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Association of gestational diabetes mellitus with vitamin D status among women attending at Bangabandhu Sheikh Mujib Medical University

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Abstract

Gestational diabetes mellitus (GDM) is an important cause of maternal and perinatal morbidities. Vitamin D is associated with glucose metabolism. The present study was aimed to assess the association of maternal serum vitamin D level with GDM. This case-control study was conducted among 80 pregnant women at the Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Among the 80 patients, 40 were GDM patients (cases) and 40 pregnant women without GDM (controls). The serum vitamin D level was measured for all of them. The mean vitamin D level of the cases and controls were 18.8±5.5 ng/ml and 22.1±7.3 ng/ml, respectively (*P*=0.025). There was significant difference regarding the vitamin D adequacy in between case and control groups (*P*= 0.006) and the respondents with vitamin D <30.0 ng/ml had 7.2 times more chances to have GDM compared to that of the respondents with vitamin D ≥30 ng/ml (OR=7.2; 95% confidence interval =1.5-35.1). There was a significant negative correlation between serum vitamin D level and plasma glucose level 2-hour after 75 gm glucose drink (r= -0.33, *P*= 0.004). In conclusion, serum vitamin D level was found low in patient with GDM compared to those without GDM.

Keywords: Gestational diabetes mellitus, Vitamin D level

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Introduction

Gestational diabetes mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] It adversely affects the pregnancy outcome and has long term negative health impact on the mother as well as the offspring. Its incidence is increasing rapidly worldwide. Globally its prevalence varies from <1-28% due to different screening strategies, diagnostic criteria and population characteristics.[2] In Bangladesh the prevalence of GDM is 8.2% and 12.9% in rural and urban population respectively.[3] However, in our country the antenatal care coverage is only 55%.[3] So, we do not know the glycemic status of the rest 45% pregnant women.

Insulin resistance and resultant hyperinsulinemia are characteristic of normal pregnancy. The resistance results from the placental secretion of diabetogenic hormones i.e., placental lactogen, estrogen and progesterone. Insufficient pancreatic

function fails to overcome the insulin resistance in pregnancy.[4] As placental hormone mediated insulin resistance increases during the second half of pregnancy, usually screening for GDM is done after 24 weeks.

Vitamin D is essential for intestinal absorption of calcium, magnesium and phosphate and thus plays important role in the maintenance of general cellular function. It plays a vital role in glucose metabolism and it improves insulin secretion by stimulating vitamin D receptors in pancreatic islet cells.[5] Activated vitamin D [1,25$(OH)_2$D] directly facilitates the human insulin receptor gene, helps in activation of the peroxisome proliferator-activator receptor gene, thus stimulates the expression of the insulin receptor and helps in insulin-mediated glucose transport.[6] As a result, patients with vitamin D deficiency have an increased risk of developing insulin resistance and diabetes.[7]

GDM is considered one of the most common medical disorders during pregnancy that could lead to severe morbidities. Hence the identification of causative factors for this disease and establishing pathophysiology seems vital and might help take preventive measures. It is important to establish a definite association between maternal serum vitamin D and GDM. So, this study has been designed to estimate the serum vitamin D level and determine its association with GDM in the women of our country.

Methods

This prospective case control study was conducted in the Department of Obstetrics & Gynecology of Bangabandhu Sheikh Mujib Medical University (BSMMU) during November 2019 to October 2021 after obtaining Institutional Review Board approval. Total 80 study subjects attending the out-patient and in-patient department of Obstetrics & Gynecology BSMMU were enrolled upon fulfilling inclusion and exclusion criteria. The study population was divided into two groups: case (n=40) consisting of patients with GDM and control (n=40) comprising women without GDM matched for age and gestational age. Inclusion criteria for cases were: singleton pregnancy with GDM (confirmed by OGTT) within the age range of 18 to 40 years with gestational age between 24 to 40 weeks. Control group bears the above-mentioned same characteristics except their being non diabetic as determined by OGTT. Exclusion criteria were: pre-existing Type 2 DM, multiple pregnancy, diagnosed cases of chronic renal disease, liver disease, polycystic ovary syndrome, any autoimmune disease, metabolic bone disease or receiving vitamin D supplementation. The purpose and procedure of the study was discussed with the participants and informed written consent was taken. The study was conducted anonymously and confidentiality of information was assured. An interviewer-administered questionnaire was used for data collection. Comprehensive sociodemographic history, obstetric history, gestational age, family history and medical history were recorded in the predesigned data sheet. Their antenatal records, early ultrasound scans and medical records of GDM diagnosis were reviewed. Pregnant mothers who had undergone GDM screening and were diagnosed as GDM by WHO criteria with fasting blood sugar 5.1 to 6.9 mmol/L and 2 hours after 75gm glucose of ≥8.5 to 11.0 mmol/L were enrolled for the study as a case group.[8] Routine physical examination and anthropometric measurements (height, weight) were taken and obstetric examinations were conducted and recorded.

