



Original Research Article

The relationship between serum ferritin and gestational diabetes mellitus- A cross sectional study

Poonguzhalai S¹, Kalyanikutty K P^{2,*}¹JIPMER, Puducherry, India²Dept. of Physiology, Government Medical College, Kerala, India

ARTICLE INFO

Article history:

Received 17-04-2019

Accepted 30-05-2019

Available online 12-09-2019

Keywords:

Pregnant women

GDM

Iron Stores

Serum Ferritin

ABSTRACT

Introduction: The incidence of Gestational Diabetes Mellitus (GDM) worldwide is on an increase with approximately 40 percent between 1989 and 2004. Serum Ferritin level is an index of iron overload. This study estimates serum Ferritin level which may contribute for the pathogenesis of GDM.

Materials and Methods: Pregnant women are divided into 2 groups those with GDM and another without GDM by screening for Glucose challenge test. Blood sugar after 12 hours of fasting and 2 hours Post prandial is done for diagnosis of GDM. Serum Ferritin of both groups are also estimated and compared.

Results: The mean rank of serum Ferritin in subjects with diabetes mellitus is 33.02 compared with the mean rank of serum Ferritin in subjects without diabetes mellitus which is 27.98. Since the mean rank of serum Ferritin in subjects with diabetes is higher, there is a positive relation between serum Ferritin and diabetes mellitus.

Conclusion: It seems that routine administration of iron supplements to all pregnant women without estimating serum Ferritin needs more evaluation since a positive relationship has been found between GDM and increased serum Ferritin level.

© 2019 Published by Innovative Publication.

1. Introduction

The incidence of Gestational Diabetes Mellitus (GDM) is increasing rapidly worldwide. Women with Gestational Diabetes Mellitus have type 2 diabetes (Insulin resistance state). Incidence of diabetes complicating pregnancy has increased approximately 40 percent between 1989 and 2004.¹ It is also estimated that this incidence will increase 165 percent by 2050. There are many factors that influence the pathogenesis of GDM. In many recent studies, it is found that serum Ferritin has a positive correlation with GDM. Women who developed GDM have a higher concentration of serum Ferritin than women who do not develop GDM. In a developing country like India all pregnant women are supplemented with iron without investigating the iron status. This is because iron deficiency anemia is one of the important problem in developing countries. But now it is estimated that increased iron load in a pregnant

women is linked to maternal complications like GDM.² We measure serum Ferritin level to estimate the iron overload in pregnant Women. We know serum Ferritin is one of the acute phase protein, the concentration of which increased in acute infections. Pregnant women may be prone for acute infections, this may account for the increased serum Ferritin. But we have studies that suggest the possible link between elevated serum Ferritin and low grade inflammation.^{2,3} Studies also associate elevated serum Ferritin concentration with increased risk of GDM, independent of C-reactive protein (acute phase protein) and BMI. This study tries to co-relate elevated serum ferritin concentration with gestational diabetes mellitus in one of the tertiary care center in Kerala, south India.

2. Materials and Methods

A total of 60 pregnant women of gestational age 16-32 weeks are chosen. This included 30 subjects with normal pregnancy and without GDM and 30 subject with normal

* Corresponding author.

E-mail address: poongu85@gmail.com (Kalyanikutty K P).

pregnancy and with GDM. Their serum Ferritin levels are assessed.

2.1. Inclusion criteria

Pregnant females between 16-32 weeks of gestation and the females are on Iron supplementation

2.2. Exclusion criteria

1. Acute and chronic infections
2. History of malignancy
3. Previous history of Diabetes mellitus
4. History of seizure
5. History of renal disease
6. History of liver disease
7. History of drug abuse
8. Women with Iron deficiency anaemia

2.3. Sample size calculation

$$\text{Sample Size (n)} = [(Z\alpha + Z\beta)^2 \times SD^2 \times 2] \div d^2$$

$Z\alpha$ = Z score of α error of 5% (1.96)

$Z\beta$ = Z score of β error of 20% (0.843)

