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Dietary Patterns and Vitamin B12–Folate Axis in Gestational Diabetes Mellitus: A Comparative Analysis

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ABSTRACT

Introduction:

Gestational Diabetes Mellitus (GDM) is a common metabolic disorder that occurs during pregnancy. GDM has been related to adverse maternal and child health. Dietary patterns and levels of micronutrients such as vitamin B12 and folate have been identified as key modifiable risk factors for GDM. However, there has been little research on the combined impact of these factors, particularly in Indian women.

Methodology:

A comparative cross-sectional study design was followed among a sample of 200 pregnant women, comprising 100 GDM and 100 non-GDM pregnant women. The study participants were recruited from the districts of Kurukshetra and Karnal. Data collection was conducted based on socio-demographic variables, dietary intake by the use of a 24-hour recall method and food frequency method, and biochemical variables such as vitamin B12 and folate levels.

Results:

The GDM subjects had significantly higher energy, carbohydrate, and fat intakes, whereas they had lower folate and vitamin B12 intakes. The GDM subjects also had lower fruit, dairy product, and green leafy vegetable intakes, whereas they had higher cereal and sweet food intakes. The prevalence of vitamin B12 and folate deficiencies was higher in GDM women. High BMI, lower vitamin B12, lower folate, higher carbohydrate, and lower fruit intakes were significant predictors of GDM, as confirmed by logistic regression analysis.

Discussion:

The findings of the study, therefore, suggest that dietary imbalance, as well as deficiencies of various micronutrients, contribute to the development of GDM. The interaction of vitamin B12 and folate levels may affect metabolic pathways, leading to insulin resistance. Nutritional imbalance, therefore, adds to the risk of developing GDM.

Conclusion:

It is observed that there is a strong association between dietary habits, micronutrients, and GDM risk. Improvement of dietary quality and adequate intake of vitamin B12 and folate may be helpful in reducing the burden of GDM. Nutritional interventions and screening of micronutrients should be undertaken to improve maternal and fetal outcomes.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as “glucose intolerance diagnosed in pregnancy, which is thought to result from hormonal changes in pregnancy such as an insulin antagonist, human placental lactogen. GDM is considered to be one of the common metabolic complications of pregnancy. The incidence of GDM is increasing globally due to various factors such as an increase in the average age of pregnant women, an increase in urbanization rates, an increase in sedentary lifestyle, and an alteration in dietary habits. GDM is considered to be affecting 10 to 20 percent of pregnancies worldwide. In South Asian women, it is found to be higher. GDM is known to cause complications such as preeclampsia, cesarean deliveries, macrosomia, hypoglycemia in newborn babies, and an increased risk of type 2 diabetes in both mother and child in the future. Thus, considering its rising incidence and its implications in future health, it is of prime importance to focus on finding modifiable risk factors. Nutritional habits during pregnancy are known to play an important role in influencing metabolic health in pregnant women. Adverse nutritional habits such as an excessive intake of refined carbohydrates, saturated fats, and an insufficient intake of fruits and vegetables are known to cause an increased risk of GDM. Recent evidence also indicates that vitamins play an important role in influencing GDM. Nutritional imbalances are known to cause alterations in insulin sensitivity, which in turn may cause metabolic complications. Thus, it is of prime importance to focus on understanding the relationship between dietary intake and vitamins in order to understand the cause of GDM.

Vitamin B12 is an important micronutrient that plays a key role in DNA synthesis, red blood cell production, and one-carbon metabolism. Deficiency of vitamin B12 is highly prevalent among pregnant women, especially in those with predominantly vegetarian dietary habits, such as in India. Various studies have documented a strong positive correlation between low levels of vitamin B12 in pregnant women and an increased risk of GDM (3, 6, 11). Studies based on systematic reviews and meta-analyses have shown that vitamin B12 deficiency is an independent factor for GDM, which may play an important role in its prevention (6, 11). These mechanisms may include impaired methylation and insulin resistance, which may cause an abnormal metabolic response in glucose homeostasis in pregnant women.

