Original Article

ASSOCIATION BETWEEN HIGH SERUM FERRITIN LEVELS AND MID-PREGNANCY GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Introduction: Ferritin levels found to have an important role in the development of many syndromes during pregnancy. To compensate for the risk of low ferritin levels in pregnant females, usually iron and vitamin supplements have been prescribed. The use of these supplements may increase the ferritin level in normal pregnancy and can cause several syndromes including gestational diabetes mellitus.

Objective: To determine the association of high serum ferritin level with gestational diabetes mellitus

Material and methods: This Case-Control study was conducted at the Department of Obstetrics & Gynecology, Sheikh Zayed Hospital, Lahore for six months. Using Non-probability consecutive sampling 70 pregnant women were divided into cases and controls. Patients with high serum ferritin (149 µg / L) were calculated in both groups and then Odds ratio and Relative Risk were estimated to find an association between high serum ferritin levels and mid-pregnancy GDM.

Results: Patients with mid-pregnancy GDM had statistically significantly higher serum ferritin levels. (36.21 ± 59.07 µg/L) compared to controls (12.46 ± 13.87 µg/L) (t (68) = 2.316, p = 0.024) 15% GDM cases (n=35) had high serum ferritin level, while in the controls group (n=35) no change in the serum ferritin observed. Relative Risk estimates showed a doubling of the risk of having mid-pregnancy GDM with high serum ferritin concentration [RR=2.167 (95% CI = 1.66 – 2.81)]

Conclusion: High serum ferritin level is associated with GDM.

Key Words: Ferritin, Gestational Diabetes, Insulin Resistance

INTRODUCTION:

Anemia during pregnancy is prevalent world over but is much more severe in the developing nations like Pakistan. As per UNO reports, prevalence of anemia is about 56% in low socioeconomic groups.[1] Iron deficiency anemia is the commonest type of anemia in Pakistani population overall and is more prevalent among females.[2,3] Iron deficiency is the commonest cause of anemia in pregnancy which affects 54% of women in developing countries.[4] In under developed area of Khanewal District, 250 pregnant women (17 – 39 years of age) were studied for 6 months. Out of these, 55% were found anemic (83 % of these were moderately anemic: Hb 8-9.9g/dL).[5] A much larger study *(*enrolling 1,369 pregnant women at 20 to 26 weeks of gestation and followed to 6 weeks postpartum*)* on urban population of Hyderabad showed 90.5% of women being anemic according to WHO cut off of Hb<11g/dL.[6] In pregnancy, iron supplementation is routinely recommended all pregnant women[8] irrespective of their serum ferritin and/or haemoglobin (Hb) levels. Increasing evidence suggests that iron, a strong per-oxidant, influences glucose metabolism, even in the absence of significant iron overload.[9] Large prospective cohort studies found that dietary iron intake, particularly heme iron derived from meat, is associated with a significant increased risk of type II Diabetes.[10,11]

Serum ferritin levels (a biomarker of body iron stores) however have also been shown to be positively associated with diabetes risk,[12] hypertension,[13] the metabolic

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syndrome,[14] cardiovascular risk factors, and inflammation.[15] Although there have been several studies investigating the possible role of dietary and serum iron on glucose metabolism, only a few studies are available about these association during pregnancy.

Adverse effects of routine iron supplementation in Pakistani population has not been researched extensively. The rationale of this study was to find out association between high serum ferritin & risk of Gestational Diabetes Mellitus (GDM). On the basis of results recommendations could be made to abandon iron to all pregnant women routine and instead judicious iron supplementation to only severely anemic women(followed by close monitoring for GDM) can be made.

MATERIAL AND METHODS:

A case control study was planned in department of Gynae & Obstetrics in Sheikh Zayed Hospital Lahore from April to September 2012.

In this study 70 participants were enrolled between the age group of 20–35 years through non probability consecutive sampling. Out of these 70 participants, 35 females were controls, who were not pregnant & 35 females were taken as cases who were diagnosed case of gestational diabetes at more than 24 weeks with oral glucose tolerance test. If the BSL was more than 186 mg/dl after 1 hour of glucose tolerance test they were labelled as cases. Controls were without gestational diabetes mellitus. Serum ferritin was tested in both cases & controls**.** All those females were exluded who were known to have pre-pregnancy diabetes mellitus, diseases affecting glucose metabolism e.g. thyrotoxicosis, Cushing syndrome, hemochromatosis, Hypertensive or having Blood Pressure ≥ 140/90 mmHg on 2 consecutive occasions, current medical treatments (including hormonal preparations, corticosteroid therapy), and supplementation with micronutrients other than iron-on history.

A value of serum ferritin >149µg/L was considered as a high level. Females with high ferritin levels and diabetes were managed as per standard protocols.

