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ANAEMIA AND HAEMOGLOBIN A1C: IN NON DIABETIC PATIENTS.

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ABSTRACT

BACKGROUND: Haemoglobin A1c (HbA1c) has been adopted by physicians as a surrogate for monitoring glycemic control. There exists concern that other factors beyond serum glucose concentration may affect glycation rates and by extrapolation HbA1c levels.

AIMS AND OBJECTIVE: The aim of this study was to determine the effect of IDA on the HbA1c levels in non diabetic patients, so as to consider IDA as an important factor which influenced the HbA1c levels, while monitoring the glycemic status of diabetics.

METHODS: The study group comprised 620 non diabetic aged > 20 years (290 patients with IDA and 330 patients without IDA)

RESULTS: The mean HbA1c (7.6 ± 0.9%) level in the patients with IDA was higher than that in the control group (5.5 ± 0.8%) (p < 0.05).

CONCLUSION: The study emphasizes the need to exercise caution when Applying HbA1c reference ranges to anemic populations

KEYWORDS : Iron Deficiency Anemia [ida], Non Diabetes Mellitus, Hba1c

INTRODUCTION:

Iron deficiency anaemia (IDA) is one of the most prevalent types of malnutrition and common in India. Ferritin is the form in which iron is stored, and testing amount of ferritin reflects the iron status. HbA1c levels are not influenced by blood glucose levels alone, studies suggested that conditions like IDA, haemolytic anaemia , alcohol ingestion, pregnancy, blood loss, uraemia, may alter HbA1c levels independent of glycemic status(1) Globally, 50% of anaemia is attributed to iron deficiency (2). Studies have shown that reduced iron levels are correlated with increased levels of HbA1c leading to false high levels of HbA1c in non-diabetic individuals [3,4]. The earliest study to investigate the effects of iron deficiency anaemia on HbA1c levels was conducted by Brooks et al. [3] who assessed HbA1 levels in 35 non-diabetic patients having iron deficiency anaemia both before and after treatment with iron. They observed that HbA1 levels were significantly higher in iron deficiency anaemia patients and decreased after treatment with iron.

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). According to studies conducted by Kalasker V et al., there were no variation between HbA1C levels in patients with IDA and controls (5).English E et al., reported a recent review in 2015 about the controversies, in this issue and highlighted the need for further studies in this field to confirm and elucidate the role of anaemia on HbA1C results [8].

A high incidence of anaemia was observed in diabetics without renal insufficiency, and also suggested that poor glycemic control and old age are associated with the incidence of anaemia in diabetic patients with normal renal function (9).

Since only limited number of studies has been carried out in Indian population, thus, the objective of the present study was to determine whether the HbA1c levels were increased among the anemia patients without diabetes. If so, the iron deficiency had to be corrected before any diagnostic or therapeutic decision was made based on the HbA1c level. We also analyzed the variation of HbA1c according to the degree of anemia.

MATERIALS AND METHODS:

This was a descriptive analytical case control study carried out at Bowring & Lady Curzon Medical College & Research Institute, Bangalore, and Karnataka between April 2019 to December 2019. Totally 620 non diabetic aged > 20 years (290 patients with IDA and 330 patients without IDA) were included in our study. The anemic patients were selected, based on their hemoglobin levels (Hb < 11 g/dl), ferritin levels (<9 ng/ml for women, <15 ng/ml for men) and on their peripheral blood smears (mostly microcytic hypochromic), which suggested iron deficiency anemia and on their hematologic investigations and serum fasting and postprandial glucose levels. The patients who had glucose tolerance abnormalities (impaired glucose tolerance or diabetes mellitus), hemoglobinopathies, hemolytic anemia, chronic alcohol ingestion, and chronic renal failure and pregnant women were excluded from the study.

A total of 330 non diabetics without IDA were enrolled to serve as controls. All the laboratory parameters analysed for study group and for the control group as well.

On the basis of Hb level, anemic 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) .Hb,Hct, MCV, MCH, MCHC were measured by XT 1800i-sysmex haematology analyzer .HbA1c measured by Beckman coulter Au480 auto analyzer. Plasma glucose and serum ferritin Mini vidas automated Immuno analyzer.

Absolute HbA1c levels were calculated from the measured HbA1c levels by using formula

$$\text{Absolute HbA1C (gm/dl)} = \frac{\text{HbA1C (\%)} \times \text{Hb (gm/dl)}}{100}$$

STATISTICAL ANALYSIS:

The data were analysed using SPSS version 20 and presented as mean±S.D for continuous variables. Pearson's coefficient was calculated to determine correlation between two variables. p-value <0.05 was considered statistically significant.

