TO STUDY THE EFFECT OF IRON DEFICIENCY ANAEMIA ON HbA1C IN NON-DIABETIC

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ABSTRACT

BACKGROUND

The most common form of anaemia plaguing our country is Iron deficiency anaemia. The extent of diabetic control is measured by HbA1c, which is the average blood glucose level of the patient over the past 3 months. HbA1c levels depend upon a multitude of factors such as the presence of different types of haemoglobins, any haemolytic anaemia, any nutritional deficiency anaemias, uraemia, pregnancy and acute blood loss. Older studies suggest that Iron deficiency anaemia is another one of the factors affecting HbA1C levels.

We conducted a prospective observational study to analyse the effect of iron deficiency anaemia on glycated haemoglobin (HbA1c) in non-diabetic Indians.

MATERIALS AND METHODS

A prospective observational study on 500 iron deficiency patient cases was carried out in SGM Hospital, Rewa from the period July 2016 to June 2017. Exclusion and inclusion criteria were used to recruit cases from the wards and OPDs of the hospital. Appropriate descriptive statistics was used to analyse the data.

RESULTS

The mean HbA1c level in the patients with iron deficiency anaemia (IDA) is 6.19 ± 0.58 . In our study, we found increased severity of iron deficiency anaemia is associated with increased level of HbA1c. In female patients (379 out of 500) mild anaemia (73)- mean HbA1c 5.79 ± 0.35 ; moderate anaemia (242)- mean HbA1c 6.16 ± 0.39 ; and severe anaemia (64)- mean HbA1c 7.2 ± 0.46 . In our study in male patients (121 out of 500) mild anaemia (34)- mean HbA1c 5.79 ± 0.35 ; moderate anaemia (73)- mean HbA1c 5.86 ± 0.26 ; and severe anaemia (14)- mean HbA1c 6.80 ± 0.354 .

CONCLUSION

It was found that IDA was more common among the reproductive age group women. It was associated with shift in the HbA1c levels to higher side with severity of anaemia.

KEYWORDS

Non-Diabetic Patient, Glycosylated Haemoglobin, Iron Deficiency Anaemia.

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BACKGROUND

HbA1c is used as the gold standard for monitoring glycaemic control and used as a foreseer of diabetic complications.^[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.

This process is non-enzymatic and reflects the average exposure of haemoglobin to glucose over a period of nearly 70 - 90 days. HbA1c has been defined as the fast fraction haemoglobin (HbA1a, A1c), which elute first during column chromatography with cation-exchange resin. HbA1c levels are not influenced by only blood glucose levels.

Any condition that decreases the average length of life of erythrocytes is also responsible for decreased HbA1c level. These conditions are acute or chronic blood loss, sickle cell anaemia, thalassaemias, haemolytic anaemia, aplastic anaemia, splenectomy, pregnancy, chronic kidney diseases, vitamin-B12 and folate deficiency anaemia.^[2,3]

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Falsely raised HbA1c can be seen during the increased lifespan of circulating erythrocyte. These conditions are alcoholism, hyperbilirubinaemia and iron deficiency anaemia.^[4,5] According to WHO, iron deficiency is the commonest of all deficiency diseases worldwide.^[6]

Iron deficiency anaemia is the most common in India.^[7] Some studies show that HbA1c levels are increased in iron deficiency anaemia and attempted to explain on the basis of both modifications to the structure of haemoglobin and levels of HbA1c in old and new red blood cells.^[8,9]

According to some studies, there were no differences between HbA1c levels of anaemic patients and controls.^[10,11] Study conducted by El-Agouza L et al showed that higher level of HbA1c seen in patients suffering from iron deficiency anaemia and with correction of anaemia fall in HbA1c is seen.^[12] Recently, Sinha et al showed that HbA1c levels and absolute HbA1c levels increased with treatment of iron deficiency anaemia.^[13]

MATERIALS AND METHODS

Type of Study

Prospective observational study.

Place of Study

Department of Medicine, SS Medical College and SGMH, Rewa, MP.

Sample Size

The studies was carried out on 500 non-diabetic patients with iron deficiency anaemia attending the OPD and admitted in medicine ward.

Study Duration

From July 2016 to June 2017.

The iron deficiency anaemic patients were recruited on their haemoglobin levels (Hb < 12 in non-pregnant female and 13 in male), ferritin levels (< 9 ng/ mL for women, < 15 ng/ mL for men) and on their peripheral blood smears which indicate iron deficiency anaemia.¹⁴

The levels of haemoglobin, mean corpuscular haemoglobin (MCH), haematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), platelet count, total leucocyte count (TLC) and differential leucocyte count (DLC) were measured by an automated analyser.

