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ASSOCIATION OF VITAMIN 12 DEFICIENCY WITH GESTATIONAL DIABETES MELLITUS

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Abstract

Introduction: *Gestational diabetes mellitus (GDM) is a common pregnancy complication associated with adverse maternal and fetal outcomes. Vitamin B12 deficiency has been linked to insulin resistance and metabolic dysfunction, but its association with GDM remains unclear. This study aimed to evaluate the relationship between vitamin B12 deficiency and GDM in pregnant women.*

Methodology: *A case-control study was conducted at the Department of Obstetrics & Gynecology, National Hospital, Lahore, over six months. A total of 60 pregnant women (>24 weeks gestation) were enrolled, with 30 cases (GDM) and 30 controls (non-GDM). Vitamin B12 levels were assessed, and deficiency was defined as <150 pg/ml. Data were analyzed using SPSS, with odds ratios (OR) and p-values calculated to determine associations.*

Results: *Vitamin B12 deficiency was significantly higher in GDM cases (40.0%) compared to controls (13.3%) (p = 0.020, OR = 4.333). The mean vitamin B12 level was lower in cases (196.01±66.61 pg/ml) than in controls (219.09±50.39 pg/ml) (p = 0.001).*

Conclusion: *Vitamin B12 deficiency was significantly associated with GDM, with a higher prevalence in younger, primiparous women and those lacking folic acid intake. These findings highlight the need for early screening and nutritional interventions to prevent B12 deficiency in pregnant women at risk of GDM.*

INTRODUCTION

A healthy maternal environment is crucial for fetal development, with gestational diabetes mellitus being a common pregnancy disorder linked to insulin resistance. Risk factors for gestational diabetes include family history of diabetes, BMI >30, prior gestational diabetes, having had a macrosomic baby weighing ≥4.5 kg, and ethnicity.[1] Globally, gestational diabetes prevalence is around 17%, with some Asian countries exceeding 20%.[2] Deficiency of B12 affects fatty acid transfer into mitochondria, hindering beta-oxidation and boosting lipogenesis, adipogenesis, and insulin resistance risk.[3-4]

Vitamin B12 deficiency is a significant issue during pregnancy, impacting both mothers and infants globally; however, it is more prevalent in populations with lower socio-economic statuses.[5] Impaired maternal vitamin B12 status during pregnancy can increase infants' risk of B12 deficiency. Interventions are required to enhance peri-conceptional B12 status for pregnant women and their children's optimal health.[6-7] Gestational diabetes mellitus is on the rise globally across ethnicities, potentially linked to vitamin B12 and folate levels. Evidence on their impact remains inconclusive.[8]

Sukumar et al., reported in a case-control study, conducted in the West Midlands, UK, that vitamin B12 deficiency was present in 51.1% females with gestational diabetes while in 38.2% females without gestational diabetes ($p<0.05$).[9] While Saravanan et al., conducted another study in UK and found that vitamin B 12 deficiency was present in 11.5% females with gestational diabetes while in 10.1% females without gestational diabetes ($p>0.05$).[8]

The study aimed to link vitamin B12 deficiency with gestational diabetes. Pregnant women are not usually screened for this deficiency. Past research has shown a significant association with gestational diabetes, but there are conflicting reports. As existing studies were conducted in the UK, where healthcare is better, this study seeks evidence from the local population to improve practices. Screening for vitamin B12 deficiency in early pregnancy could predict and prevent gestational diabetes.

METHODOLOGY

A case-control study was conducted in the Department of Obstetrics & Gynecology at National Hospital, Lahore, over a period of six months following the approval of the synopsis. The study aimed to assess the association between gestational diabetes mellitus (GDM) and vitamin B12 deficiency in pregnant women in their third trimester. A total of 60 participants were enrolled, including 30 cases (females diagnosed with GDM) and 30 controls (females without GDM). The sample size was determined using the WHO sample size calculator, with a 5% significance level, 80% power, and based on the percentage of vitamin B12 deficiency in females with GDM (51.1%) and without GDM (10.1%).[8-9]

Females aged between 18 and 40 years with a gestational age of more than 24 weeks, as determined by the last menstrual period (LMP), and with parity less than five were included in the study. Participants were categorized into cases (females diagnosed with GDM based on fasting OGTT >92 mg/dl, 1-hour postprandial OGTT ≥180 mg/dl, or 2-hour postprandial OGTT >153 mg/dl in the third trimester) and controls (females without GDM). Exclusion criteria included patients with a history of GDM in a previous pregnancy, those with known diabetes, and those with multiple pregnancies.