After selecting cases and controls, with all aseptic measures 5 ml blood was drawn from the antecubital vein to estimate serum vitamin D. Then the blood sample was sent for analysis in the laboratory of Department of Biochemistry & Molecular Biology of BSMMU. Serum vitamin D level was measured using chemiflex technology in an automated analyzer (Atellica™ IM analyzer, Siemens, Germany). The serum vitamin D level was categorized based on the cut off value as low (<30ng/ml) and normal (>30ng/ml). The low vitamin D level was again categorized as deficient (<20ng/ml) and insufficient (21-29ng/ml). Fisher's Exact test, unpaired t-test and Chi-square tests were done for statistical analysis. Odds ratio (95%Confidence Interval, [CI]) was calculated to see the association of maternal serum D level with GDM. A *P-value* <0.05 was considered as statistically significant.

Results

Among the 80 patients, 40 were GDM patients (cases) and 40 pregnant women without GDM (controls), who were chosen according to the selection criteria. The mean age of the cases was 28.75±5.21 years and 28.45±4.64 years in control. More than 80% were from

TABLE 1 The background characteristics of the study participants

Characteristics	Case (n=40)	Control (n=40)	P*
Age (mean ± SD)	28.7 ± 5.2	28.4 ± 4.6	0.786
Residence			
Rural	05 (12.5)	08 (20.0)	0.363
Urban	35 (87.5)	32 (80.0)	
Monthly family income (in Taka)**			
Lower class (≤ 7,378)	04 (10.0)	03 (7.5)	0.699
Lower middle class (7,379–28,810)	29 (72.5)	27 (67.5)	
Upper middle class (28,811–89,280)	05 (12.5)	09 (22.5)	
Upper class (≥ 89,281)	02 (5.0)	01 (2.5)	
Gravida			
Primi-gravida	12 (30.0)	08 (20.0)	0.302
Multi gravida	28 (70.0)	32 (80.0)	
Gestational age in weeks (mean ± SD)	33.1 ± 4.8	33.7 ± 4.8	0.595
Family history of diabetes mellitus			
Present	13 (32.5)	11 (27.5)	0.626
Absent	27 (67.5)	29 (72.5)	
BMI (kg/m^2) Mean ± SD	26.6 ± 1.8	25.9 ± 1.5	0.087

Results are n (%) unless indicated otherwise; *Fisher's Exact test was or Student's t-test as appropriate; Figure within parentheses are percentages; **World Bank data team on July 2020

urban areas and more than 70% were multiparous (**Table 1**).

The cases and controls were similar in terms of the history of GDM, still birth and congenital malformation (**Table 2**).

TABLE 2 Past obstetric history of multigravida patients (n=60)

Characteristics	Case (n=28)	Control (n=32)	P*
History of gestatinal diabetes			
Present	02 (7.1)	0 (0.0)	0.214
Absent	26 (92.9)	32 (100.0)	
History of stillbirth / intrauterine death			
Present	02 (7.1)	01 (3.1)	0.594
Absent	26 (92.9)	32 (96.9)	
History of congenital malformation of the foetus			
Present	01 (3.6)	0 (0.0)	0.467
Absent	27 (96.4)	32 (100.0)	

*Fisher's Exact test was appropriate; Numbers in parentheses are percentages

The mean vitamin D levels of the cases and controls were 18.8 ng/ml and 22.1 ng/ml, respectively (*P*=0.025). There was a significant difference (*P*= 0.024) of vitamin D adequacy between cases and controls (**Table 3**).

TABLE 3 Vitamin D levels and categories in the cases and controls

Vitamin D (ng/ml)	Case (n=40)	Control (n=40)	P*
Deficient (≤ 20)	28 (70.0)	21 (52.5)	0.024[a]
Insufficient (21-29)	10 (25.0)	8 (20.0)	
Sufficient (≥ 30)	2 (5.0)	11 (27.5)	
Mean ± SD	18.82 ± 5.46	22.12 ± 7.31	0.025[b]

*Fisher's Exact test was or Student's t-test as appropriate; Numbers in parentheses are percentages;

There was a significantly negative but weak correlation (r= -0.32) between serum vitamin D level and 2 hours after 75 gm of glucose drink (**Figure I**). A similar negative correlation was observed for fasting glucose also (r= - 0.31).

TABLE 4 Odds ratio (95% confidence interval) of insufficient vitamin D level for having gestational diabetes mellitus

Vitamin D (ng/ml)	Case (n=40)	Control (n=40)	Odds Ratio (95% CI)
Insufficient/ deficient (<30)	38 (95.0)	29 (72.5)	7.2 (1.5-35.1)
Sufficient/ normal (≥30)	2 (5.0)	11 (27.5)	Reference category