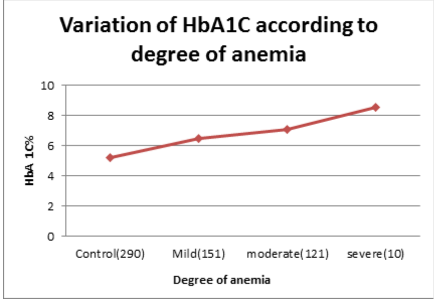
RESULTS:

The mean HbA1c (7.6 ± 0.9%) level in the patients with IDA was higher than that in the control group (5.5 ± 0.8%) (p < 0.001). All the parameters which were tested in both the groups have been reported in [Table1]. The fasting and the postprandial blood glucose levels confirmed the non diabetic status. The serum ferritin levels (index of the iron deficiency status) were low among the iron deficient subjects (3.68±1.8 ng/ml) and the peripheral blood smears showed a hypochromic microcytic picture. Absolute HbA1C (gm/dl) in those patients with IDA and non anemic group were 0.78±0.01 and 0.73±0.01 respectively which was also statistically significant (p <0.05).

Parameter	IDA (n=290)	control(n=330)
Hb(g/dl)	10.6±1.1	14.4±0.96

HCT(%)	33.2±3.0	41.4±2.7
MCV(fl)	72.3±4.2	84.2±4.6
MCH(pg)	22.6±2.2	32.9±1.7
Ferritin(ng/ml)	3.68±1.8	22.3±6.1
FBS(mg%)	92.8±9.4	90.7±10.6
PPBS(mg%)	104.6±6.1	101.9±5.8
HbA1C(%)	7.6±0.9	5.5±0.8

290 non-diabetics with IDA were further categorized according to degree of anaemia as mild(159), moderate (121) and severe (10). We also analysed HbA1C level in various degree of anaemia and observed that HbA1C increases as severity of anaemia worsen which was statistically significant ($p < 0.05$) [Fig-1].



DISCUSSION:

HbA1C is the most frequently occurring fraction of haemoglobin A_1. HbA1C reflects glycemic status for the previous three months. ADA guidelines have not only considered it as the primary target for glycemic 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]

In the present study we investigated the effect of iron deficiency anaemia (IDA) on HbA1c levels in non diabetic adults. HbA1c results were higher in patients with IDA than in patients without anemia. Similarly, Brooks et al., [10] showed higher HbA1c concentrations in iron-deficient non diabetic adults, which decreased to normal after iron replacement. Hansen et al., [11] showed normal HbA1c concentrations in iron deficiency, which dropped to subnormal levels after iron supplementation.

Several other studies done before also showed similar results as our present study [4,6,13,14,16] (Table2)

Comparison of present study HbA1C levels with previous studies having similar results.

Study	Year	Number screened	IDA	Non anaemic	Significance
El-Agouza I et al.	2002	81	6.1±0.6	5.2±0.4	$p < 0.05$
Coban E et al.	2004	100	7.4±0.8	5.9±0.5	$p < 0.05$
Shanthi B et al.	2013	100	7.6±0.5	5.5±0.8	$p < 0.05$
Silva JF et al.,	2016	122	5.6±0.4	5.3±0.4	$p < 0.05$
Nachiappan et al	2017	460	6.8±0.07	5.1±0.04	$p < 0.05$
Present study	2020	620	7.6±0.9	5.5±0.8	$p<0.05$

In anemic patients, the concentration of glycated hemoglobin has been reported to be increased despite the shortened life span of the erythrocytes. Several mechanisms have been advocated for this increase in the levels of glycated hemoglobin in anemic patients. It has been proposed that in iron deficiency, the quaternary structure of the hemoglobin molecule may be altered, and that the glycation of the β-globin chains occurs more readily. According to some investigators, the increase in the glycated hemoglobin levels in non-diabetic anemic patients has been mainly attributed to the decrease in the hemoglobin levels.(6). But studies which have investigated the glycation levels of other proteins have not been carried out.

This study has got a significant relevance because iron deficiency anaemia is very highly prevalent in a tropical country like India. HbA1c is commonly used to assess the long-term blood glucose control in the patients with diabetes mellitus, because the HbA1c value has been shown to predict the risk for the development of many of the chronic complications in diabetes [11,12].

