MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.78.82

Hemoglobin and Packed Cell Volume in Gestational Diabetes Mellitus: A Case Control study

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Key Words
Diabetes, pregnancy, haemoglobin, insulin, India

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Received: 24 February 2023
Accepted: 13 March 2023
Published: 16 April 2023

Citation: Sonu Kumar Batham, Archana Kori, Abhinav Junwal and Manisha Chauhan 2023. Hemoglobin and Packed Cell Volume in Gestational Diabetes Mellitus: A Case Control study. Res. J. Med. Sci., 17: 78-82, doi: 10.59218/ makrjms.2023.78.82

ABSTRACT

Gestational diabetes mellitus (GDM) poses significant health risks to both mothers and babies, arising from insulin resistance linked to oxidative stress caused by excess iron. The aim of this study was to compare hemoglobin and packed cell volume (PCV) levels in pregnant women with and without GDM, as these parameters reflect body iron status. Understanding the association between hemoglobin, PCV and GDM can contribute to improved management and prevention strategies for this condition during pregnancy. In a case-control study conducted at a tertiary care center in Central India, 100 cases and 100 controls were included. The cases consisted of pregnant women diagnosed with GDM according to the guidelines set by the American Diabetes Association (ADA), during the gestational period of 24-28 weeks. The control group consisted of pregnant women without GDM at the same gestational age. Data collection involved the use of a validated questionnaire. All participants received iron supplementation based on the national program. Hemoglobin and PCV levels were measured using a 2 mL blood sample obtained through venepuncture and analyzed using an automated analyzer. The association between elevated hemoglobin and PCV levels and the risk of developing GDM was assessed using Chi-square analysis, with a significance level of $p \leq 0.05$. A notable distinction was observed in hemoglobin levels between the cases and controls, indicating a statistically significant difference. Additionally, the cases exhibited significantly higher packed cell volume (PCV) values compared to the controls. The study identified a statistically significant correlation between elevated maternal hemoglobin levels and PCV with GDM.

INTRODUCTION

Gestational diabetes mellitus (GDM) is characterized by the onset of insulin resistance during the second trimester of pregnancy, with the condition typically resolving after childbirth. GDM poses an increased risk of infections and pregnancy-induced hypertension (PIH) for the mother. Infants born to diabetic mothers are more likely to have a larger birth size, which can lead to complications such as instrumental delivery and lower segment cesarean section[1]. Consequently, there is an elevated risk of birth trauma and perinatal mortality. Furthermore, mothers experiencing 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, as it affects the developing fetus. Glucose, serving as the primary energy source, crosses the placenta through facilitated diffusion. Consequently, the fetus is exposed to elevated levels of maternal circulating glucose, leading to an increase in fetal insulin production caused by β cell hyperplasia. Consequently, newborns are susceptible to hypoglycemia shortly after birth. Additionally, unexplained intrauterine death may occur near term in cases of GDM[3].

Previous study has established that insulin resistance serves as the fundamental pathology in gestational diabetes mellitus (GDM)[4]. There are various molecular mechanisms contributing to insulin resistance, including downregulation of the insulin receptor, impairments in glucose transport into cells and abnormalities in post-receptor insulin actions[5,6]. Additionally, insulin resistance in GDM can be linked to oxidative injury mediated by free radicals, which reaches its peak during the second trimester of pregnancy[7].

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

During the last 6-8 weeks of pregnancy, the iron requirement may rise to 10 mg per day[19-22]. To meet this increased iron demand, iron supplementation is provided to all pregnant women[23,24]. However, it is essential to exercise caution when prescribing iron tablets to all pregnant women, regardless of their total body iron content, as ferrous iron can generate free radicals through Fenton's reaction[25].

Elevated serum ferritin, hemoglobin and packed cell volume (PCV) levels are indicative of higher iron stores[16]. In a study conducted by Lao *et al.*[15], was found that a hemoglobin level of $\geq$13 g dL^{-1} was identified as an independent risk factor for the development of gestational diabetes mellitus (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 a reflection of the red blood cell (RBC) mass and, consequently, iron stores[16]. During normal pregnancy, PCV tends to decline due to hemodilution. However, the absence of this expected decline is associated with adverse pregnancy outcomes. Studies conducted by Lao *et al.*[9] and Afkhami-Ardekani revealed a significant association between elevated PCV and the risk of GDM, while the Camden study failed to demonstrate such a relationship[13].

Based on the aforementioned evidence, the practice of universal iron supplementation for pregnant women becomes a subject of debate. When the mother is iron deficient, there is an increased risk of neonatal and maternal morbidity[15]. Conversely, elevated maternal iron levels have been associated with an increased risk of low birth weight, preterm birth, pregnancy-induced hypertension (PIH) and stillbirth[28]. Furthermore, studies have indicated a correlation between elevated body iron levels and an augmented risk of insulin resistance during pregnancy[17,18].

