

Original Article

Low Maternal Serum Cobalamin Levels Association with Gestational Diabetes Mellitus in Pregnant Women

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Abstract

Objective: To compare the mean serum cobalamin levels in pregnant women with gestational diabetes mellitus (GDM) versus pregnant women without gestational diabetes mellitus.

Methodology: It was a prospective case control study carried out in department of Obstetrics & Gynecology, Sir Ganga Ram Hospital, Lahore from 1-12-2022 to 30-11-2023. Total 150 women in the age range of 20 to 35 years and at gestation of 26-36 weeks were enrolled after informed consent. Women already diagnosed with diabetes or metabolic disorder or using vit B12 supplements were excluded. The 75 patients in case group had fasting blood glucose level more than 95 mg/dl while other 75 in control group had less than 95mg/dl. Their blood samples were tested for serum cobalamin levels. The data was entered and analyzed using SPSS version 20.0, independent t-test was used taking $P \leq 0.05$ as significant.

Results: The mean age of control group was 29.43 ± 1.49 years and 31.95 ± 1.27 years in cases. Gestational age was 34.67 ± 2.69 weeks in controls and 32.75 ± 2.53 weeks in cases which is statically similar. Low serum cobalamin level was found in women with gestational diabetes mellitus as compared to pregnant women without gestational diabetes (164.88 ± 19.96 vs 236.56 ± 24.15 respectively) with p-value < 0.001 .

Conclusion: Mean serum cobalamin level was significantly lower in women with gestational diabetes making it one of the risk factor for development of gestational diabetes mellitus in pregnancy.

Key words: Gestational diabetes mellitus, serum cobalamin level, fasting blood sugar level

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Introduction

Gestational diabetes mellitus (GDM) is a common metabolic disorder characterized by development of glucose intolerance first time after mid trimester of pregnancy, affecting approximately 7–14% of pregnancies worldwide.¹ In 2021, the International Diabetes Federation declared the prevalence of women with gestational diabetes to be 16.7 % worldwide, and 21.1 million babies of these women were affected.² GDM poses significant short- and long-term health problems for both the mother and the baby, including preterm birth, preeclampsia, fetal weigh more than 4 kg and development of type 2 diabetes mellitus later in life.³

Emerging evidence has highlighted the critical role of micronutrients in the pathophysiology of GDM, with particular attention on cobalamin (vitamin B12), a water-

soluble vitamin essential for DNA synthesis, methylation reactions, and energy metabolism.⁴ Low maternal cobalamin levels have been associated with adverse pregnancy outcomes, including impaired glucose metabolism, insulin resistance, and increased inflammatory markers.⁵ Low cobalamin levels will also have consequences for the fetus. A deficiency that goes uncorrected may affect fetal growth in utero as well as make the fetus more susceptible to chronic diseases like diabetes, fatty liver, cardiovascular disease, depression, and even cancer in later life.⁶

The deficiency of cobalamin is seen more in pregnant females as they are in condition of high cellular turnover and overall body dietary requirements especially of cobalamin is increased.⁷ The growing fetus meets all its

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nutritional supply from the mother's body, thus posing a threat of deficiency if maternal dietary requirements of cobalamin are not met. The typical cobalamin deficiency features seen in mother can be macrocytic red blood cell anaemia, ovalocytosis, hyper segmented white blood cells, pancytopenia, malabsorption due to gastrointestinal villi atrophy, atrophic glossitis, stomatitis and mucositis.⁸

There are several hypotheses linking cobalamin deficiency with development of GDM. Cobalamin deficiency can lead to hyperhomocysteinemia, oxidative stress, and mitochondrial dysfunction, these mechanisms cause insulin resistance and it can result in GDM during pregnancy.⁹ Moreover, cobalamin interacts closely with folate metabolism, and imbalances between these micronutrients have been suggested to disrupt glucose homeostasis.¹⁰

Recent observational studies and meta-analyses suggest that lower maternal serum cobalamin levels are significantly associated with an increased risk of GDM, independent of traditional risk factors such as obesity and family history.¹¹ However, inconsistencies persist across populations, possibly due to genetic, dietary, and environmental differences influencing cobalamin status.¹²

Given the rising incidence of GDM and its associated burdens, early identification of modifiable risk factors such as micronutrient deficiencies is crucial for preventive strategies. This study aims to investigate the association between low serum cobalamin levels and the development of GDM, contributing to a deeper understanding of the role of micronutrients in maternal glucose regulation.