Folate is another vital micronutrient in one-carbon metabolism. Folate is widely recommended during pregnancy to prevent neural tube defects. However, it has also been shown in recent studies that excessive intake of folate may cause adverse metabolic effects, especially in the context of vitamin B12 deficiency. High doses of folic acid supplements have been shown to cause an increased risk of GDM in some populations, although findings are inconsistent (5, 9). Although adequate intake of folate is vital for fetal health, an imbalance of folate and vitamin B12 may cause metabolic abnormalities. Thus, an optimal balance of these nutrients is vital.

The interrelation of folate and vitamin B12 is a key factor in the development of GDM. High levels of folate in combination with low levels of vitamin B12 have been found to significantly increase the risk of GDM (4,10). The interrelationship of both vitamins affects one-carbon metabolism, which in turn affects homocysteine levels, oxidative stress, and insulin signaling. Furthermore, high levels of folate have been associated with masking symptoms of vitamin

B12 deficiency, which in turn affects metabolic dysfunction (7). The interrelationship of folate and vitamin B12 in the development of GDM is likely an important hypothesis in linking micronutrient status with glucose metabolism in pregnancy.

The interrelationship of both vitamins in the development of GDM at the molecular level is also evident. Both vitamins are central in one-carbon metabolism, which affects methylation reactions and DNA synthesis. Glucose metabolism is impacted by insulin resistance, which is linked to elevated homocysteine levels. Moreover, insulin resistance, which impacts glucose metabolism, has been linked to elevated homocysteine levels. Insulin resistance, which impacts glucose metabolism, is probably made worse by a high folate level combined with low vitamin B12 levels (7,8). Several observational and cohort studies have revealed significant correlations between maternal micronutrient levels and GDM. An increased prevalence of GDM has been linked to lower vitamin B12 levels and higher folate levels (10,12). Furthermore, pregnant women with GDM had considerably lower vitamin B12 levels than pregnant women without GDM, according to clinical investigations (14). Moreover, dietary studies revealed that inadequate consumption of foods rich in micronutrients is responsible for this imbalance (3,13). However, results are inconsistent due to differences in study population, methodology, and dietary assessment methods.

Despite extensive evidence, the role of dietary habits, vitamin B12 levels, and folate levels in GDM is not sufficiently studied in the Indian population. Most studies have reported results for dietary habits and biochemical parameters separately without taking into account the combined role of dietary habits and biochemical parameters in GDM. Moreover, dietary habits and biochemical parameters may play different roles in GDM in different regions due to differences in dietary habits and lifestyle. Therefore, it is essential to conduct comprehensive studies that include dietary habits and biochemical parameters to understand the combined role in GDM. With this background, the present study aimed to assess the association between dietary habits, vitamin B12 and folate levels, and gestational diabetes mellitus in pregnant women from Kurukshetra and Karnal districts.

METHODOLOGY

This study has been done in the form of a comparative cross-sectional study to evaluate the relationship of dietary habits, vitamin B12, and folate status of mothers with gestational diabetes mellitus. This study has been carried out among pregnant women in the districts of Kurukshetra and Karnal in Haryana. A total of 200 pregnant women were selected for this study, of which 100 were cases of gestational diabetes mellitus, and 100 were non-GDM cases. A sampling technique used in this study is a purposive sampling technique. GDM cases were selected based on the criteria of oral glucose tolerance tests recorded in hospital records. Pregnant women between 18 and 40 years of age willing to participate in this study were considered for data collection. Those pregnant women with existing diabetes mellitus, metabolic syndromes, and other medical complications, and those who were not willing to participate in this study, were excluded. Data was gathered through in-person interviews using a pre-tested, standardized questionnaire style. Relatives of pregnant women were asked about their obstetric history, diabetes history, and sociodemographic information. Pregnant women's

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weight and height were noted. The traditional method of dividing weight in kilos by height in meters was used to get the body mass index of pregnant women. Hemoglobin and blood pressure of pregnant women were recorded from medical records.

