



RESEARCH ARTICLE

RELATIONSHIP OF HBA1C AND PREGNANCY – RELATED IRON DEFICIENCY ANEMIA

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ARTICLE INFO

Article History:

Received 29th July, 2017

Received in revised form

17th August, 2017

Accepted 11th September, 2017

Published online 31st October, 2017

Key words:

Iron deficiency anemia,
Glycated protein,
HbA1c, pregnancy,
Glycemic index,
Non- diabetics.

ABSTRACT

Background: Iron deficiency anemia is most common nutritional deficiency in pregnant women due to increased iron turnover and additional requirement by fetus. Glycemic index is popularly measured by assessing glycated proteins. HbA1c is affected by several factors including pregnancy.

Objective: The aim of this study is to assess the relationship between iron deficiency anemia in pregnant women and glycated protein (HbA1c).

Patients and Methods: It is a prospective study conducted at Department of Gynecology and Obstetrics, and Department of Pathology, Pakistan Institute of Medical Science, Islamabad, Pakistan between the duration of April 2017 to June 2017. Total of 40 normal females were taken as control group, while 42 pregnant non – diabetic iron deficient patients.

Results: Both groups included females of reproductive age. All parameters including hemoglobin, serum iron, serum total iron – binding capacity (TIBC), serum transferrin saturation and serum ferritin showed statistically significant between two groups ($p < 0.001$). HbA1c also showed statically significant difference ($p = 0.021$).

Conclusion: Study showed strong correlation between iron deficiency anemia and glycated proteins as it is increased as iron deficiency develops. So it may give false increase in levels in evaluation of glycemic index.

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Citation: Noreen Atzaz, Shahzad Ali Jiskani and Siraj Muneer, 2017. "Relationship of hba1c and pregnancy – Related iron deficiency anemia", International Journal of Current Research, 9, (10), 59527-59530.

INTRODUCTION

Iron deficiency anemia is most common deficiency caused by nutrition in the world. It is also the most common anemia occurring during pregnancy. Beside nutritional deficiency, other causes include infections by parasites for example hookworm and schistosomiasis and malaria. According to Nutrition Impact Model Study 2011, the prevalence of anemia in pregnancy is 32% (Haider et al., 2013; Haniff et al., 2007). The HbA1c is a glycated hemoglobin that is extensively used for long term glycemic status on routine level for evaluation of both type 1 and type 2 diabetes mellitus. Practically, HbA1c is the index of mean glycemia and helps to document the extent of glycemic control, patient's response to treatment and assessment of risk factor development or complications that worsens the diabetes (Saudek and Brick, 2009). World Health Organization (WHO) has recommended that for diabetes, HbA1c can be used as a diagnostic test, on condition that rigorous quality assurance tests are in correct position and presence of standardized methods as criteria allied to the internationally accepted reference values and to be sure that

there are no any condition that can affect its accuracy. These conditions are pregnancy, supposed diabetes type 1, diabetes with short duration of symptoms, acute problems, getting medications that speedily increase the level of glucose, any damage in the pancreas, defects of hemoglobin, anemia, kidney injury and infection with human immunodeficiency virus (HIV) (Sinha et al., 2012; Hughes et al., 2014). In pregnancy, HbA1c concentration measurement is used in patients with diabetes to assess the degree of perinatal risk for mother and health of the fetus (Weykamp, 2013). American Diabetes Association recommended the cut – off value of ≥ 48 mmol/mol ($\geq 6.5\%$) as diagnostic for diabetes (Florkowski, 2013). Decrease in iron stores has been associated with increase in glycated hemoglobin A1C (HbA1c). It is also important to understand that iron deficiency anemia is common among diabetes mellitus type 2 patients especially those presented with diabetic neuropathy. Exact pathophysiology is not understood yet but it has been estimated that diabetes cause anemia by decreasing absorption of iron, bleeding from gastrointestinal tract and diabetic complications (Soliman et al., 2017). HbA1c concentration is affected by turnover of erythrocyte, as by glucose levels in plasma. Pregnancy is usually associated with dilutional anemia, and additionally in late pregnancy, iron deficiency anemia is seen which is caused

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by increase in iron demands. It showed to be increased in iron deficiency anemia as compared to glycemia in patients (Hashimoto *et al.*, 2008).

MATERIALS AND METHODS

This is a prospective study performed at Department of Gynecology and Obstetrics and Department of Pathology, Pakistan Institution of Medical Sciences, Islamabad, Pakistan. This study was performed from April 2017 to June 2017. A total of 42 patients were included in group A and 40 were included in normal control group. Inclusion criteria in group A was patients between age 20 to 40 years, gestational age 20 – 40 weeks and uncomplicated single pregnancy having iron deficiency anemia. Patients with multiple pregnancies, diabetes, hypertension, chronic kidney disease, cardiovascular disease, bleeding disorders and patients taking oral iron therapy or other medication therapy were excluded from the study. Group B consists of healthy non-pregnant women of childbearing age and having no iron deficiency anemia. Cut – off values for iron deficiency anemia was hemoglobin less than 11 mg/dL, serum ferritin < 12 µg/L, serum iron <10 mmol/L, TIBC >81 mmol/L and transferrin saturation <10%. A detailed medical history along with investigation including complete blood count, serum iron, total – iron binding capacity, serum ferritin and serum HbA1c. All data were collected and analyzed using SPSS version 21.0.

