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Original Research Article

Estimation of maternal serum vitamin D levels and its correlation with gestational diabetes mellitus

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ABSTRACT

Background: Several studies in the past two decades have proved beyond doubt that there is a high prevalence of hypovitaminosis D worldwide including India which has almost taken the shape of a pandemic. The study aims to determine the prevalence of hypovitaminosis D in the pregnant population of Delhi and its correlation with gestational diabetes mellitus.

Methods: This prospective cross sectional observational study was conducted at the Department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research (PGIMER), Dr R.M.L Hospital, New Delhi over a period of 1 year and 4 months. Four hundred term patients were enrolled randomly from amongst the patients admitted in labor room or antenatal ward at PGIMER, Dr. Ram Manohar Lohia Hospital who fulfilled the inclusion and exclusion criteria. 3-4ml of fasting blood samples were collected of all the enrolled women and were analysed for total serum calcium levels and serum vitamin D levels. History of presence of gestational diabetes mellitus was noted along with any treatment history. The 25(OH)D levels for each subject was recorded and correlation of vitamin D levels with gestational diabetes mellitus was analysed. Statistical analysis was done using ANOVA/ Kruska Wallis test and Chi-Square test/ Fisher's exact test. A p value of <0.05 was considered statistically significant.

Results: The overall prevalence of vitamin D deficiency in the present study was 86.25%. The overall mean serum vitamin D level was 14.06±9.43 ng/ml. Thirty five out of 37 GDM patients had hypovitaminosis D i.e. 94.59%. The prevalence of hypovitaminosis D among non-GDM population was 85.40%. The association between GDM and Vitamin D deficiency was statistically non-significant in the present study with p value=0.186.

Conclusions: There is a very high prevalence of hypovitaminosis D in pregnant females attending present institute i.e. 86.25%. Although 94.59 % of Gestational Diabetes Mellitus patients had vitamin D deficiency, there is no statistically significant association between Gestational diabetes mellitus and serum vitamin D levels.

Keywords: Gestational diabetes mellitus, Hypovitaminosis D, Vitamin D deficiency

INTRODUCTION

Vitamin D is a fat-soluble vitamin having functions related to calcium metabolism and bone health. Vitamin D can be synthesized in the skin through exposure to sunlight, which remains the major source. Vitamin D deficiency is unexpected in a tropical country like India

where there is abundant overhead sun for most or all of the year. The burden of vitamin D deficiency was found to be alarmingly high in pregnant women with serum levels <15 ng/ml recorded in 66.7% population in a study done in Lucknow.¹ However extrapolation of one data to any other population is elusive as the vitamin D status in the body remains influenced by skin colour, latitude,

season, diet as well as life style and cultural practices which determine the amount of sun exposure.

There is little information on the ideal vitamin D regimen to prevent and treat vitamin D insufficiency. The existing guidelines suggest the RDA of vitamin D as 600 IU/day during pregnancy. Newer studies have found doses of even up to 4000 IU/ day to be safe and more efficacious.² Currently there are no separate cut off levels of vitamin D insufficiency and deficiency in pregnancy. The existing cut off levels might be erroneous for pregnant and lactating females. This warrants the need for further studies for setting appropriate threshold values for initiating vitamin D therapy during pregnancy.

It has been estimated that the total prevalence of GDM is almost 15-20%.³ In vitro and animal studies have also suggested that vitamin D has important roles in glucose and insulin metabolism.⁴⁻⁶ There are evidences which suggest that vitamin D improves the insulin sensitivity by enhancing insulin responsiveness to glucose transport.⁶

Several Indian studies have shown high incidence of vitamin D deficiency in India despite plenty of sunshine in most parts of India. Current study attempts to find the status of vitamin D deficiency in pregnant women attending present hospital and to determine whether this deficiency is also associated with higher incidence of gestational diabetes mellitus.

METHODS

This prospective cross sectional observational study was conducted at the Department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research (PGIMER), Dr R.M.L Hospital, New Delhi over a period of 1 year and 4 months from November 2015 to March 2017.

This study was approved by the institutional ethics and research review board. Four hundred patients were enrolled randomly from amongst the patients admitted in labor room or antenatal ward at PGIMER, Dr. Ram Manohar Lohia Hospital who fulfil the inclusion and exclusion criteria.

Inclusion criteria

All term (37 weeks-42 weeks) singleton pregnancies booked in the Dr. RML Hospital antenatal clinic within the study period.

Exclusion criteria

- Patients with history of recent intake (i.e. within one year) of therapeutic doses of vitamin D.
- With known hypertension, renal disorders and Diabetes mellitus.
- Untreated and uncontrolled thyroid disorder.

