Association of First Trimester Vitamin D Concentration with development of Gestational Diabetes Mellitus

Abstract

Pregnant Indian women have a high Vitamin D deficiency prevalence (approx. 90%). Mounting evidence suggests that Vitamin D may be essential for maintaining healthy glucose homeostasis.

Aims:

We aimed to determine the relationship between the GDM risks and maternal concentrations of Vitamin D in early pregnancy.

Settings and Design:

An observational study was performedon 114 healthy pregnant women in their first antenatal (<twelve weeks) visit during a regular antenatal check-up at the Department of Obstetrics and Gynaecology,Rajarajeshwari Medical College and Hospital, Bangalore, India.

Methods and Material:

Venous plasma total Vitamin D concentration was evaluated with the help of tandem LC-MS/MS (liquid chromatography-mass spectrophotometry). A screening OGCT (oral glucose challenge test) was performed during the first visit and OGCT was repeated in mid-pregnancy between (24-28 weeks). Applying DIPSI criteria, gestational diabetes mellitus was identified and confirmed.

Results:

Of 114 women, 54(47.3%) were obese,25(21.9%) were overweight, 19(16.6%) were normal weight, and 16(14%) were underweight. A statistically considerable correlation was seen between Vitamin D status and OGCT ($\varkappa2$= 57/07, p=0.01). The mean OGCT levels were higher in Vitamin D deficiency patients, which showed a statistically significant difference among the group (p=0.001). No statistically considerable correlation was seen between OGCT and BMI ($\varkappa2$= 10.85, p=0.093).

Conclusions:

Increased GDM risk might be linked to low plasma total Vitamin D concentrations in early pregnancy.

Key-words: Vitamin D, Early pregnancy, Oral Glucose challenge Test, Gestational diabetes mellitus **.** Key Messages:Evaluation of the Vitamin D status of every pregnant woman at their first ANC visit is of utmost importance .

Introduction:

Gestational diabetes mellitus (GDM) is an early glucose intolerance marker that occurs in pregnancy. With respect to the fetal origins of adult disorders, infants of GDM mothers have higher diabetic and obesity risks in later life than their siblings who were not exposed to it.[1] The development of Gestational diabetes mellitus in second trimester has been linked to maternal serum Vitamin D concentrations in the first trimester in several investigations, whether prospective, observational, or nested case-control designs.[2-4] Due to the high Vitamin D deficiency prevalence (70 to 100%) in developing countries, particularly in pregnant women from India,[5,6]its crucial to assess the correlation between gestational diabetes mellitus with severe deficiency of Vitamin D. Thus, to investigate the association between first-trimester levels of Vitamin D and status of GDM in pregnancy, a hospital-based observational research study was carried out with healthy pregnant women.

Subjects and Methods:

This hospital-based observational research was carried out in the Department of Obstetrics and Gynaecology, Rajarajeshwari Medical College and Hospital in Bangalore, India. The study included women who were pregnant between the ages of 20 and 40 and who registered for antenatal screening during their 1st trimester between January 2021 and May 2022.

Exclusion criteria :

- Women with past historyofGDM
- Family history of Type II or Type I diabetes mellitus,
- Past history of type II diabetes mellitus
- Chronic hypertension,
- Abnormal liver function tests
- Metabolic bone disease.

The study participants were chosen using a suitable sampling technique. At enrolment, venous blood samples from 114 individuals in the first antenatal phase (less than 12 weeks) was taken. The Oral Glucose Challenge Test (OGCT) was done on all patients at enrolment as a screening test for gestational diabetes mellitus.OGCT was repeated during 24-28 weeks,utilizingDiabetes in Pregnancy Study Group India (DIPSI) criteria, which highly suggest 75g of oral glucose regardless of the last meal, and after two hours, levels of venous blood glucose wereanalyzed. GDM can be diagnosed if the result is greater than 140 mg/dl.[7]. At the time of recruitment, a standardized questionnaire was used to gather socio-demographic data on the participants, including their obstetric history, age, family structure, as well as SES (socio-economic status). The gestational age (measured in weeks) was determined from the last menstrual cycle day and verified using ultrasonographic measurements. Each antenatal appointment included the recording of the mother's weight to the closest 100 g using a digital weighing scale. A stadiometer was used to measure height to the nearest 0.1 centimetres. Mothers' BMI (body mass index) was determined by dividing their weight in kilograms by their height in metres squared (kg/m^2). A trained phlebotomist collected venous whole blood samples and placed them in EDTA (ethylenediaminetetraacetic acid) and plain vacutainers. Liquid chromatography-mass spectrometry was used to quantify concentrations of Vitamin Din maternal plasma samples at enrollment. Pregnant women with Vitamin D levels between 30-100ng/ml were labelled as normal , those with Vitamin D levels between 10-29ng/ml were labeled as Insufficiency of Vitamin D, those below 10 ng/ml as Vitamin D Deficiency.