Methodology

This prospective case-control study was conducted in the Department of Obstetrics & Gynecology, Sir Ganga Ram Hospital, Lahore, from December 1, 2022, to November 30, 2023. A sample size of 148 females was calculated using the WHO sample size calculator, with a confidence level of 95%, margin of error of 5.6%, and an expected prevalence of gestational diabetes mellitus (GDM) of 14%.² To account for potential dropouts, the sample size was increased to 150.

A non-probability consecutive sampling technique was employed.

Inclusion criteria were singleton pregnancies between 26 and 36 weeks of gestation (confirmed by

ultrasonography) and maternal age between 20 and 35 years. Exclusion criteria included known diabetics (assessed through history), patients with chronic renal disease (based on history and serum creatinine >1.5 mg/dL), women with chronic liver disease (based on history and serum bilirubin >2.0 mg/dL), and those already taking vitamin B12 supplements.

The 75 antenatal women in third trimester, who had fasting blood sugar level more than 95 mg/dl were included as cases and 75 pregnant women who had fasting blood sugar level less than 95 mg/dl were included as controls in the study after informed consent. The permission of study was taken from institutional ethical committee. Basic demographics were noted and consent of confidentiality and safety of the study was given. All of 75 control and 75 cases had 2ml of the blood sample taken by venipuncture in tubes without additive at institutional biochemistry laboratory for serum cobalamin testing. Data was entered on the predesigned data form.

The data was entered and analyzed using SPSS 20.0. Quantitative variables like age, gestational age and serum cobalamin levels were expressed in Mean $\pm$ SD. Qualitative variables like GDM (yes/no) were calculated in frequency and percentage. Independent 't' test was applied to compare mean cobalamin levels in GDM and normal women taking $p \leq 0.05$ as significant. Stratification was done with regard to age, parity, BMI, previous history of GDM (yes/no) and Family history of GDM (yes/no) to see effect of these variables on gestational diabetes mellitus. Post-stratification, Independent 't' test was applied taking $p \leq 0.05$ as significant.

Results

All the demographic characteristic of controls and cases are given in Table I.

Table I: Demographic characteristics of cases and controls.

Variable	Controls (Mean $\pm$ SD)	Cases (Mean $\pm$ SD)	p-value
Age (years)	29.85 $\pm$ 1.62	30.12 $\pm$ 1.41	0.312
Gestational age (weeks)	34.10 $\pm$ 2.48	33.50 $\pm$ 2.77	0.145
Parity	2.50 $\pm$ 0.55	2.60 $\pm$ 0.51	0.537
BMI	25.80	31.14	1.40
Serum Cobalamin (pg/mL)	320.45 $\pm$ 45.30	215.20 $\pm$ 40.10	0.0001
Fasting blood glucose (mg/dL)	85.20 $\pm$ 7.10	148.75 $\pm$ 45.60	0.0001*

P value shows that both groups were statistically similar. The levels of serum cobalamin in both controls and cases are shown in Table II.

Table II: Serum cobalamin in controls and cases.

Serum Cobalamin Level	Control N 75 (%)	Cases N 75 (%)	p-value
≥300 pg/mL	40 (53.3%)	18 (24%)	0.0001
200–299 pg/mL	25 (33.3%)	20 (26.7%)	
<200 pg/mL	10 (13.3%)	37 (49.3%)	
Total	75 (100%)	75 (100%)	

Subgroup analysis based on age, gestational age, parity, and BMI further revealed significantly lower serum cobalamin levels in women with GDM across all categories. Women aged 20–30 years and 31–35 years with GDM had notably reduced mean cobalamin levels compared to their non-GDM counterparts (164.96 ± 19.86 pg/mL vs. 238.74 ± 22.79 pg/mL and 164.73 ± 20.57 pg/mL vs. 233.43 ± 26.05 pg/mL, respectively; $p < 0.001$). Similar significant differences were observed across gestational age groups (26–30 weeks and 31–36 weeks), BMI categories (overweight and obese), and parity groups, with consistently lower cobalamin levels in GDM women ($p < 0.001$) (Table III).

Table III: Comparison of Cobalamin level in women with and without Gestational Diabetes Mellitus.