- Detailed history followed by general physical and systemic examination was done.

Gestational diabetes mellitus was defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy; diagnosed by 1 or more abnormal values in 75 gm glucose tolerance test. History of presence of gestational diabetes mellitus was noted along with any treatment history.

3-4ml of fasting blood samples were collected of all the enrolled women by venipuncture in a plain vacutainer and kept at room temperature for 30-60 minutes. It was then transported to laboratory and serum was separated by centrifugation at 3000 rpm for 10 minutes and transferred to Eppendorf tubes. Serum was analysed for total serum calcium levels by Arsenazo colorimetric method on fully automated clinical chemistry analyser. Serum were stored -20degree centigrade for batch analysis of serum 25(OH) vitamin D. Samples were then analysed for serum vitamin D levels by chemiluminescence immunoassay method on ECiQ vitros from Johnson's and Johnson's.

Serum calcium levels between 8.5 and 10.5mg/dl was considered normal. The 25(OH)D levels for each subject was recorded. Correlation of vitamin D levels with gestational diabetes mellitus was analysed.

As per the recommendation of Institute of Medicine classification of 25(OH) vitamin D levels were taken as follows:

- <20ng/ml: deficiency
- 20-<30 ng/ml: insufficiency
- 30-100 ng/ml: sufficiency
- >100 ng/ml: potential toxicity.

RESULTS

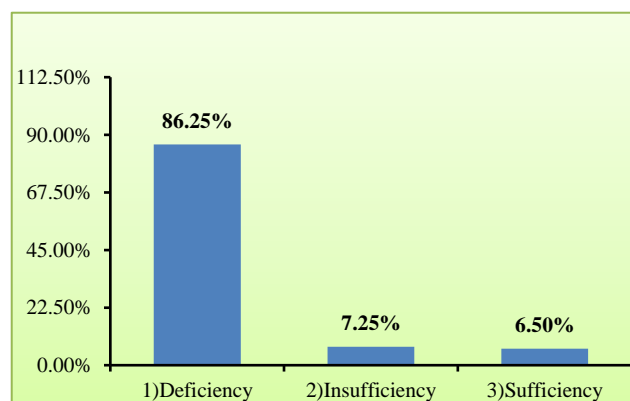


Figure 1: Vitamin D levels distribution in the study population.

The overall prevalence of vitamin D deficiency in the present study was 86.25%.

Another 7.25% were vitamin D insufficient and only 6.5% had sufficient vitamin D levels (Figure 1).

No patient had toxic levels of vitamin D. The overall mean serum vitamin D level was 14.06 ± 9.43 ng/ml.

The mean serum vitamin D levels in the control (uncomplicated group) and GDM was 14.4 ng/ml and 11.65 ng/ml respectively (Figure 2).

Thus, it was found that the mean vitamin D levels in the GDM group was lower than the uncomplicated group.

However, this association was not statistically significant (p-value=0.339).

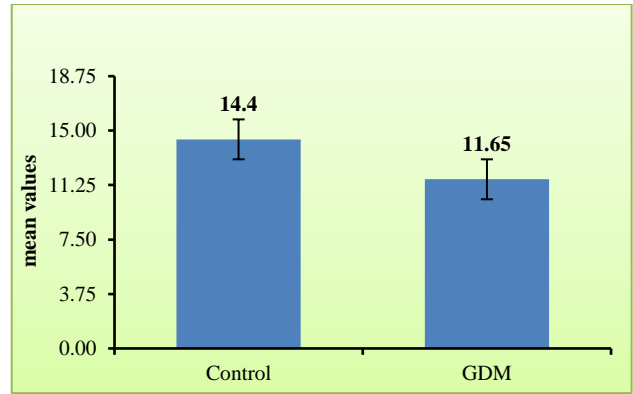


Figure 2: Bar graph for mean serum vitamin D levels in control and GDM group.

Table 1: Correlation between serum calcium and serum vitamin D level.

