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Research Article

Analysis of effect of iron deficiency anemia on HbA1c in diabetic patients in Pakistan

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ABSTRACT

Introduction: Iron deficiency is one of the most prevalent forms of malnutrition. Globally, 50% of anemia is attributed to iron deficiency.**Aims and objectives:** The basic aim of the study is to analyse the effect of iron deficiency anemia on HbA1c in diabetic patients in Pakistan.**Material and methods:** This cross sectional study was conducted in University College of Medicine & Dentistry, University of Lahore during January 2019 to October 2019. This study include all diabetic patient who visited the OPD of the hospital. Socio-demographic characteristics were collected using structured questionnaires. An enrollment form containing past medical history pertaining to chronic diseases such as kidney disease, heart related problem, skin diseases, blood coagulation disorders and other medical complaints were completed for every individual.**Results:** In 120 cases of this study, mean HbA1c value was found to be 6.87 ± 1.4%. The mean ferritin levels in male and female cases were 14.88 ± 8.62 and 8.92 ± 5.72 ng/ml, respectively. Also, mean FPG concentration was 99.66 ± 14.73 mg/dl in total cases. Hemoglobin levels in male and female cases were 9.54 ± 1.4 and 9.37 ± 1.33 g/dl, respectively. The mean MCV was 53.2 ± 8.16 fL and mean MCH was 17 ± 3.7 pg/cell for the all cases (both males and females).**Conclusion:** It is concluded that Iron deficiency anemia elevates HbA1c levels in diabetic individuals with controlled plasma glucose levels. The elevation is more in patients having plasma glucose levels between 100 to 126 mg/dl. Hence, before altering the treatment regimen for diabetes, iron deficiency anemia should be considered.

Keywords: iron deficiency, anemia, HbA1c, diabetes

INTRODUCTION

Iron deficiency is one of the most prevalent forms of malnutrition. Globally, 50% of anemia is attributed to iron deficiency. Ferritin is the storage form of iron, and it reflects the iron status accurately. An earlier study showed that reduced iron stores have a link with increased glycation of hemoglobin A1C (HbA1c), leading to false-high values of HbA1c in non-diabetic individuals[1]. HbA1c is the most predominant fraction of HbA1, and it is formed by the glycation of terminal valine at the β-chain of hemoglobin. It reflects the patient's glycemic status over previous 3 months. HbA1c is widely used as a screening test for diabetes mellitus, and American Diabetes Association has recently endorsed HbA1c ≥ 6.5% as a diagnostic criterion for diabetes mellitus. Its alteration in other conditions, such as hemolytic anemia, hemoglobinopathies, pregnancy, and vitamin B12 deficiency has been explained in a study conducted by Sinha *et al*. Although iron deficiency is the most common nutritional

deficiency, reports of the clinical relevance of iron deficiency on HbA1c levels have been inconsistent[2].

Hgb A to HbA1c conversion takes place during the entire life span of the red blood cell and the rate of this reaction is faster in diabetics because of the higher prevailing glucose concentration, resulting in a higher concentration of HbA1c[3].Red blood cells (RBC) are freely permeable to the plasma glucose molecules, and hemoglobin is practically exposed to the same glucose concentrations as plasma. Therefore, HbA1c level is directly proportional to average blood glucose concentration over the previous 4weeks to 3months or the average lifespan of the erythrocyte[4].

There are a number of methods available to estimate glycatedhemoglobin like immunoturbidimetry, ion exchange high-performance liquid chromatography (HPLC), boronate affinity, and enzymatic method. HbA1c level of ≥6.5% is sufficiently sensitive and specific to identify individuals who are at risk for developing retinopathy and who should be diagnosed as diabetic[5].

Aims and objectives

The basic aim of the study is to analyse the effect of iron deficiency anemia on HbA1c in diabetic patients in Pakistan.

Material and methods

This cross sectional study was conducted in University College of Medicine & Dentistry, University of Lahore during January 2019 to October 2019. This study was done with the approval of ethical committee of hospital. This study include all diabetic patient who visited the OPD of the hospital.

Data collection

Socio-demographic characteristics were collected using structured questionnaires. An Enrollment form containing past medical history pertaining to chronic diseases such as kidney disease, heart related problem, skin diseases, blood coagulation disorders and other medical complaints were completed for every individual. All patients were asked to provide a detailed history and were subjected to a physical examination. The levels of hemoglobin, MCH, hematocrit, MCV, MCHC, platelet count, total leucocyte count (TLC), and differential leucocyte count (DLC) were measured.