On the basis of haemoglobin level patients were categorised as having mild, moderate or severe anaemia. Mild anaemia (male patients 12 - 12.9 gm/ dL and female patients 11 - 11.9 gm/ dL).

Moderate anaemia (male patients 9 - 11.9 gm/ dL and female patients 8 - 10.9 gm/ dL) and severe anaemia (male patients < 9 gm/ dL and female patients < 8 gm/ dL). Those with predominantly microcytic indices (MCV < 80 fL), hypochromic indices (MCH < 26 pg/ cell) were considered to have iron deficiency anaemia.¹⁴ Normal HbA1c in non-diabetic individuals is < 5.6%.¹⁵

Inclusion Criteria

1. Patient without diabetes.
2. Patient belonging to rural and urban area.
3. > 18 yrs. of age.
4. Giving consent for study.

Exclusion Criteria

Patients with history of acute or chronic blood loss, haemolytic anaemia, haemoglobinopathies, kidney diseases, diabetics, pregnancy, chronic alcohol ingestion and impaired glucose tolerance are excluded.

The blood specimens were drawn after an 8-hourly fasting period. A Sysmex automated haematology analyser (MINDRAY) was used for the whole blood counts [haemoglobin (Hb), mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH)]. The serum ferritin levels were measured by using a Diatek kit in a Labowind semiautomated analyser and the peripheral blood smears were examined in all the patients. The HbA1c levels were determined by turbidimetric immunoinhibition.

Statistical Analysis

Continuous data were expressed as mean $\pm$ SD and median, and analysed by unpaired 't' test. Categorical data was represented as numbers and percentages and was analysed using the Chi-square test. P value of 0.05 or less was considered as statistically significant. Study was analysed by SPSS version 22.0.

RESULTS

In our study mean age is 37.10 ± 12.39 , mean serum ferritin is 18.45 ± 6.39 , mean haemoglobin is 9.51 ± 1.86 , mean HbA1c is 6.19 ± 0.58 , mean MCV is 68.22 ± 6.03 , mean MCH is 22.87 ± 1.77 , mean FBS is 81.26 ± 6.99 , mean PPBS is 112.65 ± 10.50 . In our study, increase in severity of anaemia is associated with increased HbA1c level.

In our study in female patient (379 out of 500)- mild anaemia (73)- mean HbA1c 5.79 ± 0.35 ; moderate anaemia (242)- mean HbA1c 6.16 ± 0.39 ; and severe anaemia (64)- mean HbA1c 7.2 ± 0.46 .

In our study in male patient (121 out of 500)- mild anaemia (34)- mean HbA1c 5.79 ± 0.35 ; moderate anaemia (73)- mean HbA1c 5.86 ± 0.26 ; severe anaemia (14)- mean HbA1c 6.80 ± 0.354 .

Out of 500 cases 107 (21.4%), 315 (63%) and 78 (15.6%) have mild, moderate and severe anaemia respectively. Out of 121 male patients, 34 (28.09%) have mild anaemia, 73 (60.33%) have moderate anaemia and 14 (11.57%) have severe anaemia. Out of 379 female patients, 73 (19.26%) have mild anaemia, 242 (63.85%) have moderate anaemia and 64 (16.88%) have severe anaemia.

Out of 500 patients, easy fatigability are present in 100% (500), dyspnoea on exertion present in 75% (375), melena present in 22.6% (113), giddiness in 20.2% (101), palpitation in 15.6% (78) and fever present in 13.4% (67). Out of 500 patients 500 (100%) patients have pallor, 134 (26.8%) have bald tongue, 136 (27.2%) have koilonychia, 47 (9.4%) have ejection systolic murmur and 43 (8.6%) have bilateral pedal oedema.

Parameter in Study	Mean Value in Study
HbA1c (%)	6.19 ± 0.58
Serum ferritin (ng/ mL)	18.45 ± 6.39
Haemoglobin (gm/ dL)	9.51 ± 1.86
MCV (fL)	68.22 ± 6.03
MCH (pg/ cell)	22.87 ± 1.77
FBS (mg/ dL)	81.26 ± 6.99
PPBS (mg/ dL)	112.65 ± 10.50
Mean Age (in yrs.)	37.10 ± 12.39

Table 1

Sl. No.	Gender	Number of Cases	Percentage
1	Male	121	24.2
2	Female	379	75.8
	Total	500	100.0

Table 2. Distribution of Cases according to Gender

Out of 500 patients, female patients are 379 (75.8%) and male patients are 121 (24.2%).