Dietary intake was measured using the 24-hour recall method, which was conducted for three consecutive days, including both weekdays and weekends. Nutrient intake, such as energy, carbohydrates, proteins, fats, folate, vitamin B12, and iron, was calculated using standard food composition tables. A food frequency questionnaire (FFQ) was also used to assess the dietary habits of participants, including the consumption of cereals, pulses, dairy products, fruits, vegetables, and sweet foods. Dietary Diversity Score (DDS) was also calculated on the basis of food groups consumed by the subjects.

Biochemical variables such as fasting blood glucose, postprandial blood glucose levels, HbA1c levels, vitamin B12 levels, and folate levels were recorded from the lab reports. Vitamin B12 levels were classified into deficient and normal by referring to reference ranges. All the data were analyzed by using suitable statistical software. Whereas categorical data were reported as frequency and percentage, continuous variables were expressed as mean + SD. The independent t-test for continuous variables and the chi-square test for categorical variables were used to compare the variables. Similarly, independent risk variables for GDM were assessed using logistic regression analysis. Statistical significance was defined as a p-value of less than 0.05.

Results

The results of this study are presented in this section to highlight the association of dietary habits, maternal vitamin B12 and folate levels, and gestational diabetes mellitus in pregnant women. The study subjects, a total of 200, comprising 100 GDM and 100 non-GDM pregnant women, are considered for the analysis. The results of this study are presented in a systematic manner, highlighting the differences and comparisons of socio-demographic and clinical characteristics, dietary habits, and vitamin and mineral levels between the two groups. The differences in dietary habits and nutrient and food group intake, and the biochemical values, are also presented. Regression analysis was carried out to identify the independent predictors of gestational diabetes mellitus. The results are presented in a tabular form to understand the results of this study in a comprehensive manner.

TABLE 1: Distribution of Study Participants by Demographic and Clinical Variables (n=200)

(n = 100 GDM, 100 Non-GDM)

S. No	Variables	Categories	Total (n=200)	GDM (n=100) n (%)	Non-GDM (n=100) n (%)
1	Age (years)	<25	30	8 (8.0)	22 (22.0)
		25–30	95	52 (52.0)	43 (43.0)
		>30	75	40 (40.0)	35 (35.0)
2	BMI (kg/m^2)	<18.5	32	2 (2.0)	30 (30.0)
		18.5–24.9	65	15 (15.0)	50 (50.0)
		≥25	103	83 (83.0)	20 (20.0)

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3	Gravida	1	80	35 (35.0)	45 (45.0)
		≥2	120	65 (65.0)	55 (55.0)
4	Family History of Diabetes	Yes	65	40 (40.0)	25 (25.0)
		No	135	60 (60.0)	75 (75.0)
5	Education	≤10th	85	48 (48.0)	37 (37.0)
		>10th	115	52 (52.0)	63 (63.0)
6	Occupation	Housewife	178	90 (90.0)	88 (88.0)
		Working	22	10 (10.0)	12 (12.0)
7	Family Income (₹)	<1 lakh	60	32 (32.0)	28 (28.0)
		1–2 lakh	85	45 (45.0)	40 (40.0)
		>2 lakh	55	23 (23.0)	32 (32.0)

The nutritional consumption of GDM women and non-GDM women differed significantly, according to the comparison. The study also found that women with GDM consumed large amounts of lipids, proteins, carbs, and energy. They did, however, consume very little in the way of micronutrients, including folate and vitamin B12. The study also revealed that women with GDM had high intakes of cereals and sugary foods. However, their intake of protective foods, such as dairy products, fruits, and green leafy vegetables, was significantly low. Moreover, the study also revealed that more women with GDM were deficient in vitamin B12 and folate. Logistic regression analysis revealed that high BMI, low vitamin B12, low folate, high carbohydrate, and low fruit consumption were significant independent predictors of GDM.

