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EFFECT OF IRON DEFICIENCY ANEMIA ON HAEMOGLOBIN A1C LEVELS

Pathology

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ABSTRACT

Background: Iron deficiency anemia is the most common form of anemia in India. It is the one of the most prevalent forms of malnutrition. Previous studies have reported that iron deficiency may elevate HBA1C concentrations, however reports are inconsistent.
Aim: This study aimed to analyze the effect of iron deficiency anemia on HB1AC levels.
Methods: This study was a retrospective case control study with 67 diagnosed cases of iron deficiency anemia and 50 healthy controls. Iron profile and Hb1Ac levels were taken in both study groups.
Results: Out of 67 cases, there were 45 females(67.16%),22 males(32.83%) as compared to 14 females (28%) and 36males (22%) in 50 controls, the mean age of patients in study group was 46.29±13.59 years as compared to 46.84±14.00 years in controls, the mean haemoglobin value of patients in study group at baseline was 10.66±1.87g/dl as compared to 13.63±1.88 g/dl in control group. Mean serum iron, TIBC and transferring saturation at baseline in study group was found to be 25.07±11.52 mcg/dl, 366.98±68.39mcg/dl and 7.18±3.36% as compared to 76.85±30.75mcg/dl, 314.0±54.10mcg/dl and 25.98±11.04% respectively in control group. The mean HbA1c value in patients of study group at baseline level was 6.17±0.86% as compared to patients in control group that is 5.72±0.65 %. Mean of other variables like MCV, MCH, MCHC in patients of study group was 75.55+6.67fl, 23.06+2.89pg, 29.93+1.65gm/dl as compared to 86.50±4.93fl, 28.68±1.66pg, 32.91±1.24gm/dl in individuals of control group, difference of means variables between study cases and controls found statistically significant at baseline level. There found no statistically significant correlation between serum iron and HbA1c in anaemic cases.
Conclusion: In contrast to the observations of previous studies, present study could not establish the effect of iron deficiency anaemia on HbA1c levels.

KEYWORDS

Iron deficiency anemia, HbA1c level.

Introduction

Iron deficiency is one of the most prevalent forms of malnutrition. In India, more than half (51%) of all women of reproductive age have anemia, globally 614 million women aged 15-49 years were affected by anaemia as per WHO report in 2017.Iron deficiency anaemia is the most common form of anaemia observed in India[1].Earlier studies showed that reduced iron stores have a link with increased glycation of HbA1c leads to false high values of HbA1c in non diabetic individuals[2].HbA1c reflect the patient's glycemic status over past 3 months and is widely used as a screening test for type2 diabetes and American Diabetes Association has mentioned HbA1c≥6.5% as a diagnostic criterion for diabetes mellitus[3].HbA1c levels not affected by blood glucose only but they are also altered in hemolytic anemias[4], haemoglobinopathies[5],acute and chronic blood loss[6],pregnancy[7,8] and chronic renal failure[9].Vitamin B12,folate and iron deficiency anaemia also affect HbA1c levels. Earlier studies reported that iron deficiency falsely elevates HbA1c levels and different theories are suggested behind this mechanism, yet reports are inconsistent. Iron deficiency anaemia is very common in Indian settings and should always be ruled out when high HbA1c levels are detected and should be corrected on priority before making diagnosis of Diabetes Mellitus or altering treatment regimen for diabetic patients.

Material and Methods

The study data was taken from Modern Diagnostic laboratory, Kurukshetra (Haryana) in May2020, 67 confirmed cases of iron deficiency anaemia with haemoglobin <12gm/dl in females and 13gm/dl in men, serum iron<35mcg/dl, TIBC(Transferin Iron Binding Capacity)>450mcg/dl and Transferrin saturation<16% with automated haematological indices like MCV<80fl/cell, MCH <27pg/cell, MCHC<30g/dl and HbA1c≥6.5 were taken into consideration. Individuals with history of haemolytic anaemia, renal failure, pregnancy and established diabetes (FPG>126mg/dl and random plasma glucose >200mg/dl) were excluded from this study. 50 healthy controls with all parameters normal with the same exclusion criterion were taken into study for comparison. Since it was a retrospective study, I had no clinical presentation and peripheral picture of these cases. Complete blood counts measured by Sysmex, HbA1c was measured by HPLC using HLC-723GX analyzer and iron profile based on Ferrozine, Chromazurol B measured by Biosystem A-25 and blood glucose estimated by oxidase peroxidase method using Biosystem A-25.

