Association of Maternal Serum Ferritin Level in Gestational Diabetes Mellitus and its Effect on Cord Blood Hemoglobin

Preeti Chauhan¹, Parijat Gogoi², Smita Tripathi³, Sanjukta Naik⁴

ABSTRACT

Introduction: Gestational Diabetes Mellitus is the development of carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Many studies had suggested that an elevated serum ferritin level in maternal blood in early as well as mid-pregnancy is an independent risk factor for development of GDM. In the present study we aim to find the association of serum ferritin levels with serum iron and Hb% in the GDM patients at the time of delivery and also correlate it with cord blood Hb% and iron levels of the new born.

Material and Methods: The study group was composed of 50 diagnosed cases of GDM and the control group comprised of age matched 50 cases of normal pregnancy. Maternal blood was used to measure mother’s hemoglobin, iron levels, serum ferritin and hsCRP. Cord blood sample was used to estimate hemoglobin and iron levels of the newborns.

Results: Our study shows that in the GDM cases the level of serum ferritin was significantly higher (p <0.001) than in the non GDM controls at the time of delivery. Cord blood hemoglobin is negatively correlated with maternal serum ferritin levels in GDM.

Conclusion: Elevated serum ferritin level in GDM is a marker of inflammation due to increased ROS production caused by iron overload. This oxidative stress might affect the placental iron transfer to the fetus and fetal Hb synthesis.

Keywords: Gestational Diabetes Mellitus (GDM), Ferritin, Reactive Oxygen Species (ROS), Hemoglobin (Hb), Serum Iron (SI), Cord Blood Hemoglobin, Cord Blood Iron

INTRODUCTION

Gestational Diabetes Mellitus is the development of carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Globally, the prevalence of GDM is estimated to be ~15%,¹ Indian women are known to have 11-fold higher risk of developing GDM compared to Caucasian women.² Diagnosis of GDM is essential for identifying the new born at risk of adverse outcome like macrosomia, hypocalcemia, hypoglycaemia, hyperbilirubinemia, preterm delivery etc.³ There are multiple risk factors for development of GDM like increased BMI, increased maternal age, family history of diabetes mellitus etc. Recently many studies are suggesting that an elevated maternal serum ferritin level, in early as well as mid-pregnancy is an independent risk factor for development of GDM.⁴⁻⁵ Ferritin is an iron storage protein. Serum ferritin concentration provides an indirect estimate of body iron stores because it is highly correlated with bone marrow iron. It is also a positive acute phase protein and is so an equally accepted marker of inflammation.⁶ Elevated levels of ferritin has been associated with many acute and chronic inflammatory diseases including diabetes and cardiovascular disease. Hence an elevated ferritin level may indicate iron overload or an inflammatory process.

Although the exact mechanism for its association with GDM is not very clear, it has been postulated that it is due to the effect of iron overload, which it reflects. In pregnancy, the placental environment is one of enhanced oxidative stress, producing huge amount of free radicals, but the body has mechanisms to counteract it in normal pregnancy. If this fine equilibrium is disturbed, it will lead to free radical injury.⁷ Some studies have also raised concern about the association of excess iron in non-pregnant people, including hereditary hemochromatosis, as a risk factor for development of insulin resistance.⁸ Iron deficiency is very common among pregnant women and remains a global public health concern. The World Health Organization (WHO) recommends intake of 30–60 mg of elemental iron by all pregnant women to prevent maternal iron deficiency anemia and to ensure adequate fetal iron stores.⁹ But various studies have shown that although adequate maternal iron is necessary for normal fetal growth and development, iron overload has adverse effects as iron is a strong pro-oxidant. Adequate iron is required for β cell function and glucose homeostasis, but excess maternal iron leads to generation of increased amount of free radicals which is toxic to the pancreatic beta cells. This leads to and impairment in the glucose metabolism and insulin resistance. Thus iron might act as a double edged sword in pregnancy.¹⁰⁻¹²

