



EFFECT OF IRON DEFICIENCY ANEMIA ON HbA1C IN NON-DIABETIC PATIENTS AT A TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN.

Pathology

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ABSTRACT

Introduction: Anaemia has a high prevalence in the third world countries like India and it potentially contributes to the pathogenesis of various chronic diseases. Amongst nutritional anemia 1/3rd of patients have iron deficiency. American Diabetes Association (ADA) has affirmed Glycated Haemoglobin (HbA1C) $\geq 6.5\%$ as a diagnostic criterion for Diabetes Mellitus (DM) as it is a well-known indicator of glycemic control in diabetes patients. It constitutes of 5% of total hemoglobin in non-diabetic patients as well. Variation of HbA1C in Iron Deficiency Anaemia (IDA) has clashing results.

Aim: To study the impact of IDA on HbA1C levels among non diabetics.

Materials and Methods: This cross-sectional study was carried out in Medipulse Hospital, Jodhpur, Rajasthan. 200 patients who were non diabetics (100 with IDA and 100 without IDA) were included in this study. Medical history was recorded and HbA1C, Haemoglobin (Hb), Haematocrit (Hct), red cell indices, serum iron, ferritin and Random Plasma Glucose (RPG) were tested.

Results: The IDA patients in this study had a mean HbA1C (6.15 $\pm$ 0.04%) which was higher than the non anaemic group (5.06 $\pm$ 0.32 %) and this difference was statistically significant ($p < 0.05$). HbA1C level was increased when severity of anaemia worsened.

Conclusion: In this study, we observed a positive correlation between IDA and elevated HbA1C level in non-diabetic population.

KEYWORDS

Glycated hemoglobin, Iron status

INTRODUCTION

Anaemia is a major health issue that has adverse impact in the third world countries like India. Nutritional anemia due to iron deficiency constitutes more than 1/3rd of patients [1]. Throughout the circulatory life of the red blood cell, HbA1c is formed continuously by adjoining of glucose to the N terminal of the haemoglobin beta chain. HbA1C has been broadly utilized as a marker of glycaemic status overpast three months [2]. According to ADA guidelines, HbA1C levels need to be kept underneath 6.5% in every diabetic patient to prevent the progression of various micro vascular complications [3].

HbA1C levels are not influenced by blood glucose levels alone. Studies suggest that conditions like IDA, haemolytic anaemia, alcohol ingestion, pregnancy, blood loss, uraemia may alter HbA1C levels independent of glycaemic status [4].

The relationship between iron status and HbA1C level has long been a topic of debate in the literature [5]. Few studies report that iron deficiency increases HbA1C level and intend to explain on the basis of both modification of the quaternary structure of haemoglobin and HbA1C levels in old and new red blood cells [4-7].

English E et al., highlighted the need for further studies in this field to confirm and elucidate the role of anaemia on HbA1C results [8].

Since only few studies has been carried out in western India, we were prompted to conduct this study to determine the impact of IDA on HbA1C in non diabetic population to determine the effect of glucose on HbA1C.

MATERIALS AND METHODS

This was a cross-sectional descriptive study carried out in Medipulse hospital, Jodhpur between July 2021 to January 2021. Totally 200 non diabetics aged >18 years (100 patients with IDA and 100 patients without IDA) were included in our study. An informed consent was obtained from all the subjects. Those having Hemoglobin <12 gm/dl in males and <11 gm/dl in females, and peripheral smear showing microcytic hypochromic picture were considered to have IDA and confirmed by their serum iron (<60 μ g/dl) and ferritin levels (<15 μ g/l) and TIBC levels [9].

A total of 100 non diabetics without IDA were included to serve as controls. All the laboratory parameters analysed for study group and for the control group as well.

Medical history was taken to exclude DM, the patients had to have no history of DM and two FPG <126 mg/dl, performed close to the date of

the complete blood count. Patients with history of chronic alcohol ingestion, kidney diseases, blood loss, haemolytic anaemia and pregnant patients were excluded from both the study and control group.

On the basis of Hb level, anaemic patients were categorized as mild anaemia (12-12.9 gm/dl for males and 11-11.9 gm/dl for females), moderate anaemia (9-11.9 gm/dl for males and 8-10.9 gm/dl for females), and severe anaemia (<9 gm/dl for males and <8 gm/dl for females).