The predesigned excel spreadsheet was filled out using the data that had been gathered. Windows version 20.0 of the SPSS application was used to conduct the statistical analysis. The proportion was compared between the groups using the Chi-Square test, and the mean was compared using the ANOVA test. A p-value of <0.05 was considered statistically significant.

Results:

Out of a hundred and fourteen patients, thirty-six had a deficiency of Vitamin D, thirty-seven had insufficient Vitamin D, and forty-one had sufficient Vitamin D. More than half of the patients- 59(51.75%) hada deficiency of Vitamin D aged from 19-25 yrs. The status of Vitamin D and age groups were statistically considerably correlated (Chi-square testϰ2= 10.02, p=0.04). (Table 1)

Among 114 patients studied, 54(47.3%) were obese, 19(16.6%) were normal weight, 25(21.9%) were overweight, and 16(14%) were underweight. There was a statistically significant association between BMI and Vitamin D status (ϰ2=18.34, p=0.005). (Table 2)

Among 114 (100%) patients, 86(75.4%) patients were non-GDM, 16(14%) patients had Gestational glucose intolerance, 12(10.5%) were GDM, and none were overt-Diabetes. (Table 3)

Out of 36 patients who were Vitamin D deficient, 10(27.7%) were non-GDM, 14(38%) had gestational glucose intolerance, and 12(33%) patients had GDM. There was a statistically significant association between OGCT and Vitamin D status (χ^2= 57/07, p=0.01). (Table 4)

The mean OGCT levels were higher in Vitamin D deficiency patients- 123.38 ± 15.354. Three (3) patients with Vitamin D sufficiency had normal OGCT values, followed by patients with Vit D sufficiency – 116 ± 12.767. ANOVA test showed a statistically significant difference among the group (p=0.001). (Table 5)

Twelve patients who had GDM were obese, 15 (93.8%) patients who had gestational glucose intolerance were obese, and 56 (65.1%) patients who were obese were non-GDM. There was no statistically significant association between BMI and OGCT (χ^2= 10.85, p=0.093). (Table 6)

Discussion:

Obstetric complications like GDM put the health of the mother as well as the infant at serious risk. There is no agreement on the association between GDM, and Vitamin D. First-trimester antenatal women were the subjects of this investigation, which was carried out at the Rajarajeswari Medical College and Hospital's Department of Obstetrics and Gynaecology. In this research, which involved 114 pregnant women, the association between GDM and serum Vitamin D levels during their 1st trimester of pregnancy was examined. In our investigation, thirty-seven patients had concentrations of plasma Vitamin D that would be classified as "insufficient," while roughly thirty-six patients had concentrations that would be termed "deficient". In our research study, of 114 (100%) patients, eighty-six (75.4%) patients were non-GDM, and 12 (10.5%) were GDM. Among 74 patients who were deficient in Vitamin D, 48 (64.9%) were non-GDM, and 12 (16.2%) patients suffered from gestational diabetes mellitus and were seen to have a statistically considerable correlation between Vitamin D status as well as OGCT (χ^2= 13.26, p=0.01)

Domenech *et al*. findings also showed that pregnant women (55.5%) had a high prevalence of Vitamin D deficiency.[8] This result is in line with previously published findings. In the research carried out by Dwarakanath P *et al*., around 50% of the GDM-diagnosed women had concentrations of Vitamin D below 30 nmol/L, and around 81.5% of the women with plasma Vitamin D concentrations were classed as "insufficient."[9]

According to Iqbal *et al*., 80.6% of the women had classified 'insufficient' plasma Vitamin D concentrations.[10] Yue and Ying discovered that 48.1% of 8468 pregnant women had Vitamin D deficiency, 40% had insufficiency of Vitamin D, and 11.9 % had sufficient Vit D.[11] In our research, the majority of Vitamin D deficient patients, i.e., 39 (52.7%) were between the ages 19- 25 yrs. Several aspects, including primipara mothers over the age of thirty, women with maternal obesity, DM (diabetes mellitus), family history, glycosuria, as well as macrosomia history, have been linked to a higher GDM risk. In our research study, nearly 82 (71.9%) patients were multigravida. Dwarknath *et al*. found that 43.1% of the women were multiparous and 56.9% were nulliparous, and Iqbal *et al*. found 46.2% were multiparous and about 53.7% were nulliparous.[10,11] Primigravida accounted for 50.3percent (95%CI = 47.1–53.6), two pregnancies for 37.5% (95%CI = 34.3–40.7), and 3 or more pregnancies for 12.2% (95%CI = 10.2–14.5) of the sample was found in Domenech *et al*. study.[8] In the current research study, out of 82 (71.9%), 53 patients had VDD, and 26 patients were Vitamin D insufficient. About 59 (51.8%) patients had 1 child,and 86 (75.4%) patients had no abortions, which is a statistically significant association between abortions and Vitamin D status (insufficiency +deficiency) ($\varkappa 2$= 15.37, p=0.018).

