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Vitamin D3 Levels in Gestational Diabetes Mellitus: A Tertiary Care Hospital Case Control Study in North India

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ABSTRACT
Gestational diabetes mellitus (GDM) is the development of either temporary during the pregnancy period only or may carry forward afterwards also. The clinical manifestations may range from undetectable diabetes to full blown hyperglycemia. Low levels of Vit D3 are linked to bacterial vagueness and prevalent across populations, increasing risks like stillbirth and HIV transmission in affected mothers. The present study was conducted on 120 women aged 18-35 years, of gestational age above 20 weeks visiting for antenatal care in the Department of Obstetrics and Gynecology dividing them into two groups of 60 each, group 1 comprising of subjects with diagnosed GDM and group 2 with pregnant women without any complication. The study compared key demographic and biochemical variables between cases and controls (n=60 each). Cases had significantly higher mean fasting blood sugar (155.11±36.66 vs. 95.16±19.08 mg/dL, P<0.001) and older mean age (28.15±4.56 vs. 26.16±4.14 years, P=0.01). Serum Vitamin D3 levels were comparable (P=0.69). The study concluded that levels of vitamin D3 remained comparable in the two groups i.e subjects with GDM and normal gestation.

INTRODUCTION

Gestational diabetes mellitus (GDM), or pregnancy-related glucose intolerance, is defined by the emergence or identification of diabetes during gestation. The condition has a range of clinical symptoms, from asymptomatic instances to severe hyperglycemia with potentially fatal outcomes[1]. The primary cause of gestational diabetes mellitus (GDM) is insulin resistance, a physiological adaptation during pregnancy that ensures sufficient glucose supply for fetal development. However, when pancreatic beta cells do not sufficiently compensate for this resistance through increasing insulin secretion and proliferation, gestational diabetes mellitus (GDM) ensues. The etiology of gestational diabetes mellitus (GDM) is multifaceted, involving both hereditary and non-genetic determinants. Genetic predisposition is evidenced by familial clustering and the discovery of potential genes associated with gestational diabetes mellitus (GDM). Nonetheless, the exact procedures are inadequately comprehended. Non-genetic variables, including advanced maternal age, obesity, inadequate dietary practices and sedentary lifestyles, are significantly correlated with heightened risk. Collectively, these elements establish a multifaceted interaction that predisposes specific individuals to manifest gestational diabetes mellitus during pregnancy[2-5]. Globally, gestational diabetes mellitus (GDM) is a considerable public health issue, with problems impacting 5-7% of pregnancies in high-income nations. In India, the estimated prevalence of gestational diabetes mellitus (GDM) is 1.3%, while recent statistics suggest an increasing frequency[1]. This trend highlights the increasing necessity for awareness and intervention. Gestational diabetes mellitus (GDM) presents risks to both the mother and fetus, including obstetric problems such as macrosomia, stillbirth, neonatal hypoglycemia and pre-eclampsia. Women with a history of gestational diabetes mellitus (GDM) face an elevated risk of acquiring type 2 diabetes, cardiovascular illnesses and recurrent GDM in future pregnancies over the long term[6-11]. Vitamin D has become a vital biomarker in pregnancy owing to its various physiological functions, including in immune system modulation, cytokine regulation and antibacterial peptide production. Notwithstanding its significance, vitamin D insufficiency is widespread among pregnant women globally. Research has associated insufficient vitamin D levels with several negative pregnancy outcomes, such as bacterial vaginosis during the first trimester and heightened chances of stillbirth and vertical transmission of HIV in impacted groups. These findings underscore the necessity to investigate the correlation between vitamin D and pregnancy-related disorders more thoroughly[12-15]. Recent data indicates that vitamin D insufficiency may have a role in the onset of gestational diabetes mellitus (GDM). Active vitamin D (1,25-dihydroxyvitamin D3) engages with its receptor on pancreatic beta cells, affecting their functionality and secretion ability. Vitamin D enhances insulin sensitivity by altering intracellular and extracellular calcium balance, which supports glucose transport and insulin receptor activation. Moreover, it promotes trans membrane calcium transport into the intra cellular matrix, guaranteeing sufficient calcium availability for insulin-dependent functions in sensitive tissues. These processes indicate that sustaining normal vitamin D levels during pregnancy may contribute to lowering the risk of gestational diabetes mellitus and enhancing maternal metabolic health[16,17]. Considering the increasing incidence of gestational diabetes mellitus (GDM) and its related complications, it is essential to investigate modifiable risk factors, including vitamin D deficiency. The primary objective of this research was to evaluate the vitamin D status of pregnant women attending this tertiary care facility and to ascertain any correlation between vitamin D levels and gestational diabetes mellitus.

