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Research Article

**STUDY TO KNOW THE ASSOCIATION BETWEEN LOW
MATERNAL SERUM VITAMIN “D” LEVELS AND
GESTATIONAL DIABETES MELLITUS**¹Dr Omer Haseeb Khan, ²Dr Maham Zafar, ³Dr Anmol Nageen¹Lahore Medical and Dental College, Lahore²Nishtar Medical College, Multan³Islamabad Medical and Dental College, Islamabad

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Abstract:

Background: The deficiency of maternal vitamin D is more critical during pregnancy. Maternal vitamin D status has directly relation with gestational diabetes mellitus (GDM). The aim of this study is to determine the relationship between low maternal serum vitamin d levels and gestational diabetes mellitus.

Study Design: This is a cross-sectional study, conducted in the department of obstetrics and gynecology of Mayo Hospital Lahore for the duration of one year from January 2019 to January 2020.

Materials and Methods: 140 pregnant women were included in this study. Out of 140 subjects, 70 women already diagnosed with GDM were taken as cases and 70 normal pregnant women were taken as control. All the patients included were subjected to detailed history taking. Blood samples were taken from both cases and control and sent for Vitamin-D level, HbA1c, Fasting blood glucose and 2hrs postprandial glucose test.

Results: An attempt has been made to assess the association of maternal serum vitamin D with Gestational diabetes mellitus and also to see its relation with glycemic control in patients with GDM. Overall 71% women are vitamin D deficient in our study. The mean maternal serum vitamin D levels were 8.83 ± 5.77 ng/ml in Group A and 17.04 ± 8.67 ng/ml in group B. The difference was statistically significant reflecting that the mean serum vitamin D was decreased in women with GDM. (P value=0.001).

Conclusions: Low maternal serum vitamin D levels were associated with gestational diabetes mellitus. There is a statistically significant negative correlation between the glycemic control and vitamin D levels in serum in the whole study population.

Keywords: vitamin D levels, gestational diabetes mellitus, maternal serum.

Corresponding author:**Dr Omer Haseeb Khan,**

Lahore Medical and Dental College, Lahore

omerhaseebkhan@yahoo.com

QR code



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INTRODUCTION:

In our present lifestyle, standard of living and in turn dietary changes as well as patterns of disease have been changed. With increasing obesity, insulin resistance and better Screening protocols, GDM is increasingly being diagnosed in our women. Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy [1]. Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. The disease has important health implications for mother and child. Early diagnosis and treatment of GDM can reduce adverse pregnancy outcomes, including stillbirth, neonatal macrosomia, neonatal hypo-glycaemia, birth trauma and neonatal respiratory distress syndrome as well as decrease the risk of preeclampsia in the mother [2]. Vitamin D deficiency is closely associated with Gestational Diabetes Mellitus (GDM). Vitamin D induces insulin receptor expression through Vitamin D receptor (VDR), enhancing insulin dependent glucose transport. Vitamin D is also a potential immunosuppressant, which down regulates the expression of pro-inflammation markers, such as TNF- α and IL-2, among pregnant women with GDM [3]. In recent years, vitamin D deficiency has been increasingly recognized as one potential contributor [4]. While epidemiologic studies have shown a fairly consistent link between vitamin D deficiency and a higher risk of type 2 diabetes[5, 6], and obesity is strongly associated with both GDM [7, 8] and vitamin D deficiency [9, 10,], it remains unclear whether vitamin D deficiency contributes to a mother's risk of developing GDM. Compelling evidence suggests a role of vitamin D deficiency in the pathogenesis of insulin resistance and insulin secretion derangements [11]. The coexistence of insulin resistance and vitamin D deficiency has generated several hypotheses as worsening insulin resistance [12]. Immense interest persists in vitamin D and its potential effects on several pregnancy outcomes including fetal growth, hypertensive disorders and gestational diabetes mellitus (GDM) [13]. Two factors make vitamin D intriguing to perinatal investigators studying GDM. First, vitamin D has been shown to improve pancreatic exocrine function and insulin sensitivity in animal models. Second, vitamin D status, like most micronutrients, is easily modified by dietary supplementation [13].

OBJECTIVE OF THE STUDY

To determine the relation between low maternal serum vitamin D levels and gestational diabetes mellitus (GDM) and the relation between vitamin

D and the glycemic control in-patient with GDM assessed by HbA1c and blood glucose levels.