Among 114 patients studied, 83(72.8%) were obese, 16(14%) were normal weight, 13(11.4%) were overweight, and 2(1.8%) were underweight. Most of the obese had Vitamin D deficiency- 60(81%) and was statistically significant association was seen between BMI and Vitamin D status ($\varkappa 2$=26.51, p=0.001). In Domenech *et al*. study, they observed that 115 (13%) of the patients were obese and 234 (26%) were overweight, and 532 (60.4%) were in normal BMI.[8] Dwaraknath *et al*. observed that 5(1.3%) of pregnant women were obese, 55 (14%) were overweight, 240 (61.2%) were in normal BMI, and 90 (23%) were underweight.[9] In the study of Iqbal, all the patients (290/100%) were overweight. In contrast to these studies, our study found most of the patients were obese. As per the observation, most of the Vitamin DDeficiency group patients (60/81.1%) and the Vitamin D insufficiency group (22/59.5%) were obese.

In our research study, of 114 (100%) patients, About 12 patients who had GDM were obese, 15(93.8%) patients who had gestational glucose intolerance were obese, and 56(65.1%) patients who were obese were non-GDM. In India, the GDM prevalence has been estimated to range from 3.8 – 21%, with higher rates in urban versus rural populations.[12-14] In our investigation, GDM prevalence (10.5%) was comparable to that of the Spanish pregnant women's populace. Domenech also found that roughly 1 in 10 pregnancies receives this diagnosis, which is a relevant health problem. In this research, we discovered that obese patients and pregnant women having GDM had higher levels of Vitamin D deficiency. Our study results matched with the study results of Domenech *et al*. discovered that Gestational diabetes mellitus pregnant women had obesity as well as higher levels of Vitamin D deficiency.[8]

Our study results showed that low concentrations of maternal plasma Vitamin D in early pregnancy are associated with a significant GDM risk and are consistent with 3 separate meta-analyses of published studies.[15,16]Around 40 to 60% increased GDMrisk in women with a deficiency of Vitamin D in the second trimester of pregnancy[16-18] has been demonstrated previously. In a study of 2,643 pregnant women, Roth *et al*. discovered that Vitamin D might play an important role in lowering the GDM risk (RR: 0.61, 95% CI 0.34-0.83).[19] Clifton-Bligh *et al*. conducted a cross-sectional research study at mid-pregnancy (24 to 28 gestation weeks) and found that a low Vitamin D status was a factor of risk for poor control of glucose.[18] According to Aghajafari *et al*. and Wei *et al*., women with a deficiency of Vitamin D have a 60% higherGDM risk.[16,17] Another research by Roth *et al*. found that Vitamin D can help reduce GDM risk.[19] Another study by Clifton Bligh *et al*. found that poor glucose control is associated with low levels of Vitamin D.[18]

In the Chinese populace, the association between deficiency of Vitamin D and Body Mass Index, as well as the possible impact of Body Mass Index, has been investigated. An association has been outlined, being stronger in the obese as well as overweight groups.[20] The relation between GDM and deficiency of Vitamin D allows us to target a specific population for intervention. We suggest further longitudinal studies to establish any relation of causality. This might contribute to intervention with supplementation of Vitamin D and a possible impact on the incidence of GDM, possibly preventing future ailments like metabolic syndrome and diabetes mellitus. Because of the regional nature of the research, a few drawbacks must be acknowledged; our findings may not be generalizable. Additional studies are necessary to corroborate our findings in other locations around the world.

There are several proposed mechanisms for the link among the low concentrations of Vitamin D and GDM risk. Vitamin D is assumed to modulate pancreatic β-cell function and secretion by binding to its circulating active Vitamin D form with β-cell Vitamin D receptors and regulating the balance between intracellular as well as extracellular β-cell calcium pools.[21] It's also been postulated that Vitamin D can promote insulin sensitivity by stimulating insulin receptor expression as well as improving insulin responsiveness for transporting glucose. Low levels of Vitamin D may result in insufficient intracellular cytosolic calcium, which is considered necessary in regulating glucose as well as for insulin-mediated intracellular processes because Vitamin D is also known for regulating extracellular calcium.

Several aspects may confound the association between early pregnancy status of Vitamin D as well as gestational diabetes mellitus. One such aspect is body weight. In our research, maternal deficiency of Vitamin D in early pregnancy was found to be considerably related to a higher GDM risk in South Indian pregnant women. The population in India is variable and diverse, and the current investigation of women might not be representative of the entire population. The assessment of the maternal status of Vitamin D in the first trimester of pregnancy as a surrogate of the pre-pregnancy state was the study's strength.