SD = Standard Deviation

$$= (SD_1 + SD_2) \div 2$$

$$= (17 + 9) \div 2$$

$$= 13 \text{ (Based on The Camden Study}^2 \text{ by Xinhua chen et$$

al)

d = allowable error(10)

$$n = [(1.96 + 0.843)^2 \times 13^2 \times 2] \div 10^2$$

$$= (7.856809 \times 169 \times 2) \div 100$$

$$= 26.55$$

$$= 27 \text{ in each arm}$$

2.4. Methodology

Pregnant women of gestational age 16-32 weeks is included in the study after getting ethical clearance and Institutional Research clearance from Govt medical college, Thrissur. They are divided into 2 groups women with GDM and women without GDM. This is done by screening the subject for Glucose challenge test by asking them to take 75 gm of glucose and the 2hr OGTT was taken. Diagnosis of GDM is done by estimating Fasting blood sugar after atleast 12 hours of fasting and Post prandial blood sugar after 2 hours of meal. Pre pregnant weight is used to calculate approximate value of body mass index (BMI). Serum Ferritin of both groups are estimated and compared. Estimation of plasma glucose is by Glucose oxidase peroxidase method. Estimation of serum Ferritin by two site sand which immunoassay using Direct chemiluminomeric technology. Analysis was done by software SPSS version 20. Non parametric analysis was done (Mann-Whitney Test).

3. Results

Analysis was done by software SPSS version 20. Non parametric analysis was done (Mann-Whitney Test)

The results obtained are discussed further

Normal values: (According to WHO recommendation).⁴⁻⁷

GCT : < 140mg/ dl

FBS: 110-125mg/dl

Serum Ferritin: 10-230ng/ml(5-216pmol/l).⁸

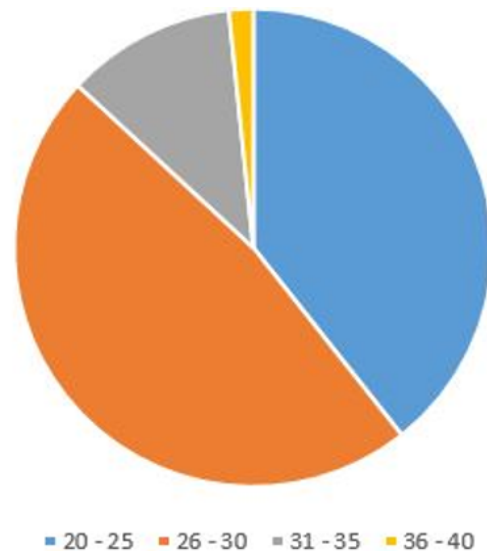


Fig. 1: Distribution According to the age of the pregnant women Maximum number of the subjects belong to 26-30 age group

Mean serum Ferritin level of pregnant women with GDM (30.83 +/-20.61) was higher than those without GDM (23.48+/-10.91). Median serum Ferritin level was comparable (20.950+/-23.8 vs 20.050+/-13.2). The difference is not statistically significant (p=0.264). According to Mann-Whitney test, the mean rank value of serum ferritin in subjects with diabetes mellitus is 33.02 compared with the mean rank value of serum ferritin in subjects without diabetes mellitus which is 27.98. Since the mean rank of serum ferritin in subjects with diabetes is higher, there is a positive relation between serum ferritin and diabetes mellitus.

4. Discussion

Analysis of the data was done by Mann Whitney, a Non Parametric analysis in which a mean rank value of serum ferritin in subjects with diabetes mellitus is 33.02 compared to the mean rank value of serum ferritin in subjects without diabetes mellitus which is 27.98. This proves there is a positive relation between serum Ferritin and Gestational Diabetes Mellitus although not significant. A study was done in South Indian population belonging to a different ethnic group. This population was highly prone for iron

Table 1: Comparison of serum ferritin with diabetes mellitus: Mann-Whitney Test

	Diabetes mellitus	Number	Mean rank	Sum of ranks
S.Ferritin	0	30	33.02	990.5
S.Ferritin	1	30	27.98	839.5

Code 0 : Pregnant ladies with GDM
 S. Ferritin: Serum Ferritin
 Code 1 : Pregnant ladies without GDM

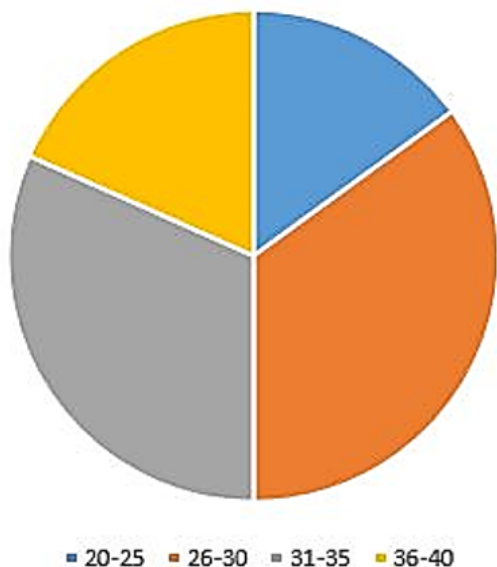


Fig. 2: Distribution according to the gestational age of the pregnant women
 Maximum number of the subjects belong to 26-30 weeks of pregnancy

