

## HbA<sub>1c</sub> status in iron deficiency anemia

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### Abstract

**Introduction:** Iron deficiency anemia (IDA) is a major public health problem in world and India too. It has been found that HbA<sub>1c</sub> level rise in patients of IDA without raised blood glucose level.

**Materials and Methods:** Study consists of 30 cases of Iron deficiency anemia and 30 controls of age and sex match between the ages of 18 to 60 years. This is a prospective case controlled study done over a period of two years. Blood samples were collected from subjects and HbA<sub>1c</sub>, Serum iron, TIBC, Serum ferritin, Blood glucose level and Hematological parameters were measured.

**Observations and Result:** Serum iron and Ferritin levels were highly significantly decreased ( $p < 0.001$ ) in IDA group patients compared to controls. TIBC levels were highly significantly increased ( $p < 0.001$ ) in IDA group patients compared to control. HbA<sub>1c</sub> levels were also highly significantly increased ( $p < 0.001$ ) in IDA group patients compared to control. Mean BSL-F and BSL-PP showed no significant difference in glycemic status of both case and control groups.

**Conclusion:** Apart from blood glucose, iron deficiency anaemia also affects HbA<sub>1c</sub> level.

**Keywords:** HbA<sub>1c</sub>, Iron deficiency anemia, Serum iron, Serum ferritin, TIBC.

**Received:** 03<sup>rd</sup> August, 2017

**Accepted:** 08<sup>th</sup> September, 2017

### Introduction

Protein glycation is a spontaneous reaction that is believed to play a key role in the pathogenesis of many clinical disorders. The glycation of proteins is enhanced by elevated blood glucose concentrations. The major form of protein glycation with a clinical consideration is glycated haemoglobin (HbA<sub>1c</sub>).<sup>1</sup> HbA<sub>1c</sub> is majorly affected by the blood glucose levels alone. However, certain studies have proven that the HbA<sub>1c</sub> levels are altered by various other coexisting factors, along with diabetes, especially that of iron deficiency anaemia which is a major public health problem in developing countries like India. Therefore, this study have been planned to assess the level of HbA<sub>1c</sub> in IDA patients.

### Aims and Objectives

To assess the status of HbA<sub>1c</sub> in patients of iron deficiency anaemia & compare with age and sex matched controls.

### Materials and Methods

It is a cross sectional comparative study conducted in 2 yrs of duration. A total number of 60 subjects between the ages of 18 to 60 years were enrolled for the present study. Detailed medical history and relevant clinical examination

data and written consent were obtained from all subjects by explaining the study procedure.

Considering the average of HbA<sub>1c</sub> value of 4.5 and allowable error of 1 at  $p < 0.05$  and power of the test 80%, estimated sample size is 60 which include 30 cases (clinically diagnosed patients of iron deficiency anaemia) & 30 age and sex matched controls belonging to age group of 18 to 60 years were selected.

The cases included in present study were selected from patients attending outpatient department (OPD) and indoor patient department (IPD) of internal medicine. Samples were assessed at the Central Clinical Laboratory (CCL), Department of Biochemistry.

### Inclusion criteria

Cases: Clinically diagnosed cases of IDA

### Exclusion criteria

Patients having history of Impaired glucose tolerance, Diabetes Mellitus, Haemoglobinopathy, Hemolytic anaemia, Chronic renal diseases, Chronic alcoholism, Pregnancy, Blood transfusion within a period of 6 months.

The following parameters were evaluated

- i. Haematological parameters: HiCN and Electrical impedance method<sup>2</sup>
- ii. Serum iron: Ferrozin method<sup>3</sup>
- iii. TIBC: Ferrozin method<sup>3,4</sup>
- iv. Serum ferritin: ELISA Method<sup>5</sup>
- v. Blood glucose: GOD-POD Method<sup>6</sup>
- vi. HbA<sub>1c</sub>: immunoturbidometric method<sup>7</sup>

Haematological parameters were analysed on Sysmex kx-21 autoanalyzer. All biochemical investigations were carried out on 'Erba 360 Fully automated biochemistry analyzer'.

## Observations and Results

Serum iron and Ferritin levels were highly significantly decreased ( $p < 0.001$ ) in IDA group patients compared to controls. TIBC levels were highly significantly increased ( $p < 0.001$ ) in IDA compared to control. HbA<sub>1c</sub> levels were also highly significantly increased ( $p < 0.001$ ) in IDA compared to control.

**Table I: Mean serum iron, TIBC, and serum ferritin level of case and control groups**

Parameters	Case	Control	P value
Serum Iron	31.9 ± 10.3	98.98 ± 21.25	0.0001
TIBC (µg/dl)	399 ± 27.2	302.1 ± 33.47	0.0001
Ferritin (µg/dl)	6.17 ± 3.34	62.96 ± 18.33	0.0001

$P < 0.001$  Indicate highly significant.

