Original Research Article

Correlation of iron deficiency anaemia with glycosylated haemoglobin (HbA1c) levels in non-diabetics: an observational study

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ABSTRACT

Background: Alteration of HbA1c in other conditions such as haemolytic anaemia, pregnancy and haemoglobinopathy has raised questions about its correlation with iron stores. The aim of the study was to correlate iron deficiency anaemia with glycosylated haemoglobin levels among non-diabetics.

Methods: The present study was an observational study among non-diabetic patients of iron deficiency anaemia attending our outpatient department. The study was conducted in the department of medicine of a tertiary care hospital in Maharashtra. All the non-diabetic patients more than 18 years with iron deficiency anaemia were included in the present study. Patients with acute coronary syndromes, chronic liver, chronic kidney diseases, malignancies, haemolytic anaemia, pregnancy, HIV positive with known end stage cardiopulmonary disease were excluded from the study.

Results: About 86.33% of the patients had mild to moderate anaemia and 10.7% had severe anaemia in the present study. The average values of haemoglobin, serum ferritin, total iron binding capacity, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration and hematocrit significantly improved after the treatment. With treatment of anaemia, glycosylated haemoglobin, fasting blood sugars and post prandial blood sugars also improved significantly when compared to baseline (p<0.001).

Conclusions: The average values of haemoglobin, serum ferritin, total iron binding capacity, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration and hematocrit significantly improved after the treatment. With treatment of anaemia, glycosylated haemoglobin, fasting blood sugars and post prandial blood sugars also improved significantly when compared to baseline.

Keywords: HbA1c, Iron deficiency anaemia, Non-diabetics

INTRODUCTION

Iron deficiency anaemia is one of the prevalent and preventable causes of malnutrition.[1] The most common cause of anemia worldwide is iron deficiency, which results in microcytic and hypochromic red cells on the peripheral smear.[1] Serum levels of ferritin, iron, and transferrin saturation will be decreased.[2] Ferritin is storage form of iron and reflects the iron status of the body.[2-4] Evidence suggests that reduced iron stores are associated with false high levels of HbA1c in non-diabetic individuals.[5-7] Glycosylated haemoglobin (HbA1c) is a gold standard to assess the blood sugar changes in the past 3 months.[8,9] It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycaemic control in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes. Alteration of HbA1c in other conditions such as haemolytic anaemia, pregnancy and haemoglobinopathy has raised questions about its

correlation with iron stores.[10] Various studies have been conducted to correlate iron deficiency anaemia with HbA1c among diabetic patients.[11-13] There is paucity of data among non-diabetics. The aim of the study was to correlate iron deficiency anaemia with HbA1c among non-diabetics presenting to our department of a tertiary care hospital.

METHODS

The present study was an observational study among non-diabetic patients of iron deficiency anaemia attending our outpatient department. The study was conducted in the department of medicine of a Punjabrao Deshmukh Memorial Medical College, Amravati, Maharashtra. The patients attending our outpatient department during the period of 2 years (September 2018 to October 2019) were included in the study. All the non-diabetic patients more than 18 years with iron deficiency anaemia were included in the present study. The presence of anaemia was defined by World health organisation guidelines for classification of anaemia.[14] Patients with acute coronary syndromes, chronic liver, chronic kidney diseases, malignancies, haemolytic anaemia, pregnancy, HIV positive with known end stage diseases an end stage cardiopulmonary disease were excluded from the study. The data was collected using pretested and pre-validated case record form which had demographic details of the patients. Investigations related to iron deficiency like complete blood count; serum ferritin, mean corpuscular volume and haematocrit along with it investigated fasting blood sugars, post prandial blood sugars and glycosylated haemoglobin of the patients. Approval from scientific review committee and institutional ethical committee was taken before starting study. Single dose of albendazole 400 mg was given for all the patients in the study. Iron requirement was calculated using the following formula,

Body weight (kg) × 2.3 × [15 - patient's haemoglobin (g/dl)] + 500 for stores

Patients with mild and moderate iron deficiency anemia were supplemented with oral iron (ferrous fumarate) 200 mg of elemental iron per day for 2 months. Patients of severe iron deficiency anemia were supplemented with intravenous iron sucrose 200 mg IV per day for 3 days (max 600 mg in a week) till restoration of iron stores. Patients were asked for follow up on 2nd and 3rd month.