Biochemical analysis

Five mililiter of venous blood was collected by needle and syringe technique aseptically from each of the study participants. CBC, serum ferritin and HbA1c tests were done following manufacturers procedure for running each test. CBC was done by using Cell dyn 1800 hematologyanalyzer, HbA1c by COBAS C 111 analyzer and Serum ferritin was determined.

Statistical analysis

All the data were collected and analysed using SPSS version of 20.0. All the values were expressed in mean and standard deviation.

RESULTS

In 120 cases of this study, mean HbA1c value was found to be 6.87 ± 1.4%. The mean ferritin levels in male and female cases were 14.88 ± 8.62 and 8.92 ± 5.72 ng/ml, respectively. Also, mean FPG concentration was 99.66 ± 14.73 mg/dl in total cases. Hemoglobin levels in male and female cases were 9.54 ± 1.4 and 9.37 ± 1.33 g/dl, respectively. The mean MCV was 53.2 ± 8.16 fL and mean MCH was 17 ± 3.7 pg/cell for the all cases (both males and females).

Table 1: Baseline characteristics of the study subjects

	Female			**Male**			**Total (n = 120)**	
	IDA	**NA**		**IDA**	**NA**		**IDA**	**NA**
Age	54.65 ± 12.98	54.66 ± 12.02		56.6 ± 9.5	52.1 ± 8.08		55.46 ± 11.66	53.59 ± 10.59
HbA1c	7.02 ± 1.58*	5.82 ± 0.53		6.67 ± 1.06*	5.59 ± 0.85		6.87 ± 1.4*	5.65 ± 0.69

HbA1c was significantly higher in females and in subjects above 50 years of age compared to males and subjects below 50 years of age.

Table 2: Mean HbA1c (%) genderwise in subjects stratified in two groups based on their age

	Female			Male			Total	
	IDA	**NA**		**IDA**	**NA**		**IDA**	**NA**
Age <50	6.78 ± 1.88	5.59 ± 0.51		6.54 ± 0.85*	5.48 ± 0.67		6.71 ± 1.64*	5.53 ± 0.59
Age >50	7.16 ± 1.37*	5.91 ± 0.52		6.70 ± 1.12*	5.69 ± 0.94		6.94 ± 1.27*	5.77 ± 0.72

DISCUSSION

HbA1c has emerged as a marker of glycemic control, glycemic risk and predictor of diabetic complication and as screening tool for diagnosis of DM. Anemia may either increase or reduce the HbA1c values due to changes in the half-life of RBC[7]. Numerous studies have been conducted on the effect of iron deficiency anemia on HbA1c in diabetic patient or non-diabetic patients and different results have been obtained but there is no clear explanation on mechanism how iron-deficiency affects HbA1c[8].

Iron deficiency anemia is one the most common anemia amongst the nutritional anemias in India. Initial studies conducted by Brooks *et al.,* Gram-Hansen *et al.,* and Coban *et al.* showed effects of iron therapy on glycatedhemoglobin and found a significant reduction in HbA1c levels after iron therapy in non-diabetic population[9]. According to the explanation provided by Sluiter *et al.*, hemoglobinglycation is an irreversible process. Hence, HbA1 levels in erythrocyte will be increased with cell age. In iron deficiency, red cell production decreases, consequently an increased average age of circulating red cells ultimately leads to elevated HbA1 levels[10].

According to some workers, the changes in HbA1c levels were due to different laboratory methods used to analyze it. Goldstein *et al.* demonstrated that HbA1c measured by HPLC was increased two hours after a standard breakfast and incubating the red cell in 0.9% saline at 37°C for five hours eliminated this increment, which was explained by presence of labile HbA1c. This effect was eliminated by reagents used in newer enzymatic kits. Rai and Pattabiramanconducted a study to evaluate different methods used to analyze HbA1c and found no significant difference between them[11].

CONCLUSION

It is concluded that Iron deficiency anemia elevates HbA1c levels in diabetic individuals with controlled plasma glucose levels. The elevation is more in patients having plasma glucose levels between 100 to 126 mg/dl. Hence, before altering the treatment regimen for diabetes, iron deficiency anemia should be considered.

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