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EVALUATION OF EFFECT OF DIABETES MELLITUS OF PREGNANCY ON SELECTED RED CELL PARAMETERS

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ABSTRACT

Background and Objectives: Gestational diabetes mellitus (GDM) presents notable health risks to both mothers and infants, primarily attributed to insulin resistance associated with oxidative stress resulting from excessive iron levels. This study aimed to compare the levels of hemoglobin and packed cell volume (PCV) between pregnant women with and without GDM, as these indicators reflect the body's iron status. By examining the relationship between hemoglobin, PCV, and GDM, this research seeks to enhance the understanding of this condition during pregnancy, leading to improved management and preventive strategies.

Materials & methods: A case-control study at an Indian tertiary care center included 95 cases (GDM-diagnosed pregnant women) and 105 controls (non-GDM pregnant women). Hemoglobin and PCV levels were measured using venepuncture and automated analysis. Data collection involved a validated questionnaire, and iron supplementation was provided to all participants. Chi-square analysis was used to evaluate the association between elevated hemoglobin and PCV levels and GDM risk ($p \leq 0.05$).

Results: A significant difference in hemoglobin levels was observed between the cases and controls, highlighting a notable distinction. Furthermore, the cases demonstrated significantly higher PCV values compared to the controls.

Conclusion: The research study revealed a statistically significant correlation between elevated maternal hemoglobin levels and PCV with GDM.

Key words: Gestational Diabetes, Pregnancy, Haemoglobin, Packed Cell Volume.

INTRODUCTION

Gestational diabetes mellitus (GDM) is characterized by the development of insulin resistance during the second trimester of pregnancy, typically resolving after childbirth. This condition poses increased risks of infections and pregnancy-induced hypertension (PIH) for the mother. Infants born to diabetic

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mothers are more likely to have a larger birth size, which can result in complications such as instrumental delivery and lower segment cesarean section, leading to an elevated risk of birth trauma and perinatal mortality [1]. Additionally, mothers with insulin resistance during pregnancy have a higher likelihood of developing type 2 diabetes in the future [2].

The impact of GDM extends beyond the mother and affects the developing fetus. Glucose, being the primary energy source, crosses the placenta through facilitated diffusion, leading to increased fetal insulin production caused by ß cell hyperplasia due to exposure to elevated levels of maternal circulating glucose. As a result, newborns are susceptible to hypoglycemia shortly after birth. Furthermore, cases of unexplained intrauterine death may occur near term in instances of GDM [3].

Previous research has established that insulin resistance plays a pivotal role in the pathophysiology of GDM [4]. Various molecular mechanisms contribute to insulin resistance, including downregulation of the insulin receptor, impairments in glucose transport into cells, and abnormalities in post-receptor insulin actions [5, 6]. Furthermore, insulin resistance in GDM can be attributed to oxidative injury mediated by free radicals, with its peak occurring during the second trimester of pregnancy [7].

Several studies have demonstrated a correlation between elevated iron levels and an increased susceptibility to insulin resistance, type 2 diabetes mellitus, and GDM [8-18]. Consequently, excessive iron stores have the potential to exacerbate the insulin resistance observed in normal pregnancy, ultimately contributing to the development of GDM.

During the final 6-8 weeks of pregnancy, the iron requirement may increase to 10 mg per day [19-22]. To meet this heightened demand, iron supplementation is provided to all pregnant women [23, 24]. However, caution must be exercised when prescribing iron tablets to all pregnant women, irrespective of their total body iron content, as ferrous iron has the potential to generate free radicals through Fenton's reaction [25].

Elevated levels of serum ferritin, hemoglobin, and packed cell volume (PCV) indicate higher iron stores [16]. In a study conducted by Lao et al., it was observed that a hemoglobin level of ≥13 g/dl was identified as an independent risk factor for the development of GDM, whereas iron deficiency anemia reduced the risk of GDM [15]. Similar findings were reported by Phaloprakarn [26] and Afkhami-Ardekani [27].