¹Associate Professor, Department of Biochemistry, Lady Hardinge Medical College & Assoc. Hospitals, New Delhi, ²Associate Professor, Department of Biochemistry, Lady Hardinge Medical College & Assoc. Hospitals, New Delhi, ³Professor, Department of Biochemistry, Lady Hardinge Medical College & Assoc. Hospitals, New Delhi, ⁴Senior Resident, Department of Biochemistry, Lady Hardinge Medical College & SSK Hospital, New Delhi, India

How to cite this article: Preeti Chauhan, Parijat Gogoi, Smita Tripathi, Sanjukta Naik. Association of maternal serum ferritin level in gestational diabetes mellitus and its effect on cord blood hemoglobin. International Journal of Contemporary Medical Research 2020;7(1):A1-A4.

DOI: http://dx.doi.org/10.21276/ijcmr.2020.7.1.8
The effect of GDM on the distribution of iron and the hemoglobin level in the new born is still debated and very few studies have been done on the association of elevated ferritin levels on these parameters. In the present study we aim to find the association of serum ferritin levels with serum iron and Hb% in the GDM patients at the time of delivery and also correlate it with cord blood Hb% and iron levels of the new born.

**MATERIAL AND METHODS**

This study was conducted in a 400 bedded, tertiary care, super speciality hospital in New Delhi. The study group was composed of 50 diagnosed cases of GDM in the age group of 20 to 35 years. The control group comprised of age matched 50 cases of normal pregnancy.

Diagnosis of GDM was made at 24-28 weeks of gestation according to ADA criteria. Patients with history of diabetes mellitus, hypertension, seizure disorder, malignancy, acute or chronic liver disease or history of drug abuse were excluded.

The study was approved by Institutional Review Board and Ethics Committee. Informed written consent was obtained from each participant before their inclusion in the study.

Clinical history, complete physical examination and routine blood tests were done in all the patients at the time of inclusion. At the time of delivery, blood samples were collected from the mother and cord blood was collected from the maternal end of umbilical cord to coincide precisely with the newborn’s venous blood sample. Maternal blood was used to measure mother’s Hb%, iron levels, serum ferritin and hsCRP. Cord blood sample was used to estimate Hb% and iron levels. The newborn birth weight and placenta weight were also recorded.

Hb% was measured on Sysmex auto-analyzer, model KT-21N. Serum Iron and hsCRP were estimated spectrophotometrically and serum Ferritin by Electro Chemiluminescence. All measurements were done on the same day.

**STATISTICAL ANALYSIS**

The data was analyzed using SPSS 21 software. Data was expressed as mean ±SD with mean differences and 95% confidence intervals. Student’s t-test was applied to compare data of cases and controls. Welch correction was applied where the assumption of equal variances was violated and correlations were computed using Pearson correlation coefficient. Our data followed normality and it was determined using Shapiro Wilk Test.

**RESULTS**

The mean age of the GDM cases was 29.94± 3.1 and in the non GDM control group the mean age was 26.24 ± 2.4

Table 1 shows that both Hb% and serum iron are significantly (<0.05) raised in GDM cases compared to the non GDM controls. The mean ±SD of serum ferritin levels (38.1± 4.6 µgm/L) of the GDM cases was much more than that of the controls (33.5 ± 2.7 µgm/L) (p < 0.001, highly significant). The mean ±SD of hsCRP of cases too was raised but p value (>0.05) was not significant.

Table 2 shows that mean ±SD of both the placental weight and birth weight of the newborns of cases was higher than that of the controls (p<0.001).

Among the estimations done in cord blood (Table 2), both Hb% and iron levels of the babies of the GDM mothers was very significantly (p< 0.001) higher compared to the babies of the non GDM mothers. However, 24% of newborn of GDM cases had Hb% less than 12 (p<0.001) and serum iron less than 90 µgm/dL (p<0.01).