Statistical methods: Categorical data were reported as mean and standard deviation. Table 't' value were used to test the difference between two groups means and Chi square test used to test the comparison between Hb1Ac and serum iron in both study groups. P value <0.05 was considered as statistically significant. Pearson's correlation coefficient used to see the correlation between two variables.

Results: Out of 67 cases, there were 45 females(67.16%),22 males(32.83%) as compared to 14 females (28%) and 36males (22%) in 50 controls. The mean age of patients in study group was 46.29±13.59 years as compared to 46.84±14.00 years in controls. The mean haemoglobin value of patients in study group at baseline was 10.66±1.87g/dl as compared to 13.63±1.88 g/dl in control group. Mean serum iron, TIBC and transferring saturation at baseline in study group was found to be 25.07±11.52 mcg/dl, 366.98±68.39mcg/dl and 7.18±3.36% as compared to 76.85±30.75mcg/dl, 314.0±54.10mcg/dl and 25.98±11.04% respectively in control group. The mean HbA1c value in patients of study group at baseline level was 6.17±0.86% as compared to patients in control group that is 5.72±0.65 %. Mean of other variables like MCV, MCH, MCHC in patients of study group was 75.55±6.67fl, 23.06±2.89pg, 29.93±1.65gm/dl as compared to 86.50±4.93fl, 28.68±1.66pg, 32.91±1.24gm/dl in individuals of control group.

Table 1: Baseline characteristics of the study subjects (N=67)

Sr. no	Parameters	Mean+Standard deviation
1.	Age	46.29±13.59
2.	Haemoglobin	10.66±1.87
3.	MCV	75.55±6.67
4.	MCH	23.06±2.89
5.	MCHC	29.93±1.65
6.	Serum Iron	25.07±11.52
7.	TIBC	366.98±68.39
8.	Transferrin Saturation	7.18±3.36
9.	Hb1Ac	6.17±0.86

Table 2: Baseline characteristics of control group (N=50)

Sr.No	Parameters	Mean+Standard deviation
1.	Age	46.84±14.00
2.	Haemoglobin	13.63±1.88
3.	MCV	86.50±4.93
4.	MCH	28.68±1.66
5.	MCHC	32.91±1.24
6.	Serum Iron	76.85±30.75
7.	TIBC	314.0±54.10
8.	Transferrin Saturation	25.98±11.04
9	HbA1c	5.72±0.65

Table 3: Comparison of haematlogical and biochemical variables between cases and controls

Variables	Cases	Controls	t value	P value
Age	46.29±13.59	46.84±14.00	0.189	0.850
HB	10.66±1.87	13.63±1.88	8.44	<0.0001
MCV	75.55±6.67	86.50±4.93	9.76	<0.0001
MCH	23.06±2.89	28.68±1.66	12.29	<0.0001
MCHC	29.93±1.65	32.91±1.24	10.68	<0.0001
S Iron	25.07±11.52	76.85±30.75	12.57	<0.0001
TIBC	366.98±68.39	314.0±54.10	4.51	<0.0001
TS	7.18±3.36	25.98±11.04	13.07	<0.0001
HbA1c	6.17±0.86	5.72±0.65	3.05	0.002

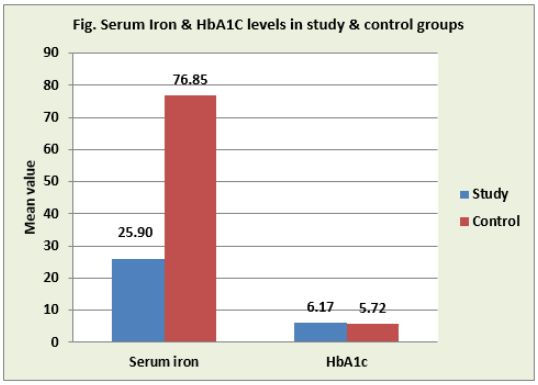

Table 3 depicts, comparison between variables of study cases and controls are statistically significant at baseline level.