This case-control study was conducted to explore the relationship between elevated maternal hemoglobin and PCV levels and the risk of developing GDM.

MATERIAL AND METHODS

The study was conducted as a case-control study at the Obstetric Department of Government Medical College in Central India. Ethical considerations were given due importance and the study obtained clearance from both the Research Committee and Institutional Ethical Committee.

The study included a total of 100 cases and 100 controls. The cases consisted of women who were diagnosed with GDM based on the established criteria outlined by the American Diabetes Association (ADA). The diagnosis of GDM was established through either a glucose challenge test with a blood sugar value exceeding 200 mg dL^{-1} 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 who did not have GDM, following the ADA criteria. Notably, all participants in the study received iron supplementation as part of the national program.

The sample size for the study was determined considering an Odds ratio of 2, which was derived from previous research findings. This resulted in a sample size of 190. Hemoglobin and packed cell volume (PCV) levels were measured using automated hematology analyzers, ensuring accuracy and reliability.

The collected data underwent statistical analysis using SPSS Version 21. The data were entered into MS Excel for systematic analysis. The association between variables was evaluated using the Chi-square test and a significance level of $p \leq 0.05$ was 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.

The difference in hemoglobin levels between the cases and controls was found to be statistically significant based on the results of the Chi-square analysis ($p<0.05$). Table 2 clearly illustrates that the cases had higher hemoglobin levels compared to the controls.

The Chi-square test revealed a significant difference in PCV levels between the cases and controls ($p<0.05$). As indicated in Table 3, the cases had higher PCV values compared to the controls.

DISCUSSIONS

The current investigation demonstrates that mothers with elevated hemoglobin levels have a higher likelihood of developing gestational diabetes mellitus (GDM). Furthermore, an association has been observed between increased body iron levels and an increased susceptibility to GDM[15,28]. This link can be attributed to the elevated production of free radicals resulting from heightened iron levels, which subsequently lead to oxidative stress and cellular damage, ultimately giving rise to insulin resistance[29]. During pregnancy, the gastrointestinal tract has a heightened capacity to absorb excess iron if presented with an abundance of this mineral[30]. Moreover, pregnancy itself is a condition that renders mothers more susceptible to oxidative stress[31]. Consequently, the provision of excessive iron supplementation, regardless of the individual's hemoglobin level, may potentially exacerbate oxidative stress and contribute to the development of GDM. In the present study, the mean PCV of cases was found to be higher compared to the mean PCV of controls. This difference was statistically significant, indicating that higher PCV is associated with an increased risk of developing GDM. The findings suggest that prophylactic iron supplementation may be beneficial for mothers with low hemoglobin levels. However, caution should be exercised when considering iron supplementation for mothers with higher hemoglobin levels, as it may predispose them to GDM. Further extensive studies are needed to establish the threshold level of hemoglobin above which iron supplementation is necessary without increasing the risk of oxidative stress and GDM. Such research will contribute to the development of more precise guidelines for iron supplementation during pregnancy, ensuring optimal maternal health outcomes. However, it is important to acknowledge the limitations of this study. The small sample size and the absence of follow-up are notable limitations. The small sample size may restrict the generalizability of the findings to a larger population. Additionally, the lack of follow-up limits the ability to assess the long-term implications and outcomes related to GDM in the study participants. These limitations should be considered when interpreting the results and further research with larger sample sizes and longitudinal follow-up is warranted to validate and expand upon these findings.

Table 1: Demographic characteristics of study population

	Cases (n = 100)		Controls (n = 100)		
	Mean	SD	Mean	SD	p-value
Age (years)	22.65	2.36	23.12	2.78	0.20
Height (cm)	154.35	3.68	155.24	2.97	0.06
Weight (kg)	61.24	5.62	62.44	4.68	0.10
BMI (kg m^{-2})	26.55	2.41	27.15	2.65	0.09

SD: Standard deviation

Table 2: Haemoglobin levels in cases and controls

	Haemoglobin (g dL^{-1})		
	Mean	SD	p-value
Cases (n = 100)	11.3	2.1	<0.05
Controls (n = 100)	10.3	0.9	

SD: Standard deviation

Table 3: PCV in study population

	PCV (%)		
	Mean	SD	p-value
Cases (n = 100)	35.8	4.2	<0.05
Controls (n = 100)	34.1	2.1	

SD: Standard deviation

CONCLUSION

The present study revealed a significant association between elevated maternal hemoglobin levels and the risk of GDM. Similarly, higher maternal PCV was also found to be associated with an increased risk of GDM. These findings suggest that assessing the body iron status of pregnant women before initiating iron therapy may be beneficial in identifying those at higher risk for GDM.

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