Discussion

In this study, the mean (sd) age of the respondents was 28.75±5.21 years in cases and 28.45±4.64 years in control. The majority (87.5%) of the cases and four-fifths (80.0%) of the controls were urban dwellers, probably because this study was conducted in an urban tertiary level hospital in Dhaka. Regarding social status, the majority of respondents belong to a lower middle class group (cases: 72.5%, controls: 67.5%) which was similar to the study done by Ahmed et al.[9] These socially neglected populations have more pregnancy complications as they fail to seek proper antenatal care. In the present study, the majority (87.5%) of the participants were in their third trimester of pregnancy and mostly multigravida (cases: 70.0%, controls: 80.0%). Ali et al, in their study showed that the mean gestational age of the patients was 33.0±6.1 weeks and 63.9% patients were multigravida.[10] But another study conducted in North India showed that 84.3% of the

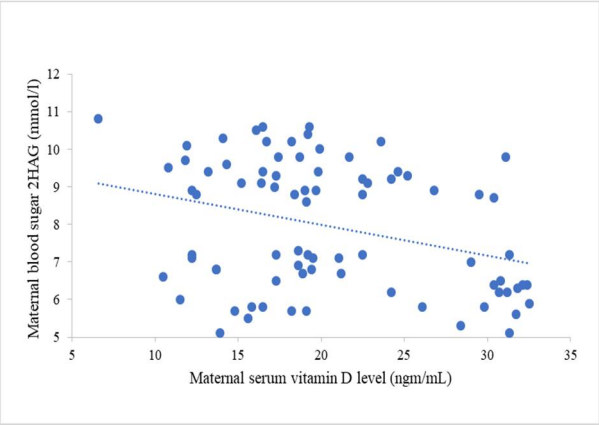

FIGURE I Scatterplot diagram showing a correlation between vitamin D level and maternal blood glucose 2HAG

GDM cases were primigravida and 61.8% of the control were multigravida.[11]

In another Egyptian study, a significant correlation was notice regarding the family history of DM where both the pregestational and gestational diabetic group compared with the control group.[12] In this study, the majority of respondent's vitamin D levels were deficient (≤ 20ng/ml) in both the case (70%) and control (52.5%) groups, whereas only 5.0% of the cases and 27.5% of the controls had vitamin D level ≥30ng/ml. Insufficient level (21-29ng/ml) was observed in 25.0% of cases compared to 20.0% controls. The mean serum vitamin D level among the cases was much lower (18.8±5.4ng/ml) than that of the controls (22.1±7.3ng/ml) which is statistically significant. The respondents with vitamin D ≤ 30 ng/ml had 7.21 times more chances of developing GDM than the control group. In Pearson's correlation analysis, vitamin D level was found negatively correlated with both the fasting blood sugar (FBS) (r= -0.310, P= 0.005) and blood sugar 2 hours after 75 gm glucose (2HAG) level (r= - 0.318, p= 0.004) which indicates that the maternal FBS and 2HAG levels tend to increase with the decline of serum vitamin D level. According to Ou et al, in Chinese pregnant women, vitamin D deficiency or insufficiency was significantly higher in the GDM group than in non-diabetic pregnant group.[14] Patients with vitamin D level <25 nmol/L had a 1.8-fold higher risk of developing GDM than those with higher vitamin D level.[14] A study done in Turkey showed the frequency of GDM was 9.38% where GDM patients have significantly lower vitamin D level in comparison to non GDM patients.[15]

Meta-analysis done by Lu et al revealed a greater risk of GDM (RR 1.45; 95%CI 1.15-1.83; p<0.001) in patients having vitamin D insufficiency.[11] It also showed that this association might differ depending on several factors like geographical variations, study design, sample size, method of measurement of vitamin D level, age of baseline and study quality.[16]

Significantly lower vitamin D level was detected in another Australian study done by Clifton-Bligh et al where separate analysis of four ethnic subgroups revealed no association between vitamin D level and GDM.[17]Another cross-sectional South Indian study done among 559 women at the gestational age of thirty weeks found no association between maternal vitamin D status and risk of GDM.[18] Another case control study done by Narain et al revealed that the prevalence of vitamin D deficiency was 86.25% where the mean serum vitamin D levels in the case and control group were 11.65 ng/ml and 14.4 ng/ml respectively but it was not statistically significant (*P*-value= 0.339).[19] Most of the studies with few exceptions revealed low levels of serum vitamin D level among the GDM patients. So, we can take some measures like proper food consumption, vitamin D supplementation and lifestyle modification to overcome vitamin D deficiency to prevent GDM and thereby improve the maternal and perinatal outcome.

Conclusion

This study attempted to find out association of vitamin D with GDM. In our study there was significant difference regarding the vitamin D level in between pregnant women with GDM group than non GDM group. Women with vitamin D less than adequate level have more chance of developing GDM than those who have adequate level. Vitamin D supplementation to improve the maternal well-being and perinatal outcomes in GDM women of our country is an easy and cheap treatment option. This may bring better health benefits for the pregnant women and their offspring.

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Author Contribution

Fl conceptualized the topic, reviewed literature, developed data collection tools, guided data analysis, interpreted results and wrote the manuscript. TRL designed the study, established methodology, monitor eddata collection, analyzed afand data analysis and revised the manuscript critically KN, TRD, NA, SSA and K revised the manuscript critically. All the authors have approved submission.

Conflict of Interest

The authors declare no conflict of interest.

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