TABLE 2: Nutrient Intake (24-hour Recall)

Parameter	GDM (Mean ± SD)	Non-GDM (Mean ± SD)	p-value
Energy (kcal)	1820 ± 120	1685 ± 110	0.01
Carbohydrates (g)	302 ± 25	265 ± 20	<0.001
Protein (g)	62 ± 6	57 ± 5	0.02
Fat (g)	42 ± 5	35 ± 4	<0.001
Folate (µg)	410 ± 80	520 ± 95	<0.001
Vitamin B12 (µg)	0.42 ± 0.15	0.88 ± 0.30	<0.001
Iron (mg)	15.5 ± 2.5	17.0 ± 2.8	0.01

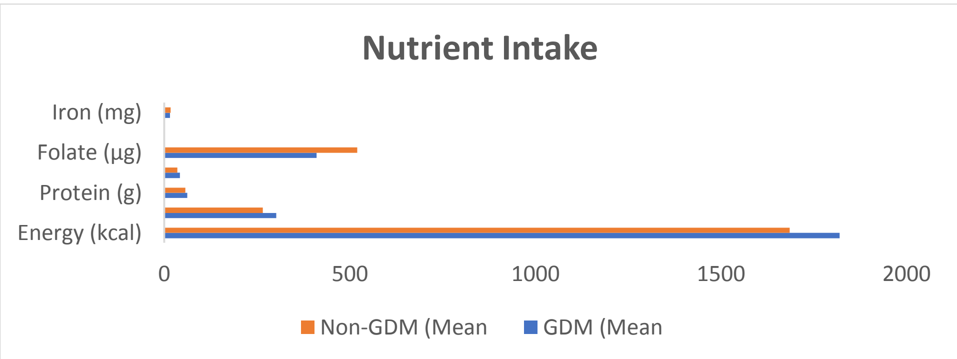

Figure 1: Nutrient intake

The analysis of the nutrient intake showed that women with GDM had significantly higher energy, carbohydrates, protein, and fat intake compared to those in the non-GDM group, with the highest significant difference in carbohydrate intake (p < 0.001). On the contrary, the women with GDM had significantly lower levels of essential micronutrients such as folate and vitamin B12. Iron levels were slightly lower in women with GDM. It can thus be concluded that dietary macronutrient-rich, micronutrient-poor foods may be associated with GDM.

TABLE 3: Food Group Consumption Pattern

Food Group	GDM (Mean intake)	Non-GDM (Mean intake)	p-value
Cereals (g)	780 ± 90	650 ± 85	<0.001
Pulses (g)	220 ± 40	240 ± 45	0.08
Dairy (ml/g)	150 ± 60	260 ± 80	<0.001
Fruits (g)	60 ± 30	140 ± 50	<0.001
Green leafy vegetables (g)	45 ± 25	95 ± 40	<0.001
Sugary foods (g)	85 ± 30	40 ± 20	<0.001

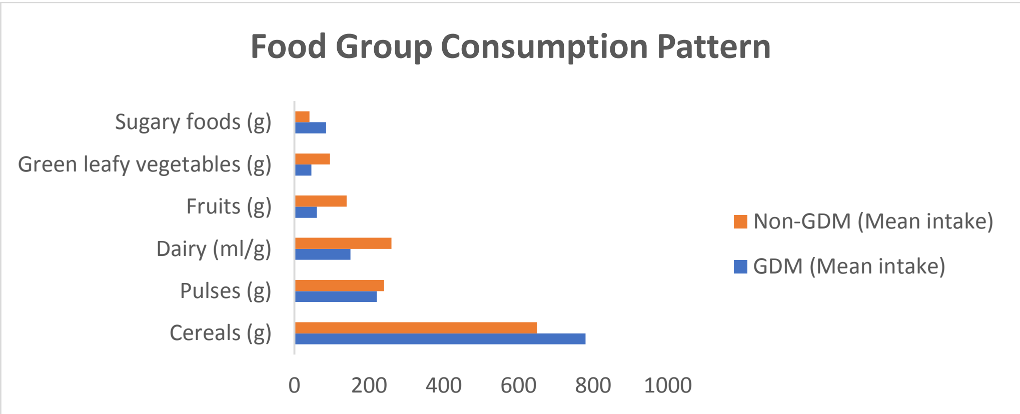

Figure 1: Food Group Consumption Pattern

The food group analysis showed that the participants in the GDM group were significantly higher in the consumption of cereals and sweet foods when compared with the non-GDM participants (p<0.001). Conversely, the participants in the GDM group were significantly low in the consumption of protective food groups such as dairy products, fruits, and green leafy vegetables. The consumption of pulses was similar in both groups. This study showed that the diet of the participants in the GDM group was high in refined carbohydrates and low in nutrient-rich foods.