RESULTS

A total of 40 normal control and 42 pregnant iron – deficient patients were included in the study (Figure 1). Age in control group was ranging between 18 to 40 years of age (Mean 29 ± 11.21 years, although age in pregnant iron – deficient patients was ranging from 20 – 40 years (Mean 30 ± 9.10 years) (Figure 2). There was no statistically significant difference in ages of both groups (p = 1.10). Hemoglobin status in control group was found to be 11.7 - 13.9 mg/dL (Mean 12.6 ± 2.93 mg/dL), while in pregnant iron deficient group it was 7.94 – 10.7 mg/dL (Mean = 9.39 ± 2.18 mg/dL) (Figure 3). Although, serum iron, serum total iron binding – capacity, serum transferrin saturation and serum ferritin showed statistically difference in all parameters among both groups (p <0.001) (Figure 4). HbA1c levels in control group was found to be 3.51 - 4.87 % (Mean = 4.10 ± 1.83 %), while in pregnant iron – deficient patients, it was increased as 5.01 - 7.65 % (Mean 6.81 ± 2.91%), showing statistically significant difference (p = 0.021) (Figure 5). Summarized difference of all difference is shown in Table 1.

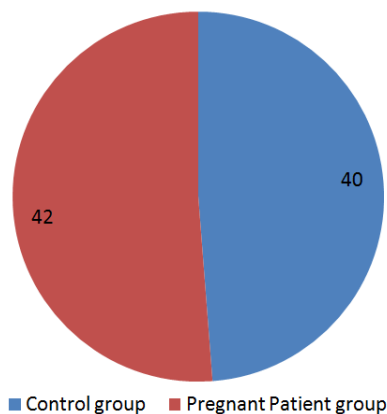


Figure 1. Number of cases

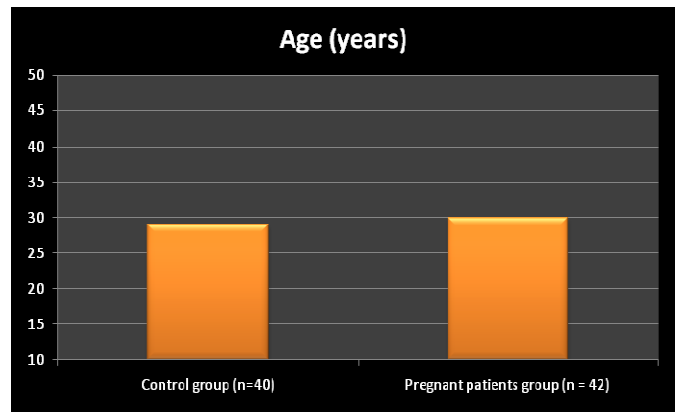


Figure 2. Age difference in both groups

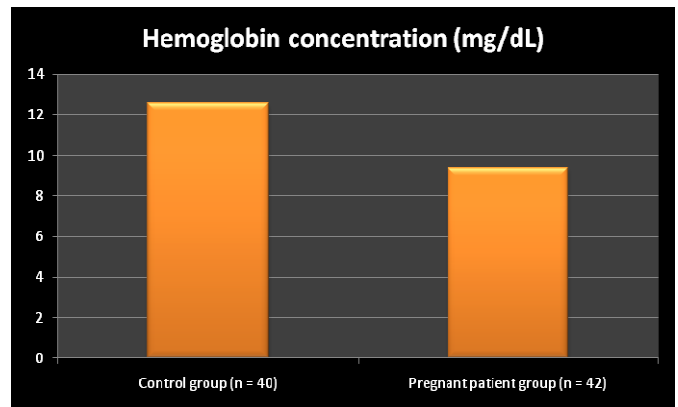


Figure 3. Hemoglobin difference in both groups

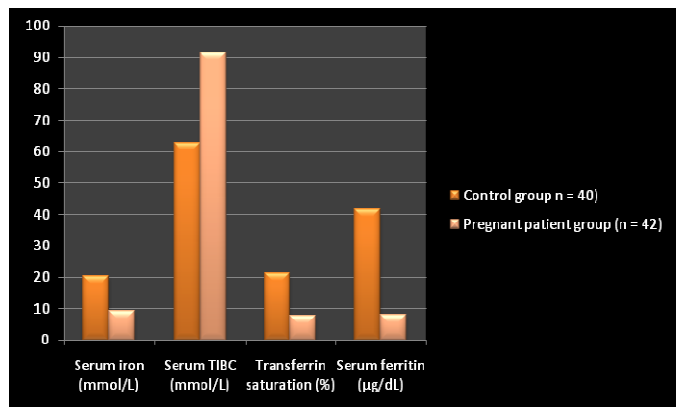


Figure 4. Serum iron, TIBC, transferrin saturation and ferritin concentration in both groups