Sl. No.	Residence	Number of Cases	Percentage
1	Urban	145	29
2	Rural	355	71
	Total	500	100.0

Table 3. Distribution of Cases according to Domicile

Out of 500 patients, 355 (71%) belonged to rural community and 145 (29%) belonged to urban community.

Sl. No.	Anaemia	Number of Cases	Percentage
1	Mild	107	21.4
2	Moderate	315	63.0
3	Severe	78	15.6
	Total	500	100.0

Table 4. Distribution of Cases according to Severity of Anaemia

Out of 500 cases 107 (21.4%), 315 (63%) and 78 (15.6%) have mild, moderate and severe anaemia respectively.

Sl. No.	Symptoms	Number of Cases	%
1	Easy fatigability	500	100
2	Dyspnoea on exertion	375	75
3	Fever	67	13.4
4	Giddiness	101	20.2
5	Melena	113	22.6
6	Palpitation	78	15.6

Table 5. Distribution of Cases according to Symptoms

Out of 500 patients, easy fatigability is present in 100% (500), dyspnoea on exertion present in 75% (375), melena present in 22.6% (113), giddiness in 20.2% (101), palpitation in 15.6% (78) and fever present in 13.4% (67).

Sl. No.	Age Group (In Yrs.)	Severity of Anaemia			Total
		Mild	Moderate	Severe	
1	18 to 30	32(29.9%)	104(33.01%)	29(37.1%)	165(33%)
2	31 to 40	30(28.03%)	98(31.1%)	29(37.1%)	157(31.4%)
3	41 to 50	18(16.8%)	72(22.8%)	12(15.3%)	102(20.4%)
4	51 to 60	14(13.08%)	30(9.5%)	06(7.6%)	50(10%)
5	>60	13(12.01%)	11(3.49%)	02(2.5%)	26(5.2%)
		107(21.4%)	315(63%)	78(15.6%)	500

Table 8. Distribution of Age Group according to Severity of Anaemia

Chi-square= 18.764, P value= 0.0162 significantly associated.

It is evident from the above table that maximum number of patients are present in 18 - 30 years of age group, that is 165 (33%) followed by 157 (31.4%) in 31 - 40 years of age group, 102 (20.4%) in 41 - 50 years of age group, 50 (10%) in 51 to 60 years of age group and minimum number of patients are present in > 60 years of age group 26 (5.2%).

Sl. No.	Male/ Anaemia	HbA1c			
		≤5.5	5.6 to 6.5	6.6 to 7.5	>7.5
1	Mild anaemia < 12 to 12.9 gm/ dL (n= 34, 28.09%)	10(29.41%)	24(70.58%)	0	0
2	Moderate anaemia 9 to 11.9 gm/ dL (n= 73, 60.33%)	3(4.10%)	68(93.15%)	2(2.73%)	0
3	Severe anaemia < 9 gm/ dL (n= 14, 11.57%)	0	3(21.4%)	10(71.42)	1(7.14%)
	Total= 121	13(10.74%)	95(78.5%)	12(9.91%)	1(0.82%)

Table 9. Correlation between HbA1c and Severity of Anaemia in Male Patient

Chi-square= 91.817, P= < 0.0001 statistically significant.

Above table shows that out of 121 male patients, 70.58% (24 of 34) patients with mild anaemia have HbA1c between 5.6% - 6.5% and there are no patients in HbA1c range between 6.6% - 7.5%, whereas 93.15%(68 of 73) patients with moderate anaemia have HbA1c between 5.6% - 6.5% and 2.73% (2 of 73) patients have HbA1c between 6.6% - 7.5%, 71.42% (10 of 14) patients in a group of severe anaemia have HbA1c range between 6.6% - 7.5%.

Sl. No.	Female/ Anaemia	HbA1c			
		≤5.5	5.6 to 6.5	6.6 to 7.5	>7.5
1	Mild anaemia < 11 to 11.9 gm/ dL (n= 73, 19.26%)	23 (31.5%)	50 (68.49%)	0	0
2	Moderate anaemia 8 to 10.9 gm/ dL (n= 242, 63.85%)	7 (2.89%)	189 (78.09)	46(19%)	0
3	Severe anaemia < 8 gm/ dL (n= 64, 16.88%)	0	2 (3.12%)	46(71.87%)	16(25%)
	Total= 379	30 (7.91)	241 (63.58%)	92(24.27%)	16(4.22%)

Table 10. Correlation between HbA1c and Severity of Anaemia in Female Patient

Chi-square= 268.16, P= < 0.0001 statistically significant.