MATERIALS AND METHODS:

This study was a hospital-based case control an observational study conducted in Department of Obstetrics & Gynaecology, Mayo Hospital Lahore for the duration of one year from January 2019 to January 2020. The pregnant women, in the third trimester, attending the antenatal care clinic, were selected. The target age group was between 20-40 years. Exclusion Criteria are H/O type 1 or 2 diabetes mellitus antedating pregnancy, medical disorders (HTN, Cardiac diseases etc.) and medical complications related to pregnancy. 70 pregnant women in their 3rd trimester with established diagnosis of GDM as per DIPSI guidelines and randomly selected 70 pregnant women with normal blood sugar attending ANC was enrolled and taken as cases and control after written and informed consent. They were subjected to detailed history taking with special focus on maternal age, parity, gestational age at diagnosis of gestational diabetes, previous history or family history of diabetes, history of gestational diabetes in previous pregnancies. Data concerning insulin regimens, insulin types and doses were also noted. Complete general physical examination, systemic examination and obstetric examination. Body Mass Index (BMI) was calculated for all subjects and matched in cases and controls. Blood sample was collected from both cases and control and sent for laboratory investigations. Assessment of serum 25(OH) Vitamin D was done by using CLIA method. The Biochemistry Department SMS Medical College Jaipur carried out chemiluminescence immunoassay. CLIA is a quantitative immunoassay method used for the determination of total 25 (OH) D in serum or plasma on a fully automated platform. It is a highly sensitive technology in which a specific antibody to vitamin D is used for coating magnetic particles (solid phase) and vitamin D is linked to an isoluminol derivative. Result of both groups was compared to evaluate association in maternal plasma 25- Hydroxyl vitamin D level and GDM. Reference value of maternal plasma 25-Hydroxyvitamin-D level-Deficiency 30ng/ml. Glycosylated hemoglobin is a blood glucose control marker in diabetic patients. HbA1c results from post-translation changes in the hemoglobin molecule, and their levels correlate well with glycemic levels over the previous six to ten weeks. HbA1c was measured by chemiluminescence to assess the glycemic control. Data collected and statistical analysis was done.

Data Analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous

variables are presented as mean \pm SD, and categorical variables are presented as absolute numbers and percentage. Data were checked for normality before statistical analysis. Categorical variables were analyzed using either the chi square test or Fisher's exact test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

RESULTS:

140 women in their third trimester were enrolled in the study. 70 women with already diagnosed GDM were taken as cases and 70 normal pregnant women as controls. The mean age of cases and controls were 27.75 ± 3.85 and 25.25 ± 3.87 . It was not statistically significant. Majority of the women belonged to Hindu religion. GDM patients were mostly from urban area. Most of the women were housewives. In Group A, 81.4% women were literate and in Group B 60% women were literate. This wide gap in the study population may be because of increase awareness and better use of health care facilities amongst the literate. The upper middle class made the majority of the study population in group A and in group B majority i.e. 31.4% belonged to lower middle class. Past h/o

GDM is an important risk factor for GDM (P value=0.013). No correlation was found with family history of Diabetes mellitus (P= 0.301). Calcium intake and periconceptional multivitamin (P value = 0.275) intake had no association with GDM. In our study vitamin deficiency was seen in 71% of the study population out of 140 subjects. The mean level of Vitamin D is 8.83 ± 5.77 in GDM cases and in the controls the mean is 17.04 ± 8.67 . Thus low level of Vitamin D was seen in patients with GDM (P value= 0.001). A significant inverse correlation was found between the HbA1C levels and Vitamin D levels (correlation coefficient $r = -0.549$, P value less than 0.05 where the higher the Levels of Vitamin D, the lower the HbA1c levels indicating a good glycemic control in women with gestational diabetes. An inverse association was also found with the fasting blood sugar levels which was statistically significant (the correlation coefficient $r = -0.570$) As regards the Vitamin D levels, Table shows that they negatively correlated with the fasting blood glucose levels and the HbA1c levels, in the whole study population including both groups; women with GDM and controls. The P value in all these correlations were <0.05 .