Measurements

Hb, Hct, MCV, MCH, MCHC were measured by SYSMEX XN1000 analyser. HbA1C measured by Nephelometry on Mispal i-2 which is based on the principle of Latex enhanced Immunoturbidimetry.

Plasma glucose was estimated by glucose oxidase/peroxidase method, serum iron (TPTZ) and serum ferritin (COBAS e 411 Roche diagnostic).

STATISTICAL ANALYSIS

The data were analysed using SPSS version 22 and presented as mean $\pm$ S.D for continuous variables. Unpaired t-test was applied for comparison of group means. Pearson's coefficient was calculated to determine correlation between two variables. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age of patients was 43.39 $\pm$ 18.14 and control was 42 $\pm$ 18.64. The mean S. Iron, S. Ferritin, S. TIBC in patients were 16.60 $\pm$ 5.20, 9.03 $\pm$ 2.05, 411.22 $\pm$ 32.48, and in control group 84.60 $\pm$ 9.03, 76.01 $\pm$ 8.04, 297.6 $\pm$ 28.46 respectively. These data provide evidence that S. ferritin, S. iron, Transferrin saturation %, were lower and S. TIBC was higher in anemic patients than in healthy controls and observe difference was statistically significant ($p < 0.001$) as shown in table.

In the present study, non diabetics with anemia (IDA) had a mean HbA1C % (5.98 $\pm$ 0.04) which was significantly higher ($p < 0.05$) than the non-anaemic group (5.06 $\pm$ 0.32). [Table/Fig-1].

Parameters	IDA (n=100) Mean $\pm$ SD	Controls (n=100) Mean $\pm$ SD	p Value
S. Iron	16.60 $\pm$ 5.20	84.60 $\pm$ 9.03	<0.001
S. Ferritin	9.03 $\pm$ 2.05	76.01 $\pm$ 8.04	<0.001
TIBC	411.22 $\pm$ 32.48	297.6 $\pm$ 28.46	<0.001
HbA1C	5.98 $\pm$ 0.04	5.06 $\pm$ 0.32	<0.001

DISCUSSION

Glycated hemoglobin A1c (HbA1c) is a major part of HbA1 and

comprises approximately 5% of the total hemoglobin non-diabetic individuals. HbA1C reflects glycaemic status for the previous three months. ADA guidelines have not only considered it as the primary target for glycaemic control but also included it as a diagnostic criterion [3]. Besides blood glucose, HbA1C levels can be affected by conditions unrelated to diabetes like anaemia [7]. Approximately 1/3rd of patients with anaemia have iron deficiency [1]. We observed that Hb, Hct, and red cell indices were lower in anaemic patients, along with a microcytic hypochromic blood picture confirming IDA. This is in accordance with results of Kalaskar *et al.*, [5].

In this study, we observed higher HbA1C level in non diabetics with IDA than those without IDA which was statistically significant. These results were obtained after excluding patients with other confounding factors known to interfere with HbA1C level. The results of the present study are consistent with those of the previous studies. The mechanisms leading to increased HbA1C levels in IDA were not clear [4].

The various theories proposed for increased HbA1C levels in IDA were alteration of quaternary structure of haemoglobin leading to more rapid glycation of globin chain [5]; Decrease in the Hb concentration might lead to an increase in the glycated fraction at a constant glucose level, because HbA1C is measured as a percentage of total Haemoglobin A [6];

Our study results are also consistent with the study done by El-Agouza *I et al.*, who reported that a decline in the Hb level might lead to increase in the glycated fraction at a fixed glucose level, because HbA1C is measured as a percentage of total Hb [6]. Similar results were also reported by Coban *E et al.*, and Kim *C et al.*, [9,10]

Coban *et al.*, showed a very large difference between HbA1C levels in non diabetic patients with and without IDA [9].

Sinha *et al.*, and few other studies contradicts with our results reporting that HbA1C levels are lowered in IDA [5,7]

Ferritin is a storage form of iron, and it reflects the true iron status [1]. In our study, serum ferritin as well as serum iron level was indirectly proportional to HbA1C. As explained previously, in IDA, ferritin is decreased with increase in the red cell life span which is associated with increased HbA1C.

CONCLUSION

This study established a positive correlation between IDA and elevated HbA1C level in non diabetic population. Elevation of HbA1C in iron depletion leads to over or under diagnosis of diabetes at the cut off point (6.5%). Thereby, this study insists on the importance to exclude IDA by iron studies and to rectify it before any diagnostic or therapeutic decision is made by clinician based solely on HbA1C level.

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