Sl. No.	Sign	Number of Cases	Percentage
1	Pallor	500	100
2	Bald tongue	134	26.8
3	Koilonychia	136	27.2
4	Ejection systolic murmur	47	9.4
5	Pedal oedema	43	8.6

Table 6. Distribution of Cases according to Sign

Out of 500 patients 500 (100%) patient have pallor, 134 (26.8%) have bald tongue, 136 (27.2%) have koilonychia, 47 (9.4%) have ejection systolic murmur and 43 (8.6%) have bilateral pedal oedema.

Sl. No.	Addiction	Number of Cases	Percentage
1	Tobacco	156	31.2
2	Smoking	49	9.8
5	Tobacco + Smoking	47	9.4

Table 7. Distribution of Cases according to Addiction

Above table shows that 156 (31.2%) are addicted for tobacco, 49 (9.8%) are addicted for smoking, addiction for both was present in 47 (9.4%).

Above table shows that out of 379 female patients, 68.49% (50 of 73) patients with mild anaemia have HbA1c between 5.6% - 6.5% and there are no patients in HbA1c range between 6.6% - 7.5%, whereas 78.09% (189 of 242) patients with moderate anaemia have HbA1c between 5.6% - 6.5% and 19% (46 of 242) patients have HbA1c between 6.6% - 7.5%, 71.87% (46 of 64) patients in a group of severe anaemia have HbA1c range between 6.6% - 7.5% and 25% (16 of 64) patients in group of severe anaemia have HbA1c > 7.5%.

Age Group (In Yrs.)	Total Patients	Mean HbA1c
18-30 yrs.	165	6.23±0.59
31-40 yrs.	157	6.27±0.60
41-50 yrs.	102	6.14±0.57
51-60 yrs.	50	6.16±0.54
>60 yrs.	26	6.02±0.47
Total (n)	500	6.19±0.58

Table 11. Mean HbA1c in Different Age Group

In our study, mean HbA1c value in all 500 patients is 6.19 ± 0.58 . In 18 - 30 yrs., mean HbA1c is 6.23 ± 0.59 . In 31 - 40 years' age group, mean HbA1c is 6.27 ± 0.60 . In 41 - 50 years' age group, mean HbA1c is 6.14 ± 0.57 . In 51 - 60 years' age group, mean HbA1c is 6.16 ± 0.54 . In > 60 years, mean HbA1c is 6.02 ± 0.47 .

X-axis- Severity of anaemia

Y-axis- Mean HbA1c level (%)

Association between Severity of Anaemia and Hba1c Level in Male

Association between Severity of Anaemia and Hba1c Level in Female

DISCUSSION

In our study, mean HbA1c value in all 500 patients is 6.19 ± 0.58 . In 18 - 30 yrs., mean HbA1c is 6.23 ± 0.59 . In 31 - 40 years' age group, mean HbA1c is 6.27 ± 0.60 . In 41 - 50 years' age group, mean HbA1c is 6.14 ± 0.57 . In 51 - 60 years' age

group, mean HbA1c is 6.16 ± 0.54 . In > 60 yrs., mean HbA1c is 6.02 ± 0.47 .

El-Agouza et al¹² and Coban⁶ et al showed that HbA1c levels were higher in patients with iron deficiency anaemia and decreased significantly upon treatment with iron. Similar results were also seen in studies carried out by Gram-Hansen et al.¹¹

In Lavanya Rajagopal¹⁶ et al study, non-diabetics with IDA had a mean HbA1c % (6.84 ± 0.07), which was significantly higher ($p < 0.05$) than the non-anaemic group (5.12 ± 0.04).

The mean HbA1c level was higher in iron deficiency anaemic patient when compared to normal healthy individual in study by Balasubramanian Shanthi et al.¹⁷

In Alap L Christy et al¹⁸ study, the mean HbA1c of cases was $6.87 \pm 1.4\%$, while it was $5.65 \pm 0.69\%$ in healthy control.

In the Ford ES et al study,¹⁹ reported no significant difference in mean HbA1C concentration according to the IDA status as well as before and after iron treatment.

In Saudek CD et al study,²⁰ suggested that red cell age was unlikely to be a significant factor in explaining the changes in HbA1C levels during the treatment of IDA and believed that the reported differences in HbA1C concentrations before and after iron supplementation were due to differences in the laboratory methods used for measuring HbA1c.

CONCLUSION

Glycosylated haemoglobin (HbA1c) values were significantly higher in non-diabetic IDA patients implying that iron deficiency anaemia leads to a rise in the glycosylated haemoglobin values. This may have a practical application in diabetic individuals with iron deficiency anaemia, where glycosylated haemoglobin alone may give a false picture of poor glycaemic control. Therefore, iron deficiency must be corrected before making diagnostic or therapeutic decision based on glycosylated haemoglobin values in diabetes mellitus.

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