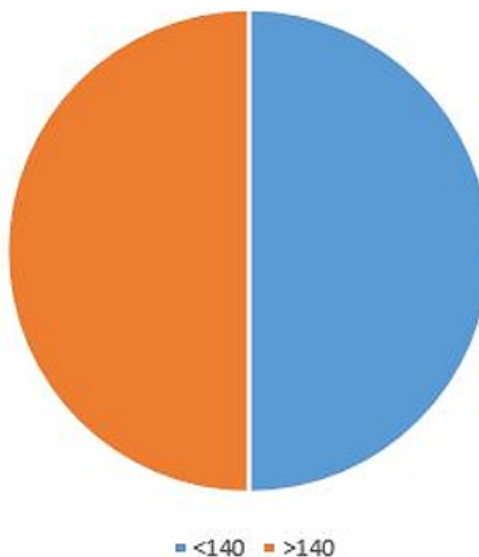


Fig. 4:

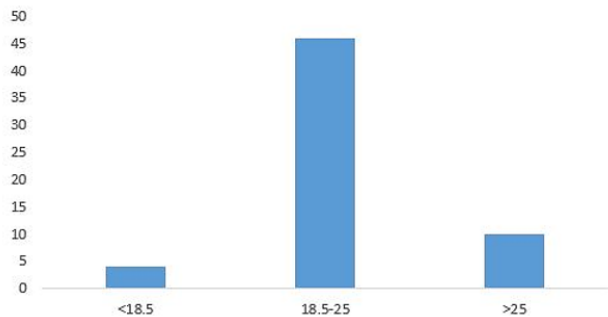


Fig. 3: Distribution According to the BMI of the pregnant women
 Most of the subjects are not obese

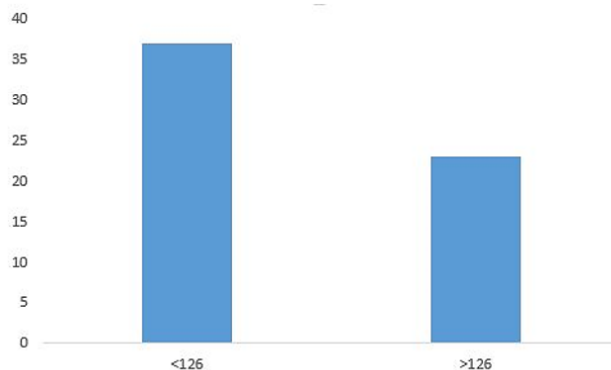


Fig. 5:

deficiency anemia so iron supplementation is mandatory here. Normal serum Ferritin value is of a wider range (10-291 μg/l) so the analysis was done by “Non Parametric Test” (MannWhitney test). Except for a positive relation between serum Ferritin and GDM a significant correlation has not been proved. Joseph Scott Gabrielsen et al^{9,10} proved the pathophysiology behind the iron stores and GDM. Increased serum Ferritin causes oxidative stress induced damage to Adipocytes by producing free radicals. One

of the stress specific gene is FOXO 1. FOXO1 gene is specific for Adipocytes is found to reduce the Adiponectin transcription.^{11,12} Hence the release of Adiponectin into circulation is reduced contributing for the Insulin resistance. Physiologically Adiponectin cause Insulin sensitive state.

In our study comparison between BMI and GDM was not analyzed. Studies shows significant correlation between iron stores (Ferritin and Hemoglobin) and GDM independent of BMI and other confounding factors like positive family history, C- reactive protein (a marker of inflammation) etc.² Serum Ferritin, the storage form of iron is also a marker of inflammation. Thus Ferritin-insulin resistance could be due to increased iron stores or inflammation or both. Most of the studies investigating serum Ferritin also measured other markers of acute phase reaction including CRP and fibrinogen. There are studies which suggest that measuring of inflammatory markers had little effect on iron-insulin resistance. This gives the evidence of Ferritin-insulin resistance relationship independent of inflammation.² In this study all confounding factors were not included

Most of the studies which investigated the iron stores not only measured serum Ferritin but also serum iron, total iron binding capacity and transferrin saturation. In this study we have measured only serum Ferritin level is measured. Since other forms of iron are not measured the precise information regarding the iron stores is not available. Hence this is a drawback of this study compared to the other studies.