Mean BSL-F and BSL-PP showed no significant difference in glycemc status of both case and control groups.

**Table II: Mean BSL-F and BSL-PP in case and control groups**

BSL (mg/dl)	Case	Control	P value
BSL-F	88.9 ± 9.03	84.70 ± 7.6	$P > 0.05$
BSL- PP	120.00 ± 10.53	124.00 ± 9.08	$P > 0.05$

$P < 0.05$  Indicates statically significant.

Mean HbA<sub>1c</sub> showed highly significant difference in both case and control groups ( $P < 0.001$ ). **Table II: Mean HbA<sub>1c</sub> level of case and control groups.**

Parameters	Case	Control	P value
HbA <sub>1c</sub>	6.55 ± 0.77	5.27 ± 0.83	0.0001

$P < 0.001$  Indicates statically significant.

Unpaired 'T' test is applied for statistical analysis of Mean Hb, HCT, MCV, MCH, MCHC levels. All levels were highly significantly decreased ( $p < 0.001$ ) in IDA group patients compared to controls. RDW levels was highly significantly increased ( $p < 0.001$ ) in IDA compared to control.

**Table III: Mean Haemoglobin (Hb), MCV, MCH, MCHC, and RDW in case and control groups**

Parameters	Case	Control	P value
Hb (g/dl)	8.9 ± 1.5	13.83 ± 1.04	0.0001
HCT (%)	26.64 ± 5.2	40.97 ± 3.4	0.0001
MCV (fl)	70.03 ± 5.1	91.44 ± 3.87	0.0001
MCH (pg)	23.51 ± 2.6	30.88 ± 1.59	0.0001
MCHC (g/dl)	28.03 ± 1.74	33.86 ± 1.86	0.0001
RDW (%)	19.14 ± 3.92	13.42 ± 0.64	0.0001

$P < 0.001$  indicate highly significant.

## Discussion

HbA<sub>1c</sub> is majorly affected by the blood glucose levels. However, certain studies showed that the HbA<sub>1c</sub> levels are altered by various other coexisting factors, along with diabetes, especially that of iron deficiency anaemia, which is a major public health problem in developing countries like India. Present study was conducted to assess the status of HbA<sub>1c</sub> in iron deficiency anaemia.

Present study was conducted on 60 subjects with IDA (n=30) and age and sex matched healthy controls (n=30) groups. Diagnosis of iron deficiency anaemia requires laboratory-confirmed evidence of anaemia, as well as low iron stores.<sup>8</sup> Complete blood count was assessed to recognize the indices of iron deficiency anaemia (reduced Hb, Hct, MCV, MCH, MCHC and raised RDW) along with peripheral smear blood smear examination. Iron study was carried

out to confirm iron deficiency (reduced Serum iron, ferritin, and increase TIBC in IDA).<sup>9,10</sup>

Several mechanisms have been advocated for this increase in the level of glycated haemoglobin in anaemic patients. It has been proposed that in iron deficiency, the quaternary structure of the haemoglobin molecule may be altered and the glycation of the beta globin chains occurs more readily.<sup>11</sup>

According to the explanation provided by Sluiter et al<sup>12</sup> the formation of glycosylated haemoglobin is almost irreversible, the concentration of HbA<sub>1c</sub> in erythrocyte will increase linearly with the cell's age. Younger population of red blood cells have lower HbA<sub>1c</sub> level as after treatment of iron deficiency anaemia but if iron deficiency has been worsening in the previous months, red cell production will fall causing not only anaemia but also increasing average age of circulating erythrocytes and thus an increase in HbA<sub>1c</sub> level.

Above discussion underline the effect of iron deficiency anaemia on HbA<sub>1c</sub> concentration. Increased level of HbA<sub>1c</sub> was observed in iron deficiency anaemia. This study has got significant relevance because IDA is highly prevalent in a tropical country like India. Recently HbA<sub>1c</sub> has been recommended as one of the diagnostic criteria of DM. Thus iron status must be considered during the interpretation of the HbA<sub>1c</sub>. Further similar study on a large sample size is needed to substantiate the results of this study.

## Conclusion

Apart from blood glucose, iron deficiency anaemia also affects HbA<sub>1c</sub> level. As IDA and Diabetes mellitus both being frequent in India, IDA is to be taken in consideration while interpreting HbA<sub>1c</sub> in diagnosis and monitoring of Diabetes mellitus. IDA can be suspected in raised HbA<sub>1c</sub> level with euglycemia

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