After obtaining informed consent, eligible participants were enrolled from the Outpatient Department (OPD). Demographic details, including name, age, occupation, socioeconomic status, parity, gestational age, family history of diabetes, history of folic acid intake in the current pregnancy, and body mass index (BMI), were recorded. Participants were then divided into the case and control groups accordingly.

A 3 ml venous blood sample was collected from each participant and sent to the hospital laboratory for vitamin B12 level assessment. A vitamin B12 level of less than 150 pg/ml was used to define vitamin B12 deficiency. Reports were reviewed, and participants with vitamin B12 deficiency and gestational diabetes were managed as per standard clinical protocols. All collected data were recorded in a structured proforma.

For statistical analysis, SPSS version 25.0 calculated mean, standard deviation for age, BMI, gestational age, vitamin B12 levels, and provided frequencies, percentages for socioeconomic status, occupation, family history of diabetes, history of folic acid intake during pregnancy, vitamin B12 deficiency. An odds ratio (OR) >1 in a 2×2 table linking vitamin B12 deficiency to GDM was deemed significant. Data were stratified by various factors, each stratum analyzed for associations between vitamin B12 deficiency and GDM using 2×2 tables with OR >1 indicating significance.

RESULTS

Table 1 presents a comparative analysis of various demographic and clinical variables between cases (women with gestational diabetes) and controls (women without gestational diabetes). The mean age of participants in both groups was similar (31.80±5.41 years in cases and 31.03±4.64 years in controls), with a majority falling in the 31-40 years category. BMI distribution showed that most participants were overweight (60.0% in both groups), with a small percentage classified as obese. The mean BMI was slightly higher in the control group (27.07±2.80) than in cases (26.63±2.70).

Regarding gestational age, the majority of participants were between 24-36 weeks (66.7% in cases and 63.3% in controls), with an overall comparable mean gestational age. Parity distribution

was also similar, with 60.0% of cases and 56.7% of controls being multiparous. Socioeconomic status varied between groups, with a slightly higher proportion of low-income individuals in cases (40.0%) compared to controls (33.3%), whereas the middle-income group was more prevalent in controls (43.3%). In terms of occupation, most participants were housewives (60.0% in cases, 63.3% in controls), with smaller proportions of self-employed and unemployed individuals. Family history of diabetes was slightly more common in cases (53.3%) compared to controls (50.0%). The history of folic acid intake differed between groups, with 56.7% of cases reporting no folic acid intake compared to 46.7% in controls.

Table 2 shows a significant link between vitamin B12 insufficiency and gestational diabetes mellitus (GDM). Among women with GDM, 40.0% had a deficiency, while only 13.3% did in the control group. The odds ratio of 4.333 indicates that pregnant women with GDM are over four times more likely to lack vitamin B12. Average B12 levels were notably lower in GDM cases (196.01±66.61 pg/ml) compared to controls (219.09±50.39 pg/ml), with a highly significant p-value of 0.001, suggesting a connection between low vitamin B12 and GDM.

Table 3 shows the link between vitamin B12 deficiency and gestational diabetes mellitus (GDM) across different groups. Significant associations were found in younger women, primiparous women, those without a family history of diabetes, and women who didn't take folic acid during pregnancy. Higher odds of deficiency appeared in obese women, housewives, and high-income groups, though not significant. The strongest link was among women without folic acid intake, hinting at folic acid's potential protective role against vitamin B12 deficiency in GDM. These findings stress the importance of targeted nutritional interventions.