Table 1: Clinical and biochemical demographic data of the studied groups Group-A

-	Group-A (n=70, cases)	Group-B (n=70, controls)	P-Value
Maternal age	27.75 ± 3.85	25.25 ± 3.87	0.99(NS)
Parity	1.79 ± 1.06	1.81 ± 2.95	0.665(NS)
H/O GDM	10%	0%	0.013(S)
Family h/o type 2DM	8.6%	4.3%	0.301(NS)
Calcium intake	64.3%	72.9%	0.275(NS)
Periconceptional multivitamin	27.1%	35.7%	0.275(NS)
Physical activity in the sun(>3hrs)	10%	30%	0.005(S)
Fasting blood sugar	93.18 ± 8.05	78.70 ± 4.54	-
HbA1c	6.62 ± 1.29	4.8 ± 0.28	-
Vitamin D	8.83 ± 5.77	17.04 ± 8.67	0.001(S)

DM: diabetes mellitus, GDM: gestational diabetes mellitus, NS: not significant, S: significant

DISCUSSION:

Vitamin D seems to have several extra skeletal functions including regulation of glucose metabolism through influencing insulin sensitivity, although the mechanisms are not fully understood. In our study we have found high prevalence of deficiency in overall study sample. This may be explained by poor sun exposure, poor dietary intake, and lack of physical activity. In our study we also tried to find a correlation between Vitamin D and Gestational diabetes mellitus in pregnant women in their third trimester already diagnosed to have GDM at previous ANC visits, and we included normal pregnant population as control. Vitamin D deficiency was the salient feature in

both groups. The mean age of group A was 27.75 ± 3.85 and for group B was 25.25 ± 3.87 . The majority of the GDM subjects came from urban population (81.4%). Upper middle class patients constituted the major part of the GDM population (40%) whereas, in the control group majority belonged to lower middle class (31.4%). There was no significant difference in distribution of study population according to religion. Maximum no. of the study population were literate (75%). Majority (82.14%) of the subjects were vegetarian (P-value is 0.010). Study population consisted mostly of Primigravida. Majority of the subjects were diagnosed at 26 weeks of gestation i.e. 44.3%. Past H/O GDM is an important risk factor for GDM. In

group A 10% had history of GDM (P value 0.013). Calcium and periconceptional multivitamin intake in both groups did not show statistical significance. Jain Madhu *et al.* [14] also had similar finding in their study. Majority of the study population were non-smokers. In group A 90% had low sun exposure (physical activity in the sun less than 3hrs) and in group B 70% had low sun exposure, (P value= 0.005). This paradox of majority of the study population having low sun exposure, in a tropical country like Pakistan in spite of abundant sunlight for most of the year, can be explained due to many prevalent social and cultural practices e.g. increased urbanization, poor outdoor activity, greater pollution that preclude exposure of women to sunlight. The mean HbA1c in group A is 6.62 ± 1.29 and in group B the mean is 4.8 ± 0.28 . Overall 71% Of the study population are vitamin D deficient. Sachan A *et al.*, reported a prevalence of 84.3% urban and 83.6% in rural area. The mean maternal serum vitamin D levels were 8.83 ± 5.77 ng/ml in Group A and 17.04 ± 8.67 ng/ml in group B. The difference was statistically significant reflecting that the mean serum vitamin D was decreased in women with GDM. (P value 0.001). Similarly zhang C *et al.* [15], and PleskaIová Anna *et al.* [18] also found similar association between Vitamin D levels and GDM. Poel *et al.* in a meta-analysis of four out of seven observational studies have reported a high incidence of Vitamin D deficiency (>50%, 25 (OH) > 50 nmol/L) in pregnant women with the risk of GDM with an Odds ratio of 1.61 [17]. There is a negative correlation between the Vitamin D levels and fasting blood sugar, higher levels of fasting blood sugar were found in women with lower Vitamin D levels ($r=-0.570$). Negative correlation also seen between the Vitamin D levels and HbA1c, thus indicating poor glycemic control, this inverse relation was found to be statistically significant ($r=-0.549$). Similar observation were made by El Lithy *et al.* [18] (correlation coefficient($r = -0.492$, P value 0.05) and Debnath arijit *et al.* (r value=0.571; Spearman correlation) [16]. Thus the low serum Vitamin D levels were associated with Gestational diabetes mellitus (GDM). So finally we concluded that the maternal serum Vitamin D level could be done as a routine investigation in pregnancy and Vitamin D deficiency should be treated to avoid risk of GDM. The strength of present study was its good sample size, meticulous data collection, analysis and interpretation of the results. However, there are limitations.

CONCLUSION:

Based on this study it is concluded that there is high prevalence of Vitamin D deficiency in our study population. Low serum Vitamin D levels were associated with Gestational diabetes mellitus (GDM). Maternal serum Vitamin D level should be

done as a routine investigation in pregnancy and Vitamin D deficiency should be treated to avoid risk of GDM.

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