PCV serves as an indicator of the red blood cell (RBC) mass and, consequently, iron stores [16]. During a normal pregnancy, PCV typically decreases due to hemodilution. However, the absence of this expected decline has been associated with adverse pregnancy outcomes. Studies conducted by Lao et al. and Afkhami-Ardekani revealed a significant association between elevated PCV levels and the risk of GDM, while the Camden study did not demonstrate such a relationship [13].
Based on the evidence presented, the practice of universal iron supplementation for pregnant women becomes a topic of debate. Iron deficiency in the mother increases the risk of neonatal and maternal morbidity [15]. Conversely, elevated maternal iron levels have been linked to a higher risk of low birth weight, preterm birth, PIH, and stillbirth [28]. Furthermore, studies have indicated a correlation between elevated body iron levels and an increased risk of insulin resistance during pregnancy [17, 18].

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The purpose of this case-control study was to investigate the association between elevated maternal hemoglobin and PCV levels and the risk of developing GDM.

MATERIAL & METHODS

The study was conducted as a case-control study at a tertiary level hospital in India, with ethical considerations given due importance. The study included a total of 95 cases and 105 controls. The cases consisted of women diagnosed with GDM based on the established criteria outlined by the ADA. The diagnosis of GDM was determined through either a glucose challenge test with a blood sugar value exceeding 200 mg/dl or a glucose tolerance test with two or more abnormal blood sugar values. The control group comprised pregnant women at 24-28 weeks of gestation without GDM, following the ADA criteria. Importantly, all participants received iron supplementation as part of the national program.

The sample size for the study was determined based on an Odds ratio of 2 derived from previous research findings, resulting in a sample size of 197. Hemoglobin and PCV levels were measured using automated hematology analyzers to ensure accuracy and reliability.

The collected data underwent statistical analysis using SPSS Version 20. The data were entered into MS Excel for systematic analysis. The association between variables was assessed using the Chi-square test, with a significance level of $p \leq 0.05$ established as the threshold for determining statistical significance.

RESULTS

Table 1 shows the baseline demographic characteristics of study population. There was no significant difference between the two groups in baseline characteristics.

Table 1: Demographic characteristics of study population

	Cases (n=95)		**Controls (n=105)**		**P value**
	Mean	**SD**	**Mean**	**SD**	
Age (years)	22.7	2.31	23.08	2.82	0.18
Height (cm)	153.92	3.71	155.05	3.01	0.08
Weight (kg)	61.45	5.56	62.31	4.73	0.07
BMI (kg/m^2)	26.64	2.35	27.09	2.68	0.13

The difference in hemoglobin levels between the cases and controls was determined to be statistically significant, as indicated by the results of the Chi-square analysis ($P < 0.05$). Table 2 provides a clear depiction of the higher hemoglobin levels observed in the cases compared to the controls.

Table 2: Haemoglobin levels in cases and controls

	Haemoglobin (gm/dl)		
	Mean	**SD**	**P value**
Cases (n=95)	10.6	1.4	< 0.05
Controls (n=105)	10	1.2	

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The results of the Chi-square test demonstrated a significant disparity in packed cell volume (PCV) levels between the cases and controls ($P < 0.05$). Table 3 clearly displays the higher PCV values observed in the cases compared to the controls.

Table 3: PCV in study population

	PCV (%)		
	Mean	**SD**	**P value**
Cases (n=95)	36.21	4.17	< 0.05
Controls (n=105)	33.97	2.05	

DISCUSSION

The present study provides evidence that mothers with elevated hemoglobin levels are at a higher risk of developing GDM. Additionally, a correlation has been observed between increased body iron levels and an increased susceptibility to GDM [28, 29]. This association can be attributed to the heightened production of free radicals resulting from elevated iron levels, which subsequently leads to oxidative stress and cellular damage, ultimately leading to the development of insulin resistance [30].