Table-1: Comparison of distribution of different variables between groups

Variables		Groups	
		Cases	Controls
Age groups	18-30 years	12(40.0%)	13(43.3%)
	31-40 years	18(60.0%)	17(56.7%)
	Mean±S.D	31.80±5.41	31.03±4.64
BMI	Normal	11(36.7%)	10(33.3%)
	Overweight	18(60.0%)	18(60.0%)
	Obese	1(3.3%)	2(6.7%)
	Mean±S.D	26.63±2.70	27.07±2.80
Gestational age	24-36 weeks	20(66.7%)	19(63.3%)
	37-41 weeks	10(33.3%)	11(36.7%)
	Mean±S.D	32.90±5.62	32.70±5.33
Parity	Primiparous	12(40.0%)	13(43.3%)
	Multiparous	18(60.0%)	17(56.7%)
Socio-economic status	Low	12(40.0%)	10(33.3%)
	Middle	10(33.3%)	13(43.3%)
	High	8(26.7%)	7(23.3%)
Occupation	Self-employed	7(23.3%)	7(23.3%)
	Unemployed	5(16.7%)	4(13.3%)
	Housewife	18(60.0%)	19(63.3%)
Family history of diabetes	Yes	16(53.3%)	15(50.0%)
	No	14(46.7%)	15(50.0%)
History of folic acid intake	Yes	13(43.3%)	16(53.3%)
	No	17(56.7%)	14(46.7%)

Table-2: Association of vitamin B12 deficiency with gestational diabetes mellitus

Vit. B12 deficiency	Groups		p-value	Odds ratio
	Cases	Controls		
Yes	12(40.0%)	4(13.3%)	0.020	4.333
No	18(60.0%)	26(86.7%)		
Mean vit. B12 levels	196.01±66.61	219.09±50.39	0.001	

Table-3: Stratification of association of vitamin B12 deficiency with gestational diabetes mellitus with respect to different variables

Variables	Vit. B12 deficiency	Cases	Controls	p-value	Odds ratio
Age groups					
18-30 years	Yes	5(41.7%)	0(0.0%)	0.009	2.857
	No	7(58.3%)	13(100.0%)		
31-40 years	Yes	7(38.9%)	4(23.5%)	0.328	2.068
	No	11(61.1%)	13(76.5%)		
BMI					
Normal	Yes	4(36.4%)	1(10.0%)	0.157	5.143
	No	7(63.6%)	9(90.0%)		
Overweight	Yes	7(38.9%)	3(16.7%)	0.137	3.182
	No	11(61.1%)	15(83.3%)		
Obese	Yes	1(100.0%)	0(0.0%)	0.083	N/A
	No	0(0.0%)	2(100.0%)		
Gestational age					
24-36 weeks	Yes	7(35.0%)	2(10.5%)	0.070	4.577
	No	13(65.0%)	17(89.5%)		
37-41 weeks	Yes	5(50.0%)	2(18.2%)	0.122	4.500
	No	5(50.0%)	9(81.8%)		
Parity					
Primiparous	Yes	5(41.7%)	0(0.0%)	0.009	2.857
	No	7(58.3%)	13(100.0%)		
Multiparous	Yes	7(38.9%)	4(23.5%)	0.328	1.388
	No	11(61.1%)	13(76.5%)		
Socio-economic status					
Low	Yes	4(33.3%)	1(10.0%)	0.193	4.500
	No	8(66.7%)	9(90.0%)		
Middle	Yes	5(50.0%)	3(23.1%)	0.179	3.333
	No	5(50.0%)	10(76.9%)		
High	Yes	3(37.5%)	0(0.0%)	0.070	2.400
	No	5(62.5%)	7(100.0%)		
Occupation					
Self-employed	Yes	2(28.6%)	0(0.0%)	0.127	2.400
	No	5(71.4%)	7(100.0%)		
Unemployed	Yes	1(20.0%)	0(0.0%)	0.343	2.000

	No	4(80.0%)	4(100.0%)		
Housewife	Yes	9(50.0%)	4(21.1%)	0.065	3.750
	No	9(50.0%)	15(78.9%)		
Family history of diabetes					
Yes	Yes	4(25.0%)	1(6.7%)	0.165	4.667
	No	12(75.0%)	14(93.3%)		
No	Yes	8(57.1%)	3(20.0%)	0.039	5.333
	No	6(42.9%)	12(80.0%)		
History of folic acid intake					
Yes	Yes	5(38.5%)	3(18.8%)	0.238	2.708
	No	8(61.5%)	13(81.3%)		
No	Yes	7(41.2%)	1(7.1%)	0.031	9.100
	No	10(58.8%)	13(92.9%)		

DISCUSSION

Considering the relatively elevated incidence of Gestational Diabetes Mellitus (GDM), particularly in underdeveloped nations, the insufficient identification of both maternal and fetal etiologies and complications, as well as ongoing debates among scholars regarding the risk factors associated with GDM, this investigation sought to analyze and contrast variations in vitamin B12 concentrations between women diagnosed with GDM and a control cohort. The rate of vitamin B12 insufficiency was observed to be 26.7% among the 60 pregnant women included in the study.