Statistical analysis

The data was collected, compiled, and analyzed SPSS version 20.00. The qualitative variables were expressed in terms of percentages. The quantitative variables were both categorized and expressed in terms of percentages or in terms of mean and standard deviations. The difference between the two proportions was analyzed using chi-square or Fisher exact test. ANOVA was used to test the difference between mean of more than 2 groups. Post Hoc Bonferoni test was used to find the p value between the

groups more than 2. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS

We included 150 subjects in the present study. The mean age of the study subjects was 45.44 years with female preponderance in the present study.

Table 1: Demographics of the present sample.

Demographics	Mean/number	SD/%
Age (in years)	45.44	15.17
Gender		
Female	79	52.7
Male	71	47.3

About 6% of the cases were having mild anaemia, 80.33% had moderate anaemia and 10.7% had severe anaemia in the present study.
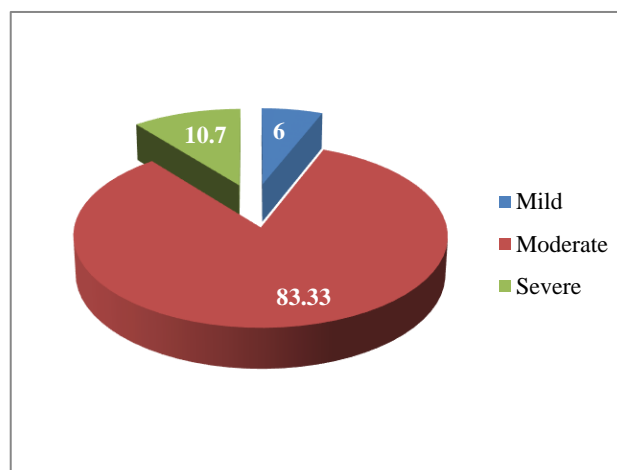
Figure 1: Distribution based on severity of the anaemia.

Table 2: Distribution of the subjects based on the chief complaints.

Chief complaints	Number	Percentage (%)
Symptoms		
Generalised weakness	125	83.30
Malaise	91	60.70
Lack of interest in work	72	48.00
Dyspnoea	30	20.00
Presence of worms in stool	13	8.70
Signs		
Nail changes	36	24.00
Mild splenomegaly	74	49.3
Ejection systolic murmur	13	8.70

Some of the major symptoms reported by the patient in present study were generalised weakness (85.30%), malaise (60.70%) and lack of interest in work (48%). Some common signs were nail changes (24%) and mild splenomegaly (49.3%).

The average values of haemoglobin, serum ferritin, total iron binding capacity, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration and hematocrit significantly improved after the treatment (p<0.001).

Table 3: Haematological parameters at baseline and follow up at 2 months and 3 months.

Haematological parameters	Baseline		2 months		3 months		P value
	Mean	SD	Mean	SD	Mean	SD	
Haemoglobin (g/dl)	8.82	1.16	12.84	0.79	13.69	0.50	0.0010
Serum ferritin (ng/ml)	7.73	2.03	152.24	30.27	247.12	37.50	0.0000
Total iron binding capacity (mcg/dl)	456.63	10.84	350.07	14.60	325.08	14.02	0.0000
Mean corpuscular volume (fl/red cell)	73.70	53.72	84.56	2.98	88.96	2.54	0.0000
Mean corpuscular haemoglobin (pg/cell)	25.55	1.91	29.99	1.34	31.23	1.39	0.0000
Mean corpuscular haemoglobin concentration (g/dl)	29.76	1.60	34.15	0.98	34.42	0.91	0.0000
Hematocrit (%)	42.91	0.57	45.07	0.59	47.98	0.60	0.0010

Table 4: Blood glucose parameters at baseline and follow up at 2 months and 3 months.