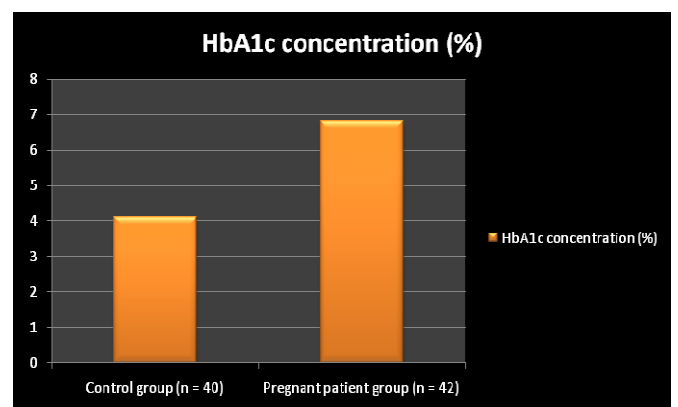


Figure 5. HbA1c concentration difference in both groups

Table 1. Statistical analysis of all parameters in both groups

	Control group	Pregnant patients group	P - value
Number of cases	40	42	
Mean age (years)	29 ± 11.21	30 ± 9.10	1.10
Mean hemoglobin (mg/dL)	12.6 ± 2.93	9.39 ± 2.18	0.031
Mean serum iron (mmol/L)	20.21 ± 6.81	7.2 ± 1.98	<0.001
Mean serum TIBC (mmol/L)	62.81 ± 11.94	91.7 ± 14.29	<0.001
Mean transferrin saturation (%)	21.2 ± 6.91	7.91 ± 4.01	<0.001
Mean serum ferritin (µg/dL)	41.6 ± 18.13	8.15 ± 9.93	<0.001
Mean HbA1c (%)	4.10 ± 1.83	6.81 ± 2.91	0.021

DISCUSSION

In present study, we found statistically significant difference in hemoglobin, serum iron, serum total iron – binding capacity, serum transferrin saturation and serum ferritin levels in both control and pregnant iron – deficient group. This change indicates the increase in turnover of iron metabolism as requirement of pregnant women is greater as compared to normal non – pregnant female. It is also important to understand that fetus needs extra iron from mother, putting extra load on stored iron of mother; thereby increasing iron requirement (Hashim, 2004). HbA1c was shown to be increased in pregnant iron – deficient group as compared to normal control group, suggestive of effect of iron deficiency and anemia on glycated hemoglobin as it is affected by altered turnover of erythrocytes (Sinha *et al.*, 2012). Several previous studies have showed to increase HbA1c in pregnancy. Hashimoto *et al.* performed a study in 2008 on 47 non – diabetic pregnant women. His study shown that in HbA1c levels are raised in late pregnancy. But his study also included serum glycated albumin which offered better glycemic index control in pregnancy (Hashimoto *et al.*, 2008). Rodrigues *et al.* in 2013 showed opposite effect of HbA1c in pregnancy; although his study included patients with no anemia or iron deficiency, which supports the hypothesis that anemia and iron deficiency in pregnancy is related with alteration in HbA1c (Rodrigues *et al.*, 2013). Sinha *et al* performed a study in 2012 on 50 iron deficient patients. His study proved that iron deficiency anemia has strong association with HbA1c as it is increased as iron deficiency develops (Sinha *et al.*, 2012). Chowdeswari *et al* performed study in 2016 including diabetic and non – diabetic patients. His study also supports the argument that iron deficiency anemia is associated with increase in HbA1c in non – diabetic patients (Chowdeswari *et al.*, 2016). Hong *et al* did a survey from 2011 to 2012. His study proved strong relationship between iron deficiency anemia and HbA1c as it was increased in iron deficient non – diabetic patients (Hong *et al.*, 2015). There was a huge survey conducted through decades by Hussain *et al.* His survey showed that HbA1c is increased in patients with non – diabetic iron deficient patients (Hussain, 2015). Another study performed by Abdel – aziz *et al* in 2017 on 50 patients showed increase in glycated proteins in non – diabetic iron deficient pregnant females (Abdel-aziz *et al.*, 2017). Previous studies strongly support the evidence of increase in HbA1c as iron deficiency anemia develops. So in this context, glycated proteins can give false increase levels in the presence of iron deficiency anemia so an accurate diagnosis of diabetes cannot be done as it is affected by presence of iron deficiency.

Conclusion

Our study strongly proves that presence of iron deficiency anemia can alter the levels of HbA1c by increasing its

concentration, suggesting of effect of iron deficiency on erythrocyte turnover and ultimately alteration of HbA1c. However our study has some limitations. There should be more studies on large population to prove more strong relationship between iron deficiency and HbA1c. Our study did not include glycated albumin as some studies showed it as better parameter. Same patients should be re – evaluated after correction of iron deficiency to assess their effect upon correction of anemia.

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