MATERIALS AND METHODS

This case-control study was performed over one year at the Department of Biochemistry and the Department of Obstetrics and Gynecology at PGIMS, Rohtak, Haryana. The research focused on pregnant women visiting the outpatient department of Obstetrics and Gynecology who were diagnosed with gestational diabetes mellitus after 20 weeks of gestation. Ethical approval for the study was obtained from the Institutional Ethical Committee prior to its commencement. All participants were enrolled after a comprehensive explanation of the study and informed written agreement was secured from each individual. The confidentiality of all data gathered during the investigation was maintained consistently. Participants were chosen as per established inclusion and exclusion criteria. The inclusion criteria included pregnant women diagnosed with gestational diabetes mellitus (GDM), aged under 35 years and with a gestational age of 20 weeks or greater. Both vertex and non-vertex fetal presentations were evaluated and only low-risk pregnancies were incorporated to reduce confounding variables. Women with atypical placental presentations or other complications of pregnancy, including pregnancy-induced hypertension (PIH), anemia, pre-eclampsia, or multiple gestations, were excluded from the study. Furthermore, women with any further medical issues or those who declined to participate were excluded. A comprehensive history was obtained from each participant, encompassing demographic, medical and obstetric data. A comprehensive clinical examination was conducted to evaluate their overall health and the development of the pregnancy. Anthropometric measurements, including weight and height, were recorded and both routine and special

biochemical analyses were planned in the department of Obstetrics and Gynecology. Blood sample collection and processing were conducted under stringent aseptic conditions. A 4mL venous blood specimen was collected aseptically from each participant using a sterile red-capped vacuum tube. Following clotting of the blood, it was centrifuged at 2000 rpm for 10 minutes to isolate the serum. The serum was subsequently divided into two aliquots. The first part was utilized promptly for standard biochemical analyses. The second half was preserved at -20°C for the batch analysis of specific biochemical markers, including Vitamin D. The procedures conformed to established standards to ensure data consistency and reliability. The study was meticulously structured to reduce variability in sample management and processing. Ethical considerations were emphasized consistently and participant rights were safeguarded at all phases. Only individuals who granted consent were included and comprehensive documentation guaranteed that participants were thoroughly informed regarding the nature and objectives of the study. The computed sample size for the study was 59.59, which was rounded up to a minimum of 60 persons with GDM. Serum samples were analyzed for routine biochemical investigations using standard protocols on an automated analyzer to measure blood urea, serum creatinine, serum uric acid, serum calcium, serum AST, serum ALT, serum alkaline phosphates, serum protein, albumin, serum triglycerides, serum cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol and blood glucose. Special investigations involved the assessment of Vitamin D via the Chemiluminescence Immuno assay (CLIA) technology.

Statistical Analysis: Statistical analysis was conducted utilizing the Statistical Package for Social Sciences (SPSS) version 20.0. Laboratory test results were presented as mean±standard deviation (SD) and group comparisons were performed using the Student's t-test for continuous variables. The chi-square test was employed to assess the frequencies of abnormal results across groups. A 95% confidence interval (95% CI) was employed and a p-value of <0.05 was deemed statistically significant. The data were thoroughly assembled and evaluated using suitable statistical methods to ensure proper interpretation of results and a relevant conclusion.

RESULTS AND DISCUSSIONS

Table 1: Showing the Variables Under Study, P-Value <0.05 was Taken as Significant. Paired T-Test and ANOVA was Used. Pearson Correlation Coefficient Ranges from -1 to +1, Showing Positive or Negative Correlation

Mean value	Group1 (n=60)	Group2 (n=60)	P-value
Age (years)	28.15±4.56	26.16±4.14	0.01*
FBS(mg/dL)	155.11±36.66	95.16±19.08	<0.001**
S. Vit D3(ng/mL)	21.98±13.43	23.01±14.77	0.69
S. Vit D3-FBS correlation (Pearson correlation)	0.16	0.02	

The table shows the demographic and biochemical characteristics of participants in both the case and control groups, each consisting of 60 individuals. A comparison of the mean values for age, fasting blood sugar (FBS) and serum Vitamin D3 levels indicates notable differences between the two groups, emphasizing specific statistically significant results except for serum Vit. D3 levels. The mean age of participants in the case group was 28.15±4.56 years, marginally exceeding the average age of 26.16±4.14 years in the control group. The observed difference was statistically significant, indicated by a P-value of 0.01, implying that age may influence the gestational outcomes in terms of diabetes. Fasting blood sugar levels exhibited a significant disparity between the groups. The case group demonstrated a mean FBS level of 155.11±36.66mg/dL, which was significantly higher than the control group's level of 95.16±19.08 mg/dL. The observed difference was statistically significant, with a P-value of <0.001 (P<0.00). Serum Vitamin D3 levels were comparable between the two groups, with the case group exhibiting a mean value of 21.98±13.43 ng/mL and the control group a mean of 23.01±14.77 ng/mL. The difference was not statistically significant, with a P-value of 0.69. The correlation coefficient calculated for the two groups separately were 0.16 for group 1 and 0.02 for group 2, showing very weak positive correlation between the FBS and Vit. D3 levels. The data reveal significant variations in age and fasting blood sugar levels between cases and controls, whereas serum Vitamin D3 levels are comparable. The findings offer insights into potential factors related to the condition under investigation and underscore the necessity for additional research to examine these associations more thoroughly. Statistical significance was assessed using a threshold of P<0.05, while P<0.001 was regarded as highly significant.

