ORIGINAL ARTICLE

Effect of Iron Replacement on Mean Decrease of Hba1c in Diabetic Type 2 Patients with Iron Deficiency Anemia

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ABSTRACT

Background: HbA1c is gold-standard for the assessment of glycemic control in diabetic patients. Studies have shown that iron deficiency anemia is associated with increased levels of glycated hemoglobin A1c (HbA1c), but the mechanism remains unclear. Several studies suggest that iron deficiency anemia affects the levels of HbA1c.
Aim: To determine mean change in HbA1c with iron supplementation in type 2 diabetic with iron deficiency anemia.
Place and duration of study: This study was carried out in Endocrine OPD, Department of Medicine, Sheikh Zayed Medical Complex, Lahore from 9-4-2019 to 9-10-2019.
Methodology: This is a Quasi experimental trial. Patients fulfilling selection criteria were enrolled in the study. At baseline, blood sample was obtained for assessment of HbA1c. Reports were assessed and HbA1c was noted. Then patients were prescribed oral ferrous sulfate at 200mg/day for 3 months. After 3 months, blood sample was obtained again for assessment of HbA1c. Reports were assessed and HbA1c was noted.
Results: Mean age of patients in this study was 54.84±8.69 years. Among patients 101(55.5%) were male and 81(44.5%) were female. Pretreatment HbA1c level was 6.99±0.32 and post treatment HbA1c level was 6.29±0.32. Mean change in post treatment HbA1c level was 0.69±0.03 (p =0.000)
Conclusion: Treating iron deficiency anemia in diabetic patients results in significant reduction of HbA1c level. It is also recommended to screen type 2 diabetic patients for iron deficiency anemia and prescribing iron supplements with uncontrolled glycemic level.
Keywords: Type-2, Diabetic, Anemia, HbA1c, Iron, Supplementation.

INTRODUCTION

Diabetes mellitus type 2 is a major public health issue all over the world. Its prevalence is alarmingly raising in Pakistani population[1]. The prevalence of diabetes and prediabetes was 11.1% and 16%, respectively[2]. The factors leading to its increases disease burden are obesity, family history, lifestyle, age, race, lack of exercise, high blood pressure, abnormal cholesterol and triglyceride[3]. Glycosylated haemoglobin (HbA1c), clinicians can get an overall picture of what is the average blood sugar levels have been over a period of weeks/month. Hba1c affect by many factors including iron deficiency anemia.[4] There are many studies which prove that iron deficiency anemia affects HbA1c. In 2014 study by Christy found a positive correlation between iron deficiency anemia and increased A1C levels, especially in the controlled diabetic women and individuals having FPG between 100-126mg/dl[5].

One study found that with iron supplementation, mean HbA1c was decreased from 7.59±1.16% to 6.80±0.85%, hence showed 0.79±0.31% decrease in HbA1c in DM2 patients who had iron deficiency anemia. This was a significant decrease (n=45, p<0.05).[6] Another study also showed that HbA1C fell significantly after iron treatment, from a mean of 6.15±0.62% to 5.25±0.45% (decrease = 0.9±0.17, n=47, P < 0.001).[7] Rationale of this study is to determine the mean decrease in Hba1c with iron supplementation in DM2 with iron deficiency anemia. Literature showed that iron supplementation decrease levels of HbA1c in iron deficiency with type 2. But not much work has been done in this regard and there is no local evidence available. Moreover previous studies were conducted on small sample size. So we want to conduct this study to find the beneficial role of iron supplementation. This will help to improve our practice and in future, we will recommend to screen DM2 patients for iron deficiency anemia and prescribe iron supplements in DM2 patients with uncontrolled glycemic level.

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MATERIALS AND METHODS

This Quasi experimental trial was carried out in Endocrine OPD, Department of Medicine, Sheikh Zayed Medical Complex, Lahore from 9-4-2019 to 9-10-2019. Sample size of 182 cases is calculated with 95% confidence level, d=1% and taking magnitude of mean decrease in HbA1c i.e. 0.79±0.31% with iron supplement in DM2 patients with iron deficiency anemia.

Inclusion criteria: Patients of age between 40 to 70 years or either gender presenting with DM2 and iron deficiency anemia (as per operational definition).