Serum calcium (mg/dl)	S. Vit D levels distribution			Total	P-value
	Deficiency	Insufficiency	Sufficiency		
<8.5	48 (92.31%)	3 (5.77%)	1 (1.92%)	52 (100.00%)	0.390
8.5-9.5	180 (85.71%)	18 (8.57%)	12 (5.71%)	210 (100.00%)	
9.5-10.5	105 (84.68%)	8 (6.45%)	11 (8.87%)	124 (100.00%)	
>10.5	12 (85.71%)	0 (0.00%)	2 (14.29%)	14 (100.00%)	
Total	345 (86.25%)	29 (7.25%)	26 (6.50%)	400 (100.00%)	

The mean serum calcium level in the present study was within normal limits i.e. 9.27 ± 0.77 mg/dl. Out of 345 vitamin D deficient patients, only 48 had calcium deficiency i.e. 13.9% as compared 3.8% of the vitamin D sufficient group. However, this was not significant with a p value=0.227. Out of 345, 297 i.e. 86.08% of vitamin D deficient patients had normal serum calcium levels. The relation between serum calcium and serum vitamin D levels was not statistically significant (p value=0.390) (Table 1). The mean calcium levels in the sufficient group was slightly higher than the deficient and insufficient group (Figure 3).

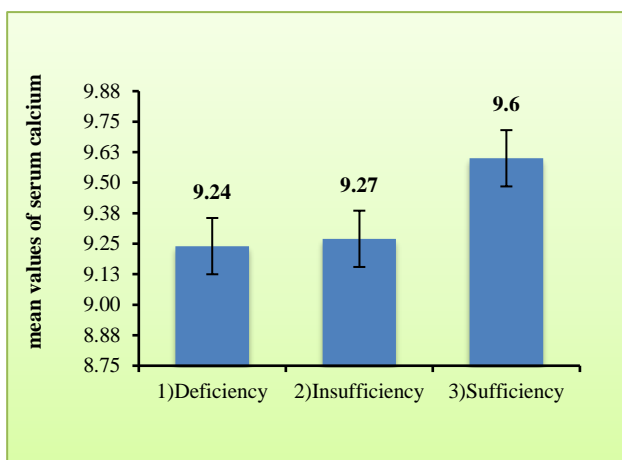


Figure 3: Correlation of mean serum calcium with vitamin D levels.

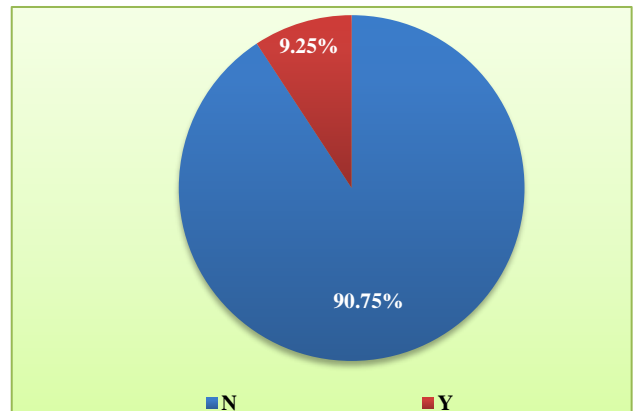


Figure 4: Incidence of GDM among study population.

Out of 400 participants, 37 had GDM (9.25%) (Figure 4). The prevalence of hypovitaminosis D amongst the GDM patients was 94.59%.

The prevalence of hypovitaminosis D among non-GDM population was 85.40%.

In the present study the incidence of GDM was 10.14% and 7.69% in the patients with and without hypovitaminosis D respectively (Figure 5).

However, the association between GDM and Vitamin D deficiency was statistically non-significant in the present study with p value=0.186.

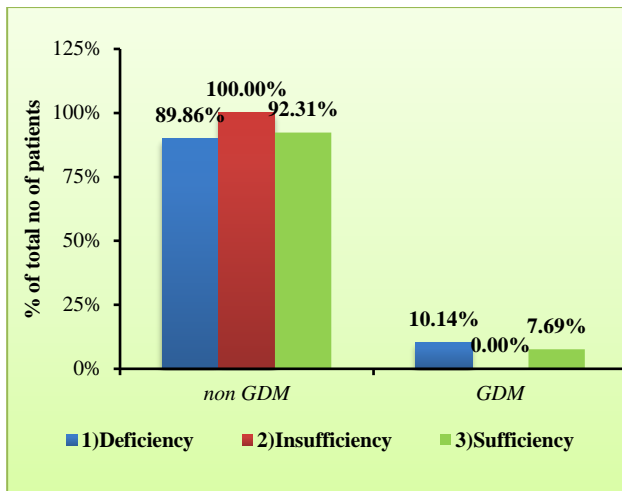


Figure 5: Correlation between GDM and vitamin D deficiency.

