.001 was found to be significant. Further, Pearson's correlation analysis reveals a positive correlation between HbA1C and Haemoglobin and it was found to be significant (r=0.632; P=0.000) in anaemic patients. The data were shown Table 3.

Table 3: Correlation between HbA1C and haemoglobin among the anaemic patients

Study Group	Haemoglobin	
	Pearson's Coefficient (R)	P value
Anaemic cases	0.632	0.000

Discussion

Previous studies display, conflicting data in the HbA1C levels alteration in iron deficiency anaemia[8, 10]. The relationship IDA and HbA1c levels is first reported by Horton in 1965[11]. Later in the year 1980, Brookesstated that, in IDA patients there is substantial increase in the level of HbA1C conflicting report in 1980 that the levels of HbA1c were rather increased in iron deficiency anemia15. So, the present study was done to detect changes of HbA1c in our setup.

In our study, the mean age among the control and anaemic cases are 40.57± 18.38 years and 44.85± 18.38 years respectively. Similar to our report, in Bansal et al study, the mean age of the patients in control and cases are 42.51 ± 18.64 and 43.39 ± 18.14 respectively[13]. Female preponderance is observed in this study, which is similar to the reports published by Bansal et al.[13].

In our study Hb levels are significantly are significantly decreased in anaemic cases as compared to the controls. Further, anaemic cases showed decreased levels of red blood indices such as mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration.Similar to the present study report, Sakamoto et al, reported decreased level of red cell indices in anaemic patients[14].

In our study, there was a significant increase in the level of HbA1C in Anaemic cases as compared to the control. Further, serum iron, ferritin levels are decreased and TIBC levels is increased in anaemic cases as compared to the controls. The findings are similar to the studies done by Rajagopal et al. where HbA1c level increased as the severity of anemia increased. In Bansal et al study, iron

deficiency anaemia patients showed increased HbA1C concentration as compared to the healthy controls, 6.11 ±0.11 vs 5.41± 0.41[7,13].

In our study, we found a significant positive correlation between HbA1C and Hemoglobin in anaemic cases (R=0.632; P=0.000). Similar to our report, Sinha et al. reported significant correlation between hemoglobin and HbA1c levels in anaemic patients (coefficient of correlation=0.593; p<0.01).

Conclusion

Thus the findings of the present study, shows that increased HbA1c level in non-diabetic subjects are independently associated with Iron deficiency anaemia. So, HbA1C level must be correctly interpreted in anaemic patient and should be treated accordingly.

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