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**Original Article**

# Effects of Nutritional Anemia on Hba1c Levels

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## ABSTRACT

**Background and Objectives**: HbA1C is measured in diabetics as well as in those with impaired glucose tolerance to assess the glycaemic status over the last two to three months. But there are numerous conditions causing falsely low or high HbA1c measurements. One condition that effect erythrocyte turnover is anemia. Here we aimed to estimate the levels of HbA1c in iron deficiency or mixed deficiency anemia patients without diabetes and to assess the changes in HbA1c levels 3 months after treatment of nutritional anemia.
**Methods**: It is a hospital based prospective interventional study done in Department of General medicine, Kozhikode medical college from June 2021 to December 2022. The study comprises 120 patients with nutritional anemia, including iron deficiency anemia and mixed deficiency anemia. We treated the patients with nutritional supplementation for three months and noted anemia parameters and HbA1c levels before and after the therapy. Data was collected using a semi structured questionnaire, entered in excel and analysed using SPSS software.
**Results**: The prevalence of nutritional anemia was found to be more common in females. After 3 months of treatment of anemia there was statistically significant increase in Hemoglobin, MCV and RBC count and a significant fall in RDW and Platelet count. The mean HbA1c of the study population decreased from 6.07(±0.53) % to 5.40(±0.52) % after 3 months of treatment which was statistically significant. (P<0.001). There was a noticeable, though statistically insignificant, inverse relationship between rising Hb levels and falling HbA1c levels in patients with anemia.
**Interpretation and Conclusions**: HbA1c in anemic subjects showed a significant decrease with appropriate therapy. As nutritional anemia and Diabetes mellitus both being frequent in India, anemia is to be taken in consideration while interpreting HbA1c in diagnosis and monitoring of Diabetes mellitus.

**Key Words**: *Nutritional, Anemia, HbA1c, Diabetes Mellitus*

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## INTRODUCTION

HbA1c is an important biomarker used to assess long-term glycemic control in individuals with diabetes. HbA1c results from the covalent attachment of glucose to the N-terminal valine of the haemoglobin β-chain in a nonenzymatic process known as glycation [1]. It is measured in diabetics as well as in those with impaired glucose tolerance to assess the glycaemic status over the last two to three months. According to the American Diabetes Association (ADA) Guidelines 2007, the value of HbAlc should be kept below 7% in all diabetics [2]. In 2009, the American Diabetes Association (ADA) also recommended that HbA1c ≥6.5% should be used as diagnostic criteria for diabetes [3].

Oral glucose tolerance test (OGTT), which is considered as the diagnostic gold standard is a time-consuming procedure; whereas measurement of HbA1c levels is rapid and convenient. HbA1c levels are also related to the progression of diabetic microvascular lesions [4]. Other advantages of measuring HbA1c include better preanalytical stability, lesser biological variability, non-requirement of pre-test preparation like fasting and lesser day to day variability. However, its utility is limited by poor sensitivity and standardization, higher cost, and various conditions affecting its accuracy [5, 6].

Various conditions can lead to falsely elevated or falsely lowered values of HbA1c. Conditions that prolong the life of the erythrocytes or is associated with decreased red cell turnover results in higher A1c levels. These include Iron deficiency, Vitamin B12 deficiency, Folate deficiency and asplenia. Other conditions associated with assay related artifacts include hypertriglyceridemia, hyperbilirubinemia, uraemia, Aspirin-induced acetylated haemoglobin and cigarette-associated carboxyhaemoglobin [7]. Conditions that shorten the life of the erythrocytes or is associated with increased red cell turnover result in lower A1c levels. Acute and chronic blood loss, hemolytic anemia, and splenomegaly can all cause falsely lowered HbA1c values [8].

One of the most prevalent confounding factors in our country is nutritional anemia. Although, there were multiple studies in the past investigating the relationship between nutritional anemia and HbA1c, the results were inconsistent. In a study by Coban et al [9], in patients with iron deficiency anemia, HbA1c decreased significantly after iron treatment. Silva et al [10], also observed that patients with IDA present higher HbA1c levels when compared with patients without anaemia. Study by Van Heyningen et al [11] found no significant change in HbA1c levels after treatment of anemia and Rai et al [12] failed to find a difference in mean HbA1c among those with and without iron deficiency. Sinha et al [13] observed that the HbA1c levels were found to be significantly lower in patients with iron deficiency anemia than in the controls. This study aimed to study the levels of HbA1c in patients with nutritional anemia and the changes in HbA1c level after the correction of anemia.

## METHODS

This was a prospective follow-up study consisting of 120 subjects with iron deficiency and mixed deficiency anemia. The study was conducted in department of general medicine, Kozhikode medical college from June 2021 to December 2022.