DISCUSSION

The overall prevalence of vitamin D deficiency in the present study was 86.25%. This was despite the fact that 100% patients had taken 400 IU vitamin D supplements per day during second and third trimester. This was similar to results obtained by Kazemi et al who also reported 86% incidence of vitamin D deficiency and by Sachan et al.^{1,7}

Another 7.25% were vitamin D insufficient and only 6.5% had sufficient vitamin D levels. The mean serum vitamin D level was 14.06 ± 9.43 .

The mean serum vitamin D levels in the control (uncomplicated group) and GDM was 14.4 ng/ml and 11.65 ng/ml respectively. Thus, it was found that the mean vitamin D levels in the GDM group was lower than the uncomplicated group. However, this association was not statistically significant (p value= 0.339).

It can be hypothesised that the high prevalence of hypovitaminosis D in the pregnant females may be secondary to the hemodilution or other physiological changes of pregnancy. Thus, similar to other biochemical parameters, separate cut off levels for vitamin D levels might be needed to diagnose hypovitaminosis D in pregnancy. Further research needs to be undertaken to strengthen or reject this hypothesis.

The mean serum calcium level in the present study was 9.27 ± 0.77 mg/dl which lies within the normal range. Out of 400, 52 patients (13%) had serum calcium below 8.5 mg/dl. The incidence of low serum calcium in vitamin D sufficient patients was 3.8% as compared to 13.9% in vitamin D deficient patients.

However, the relation between serum calcium and serum vitamin D levels was not statistically significant (p value=0.390).

Out of 400 participants, 37 had GDM (9.25%). Except 2 all the GDM patients had hypovitaminosis D i.e. 94.59%. But they constituted only 10.14% of vitamin D deficient group. This can be attributed to the overall high prevalence of vitamin D deficiency in the general population in this study. The prevalence of hypovitaminosis D among non-GDM population was 85.40%. Although the association between vitamin D levels and GDM was not found to be statistically significant, it does point towards increased prevalence of vitamin D deficiency amongst GDM group.

Similar results were obtained by Farrant et al.⁸ He reported 7% incidence of GDM in women with or without hypovitaminosis D and suggested that although vitamin D insufficiency is common in Indian mothers it is not associated with gestational diabetes. In the present study the incidence was 10.14% and 7.69% in the patients with and without hypovitaminosis D respectively. Likewise, Baker et al found no association between 25(OH)D level and the odds of GDM.⁹ In addition, Makgoba and colleagues in their case control study reported no association between first trimester blood samples and subsequent development of GDM.¹⁰

In contrast Kumari et al reported a significantly lower mean vitamin D level in GDM women 12.62 ± 6.69 ng/ml as compared to controls 24.25 ± 14.44 ng/ml (median= 18.2 ng/ml) (P<0.05).¹¹ Similarly Mojibian et al found that maternal 25(OH)D concentration at 24-28 weeks of gestation were significantly lower in women with GDM.¹² In addition to this, Aghajafari et al in their meta-analysis of 10 studies concluded that 25(OH)D levels <75 nmol/L were associated with increased odds of GDM (OR 1.49 (95% confidence interval 1.18 to 1.88)).¹³ Parlea et al after adjusting for gestational age and maternal weight, concluded that low serum 25 hydroxy vitamin D was associated with a twofold greater likelihood of gestational diabetes which was independent of race, age, season and maternal weight.¹⁴ Zhang C et al in a nested case-control study in Washington in 2008 concluded that maternal plasma 25(OH)D concentrations were 20% lower among women who subsequently developed gestational diabetes mellitus as compared to those who were not diagnosed with gestational diabetes mellitus.¹⁵

To further establish the association between glucose intolerance and hypovitaminosis D, interventional studies have been undertaken in the past few years. Jayaraman et al reported that frequency of GDM was similar irrespective of vitamin D status 67% versus 42% (p value=0.09).¹⁶ However, serum 25-OH Vitamin D levels were significantly lower in GDM $24.7 (\pm 17.6)$ ng/ml versus normal glucose tolerance group (45.8 ± 28) group (p value=0.0004). The investigators went on to conclude that replacement of vitamin D in the form of supplementation does not reverse the glucose intolerance. In a randomised controlled trial conducted in 2015, Mojibian M et al compared the effects of 50,000 IU of vitamin D every two weeks with that of 400 IU of

vitamin D daily.¹² The researchers concluded that 50,000 IU vitamin D every 2 weeks decreases the incidence of GDM.

CONCLUSION

There is a very high prevalence of hypovitaminosis D in pregnant females attending present institute i.e. 86.25%. Although 94.59% of Gestational Diabetes Mellitus patients had vitamin D deficiency, there is no statistically significant association between Gestational diabetes mellitus and serum vitamin D levels.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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