TABLE 4: Vitamin B12 and Folate Status

Parameter	Category	GDM (n=100) n (%)	Non-GDM (n=100) n (%)	p-value
Vitamin B12	**Deficient (<200 pg/mL)**	**45 (45.0)**	**20 (20.0)**	**<0.001**
	Borderline	**30 (30.0)**	**25 (25.0)**	
	Normal	**25 (25.0)**	**55 (55.0)**	

Folate	**Deficient (<5 ng/mL)**	**40 (40.0)**	**18 (18.0)**	**<0.001**
	Normal	**60 (60.0)**	**82 (82.0)**	

Compared to the non-GDM group (20%), the GDM group had a much higher proportion of vitamin B12 insufficiency (45%). Similarly, the GDM group had a higher rate of folate deficit (40%) than the non-GDM group (18%). Nonetheless, a significant portion of the non-GDM group had normal levels of both vitamin B12 and folate. This demonstrates the strong link between GDM and vitamin B12 and folate deficits.

TABLE 5: Logistic Regression Analysis for Risk of GDM

Variable	Odds Ratio (OR)	95% CI	p-value
BMI ≥25	3.8	2.1 – 6.5	<0.001
Low Vitamin B12	2.9	1.6 – 5.1	0.002
Low Folate	2.5	1.4 – 4.3	0.004
Low fruit intake	2.2	1.3 – 3.8	0.01
High carbohydrate intake	3.1	1.8 – 5.2	<0.001

The independent factors for GDM were determined using logistic regression analysis. It was observed that women with BMI ≥ 25 kg/m² had significantly higher odds of developing GDM (3.8). Low levels of vitamin B12 and folate were strong predictors of GDM, increasing the risk of GDM almost three- to two-fold, respectively. High levels of carbohydrates in the diet and lower levels of fruit intake were significantly associated with an increased risk of GDM.

DISCUSSION

The goal of the current study was to look into the connection between gestational diabetes mellitus (GDM) and dietary practices, maternal vitamin B12, and folate levels. The study's results unequivocally show how metabolic and dietary variables contribute to the development of GDM. From the findings, it is clearly evident that women with GDM consume more energy and macronutrients, especially carbohydrates, and fewer essential nutrients, vitamin B12, and folate. This is in line with the findings of previous studies that emphasize the risk of developing GDM in women who consume more dietary energy and refined sugars (2,3).

The findings of the present study clearly reflect that the consumption of more carbohydrates is significant in the development of GDM. This is in line with the findings of cohort studies that emphasize the risk of developing GDM in women who consume more carbohydrates (3). Additionally, the increased consumption of fats and energy among women with GDM is another factor that supports the findings of the study. This is in line with the findings of previous studies that emphasize the risk of developing GDM in women who consume more dietary energy (2).

The findings of the study clearly reflect the significance of vitamin B12 levels in the development of GDM. From the findings, it is clearly evident that women with GDM consume fewer vitamin B12 levels. Almost half of the women with GDM were vitamin B12 deficient. This is in line with the findings of previous systematic reviews and meta-analyses that emphasize the risk of developing GDM in women who consume fewer vitamin B12 levels (6,11). Vitamin B12 is essential in the metabolism of one-carbon compounds and methylation reactions. Vitamin B12 deficiency has been shown to affect glucose metabolism and induce insulin resistance (8). Additionally, pregnant women with GDM were shown to have low vitamin B12 levels compared to non-GDM women (14,15).