Exclusion criteria

- Patient with anemia secondary to hemolysis (on medical record)
- Active gastrointestinal bleeding (on medical record)
- Patients already taking iron therapy and have no recovery (on medical record)
- Patients with allergy to iron supplements (on history)

Data Collection Procedure: After approval from hospital ethical committee, patients fulfilling selection criteria were enrolled in the study from Endocrine OPD Sheikh Zayed Hospital Lahore. An informed consent was taken from before enrolling in the study. Demographic data (name,

age, gender, BMI, duration of DM2, treatment taking for DM2) was noted. At baseline, blood sample was obtained in a 3cc disposable syringe. All samples were sent to the laboratory of the hospital for assessment of HbA1c. Reports were assessed and HbA1c was noted. Then patients were prescribed oral ferrous sulfate at 200 mg/day for 3 months. After 3 months, blood sample was obtained again in a 3cc disposable syringe. All samples were sent to the laboratory of the hospital for assessment of HbA1c. Reports were assessed and HbA1c was noted. The difference in pretreatment and posttreatment HbA1c was calculated (as per operational definition). Quantitative variables like age, BMI, duration of DM2, pretreatment & post treatment HbA1c and decrease in HbA1c was presented as mean±SD. Qualitative variables like gender and treatment taking for DM2 was presented as frequency and percentage. Paired sample t-test was applied to check the mean decrease in HbA1c. Data will be stratified for age, gender, BMI, duration of DM2, treatment taking for DM2. Post-stratification, paired sample t-test was applied with to check the mean decrease in HbA1c in each strata with p ≤0.05 taken as significant.

RESULTS

Mean age of patients in this study was 54.84±8.69 years. Minimum and maximum age of patients was 40 and 70 years (Table 1). Among patients 101(55.5%) were male and 81(44.5%) were female (Table 2). Among patients 63(34.6%) had normal body mass index, 53(29.1%) were overweight and 66(36.3%) were obese. Mean duration of diabetes was 8.13±4.34 years. Minimum and maximum duration of diabetes was 2 and 20 years. Among patients 130(71.4%) were taking medicine for diabetes mellitus (Table 3). Pretreatment HbA1c level was 6.99±0.32. Minimum and maximum HbA1c level was 6.50 and 7.50 respectively (Table 4) Post treatment HbA1c level was 6.29±0.32. Minimum and maximum HbA1c level was 5.75 and 6.85 respectively. Mean change in post treatment HbA1c level was 0.69±0.03. Minimum and maximum post-treatment change in HbA1c level was 0.65 and 0.79. Significant difference was seen in HbA1c level pre and post treatment. i.e. p=0.000 (Table 5). Significant difference was seen in mean HbA1c level in all age groups before and after treatment. i.e. 40-50 years (Pre-Treatment: 7.03±0.33 vs. Post Treatment: 6.34±0.34, p=0.000), 51-60 years (Pre-Treatment: 6.99±0.29 vs. Post Treatment: 6.29±0.30, p=0.000) and 61-70 years: (Pre-Treatment: 6.94±0.34 vs. Post Treatment: 6.23±0.35, p=0.000) (Table 6). Among male and female patients significant difference was seen in mean HbA1c level post treatment. i.e. male (Pre-Treatment: 7.01±0.33 vs. 6.31±0.34, p=0.000) & Female (Pre-Treatment: 6.96±0.30 vs. 6.26±0.32, p=0.000) (Table 7). Significant difference was seen in post treatment HbA1c level in women with normal BMI as well as among overweight and among obese women. Normal-BMI (Pre-treatment: 7.05±0.32 vs. 6.35±0.31, p=0.000), overweight (Pre-treatment: 6.95±0.32 vs. 6.26±0.33, p=0.000) and obese women (Pre-Treatment: 6.96±0.32 vs. 6.26±0.33, p=0.000) (Table 8). Significant difference was seen in post treatment HbA1c level in patients with 1-10 years of diabetes as well as in patients with 1-10 years of diabetes. Duration 1-10 years (pre-Treatment: 7.01±0.32 vs. 6.31±0.32, p=0.000) and duration 11-20 years (pre-Treatment: 6.94±0.34 vs. 6.23±0.35, p=0.000) (Table 9).