Our study included adults aged more than or equal to 18 years with Hb < 12 gm/dL in women and < 13 gm/dL in men without diabetes, impaired fasting glucose or impaired glucose tolerance. We excluded patients who were not willing, those with established diabetes/impaired fasting glucose, impaired glucose tolerance, history of GDM, pregnancy or pregnancy related condition, chronic renal failure / liver disease, chronic infections, acromegaly or Cushing syndrome, Erythropoietin use, renal transplant patients, chronic hemolysis like thalassemia, G6PD deficiency, and patients on drugs inducing diabetes. Patients with severe anemia (Hb ≤6), anemia other than nutritional anemia, those with history of blood loss or blood transfusion within two months and those who were treated for iron/folic acid deficiency were also excluded.

After clearance from the ethical committee, 120 patients were enrolled for the study after written and informed consent. Detailed history was recorded along with complete clinical examination. Samples were collected from all the participants to estimate complete blood count, blood urea, serum creatinine, serum electrolytes, blood sugar: FBS/PPBS and urine R/E. HbA1c measurement was done using ion exchange high performance liquid chromatography in all patients. Anemia profile including peripheral smear, iron studies, vitamin B12 and folic acid levels were performed as indicated. Depending on the results, patients were classified as those with iron deficiency anemia and mixed deficiency anemia. All of them were initiated on oral supplementation. Iron deficiency anemia was managed with oral iron therapy and mixed deficiency anemia was managed with iron, folic acid and B12 supplementation for a duration of 3 months.

After 3 months, follow up evaluation was done which included history, clinical examination, relevant investigations, complete hemogram and anemia profile according to diagnosis. HbA1c levels were also repeated. For statistical analysis, data were entered into SPSS for Windows. Paired t test was used for comparison of parameters before and after therapy. Standard deviation and P values were calculated. A p value <0 .05 was considered statistically significant.

## RESULTS

The mean age of study popuation was 40.28 years. Among 120 patients with anemia, around 66.7% of the cases were females and 33.3% of the cases were males. 51.7% of the subjects were diagnosed as mixed deficiency anemia and 48.3% as iron deficiency anemia according to clinical and blood parameters.

The mean hemoglobin level before treatment of anemia was 9.85 gm/dL with a standard deviation of 1.33. Mean value of Hb after 3 months of treatment was 13.09gm/dL with a standard deviation of 0.68(figure 1). Increase in hemoglobin from baseline to 3 months post treatment had a mean value of 3.51 gm/dL with a standard deviation of 1.03. P value was less than 0.001(table 1).

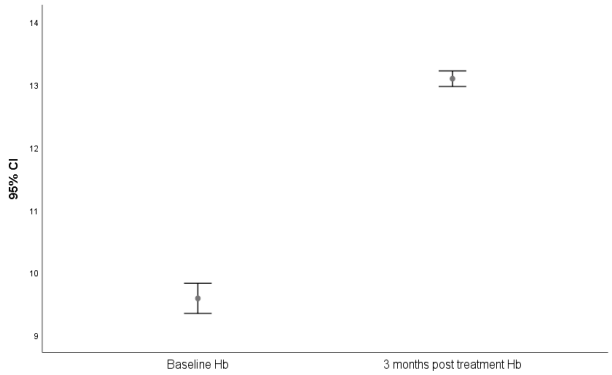


**Figure 1: Baseline Hb and post-treatment Hb distribution (original)**

**Table 1: Mean difference in Baseline Hb and post-treatment Hb**

| Variable | Mean difference ± SD | P value |
|---|---|---|
| **3 months post treatment hemoglobin – Baseline hemoglobin** | 3.51±1.03 | <0.001* |

The mean value of HbA1c in study group before treatment was 6.07% with a standard deviation of 0.53. Three months post treatment the mean value changed to 5.40 %with a standard deviation of 0.52(figure 2). The mean value of decrease in HbA1c was 0.67% with a standard deviation of 0.47.P value was less than 0.001. (Table 2).