During pregnancy, the gastrointestinal tract is capable of absorbing excessive iron if it is available in abundance. Additionally, pregnancy itself is a condition that renders mothers more susceptible to oxidative stress [31]. Therefore, the provision of excessive iron supplementation, regardless of an individual's hemoglobin level, may potentially worsen oxidative stress and contribute to the development of GDM.

In the present study, it was observed that the mean PCV of the cases was significantly higher compared to the mean PCV of the controls. This finding indicates that a higher PCV is associated with an increased risk of developing GDM.

The findings of this study suggest that prophylactic iron supplementation may be beneficial for mothers with low hemoglobin levels. However, caution is warranted when considering iron supplementation for mothers with higher hemoglobin levels, as it may increase the risk of GDM. Further extensive research is needed to determine the threshold level of hemoglobin above which iron supplementation is necessary without elevating the risk of oxidative stress and GDM. Such studies will contribute to the development of more precise guidelines for iron supplementation during pregnancy, ensuring optimal maternal health outcomes.

It is crucial to recognize the limitations of this study. The small sample size and the absence of follow-up are significant limitations. The small sample size may limit the generalizability of the findings to a larger population. Additionally, the lack of follow-up hinders the ability to assess the long-term implications and outcomes associated with GDM in the study participants. These limitations should be taken into account when interpreting the results, and further research with larger sample sizes and longitudinal follow-up is necessary to validate and enhance these findings.

CONCLUSION

The findings of the present study indicate a noteworthy association between elevated maternal hemoglobin levels and an increased risk of GDM. Similarly, a higher maternal PCV was also found

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to be associated with an elevated risk of GDM. These results suggest that evaluating the body iron status of pregnant women before initiating iron therapy may be advantageous in identifying individuals at a higher risk for GDM.

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REFERENCES

1. Blank A, Grave GD, Metzger BE. Effects of gestational diabetes on perinatal morbidity reassessed. Report of the International Workshop on Adverse Perinatal Outcomes of Gestational Diabetes Mellitus, December 3-4, 1992. Diabetes Care. 1995 Jan;18(1):127-9.
2. Vidanalage CJ, Senarth U, Silva KD, Lekamge U, Liyanage IJ. Effects of initial body mass index on development of gestational diabetes in a rural Sri Lankan population: A case-control study. Diabetes Metab Syndr. 2016 Apr-Jun;10(2 Suppl 1):S110-3.
3. Alyce TM, Gutierrez YM. Pathophysiology of GDM. In: American Dietetic Association Guide to Gestational Diabetes Mellitus; 2005.
4. Skouby SO, Andersen O, Saurbrey N, Kühl C. Oral contraception and insulin sensitivity: in vivo assessment in normal women and women with previous gestational diabetes. J Clin Endocrinol Metab. 1987 Mar;64(3):519-23.
5. Grunberger G, Taylor SI, Dons RF, Gorden P. Insulin receptors in normal and disease states. Clin Endocrinol Metab. 1983 Mar;12(1):191-219.
6. Puavilai G, Drobny EC, Domont LA, Baumann G. Insulin receptors and insulin in human pregnancy: Evidence for a post receptor defect in insulin action. J Clin Endocrinol Metab 1982;54:247-53.
7. Casanueva E, Viter FE. Iron and oxidative stress in pregnancy. J Nutr 2003;133:1700S-8S.
8. Simona BO, Menato G, Villois P, Gambino R, Cassander, M, Cotrino I, et al. Iron supplementation and gestational diabetes in mid-pregnancy. Am J Obstetr Gynaecol 2009;201:158.
9. Lao TT, Tam KF, Cham LY. Third trimester iron status and pregnancy outcome in non-anaemic women; pregnancy unfavourably affected by maternal iron excess. Hum Reprod 2002;15:1843-8.
10. O'Scholl T. Iron status during pregnancy: Setting stage for mother and infant. Am Med J Clin Nutr 2005;81:12185-225.
11. Knutson MD. Iron-sensing proteins that regulate hepcidin and enteric iron absorption. Annu Rev Nutr. 2010 Aug 21;30:149-71.
12. Qiu C, Sorensen TK, Luthy DA, Williams MA. A prospective study of maternal serum C-reactive protein (CRP) concentrations and risk of gestational diabetes mellitus. Paediatr Perinat Epidemiol. 2004 Sep;18(5):377-84.
13. 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 Mar;44(1):91-96.
14. 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, multiracial cohort. Diabetologia. 2017 Feb;60(2):249-257.
15. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of Type 2 diabetes in apparently healthy women. JAMA 2004;291:711-7.