In this study we categorized pregnant women with GDM by measuring OGCT and FBS. Many of the upcoming study measured Hb A1c as useful indicator for diagnosing GDM. Alex Fong et al¹³ analyzed Hb A1c as the early indicator of GDM. An HbA1c level of 5.7-6.4% is an effective means of identifying patients at the highest risk of developing GDM. It may be most prognostic in an obese population. Its efficacy has been demonstrated when the sample is drawn during the first trimester and may be effective up to 20 weeks of gestation. This information may help the clinicians target the patients who will benefit the most.

5. Conclusion

It seems that routine administration of iron supplements to all pregnant women without estimating serum Ferritin needs more evaluation since a positive relationship has been found between GDM and increased serum Ferritin level. Clinicians should consider the unwanted supplementation of Iron for pregnant women without estimating the Iron storage state.

6. Limitation of the study

1. Sample size is very low
2. TIBC and Transferrin saturation levels were not measured

3. Serum Insulin level is not measured to justify insulin resistance as the pathology under GDM (due to increased iron stores)
4. Confounding factors were not estimated
5. Study should be done in different parts of India

7. Source of funding

None.

8. Conflict of interest

None.

References

1. Cunningham, Leveno, Bloom, Hauth. Williams obstetrics; Chapter 52 – Diabetes; Mc - Graw Hill ; . .
2. Chen X, Scholl TO, Stein TP. Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: The Camden study. ; 2006,.
3. Khl C, Hornnes PJ, Andersen O. Review: Etiology and Pathophysiology of Gestational Diabetes Mellitus. *Diabetes*. 1985;34:66–70. Supplement 2.
4. Gestational-Diabetes-Mellitus. ; 2019,. Available from: http://164.100.154.238/New_Updates_2018/NHM_Components/RMNCH_MH_Guidelines/Gestational-Diabetes-Mellitus.pdf.
5. Foss-Freitas MC, Andrade RCD, Figueiredo RC, Pace AE, Martinez EZ, et al. Comparison of venous plasma glycemia and capillary glycemia for the screening of type 2 diabetes mellitus in the Japanese-Brazilian community of Mombuca (Guatapar-SP). *Diabetol Metab Syndr*. 2010;2:6.
6. Farrar D, Duley L, Lawlor DA ; 2011,. Internet. Available from: [10.1002/14651858.CD007122.pub2/abstract](http://dx.doi.org/10.1002/14651858.CD007122.pub2/abstract).
7. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM. Screening and diagnosing gestational diabetes mellitus. *Evid Rep Technol Assess*. 2012;(210):1–327.
8. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. *Obstet Gynecol*. 2009;114(6):1326–1357.
9. Gao Y, Li Z, Gabrielsen JS, Simcox JA, Lee S, et al. Adipocyte iron regulates leptin and food intake. *J Clin Invest*. 2015;125(9):3681–3691.
10. Gabrielsen JS, Gao Y, Simcox JA, Huang J, Thorup D, Jones D. Adipocyte iron regulates adiponectin and insulin sensitivity. *J Clin Invest*. 2012;122(10):3529–3569.
11. King SM, Donangelo CM, Knutson MD, Walter PB, Ames BN, Viteri FE. Daily Supplementation with Iron Increases Lipid Peroxidation in Young Women with Low Iron Stores. *Exp Biol Med*. 2008;233(6):701–708.
12. Swaminathan S, Fonseca VA, Alam MG, Shah SV ; 2007,.
13. Fong A, Serra AE, Gabby L, Wing DA, Berkowitz KM. Use of hemoglobin A1c as an early predictor of gestational diabetes mellitus. *Am J Obstet Gynecol*. 2014;211(6):641–642. e7.

Author biography

Poonguzhalai S Senior Resident

Kalyanikutty K P HOD

Cite this article: Poonguzhalai S , Kalyanikutty K P . The relationship between serum ferritin and gestational diabetes mellitus- A cross sectional study. *Indian J Obstet Gynecol Res* 2019;6(3):342-345.