In the research conducted by Chen et al., the occurrence rate of vitamin B12 deficiency was determined to be 22.9%.[10] The incidence of vitamin B12 deficiency observed in the present investigation was markedly greater than that reported in the study conducted by Chen and associates, a discrepancy that may be attributed to variations in lifestyle and dietary abundance prevalent in developed nations. A pivotal finding of this research was the significantly elevated prevalence of vitamin B12 deficiency among women diagnosed with gestational diabetes mellitus (GDM) compared to their non-GDM counterparts (40% versus 13.3%). To elucidate, the proportion of vitamin B12 deficiency in the cohort of women with GDM was found to be threefold that of women without GDM.

In the investigation conducted by Sukumar et al., it was observed that 51.1% of pregnant women with gestational diabetes mellitus (GDM) exhibited suboptimal levels of vitamin B12. Consequently, a correlation was established between vitamin B12 deficiency and the occurrence of GDM.[9] Wang et al. documented that the levels of aggregated serum vitamin B12 were markedly diminished in the gestational diabetes mellitus (GDM) cohort compared to the non-GDM cohort, a finding that aligns with the current investigation.[11]

In a comparable investigation, Saravanan et al. identified that diminished levels of vitamin B12 during the initial stages of gestation correlated with an increased likelihood of gestational diabetes mellitus (GDM). They asserted that to generalize these findings, additional research is necessary to examine the influence of early pregnancy on B12 concentrations and the ensuing hyperglycemic responses.[8]

In a study conducted in 2020, Liu and colleagues indicated that an inverse relationship exists between the risk of diabetes and elevated or standard levels of vitamin B12. They elaborated that additional research with a more extensive sample population from diverse geographical areas globally is imperative to bolster the existing evidence.[12]

Kouroglou et al., in their meta-analytical investigation, established a noteworthy correlation between vitamin B12 deficiency and gestational diabetes mellitus (GDM). Nonetheless, no statistically significant variation was observed in the remaining four studies.[13] Guven et al. proposed that there is no significant disparity in vitamin B12 concentrations between the gestational diabetes mellitus (GDM) cohort and the non-GDM cohort.[14]

Based on the existing literature and the findings of this investigation, the association between maternal vitamin B12 concentrations during gestation and the

susceptibility to gestational diabetes mellitus (GDM) remains ambiguous and is characterized by inconsistencies. The current research explored the influence of vitamin B12 and determined that adequate levels of this vitamin may serve as a protective mechanism against GDM, which constitutes a clinically significant observation.

In the research conducted by Maher et al., it was determined that a deficiency in vitamin B12 correlates with increased insulin resistance. They proposed a plausible strategy to mitigate the risk of GDM by improving maternal metabolic health through the administration of vitamin B12 supplements.[3]

Based on the findings presented by Xie et al., there exists a significant correlation between vitamin B12 levels and the risk of gestational diabetes mellitus (GDM).[15] Furthermore, Li et al. demonstrated that a deficiency in vitamin B12 elevated the incidence of gestational diabetes mellitus (GDM) by a factor of 1.12.[16]

This study's limitations affecting result interpretation include a small sample size (60 participants), limiting generalizability. A larger sample would offer stronger evidence on vitamin B12 deficiency and gestational diabetes mellitus. Conducted in a single hospital setting, the study's findings may not reflect nationwide nutritional and healthcare disparities. The study solely relied on serum vitamin B12 levels for deficiency assessment. Lack of functional biomarker measurements like methylmalonic acid or homocysteine levels hinders B12 status evaluation accuracy. Dietary variation in B12 intake, unaccounted for in the study, might affect deficiency rates. Future research should include comprehensive nutritional assessments and long-term follow-ups for a deeper understanding of the association.

CONCLUSION

Vitamin B12 deficiency was significantly linked to gestational diabetes (GDM), more prevalent in young, first-time mothers and those with inadequate folic acid intake. These results emphasize the importance of early screening and nutritional support for pregnant women at GDM risk to prevent B12 deficiency.

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