Gestational diabetes mellitus (GDM) is a significant health concern that impacts both maternal and fetal outcomes[1]. Vitamin D, a fat-soluble vitamin crucial for calcium homeostasis, has been hypothesized to play a role in glucose metabolism through its effects on insulin secretion and sensitivity[16,17]. Advanced maternal age is a recognized risk factor for gestational diabetes mellitus (GDM). The probability of gestational diabetes mellitus (GDM) escalates with advancing maternal age, largely attributable to age-associated insulin resistance and diminished ß-cell functionality[18]. Multiple studies, such as those conducted by Hochler[19] and Paulo[20] have established a significant correlation between maternal age and the risk of gestational diabetes mellitus (GDM). Deng[21] found that maternal age over 35 years significantly increased the risk of gestational diabetes mellitus (GDM), likely attributable to cumulative metabolic changes and decreased glucose tolerance associated with aging. The present study found a statistically significant difference in the mean age of the two groups(p value=0.01)

corroborates the findings of Hedderson[22] indicating that age significantly influences the development of gestational diabetes mellitus (GDM), even when controlling for confounding variables such as body mass index (BMI) and ethnicity. Su[23] highlighted that maternal age is a crucial factor, independent of other variables, underscoring the necessity for focused screening and management in older pregnant populations. Vitamin D regulates pancreatic ß-cell function and insulin sensitivity. The vitamin D receptor (VDR) is present in pancreatic cells and its activation correlates with enhanced insulin secretion[24]. Additionally, vitamin D plays a role in mitigating systemic inflammation, which is a recognized factor in insulin resistance associated with gestational diabetes mellitus (GDM)[25]. Our study revealed that the levels of Vit D3 were lower but not statistically significant difference was noted between GDM cases and controls, despite the proposed mechanisms. This indicates that Vitamin D3 levels may not play a significant role in patients with gestational diabetes mellitus compared to those in normal gestation. Previous studies have indicated a significant association between vitamin D deficiency and gestational diabetes mellitus (GDM). Milajerdi[26] observed a higher prevalence of vitamin D deficiency in women with gestational diabetes mellitus (GDM). Zhang[27] performed a systematic review that identified a consistent association between low vitamin D levels and an elevated risk of gestational diabetes mellitus (GDM). Nonetheless, additional research, including that conducted by Flood-Nichols[28] and Aghajafari[29], did not identify a significant correlation, consistent with the findings of our study, (person correlation calculated 0.12). Serum levels of Vit-D were reported low and negatively correlated with the fasting glucose levels in GDM subjects compared to NGDM subjects in a study by Milan[30]. The absence of a notable correlation in our study may be ascribed to: (a) Regional Variations as Vit. D deficiency is prevalent in India, attributed to limited sun exposure and dietary insufficiency[31]. This prevalent deficiency may obscure potential distinctions between GDM cases and controls. (b) Although our sample size was sufficient for initial analysis, larger cohort studies may be necessary to identify subtle associations. (c) The confounding factors including body mass index (BMI), dietary habits and genetic predisposition, which were not considered in this study, may have impacted the results.

Consequences and Prospective Directions: Our study did not identify a significant association between vitamin D levels and gestational diabetes mellitus (GDM). However, the observed significance of age and fasting blood sugar levels is consistent with established risk factors for GDM. The HAPO study in Australia found a link between mid-gestational vitamin D levels and fasting glucose in normoglycemic pregnant women, while other studies have found no such association with the development of gestational diabetes mellitus (GDM)[32,33]. Subsequent investigations should concentrate on to investigate variations in vitamin D levels throughout gestation and their effects on glucose metabolism through planned longitudinal study and intervention trials like randomized controlled trials designed to evaluate the effects of vitamin D supplementation on the prevention or management of gestational diabetes mellitus (GDM). Assessing additional vitamin D-related biomarkers, including parathyroid hormone (PTH) and 25-hydroxyvitamin D, to determine their potential involvement in gestational diabetes mellitus (GDM) may also put better light on the complex interplay.

Public Health Relevance: Given the high prevalence of both GDM and vitamin D deficiency in India, this study underscores the need for comprehensive screening and management strategies. While vitamin D supplementation may not directly impact GDM risk, ensuring optimal levels could have other health benefits, including improved bone health and immune function[34,35].

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