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16. Ford ES, Logswell ME. Diabetes and serum ferritin concentration among US adults. Diabetes Care 1999;22:1978-83.
17. Fleming DJ, Jacques PF, Tucker KL, Massano MJ, D'Agostino RB, Wilson PW, et al. Iron status of the freeliving elderly Framigham heart study cohort: An iron replete population with a high prevalence of elevated iron stores. Am J Clin Nutr 2001;73:638-46.
18. Buchanan TA, Metzger BE, Freinkel N, Bergman RN. Insulin sensitivity and ß cell responsiveness to glucose during late pregnancy in lean and moderately obese women with normal glucose tolerance or mild gestational. Am J Obstet Gynaecol 1990;162:1008-14.
19. Phelps RL, Metzger BE, Freinkel N. Carbohydrate metabolism in pregnancy XVII, diurnal profiles of plasma glucose, insulin, FFA, TG, cholesterol and individual amino acid in late normal pregnancy. Am Med J Obstet Gynaecol 1981;140:730-6.
20. Burt RL, Davidson IW. Insulin half-life and utilization during pregnancy. Obstet Gynaecol 1974;43:161-70.
21. Ciaralli TB, Kettel M, el-Roeiy A, Madar Z, Reichart D, Yen SS, et al. Mechanism of cellular insulin resistance in normal pregnancy. Am J Obstet Gynaecol 1994;170:635-41.
22. Caballero B. Guide to Nutritional Supplements. Amsterdam, Netherlands: Elsevier Ltd.; 2009. p. 13.
23. Kalkhoff R, Schalch DS, Walker JL, Beck P, Kipnis DM, Daughaday WH. Diabetogenic factors associated with pregnancy. Trans Assoc Am Physicians 1964;77:270-80.
24. Gresser P. Iron Therapy with Special Emphasis on Oxidative Stress. Switzerland: Vifor Inc.; 1998.
25. Phaloprakarn C, Tangjitgamol S. Importance of high maternal haemoglobin at first antenatal visit in pregnant outcomes: A cohort study. J Perinat Med 2008;36:115-9.
26. Afkhami-Ardekani M, Rashidi M. Iron status in women with and without GDM. J Diabetes Complications 2009;23:194-8
27. Lao TT, Chan PL, Tam KF. Gestational diabetes mellitus in the last trimester - a feature of maternal iron excess? Diabet Med. 2001 Mar;18(3):218-23.
28. Liu K, Chen Y, Tong J, Yin A, Wu L, Niu J. Association of maternal obesity with preterm birth phenotype and mediation effects of gestational diabetes mellitus and preeclampsia: a prospective cohort study. BMC Pregnancy Childbirth. 2022 Jun 1;22(1):459.
29. Thomas FB, Falko JM, Zuckerman K. Inhibition of intestinal iron absorption by laundry starch. Gastroenterology. 1976 Dec;71(6):1028-32. PMID: 11141.
30. Evans P, Kayyali R, Hider RC, Eccleston J, Porter JB. Mechanisms for the shuttling of plasma non-transferrin-bound iron (NTBI) onto deferoxamine by deferiprone. Transl Res. 2010 Aug;156(2):55-67.
31. Bjelakovic G, Nikolova D, Gluud C. Antioxidant supplements to prevent mortality. JAMA. 2013 Sep 18;310(11):1178-9.