Table 4: HbA1c levels in relation with serum Iron in study cases (N=67)

S Iron	HbA1c<6.5%	HbA1c>6.5%	x2	'P'
<50microgm/dl	54(80.59%)	11(16.42%)	0.404	0.524
>50microgm/dl	02(2.98%)	00	-	-

Table 4 depicts, majority of individuals 54(80.59%) with serum iron level below <50microgm/dl had HbA1C value of less than 6.5 which found statistically non significant. There is no single case in present study with iron level more than 50microgm/dl had Hb1Ac more than 6.5%.

Table 5: HbA1c levels in relation with serum iron in controls (N=50)

S Iron	HbA1c<6.5%	HbA1c>6.5%	x2	'P'
<50microgm/dl	03(6%)	00	-	-
>50microgm/dl	41(82%)	06(12%)	0.435	0.509

Table 5 depicts, maximum individuals 41(82%) with serum iron level >50microgm/dl have HbA1C value of less than 6.5 which found **statistically non significant.** There is no single control in present study with iron level less than 50microgm/dl had Hb1Ac more than 6.5%.

Table 6: Correlation between HbA1c, iron profile and haematological parameters using Pearson's correlation coefficient (Study cases=67)

Correlation between variables	R value	P value
HbA1c and serum iron	**0.09**	**0.944**
HbA1c and TIBC	**-0.175**	**0.803**
HbA1c and Transferrin saturation	**0.198**	**0.752**
HbA1c and Haemoglobin	**-0.086**	**0.951**
HbA1c and MCV	**-0.071**	**0.967**
HbA1c and MCH	**0.006**	**1.00**
HbA1c and MCHC	**-0.021**	**0.997**

In present study, positive correlation observed between Hb1Ac and serum iron, whereas other iron profile parameters like TIBC and transferrin saturation shown negative correlation with Hb1Ac which was **statistically non significant**. Other hematological parameters like Haemoglobin, MCV, MCHC shown negative correlation with Hb1Ac except MCH which came **statistically non significant.**

Discussion

Hb1Ac is one of the glycated haemoglobins which is used to assess the glycemic status of an individual over last 2 to 3 months and is mostly being used in diabetics and impaired glucose tolerance. Initially it was believed that Hb1Ac was only altered by glucose levels but certain studies showed Hb1Ac also affected by haemoglobinopathies, chronic kidney disease, pregnancy and other nutritional anaemias. Iron deficiency anaemia is one of the most common anaemia amongst nutritional anaemias in India, many studies in past shown Hb1Ac also affected by iron deficiency and found a significant reduction in Hb1Ac levels after iron therapy in non diabetic population. But in my study, results found inconsistent and non comparable with other studies conducted by Brooks et al[10],Sluiter et al[11],Mitcheil et al[12], Kairavi et al[13] in past. In present study, difference of means variables between study cases and controls found statistically significant at baseline level comparable with Kairavi et al[13] but on further comparison of serum iron with Hb1Ac in study cases, result came statistically non significant, majority of diagnosed anaemic cases have Hb1Ac below 6.5% at baseline level, although mean values of serum iron, heamoglobin, RBC indices found lower in diagnosed anaemic cases as compared to healthy controls with mean Hb1Ac found higher in study cases than controls. There found no statistically significant correlation between serum iron and Hb1Ac compared with Nitin et al[14],other iron profile parameters, haemologlobin and RBC indices shown negative correlation with Hb1Ac that too came statistically non significant. This study had major limitations like its small sample size which may limit generalization of results, secondly it was retrospective case control study, neither clinical data nor morphological picture could available for this study, thirdly serum ferritin values were not given in iron profile reports which is a definitive marker of iron deficiency anaemia, since serum ferritin have to advise separately besides complete iron study by clinicians if they required so and lastly I could not get the follow up data of cases after iron therapy which might have given a new dimension to this study.

Conclusion

In contrast to the observations of previous studies, present study found no significant correlation between serum iron and Hb1Ac, results might be better explained if this study had post iron therapy follow up data. Further studies are warranted.

Abbreviations: TIBC (Total Iron Binding Capacity), TS (Transferrin saturation), Hb (Haemoglobin), MCV(Mean corpuscular volume), MCH(Mean Corpuscular Haemoglobin), MCHC(Mean Corpuscular Haemoglobin Concentration).

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