Table3 shows that there was a moderately negative correlation {Pearson’s coeff r = -0.35, p> 0.001} between the maternal serum Ferritin levels of GDM cases with Cord blood Hb% of the newborns of the GDM mothers. However, there was no significant correlation of the serum Ferritin levels of the GDM mothers with the Cord blood iron levels of their newborns.

**DISCUSSION**

Our study shows that in the GDM cases the level of serum ferritin was significantly higher (p <0.001) than in the non GDM controls at the time of delivery. Many previous studies have shown that patients with raised serum ferritin levels in the early and mid-pregnancy are at more risk of developing GDM. The levels of ferritin in both the cases (38.1± 4.6 µgm/L) and control (33.5 ± 2.7µgm/L) are
CONCLUSION

Elevated serum ferritin level in GDM is a marker of inflammation due to increased ROS production caused by iron overload. This oxidative stress might affect the placental iron transfer to the fetus and fetal Hb synthesis.

REFERENCES

1. Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Res Clin Pract. 2014;103:176–185.
2. Rani PR, Begum J. Screening and diagnosis of gestational diabetes mellitus, where do we stand. J Clin Diag Res. 2016;10:QE01-4.
3. Mitandche D, Yzydorczyk C, Simeoni U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes? World J Diabetes. 2015;6:734-43.
4. Dr. V Sumathy, Dr. T Rajatharangini and S Padmanaban. Association of elevated serum ferritin levels in mid-pregnancy and the risk of gestational diabetes mellitus. International Journal of Clinical Obstetrics and Gynaecology 2018; 2: 18-21.
5. Bowers KA, Olsen SF, Bao W, Halldorsson TI, Strom M, Zhang C. Plasma Concentrations of Ferritin in Early Pregnancy Are Associated With Risk of Gestational Diabetes Mellitus in Women in the Danish National Birth Cohort. J Nutr. 2016;146:1756-61.
6. Soheilykhah S, Mojibian M, Janatii Moghadam M. Serum ferritin concentration in early pregnancy and risk of subsequent development of gestational diabetes: A prospective study. Int J Reprod Biomed (Yazd). 2017;15:155-160.
7. M Galal, M Salah. Aanj. Correlation Between First Trimester Pregnancy Serum Ferritin And Risk Of Gestational Diabetes In This Pregnancy. AAMJ. 2015:13-1-8.
8. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. Metallomics. 2014;6:748-73.
9. Halliwell, B. and Gutteridge, J.M.C., Eds., Free Radicals in Biology and Medicine, 3rd Edition, Oxford University Press, Oxford, 1-25.
10. Zhao Z, Li S, Liu G, Yan F, Ma X, Huang Z, Tian H. Body iron stores and heme-iron intake in relation to risk of type 2 diabetes: a systematic review and meta-analysis. PLoS One. 2012;7:e41641.
11. Benoist, B.D.; McLean, E.; Egll, I.; Cogswell, M. Worldwide prevalence of anaemia 1993–2005:WHO Global Database on Anaemia; Geneva, Switzerland, 2008.
12. Hansen JB, Moen IW, Mandrup-Poulsen T. Iron: the hard player in diabetes pathophysiology. Acta Physiol (Oxf). 2014;210:717-32.
13. Liu Q, Sun L, Tan Y, Wang G, Lin X, Cai L. Role of iron deficiency and overload in the pathogenesis of diabetes and diabetic complications. Curr Med Chem 2009;16:113–29.
14. Buchanan TA, Xiang A, Kjos SL, Watanabe R. What is gestational diabetes? Diabetes Care 2007;30:S105–11.