Conclusion:

A significant result of this research is the link between maternal deficiency of Vitamin D and a greater gestational diabetes mellitus risk in early pregnancy among pregnant women.This relationship suggests that 25(OH)D might play a potential role in the development of Gestational diabetes mellitus. We highly suggest that every pregnant woman should get the status of Vitamin D checked during her 1st ANC visit, particularly if there is a family history or history of GDM or DM. Clinicians must pay closer attention to the deficiency of Vitamin D in pregnant women and strengthen pregnancy supervision, which seems to have crucial clinical consequences for lowering GDM as well as preventing adverse outcomes during pregnancy.

Contribution Details :

	Contributor 1	Contributor 2
Concepts	YES	YES
Design	YES	YES
Definition of intellectual content	YES	YES
Literature search	YES	YES
Clinical studies	YES	YES
Experimental studies	YES	YES
Data acquisition	YES	YES
Data analysis	YES	YES
Statistical analysis	YES	YES
Manuscript preparation	YES	YES
Manuscript editing	YES	YES
Manuscript review	YES	YES
Guarantor	YES	YES

EthicalApprroval

All study procedures were authorized by the Rajarajeswari Medical College and Hospital's Institutional Ethical Review Board, and each respondent gave their written, signed agreement prior to enrolment.

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Table 1: Percentage of women based on age groups and Vitamin D status

Age groups		Vitamin D status			Total
		Deficiency	Insufficiency	Sufficiency	
19 to 25 yrs	Count	16	19	24	59
	%	44.4%	51.35%	58.5%	51.75%
26 to 30 yrs	Count	12	16	16	44
	%	33.3%	43.2%	39%	38.5%
> 30 yrs	Count	8	2	1	11
	%	22.2%	5.4%	2.4%	9.6%
Total	Count	36	37	41	114
	%	100.0%	100.0%	100.0%	100.0%
Chi-square value- 10.02					
p-value- 0.04*					

Table 2: BMI and Vitamin D status among patients

BMI		Vitamin D status			Total
		Deficiency	Insufficiency	Sufficiency	
Normal (18.5-22.9)	Count	4	7	8	19
	%	11.1%	18.9%	19.5%	16.6%
Overweight (23-24.9)	Count	4	7	14	25
	%	11.1%	18.9%	34.1%	21.9%
Obese (>25)	Count	22	22	10	54
	%	61.1%	59.45%	24.3%	47.3%
Underweight (<18.5)	Count	6	1	9	16
	%	16.6%	2.7%	21.9%	14%
Total	Count	36	37	41	114
	%	100.0%	100.0%	100.0%	100.0%
Chi-square value- 18.34					
p-value- 0.005*					

*Significant

Table 3: Percentage of women across OGCT

OGCT	Frequency	Percent
Non-GDM (<119)	86	75.4
Gestational glucose intolerance (120 to 139)	16	14.0
GDM (140-199)	12	10.5
Overt Diabetes (≥ 200)	0	0
Total	114	100.0

Table 4: Percentage of women with OGCT across Vitamin D status

OGCT		Vitamin D status		
		Deficiency	Insufficiency	Sufficiency
GDM (>140mg/dl)	Count	12	0	0
	%	33%	0	0
Gestational glucose intolerance (120-139mg/dl)	Count	14	2	0
	%	38%	5.4%	0
Non-GDM (<119mg/dl)	Count	10	35	41
	%	27.7%	94.6%	100%
Total	Count	36	37	41
	%	100.0%	100.0%	100.0%
Chi-square value- 57.07				
p-value- 0.001*				

*Significant

Table 5: Comparison of the mean OGCT based on Vitamin D status using ANOVA

Vitamin D status	N	Minimum	Maximum	Mean	SD	p value
Deficiency	36	98	156	123.38	15.354	0.001*
Insufficiency	37	96	136	110.14	9.253	
Sufficiency	41	102	127	116.00	12.767	

*Significant

Table 6: Association of BMI and OGCT

BMI		OGCT		
		GDM	Gestational glucose intolerance	Non-GDM
Underweight (<18.5)	Count	0	0	2
	%	0.0%	0.0%	2.3%
Normal (18.5-22.9)	Count	0	1	15
	%	0.0%	6.3%	17.4%
Overweight (23-24.9)	Count	0	0	13
	%	0.0%	0.0%	15.1%
Obese (>25)	Count	12	15	56
	%	100.0%	93.8%	65.1%
Total	Count	12	16	86
	%	100.0%	100.0%	100.0%
Chi-square value- 10.85				
p value- 0.093				