All the information collected was entered into SPSS version 15.0 and was analyzed through its statistical package. Odd's ratio and Relative Risk was calculated to see the strength of the association of High Serum Ferritin Levels and GDM. Odd's ratio > 2 was taken as significant.

RESULTS:

In our study, the mean age of patients was 26.37±3.77 years of GDM cases and 28.00±4.39year of controls. The mean gestational age was 30.21±7.47weeks of GDM cases and 29.88±8.13weeks of controls. Among cases, there was 11 (31.4%) primigravida and 24 (68.6%) multigravida while among controls, there were 17 (48.6%) primigravida and 18 (51.4%) multigravida. The mean BMI of cases was 29.63±13.97kg/m^2 while of controls was 30.22±14.82kg/m^2. (Table 1)

The patients with gestational diabetes had statistically significantly higher serum ferritin levels (36.21±59.07µg/L) than non-GDM patients (12.46±13.87µg/L, p = 0.024). There was a significant association of high serum ferritin levels with GDM i.e. 14.3% vs. 0% and the risk of developing GDM is 12.80 times high in females with high ferritin levels. (Table 2)

Table 1: Comparison of Age and Serum Ferritin between cases and controls

	Group	
	Cases	Control
n	35	35
Age (years)	26.37±3.77	28.00±4.39
Gestational age (weeks)	30.21±7.47	29.88±8.13
Gravidity		
Primigravida	11 (31.4%)	17 (48.6%)
Multigravida	24 (68.6%)	18 (51.4%)
BMI (kg/m^2)	29.63±13.97	30.22±14.82

Table 2: High and Low Serum Ferritin Counts in Cases & Controls

		Group		Significance
		Cases	Controls	
Serum Ferritin Level (µg/L)		36.21± 59.08	12.46± 13.87	0.024
Ferritin level	High	5 (14.3%)	0 (0%)	OR= 12.80
	Low	30 (85.7%)	35 (100%)	95% CI (0.68 to 241.03)
Total		35	35	

DISCUSSION:

Gestational diabetes can be linked to free radical damage caused by high serum ferritin levels.[16-18]

In one of the studies of the Pakistani population, it was observed that the pregnant ladies of community have very low serum ferritin levels (reflecting low body iron stores). Mean serum ferritin levels found in this study simulate with those found in the study conducted at the Faculty of Health Sciences, Hazara University.[19]

Although overall ferritin levels were low regardless of presence and absence of gestational diabetes later on all patients with gestational diabetes diagnosed to have high ferritin levels; the same was found in the study of 128 ladies in Iran, and positive co-relation between serum ferritin, HbA1c and fasting plasma glucose levels was discovered.[20]

Bo et al in their Chinese cohort and Caucasian cohort confirmed the positive link between serum ferritin and gestational diabetes.[21,22,24] While iron deficiency is a defensive condition. [23]

Routine iron supplementation during pregnancy is necessary or toxic, is a highly controversial topic.[25] Another large prospective cohort study, which identified the existence between pre-pregnancy dietary heme iron intake and GDM.[26]

In this study, it was found out that a single woman among controls has higher than our threshold level of serum ferritin (i.e. 149 µ /L). This resulted in a "divide by zero" error while calculating the odds ratio. Thus the odds ratio was calculated after little adjustment (*adding 0.5 to all four values to prevent a divide by zero*). Relative Risk, however, is calculated using original counts as it is not affected by "divide by zero" error

By investigation of serum ferritin either before pregnancy or in early pregnancy, it is conceivable to order ladies in three groups: (a) those with low iron status (ferritin <30 µg/L) who either have or are in danger of developing iron deficiency and IDA; (b) those with intermediate iron status (ferritin 30–70 µg/L) and moderate danger of iron deficiency and IDA; (c) those with satisfactory iron status (ferritin >70–80 µg/L) with insignificant or no danger of iron deficiency. Healthy pregnant ladies having ferritin over 70–80 µg/L give off an impression of being in safe water concerning iron deficiency as their body iron sores are 500 mg or more, which is satisfactory to finish a pregnancy without taking iron supplements. Prophylactic iron supplementation along these lines gives off an impression of being sheltered in ladies with Intermediate and low iron status yet in those with pre-pregnancy sufficient iron stores alerts must be watched.

CONCLUSION:

Higher Serum ferritin levels are associated with increased risk of mid-pregnancy GDM. Owing to a great majority of Pakistani pregnant women having very low total iron body stores, general Iron prophylaxis during pregnancy seems to be a safe option in the vast majority. Pregnant women coming from a high socioeconomic group should have their serum ferritin levels done and iron prophylaxis initiated only if low ferritin count is found.

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