Table 1: Age of the patients (n=182)

N	**182**
Mean	54.84
SD	8.69
Minimum	40
Maximum	70

Table 2: Gender of patients

	Frequency	**Percent**
Male	101	55.5%
Female	81	44.5%

Table 3: Taking Treatment for Diabetes

	Frequency	**Percent**
Yes	130	71.4%
No	52	28.6%

Table 4: Descriptive Statistics for Pretreatment HbA1c

N	**182**
Mean	6.99
SD	0.32
Minimum	6.50
Maximum	7.50
Post treatment HbA1c	
Mean	6.29
SD	0.32
Minimum	5.75
Maximum	6.85

Table 5: Change in HbA1C level before and after Treatment

	HbA1C		
	Before	**After**	**Change**
N	**182**	**182**	**182**
Mean	6.99	6.29	-0.69
SD	0.32	0.32	0.03
Minimum	6.50	5.75	-0.79
Maximum	7.50	6.85	-0.65
P value	0.000		

Table 6: Descriptive Statistics for Change in HbA1c in relation to Age Groups

(Age (years)	**HbA1c**		**Change**	**P value**
	Pre Treatment	**Post treatment**		
40-50	7.03±0.33	6.34±0.34	-0.69±0.03	0.000
51-60	6.99±0.29	6.29±0.30	-0.69±0.003	0.000
61-70	6.94±0.34	6.23±0.35	-0.71±0.004	0.000

Table 7: Descriptive Statistics for Change in HbA1c in relation to Gender

	HbA1c		**Change**	**P value**
	Pre Treatment	**Post treatment**		
Male	7.01±0.33	6.31±0.34	-0.69±0.03	0.000
Female	6.96±0.30	6.26±0.32	-0.70±0.03	0.000

Table 8: Descriptive Statistics for Change in HbA1c in relation to Body Mass Index

	HbA1c		**Change**	**P value**
	Pre Treatment	**Post Treatment**		
Normal	7.05±0.32	6.35±0.31	-0.70±0.03	0.000
Overweight	6.95±0.32	6.26±0.33	-0.69±0.03	0.000
Obese	6.96±0.32	6.26±0.33	-0.69±0.03	0.000

Table 9: Descriptive Statistics for Change in HbA1c in relation to Duration of Diabetes Mellitus

	HbA1c			p
	Pre Treatment	Post treatment	Change	value
1-10	7.01±0.32	6.31±0.32	-0.69±0.03	0.000
11-12	6.94±0.34	6.23±0.35	-0.71±0.03	0.000

DISCUSSION

HbA1c is gold standard for the diabetes care it is considered to be important parameter defining the accuracy of glycemic control is HbA1c.[9] It is a glycated product of hemoglobin No enzyme involved in glycation rather it is regulated by mean plasma glucose over the whole lifespan of RBCs[8]. Regulation of HbA1c synthesis is multi factorial [8] both physiologic and pathological. Studies revealed that HbA1c was higher in patients with iron deficiency and iron replacement therapy decreased significantly decreased A1C[10-13] The probable mechanism may be decrease in the hemoglobin concentration lead to an increased in the glycation, conditioned serum glucose remains constant[12,13]. In this study pretreatment mean HbA1c level was 6.99±0.32 and post treatment mean HbA1c level was 6.29±0.32. Significant difference was seen in mean HbA1c level pre and post treatment. i.e. (mean change in HbA1c level was 0.69±0.03, p=0.000). Iron deficiency with or without anemia leads to a spurious increase in HbA1c values, as derived from a systemic review[14].

Nasli-Esfahani in his study found that with iron supplementation, mean HbA1c was decreased from 7.59±1.16% to 6.80±0.85%, hence showed 0.79±0.31% decrease in HbA1c in DM2 patients who had iron deficiency anemia. This was a significant decrease (n=45, $p<0.05$).[6] Results of this study is consistent with the findings of Nasli-Esfahani as post treatment HbA1c level showed significant decrease showing that treatment of iron deficiency anemia had a significant impact on HbA1c level. Results of this study is also in line with the findings of El Agouza revealed a significant decline in HbA1C with iron replacement, from a mean of 6.15±0.62% to 5.25±0.45% (decrease = 0.9±0.17, n=47, $P < 0.001$)[7]. However in above mentioned studies mean decreased in HbA1c level after treatment of iron deficiency anemia was higher when compared with this study. Attard et al studied the levels of HbA1c and fasting blood glucose as diagnostic criteria to study the effect of iron deficiency anemia on diabetes. The results showed that iron deficiency and iron deficiency anemia led to changes in HbA1c, irrespective of control of glycemia[15].

In view of thought of co-existent iron deficiency in diabetics, that can lead to falsely elevated HbA1c, the diabetics patients should be advised to keep blood sugar level record and then change in treatment regimen is advised lest they suffer from hypoglycemia and fatal outcome. All diabetics with IDA should be given Iron treatment so that they should be followed through HbA1c.

CONCLUSION

The results of this study demonstrated that treating iron deficiency anemia in diabetic patient results in significant reduction of HbA1c level. It is also recommended to screen type 2 diabetic patients for iron deficiency anemia and prescribing iron supplements with uncontrolled glycemic level.

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