IDA affects HbA1c results and this effect is dependent on anaemia degree. In our study, serum ferritin 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. This goes in hand with other study results of Shanthi B et al., and Raj S et al., (13,15].

We also analysed HbA1C results in different degrees of anaemia and found that HbA1C level increases as severity of anaemia worsens. This result of ours was in accordance with the results of Silva JF et al.,(14)

CONCLUSIONS:

The study emphasizes the need to exercise caution when applying HbA1c reference ranges to anaemic populations. It makes the case for defining HbA1c reference ranges and thus, therapeutic goals for each anaemia subtype. Redefining such reference ranges may increase the sensitivity of HbA1c in diagnosing diabetes in anaemic population .

REFERENCES

1. Christy AL, Manjrekar PA, Babu RP, Hegde A. Influence of iron deficiency anaemia on haemoglobin A1C levels in diabetic individuals with controlled plasma glucose levels. Iran Biomed J. 2014;18(2):88. [PMC free article] [PubMed] [Google Scholar]
2. Nitin Sinha, Mishra TK, Tejinder Singh, Naresh Gupta; Effect of Iron Deficiency Anemia on Hemoglobin A1c Levels Ann Lab Med. 2012 Jan;32(1):17–22.
3. Brooks AP, Metcalfe J, Day JL, Edwards MS. Iron deficiency and glycosylated haemoglobin A1. Lancet. 1980 Jul;316(8186).
4. Coban E, Ozdogan M, Timuragaoglu A. Effect of iron deficiency anemia on the levels of hemoglobin A1c in nondiabetic patients. Acta Haematol. 2004;112:126–128.
5. Kalasker V, Kodliwadmath MV, Bhat H. Effect of iron deficiency anaemia on glycosylated haemoglobin levels in non diabetic Indian adults. Int J Med Hlth Sci. 2014;3(1):40–43. [Google Scholar]
6. El-Agouza I, Abu Shahla A, Sirdah M. The effect of iron deficiency anaemia on the levels of haemoglobin subtypes: Possible consequences for clinical diagnosis. ClinLabHaematol. 2002;24(5):28589. [PubMed] [Google Scholar]
7. Sinha N, Mishra TK, Singh T, Gupta N. Effect of iron deficiency anaemia on haemoglobin A1C levels. Ann Lab Med. 2012;32(1):17–22. [PMC free article] [PubMed] [Google Scholar]
8. English E, Idris I, Smith G, Dhatariya K, Kilpatrick ES, John WG. The effect of anaemia and abnormalities of erythrocyte indices on HbA1C analysis: A systematic review. Diabetologia. 2015;58(7):1409–21. [PubMed] [Google Scholar]
9. Ganesha Pandian M, Geetha H, Sundhararajan A. Risk of anaemia in Type2 diabetic patients in the absence of renal impairment. Indian Journal of Applied Research, 2017; March 7(3):50-52.
10. Brooks AP, Metcalfe J, Day JL, Edwards MS. Iron deficiency and glycosylated haemoglobin A1. Lancet. 1980;19(ii):141.
11. Hansen PG, Eriksen J, Andersen TM, Olesen L. Glycosylated hae¬moglobin (HbA1c) in iron and vitamin B12 deficiency. J Intern Med. 1990; 227:133–36.
12. Kim C, Bullard KM, Herman WH, Beckles GL. Association between iron deficiency and A1C levels among adults without diabetes in the National Health and Nutrition Examination Survey, 1999-2006. Diabetes care. 2010;33(4):780–85. [PMC free article] [PubMed] [Google Scholar]
13. Shanthi B, Revathy C, Manjula Devi AJ, Subhashree AR. Effect of iron deficiency on glycation of haemoglobin in nondiabetics. J Clin Diagn Res. 2013;7(1):15–17. [PMC free article] [PubMed] [Google Scholar]
14. Silva JF, Pimentel AL, Camargo JL. Effect of iron deficiency anaemia on HbA1C levels is dependent on the degree of anaemia. Clinical Biochemistry. 2016;49(1):117–20. [PubMed] [Google Scholar]
15. Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1C in Type 2 diabetes mellitus. Int J Res Med Sci. 2013;1(1):12–15. [Google Scholar]
16. Nachiappan R , Anitha G , Geetha H. INFLUENCE OF IRON DEFICIENCY ANAEMIA ON HBA1C IN TYPE 2 DIABETIC AND NON-DIABETIC, Indian Journal of Applied Research, 2017, August 7(8):80-82.