Folate status was also found to be significantly associated with GDM, as indicated by the higher prevalence of folate deficiency in GDM subjects. While folate is crucial for fetal development, recent evidence indicates that both deficiency and excess of folate may play a role in GDM (5,9). For instance, it has been indicated that higher levels of folic acid supplementation, especially in conjunction with lower levels of vitamin B12, may increase the risk for GDM (9). This indicates that it is crucial to focus on maintaining an optimum balance rather than focusing on individual nutrient supplements.

Folate and vitamin B12 interaction in GDM

Folate and vitamin B12 interaction plays an integral role in the development of GDM. The results obtained in this study support the notion that an imbalance in these two micronutrients leads to metabolic disorders. Previous studies have indicated that higher levels of folate in conjunction with deficiency in vitamin B12 significantly increase the risk for GDM (4,10). This imbalance in these two micronutrients leads to metabolic disorders through increased levels of homocysteine and through oxidative stress and insulin resistance (4,10). Furthermore, it is indicated that higher levels of folate may mask clinical symptoms of vitamin B12 deficiency, thus leading to metabolic disorders (7).

Mechanistically, the role of folate and vitamin B12 in the metabolism of homocysteine and in the process of methylation of DNA is well recognized. Abnormalities in these pathways have been linked with insulin resistance and endothelial dysfunction and changes in the expression of genes that regulate glucose metabolism. Increased levels of homocysteine caused by an imbalance in these two nutrients have been linked with the risk of developing GDM. In addition, hyperfolateemia in the presence of vitamin B12 deficiency has been linked with insulin resistance and the development of GDM.

The dietary pattern identified in this study further reinforces the association between diet and the development of GDM. The study found that the women with GDM had significantly low intakes of fruits, dairy products, and green leafy vegetables that are rich in various nutrients including folate and vitamin B12. In contrast, the study found that the women with GDM had significantly high intakes of cereals and sweet foods. Similar findings were reported in another study that showed that the women with GDM had low dietary diversity and low intakes of nutrient-rich foods. The study suggested that the quality rather than the quantity of the diet plays an important role in the prevention of GDM.

The logistic regression analysis in the present study revealed that high BMI, low vitamin B12, low folate, high carbohydrate, and low fruit intake are significant independent predictors of GDM. These results are in accordance with the literature, which states that obesity and micronutrient imbalance are major risk factors for GDM (6,11).

Although numerous studies have revealed the risk factors and their association with GDM, there is still controversy in the literature regarding the association of folate and vitamin B12 in GDM patients. Greater folate levels have been linked to a lower risk of GDM in some research, whereas low vitamin B12 levels and greater folate levels have been linked to a higher risk of GDM in other studies (5,9,12). These discrepancies in the results may be due to differences in the study population and methods of assessment. It is also suggested that further studies are needed to clarify the complex association of micronutrients and GDM.

The present study contributes to the already available data by providing an exhaustive insight into the dietary habits and nutrient and biochemical status in relation to GDM in the Indian population. Unlike other studies, which have concentrated only on individual factors, the present study has provided an exhaustive account of the role of dietary and biochemical factors in GDM, which is more holistic in nature. The results of the present study are also significant in the context of the high prevalence of vitamin B12 deficiency in the Indian population, especially in vegetarians.

Therefore, the present study aims to emphasize the importance of nutrients during pregnancy, not only in terms of intake but also in terms of the nutrient status, particularly the optimal nutrient status in the body, such as vitamin B12 and folate, which play an important role in the management of GDM and hence contribute significantly towards the management of the incidence of GDM in the population.

Conclusion

The present study has revealed that there is a significant association of dietary habits, vitamin B12, and folate with GDM. It has been revealed that the dietary habits of women suffering from GDM reveal higher dietary energy and carbohydrates, while the levels of essential nutrients such as vitamin B12 and folate are lower. It has been concluded that dietary habits such as lower intake of fruits, dairy products, green leafy vegetables, and higher levels of dietary carbohydrates play a significant role in GDM. It has also been revealed that higher levels of BMI, along with lower levels of essential nutrients such as vitamin B12 and folate, act as predictors for GDM. This reveals the need for adopting an integrated approach to address the problem of GDM by considering the importance of dietary habits and the need for treating vitamin B12 and folate deficiency in pregnant women.

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