15. Guo W, Wang H, Liu Q, Yuan Y, Jing Y, Yang X. Analysis of the correlation of gestational diabetes mellitus and peripheral ferritin with iron levels in early pregnancy. Minerva Endocrinol. 2019;44:91-96.
16. Zein S, Rachidi S, Hininger-Favier I. Is oxidative stress induced by iron status associated with gestational diabetes mellitus? J Trace Elem Med Biol. 2014;28:65-9.
17. McArdle HJ, Lang C, Hayes H, Gambling L. Role of the placenta in regulation of fetal iron status. Nutr Rev. 2011;69:S17-22.
18. Rawal S, Hinkle SN, Bao W, Zhu Y, Grewal J, Albert PS, Weir NL, Tsai MY, Zhang C. A longitudinal study of iron status during pregnancy and the risk of gestational diabetes: findings from a prospective, multicohort. Diabetologia. 2017;60:249-257.
19. Koenig MD, Tussing-Humphreys L, Day J, Cadwell B, Nemeth E. Hepcidin and iron homeostasis during pregnancy. Nutrients. 2014; 6:3062–3083.
20. Iron Status and Gestational Diabetes—A Meta-Analysis. Yachana Kataria, Yanxin Wu, Peter De Hemmer Horskjær, Thomas Mandrup-Poulsen and Christina Ellervik. Nutrients 2018;10:621.
21. Rajpathak SN, Crandall JP, Wylie-Rosett J, Kabat GC, Rohan TE, Hu FB. The role of iron in type 2 diabetes in humans. Biochim Biophys Acta. 2009;1790:671-81.
22. Fernández-Real JM, McClain D, Manco M. Mechanisms Linking Glucose Homeostasis and Iron Metabolism Toward the Onset and Progression of Type 2 Diabetes. Diabetes Care. 2015;38:2169-76.
23. Shukla P, Xiao X, Mishra R. Iron Biomarker in Gestational Diabetes Pathogenesis. J Mol Biomark Diagn 2014;5:205.
24. Zhiguo Wang, Hai-bo Fan, Wan-wei Yang, Xiao-dong Mao, Shu-hang Xu, Xiao-ping Ma, Gui-ping Wan, Xiao-ming Yao, Keyang Chen. Correlation between plasma ferritin level and gestational diabetes mellitus and its impact on fetal macrosomia Diabetes Investig 2018; 9: 1354–1359.
25. Ashwaq Kadhim Mohammed, Vian Hussam ALmans AlQami. The Correlation between Serum Ferritin and Fasting Blood Sugar in Iraqi Women with Gestational Diabetes. J. Pharm. Sci. & Res. 2017;9:1654-1658
26. Cynthia C Das, Sreekala K N, N Geetha. Serum Ferritin in Gestational Diabetes. JMSCR Aug 2017;5:26814-26819.
27. Chan K, Chan B, Lam K, Tam S, Lao T. Iron supplement in pregnancy and development of gestational diabetes—a randomised placebo-controlled trial. BJOG 2009;116:789–798.
28. Ke K, Shaky S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. Ann Nutr Metab. 2015;66:14-20.
29. K Saigo, M Takenokuchi, Y Hiramatsu et.al. Oxidative Stress Levels in Myelodysplastic Syndrome Patients: their Relationship to Serum Ferritin and Haemoglobin Values. J Int Medical Research.2011;39:1941-1945
30. Yoo JH, Maeng HY, Sun YK, et.al. Oxidative status in iron deficient anemia. J Clin Lab Anal 2009;23:319-323.
31. Bala J, Vercelloti GM, Jeney V et.al. Heme, Heme oxygense and ferritin: how the vascular endothelium survives (and dies) in an iron rich environment. Antioxid Redox Signal 2007;9:2119-2137
32. Samreen Siddiqui, Swati Waghdiare, Manju Panda, Shweta Dubey Sujeet Jha. Association of IL-6 and CRP Levels with Gestational Diabetes Mellitus. Diabetes 2018; 67:34-39.

Source of Support: Nil; Conflict of Interest: None
Submitted: 03-12-2019; Accepted: 27-12-2019; Published: 16-01-2020