Haematological parameters	Baseline		2 months		3 months		P value
	Mean	SD	Mean	SD	Mean	SD	
Glycosylated haemoglobin (%)	6.66	0.43	5.58	0.43	4.92	0.36	0.0000
Fasting blood sugars (mg/dl)	85.35	6.55	92.49	57.38	88.34	6.14	0.0000
Post prandial blood sugars (mg/dl)	109.83	4.42	109.66	4.35	111.78	5.27	0.0000

With treatment of anaemia, glycosylated haemoglobin, fasting blood sugars and post prandial blood sugars also improved significantly when compared to baseline (p<0.001).

DISCUSSION

Glycosylated haemoglobin basically a reaction between glucose and N-terminal valine of both beta chains of haemoglobin. Assessing this helps us to understand the long term glycemic control of the patients. Evidence says the levels of glycosylated haemoglobin are modulated by iron status of the patients.[2] With this purview we conducted a cross sectional study to understand the effect of iron treatment on the changes in glycosylated haemoglobin.

Among the 150 cases studied in the present study, 9 were mild cases, 125 were moderate cases and 16 were severe cases. Similar inferences were drawn by Kumar et al and Silva et al.[15,16] Studies conducted by Sinha et al had only moderate and severe cases in their study and study conducted by Rajagopal et al had majority of mild and moderate cases in their study.[10,17]

We found the significant improvement in haemoglobin after the treatment when compared to baseline. A study by Ganz et al found that the average HbA1c levels pretreatment were significantly higher when compared to 2

months and 3 month follow up HbA1c.[18] Similar findings were inferred by Coban et al in their study but the follow up period was small in their study.[19] A study conducted by Brooks et al inferred that the mean HbA1c levels pretreatment of anaemia in their study was 9.9 and after treatment it was 8.1 and this difference was statistically significant.[7] Another study conducted by Gram et al inferred that there was significant decrease in the HbA1c levels after the treatment of anemia in non-diabetic patients.[6] A study conducted by Agouza et al on university students revealed that the mean HbA1c levels at baseline was 6.15 and at 1 month and 2 months follow up was 5.59 and 5.54 respectively.[20] MCV in the present study improved significantly after treatment of the patients from baseline. The current results are similar to the findings of Goddard et al, Kumar et al and Coban et al.[15,19,21] The changes in total iron binding capacity in the present study were in concordant with findings of Bermejo et al.[22]

A study conducted by Sinha et al found that the baseline HbA1c levels among their study subjects was 4.6 and at 1 month follow up was 5.4 and at 2 months follow up it was 5.9.[10] This study showed increasing trend of HbA1c as compared to our study and other studies described so far. Sinha et al observed a significant correlation between hemoglobin and HbA1c levels in patients at baseline (coefficient of correlation=0.593, p<0.01) and after 1 month of treatment (coefficient of correlation=0.490, p<0.01).[10] However, there was no positive correlation

between hemoglobin and HbA1c levels at the end of the 2 months treatment period (coefficient of correlation= -0.63, p>0.05).

The present study had some limitations. Firstly, it was a cross sectional study. Randomised controlled trails would have given a better picture of the present hypothesis. Due to time limitation, we could not conduct the same. Secondly it was a single center study. Multi-centeric and multi ethnic studies would yield a better perspective of the effect on iron treatment with glycosylated haemoglobin. Nonetheless, it was one of the pioneer studies which included all the changes in haematological parameters and the study was done on non-diabetics as the sample.

CONCLUSION

More than ¾ of the present sample was having moderate anaemia. The average values of haemoglobin, serum ferritin, total iron binding capacity, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration and hematocrit significantly improved after the treatment. With treatment of anaemia, glycosylated haemoglobin, fasting blood sugars and post prandial blood sugars also improved significantly when compared to baseline (p<0.001). It can be concluded that IDA affects HbA1c results and this effect is dependent on anaemia 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 anaemia is likely to have a minor effect on HbA1c levels favouring its use to diagnose diabetes in patients with mild anaemia. This study concluded that before considering HbA1c as a diagnostic parameter and glycemic control in diabetes, iron deficiency anaemia should be ruled out; as the severity of the anaemia has effect on quantity of HbA1c.

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