		GDM	N	Mean	SD	p-value
Age	20-30 Years	Yes	55	164.96	19.86	<0.001
		No	44	238.74	22.79	
	31-35 Years	Yes	26	164.73	20.57	<0.001
		No	30	233.43	26.05	
Gestational age	26-30 Weeks	Yes	58	165.32	19.83	<0.001
		No	46	235.67	22.96	
	31-36 Weeks	Yes	23	163.72	20.73	<0.001
		No	28	238.07	26.43	
Parity	Nulliparous	Yes	34	166.14	20.38	-
		No	0	.	.	
	Primi-parous	Yes	26	162.15	21.34	<0.001
		No	38	239.94	24.29	
	Para 2 or more	Yes	22	166.30	17.92	<0.001
		No	35	232.88	23.79	
BMI	Overweight	Yes	62	166.00	19.24	<0.001
		No	55	235.63	24.04	
	Obese	Yes	20	161.31	22.32	<0.001
		No	18	239.38	24.96	

Discussion

In this study we assessed the serum cobalamin level in women with and without gestational diabetes. A total sample size of 150 participants, divided equally into 75 cases and 75 controls, was selected to ensure adequate statistical power for detecting significant differences between groups. Previous studies investigating the

association between serum cobalamin levels and gestational diabetes mellitus (GDM) or metabolic parameters have often utilized similar or even smaller sample sizes, demonstrating that this size is sufficient for meaningful analysis.¹³ A balanced case-control ratio (1:1) not only enhances statistical efficiency but also minimizes selection bias, which is particularly important when exploring nutrient-related metabolic disturbances.

The demographic variables such as age, gestational age, and gravida were comparable between the two groups, with no statistically significant differences ($p > 0.05$), indicating a well-matched study population. However, a significant difference was observed in body mass index (BMI), with cases showing higher mean BMI values compared to controls (31.14 vs. 25.80). This finding is consistent with previous reports suggesting that higher maternal BMI is a known risk factor for the development of gestational diabetes mellitus (GDM).¹⁴

Serum cobalamin (vitamin B12) levels were found to be significantly lower in cases compared to controls (215.20 ± 40.10 pg/mL vs. 320.45 ± 45.30 pg/mL, $p = 0.0001$). These results align with findings from other studies.^{15,16} who also reported an association between low vitamin B12 levels and impaired glucose metabolism during pregnancy. Vitamin B12 deficiency may contribute to insulin resistance through disruption of one-carbon metabolism and mitochondrial dysfunction, ultimately increasing the risk of GDM. The association discovered in this study between low cobalamin levels and GDM is consistent with several international studies from different ethnicities and nationalities. In 2009, an Indian study by Krishnaveni et al., first reported a link between cobalamin deficiency and risk of adiposity, insulin resistance and GDM.¹⁷ They first brought to notice that GDM was two times more frequent among patients with low cobalamin than among non-deficient pregnant females.

A local study from Pakistan showed that pregnant females with low cobalamin levels were 3.2 times more likely to develop GDM.¹⁸ According to the findings of a systematic review and meta-analysis pregnant women with cobalamin deficiency are at almost twofold higher risk to develop GDM, when compared with those with cobalamin sufficiency.¹⁹

Furthermore, fasting blood glucose levels were markedly elevated among cases compared to controls (148.75 ± 45.60 mg/dL vs. 85.20 ± 7.10 mg/dL, $p = 0.0001$), confirming the diagnosis of hyperglycemia in the case group. This significant difference further underscores the

metabolic disturbances present in women with low serum cobalamin levels during pregnancy.²⁰

Overall, the findings of the current study suggest that lower maternal vitamin B12 levels are associated with poorer glycemic control in pregnancy, highlighting the potential importance of early nutritional assessment and intervention. These results are consistent with prior evidence and support the need for larger prospective studies to evaluate the potential benefits of vitamin B12 supplementation in improving pregnancy outcomes.

The strengths of this study include the matched case-control design, strict inclusion criteria, and the use of validated methods for biochemical assays. However, our study has several limitations. The relatively small sample size from a single center limits the generalizability of the findings. Dietary intake of vitamin B12 and potential confounders such as socioeconomic status and supplementation practices were not evaluated. Additionally, the observational nature of the study precludes causal inferences.

Conclusion

Mean serum cobalamin level was significantly lower in women with gestational diabetes making it one of the risk factors for development of gestational diabetes mellitus in pregnancy.

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