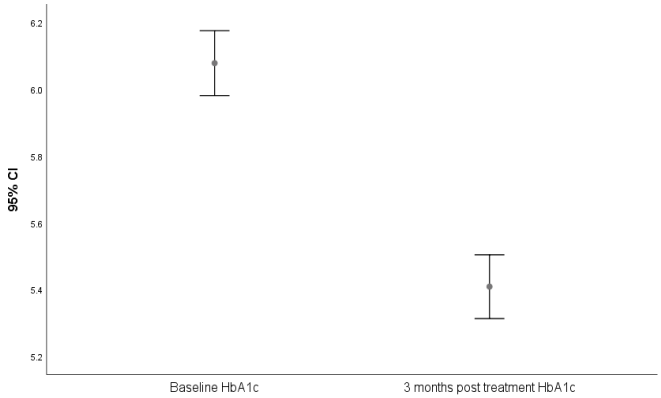


**Figure 2: Distribution of HbA1c in study group pre and post correction (original)**

**Table 2: Mean difference in post treatment HbA1c and Baseline HbA1c**

| Variable | Mean difference ± SD | P value |
|---|---|---|
| **3 months post treatment HbA1c – Baseline HbA1c** | 0.67±0.47 | <0.001* |

While plotting decrease in HbA1c versus increase in Hb after treatment we got a positive correlation indicating that rise in Hb correlates with fall in Hba1c levels with a r value of 0.153(Figure 3). However, the P value was 0.095.

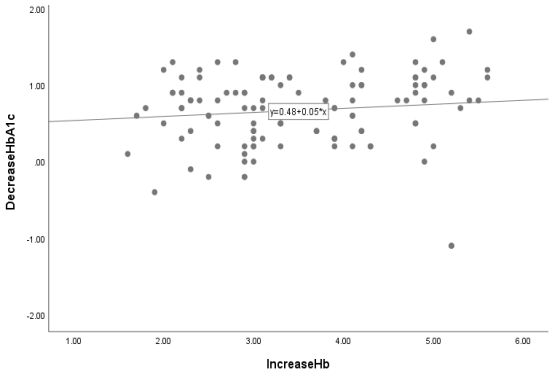


**Figure 3: Correlation between increase in hemoglobin and decrease in HbA1c (original)**

**DISCUSSION**

In our study comprising of 120 patients, the effects of nutritional anemia (iron deficiency and mixed deficiency anemia) on HbA1c levels were studied. After analysis if was found that there was a clinically significant rise in Hb after 3 months (3.51± (1.03) gms).The mean HbA1c of the study population decreased from 6.07(±0.53) % to 5.40(±0.52) % after 3 months of treatment which was also statistically significant. We got a positive correlation between rise in hemoglobin and decrease in Hba1c indicating that rise in Hb leads to fall in Hba1c levels with a correlation coefficient of 0.153. But the P value was 0.095 indicating this change was not statistically significant.

In study by Coban et al, in patients with iron deficiency anemia , HbA1c decreased significantly after iron treatment from a mean of 7.4 ± 0.8 to 6.2 ± 0.6 % ($p < 0.001$)(9)

In a study conducted in India by Rakesh Pilla et al, HbA1c levels were studied in patients with iron deficiency anemia and Vitamin b12 deficiency anemia. They found that there was a significant decrease in HbA1c in both groups of iron deficiency patients and Vitamin B12 deficiency anemia after treatment [14].

The results of the studies by Ford et al [15], El Agouza et al [16] also showed that HbA1c concentrations tended to be higher in the presence of iron deficiency and level of HbA1c decreased after treatment of anemia.

In a study conducted by Silva et al, it was observed that patients with IDA present higher HbA1c levels when compared with patients without anaemia. This difference rises as total Hb falls. Besides, there were regular negative correlations between haematological indices and HbA1c, which were stronger when HbA1c was measured by immunoturbidimetry [10].

A study by P.S Hardikar et al [17], studied about high prevalence of prediabetes spuriously diagnosed by HbA1c in Young Indians after comparing with the results of OGTT and found that anemia is a responsible factor for this.

Sinha et al conducted a similar study, but the HbA1c levels were found to be significantly lower in patients with iron deficiency anemia than in the controls. Moreover, the HbA1c levels increased after treatment of anemia [13].

Our results suggest that correction of nutritional anemia that is both iron deficiency and mixed deficiency anemia leads to a significant reduction in HbA1c levels. A positive correlation was found with decrease in HbA1c and increase in Hb though statistically insignificant. Hence it is important to correct nutritional anemia before using HbA1c levels as an indicator of glycemic control and for the diagnosis of diabetes.

The present study was hospital-based, so our findings should not be generalized to the whole population. The study period was short and other factors that alter HbA1c values in a general population should also be considered.

## CONCLUSIONS

There was a statistically significant reduction in HbA1c levels in the patients after treatment of nutritional anemia. We could also find an observable, though statistically insignificant, inverse relationship between rising Hb levels and falling HbA1c levels in patients with nutritional anemia. As nutritional anemia and Diabetes mellitus both being frequent in India, anemia is to be taken in consideration while interpreting HbA1c in diagnosis and monitoring of Diabetes mellitus. Anemia should be treated before using HbA1c as a diagnostic tool for diabetes. More extensive studies are needed to highlight the effect of anemia on HbA1c levels in general population.

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