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Original Article

Effect of gestational diabetes on the vitamin D levels in the neonates: a case control study

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ABSTRACT

Background and objectives. The present study was conducted to determine the effect of maternal gestational diabetes on the Vitamin D levels of the mother and their newborns and to compare it with healthy mother-infant pairs.

Methods. The study design was a Case Control study. It was conducted at the antenatal unit of Obstetrics and Neonatal unit of Pediatrics department of a tertiary care hospital in costal Karnataka. Consecutive sample of otherwise healthy pregnant women presenting with Gestational Diabetes Mellitus (GDM) and their healthy term neonates were taken as study group. The weight matched healthy mothers and their healthy term neonates were taken as controls. The blood samples of the mothers, at term and the cord blood samples of the neonates were collected for estimating the Vitamin D levels. Vitamin D levels in the cases and controls were the primary outcome measures.

Results. The mean value of Vitamin D levels in the GDM mothers was 10.74 ng/ml and in the mothers forming the control group was 23.53ng/ml (p value <0.001). The mean value of Vitamin D levels in GDM babies was 8.47ng/ml and was 19.51ng/ml in the control (p value <0.001).

Conclusion. Comparison of Vitamin D levels of mothers and infants of both groups showed a positive correlation. GDM seems to exacerbate the Vitamin D deficiency in the mothers and their neonates.

Key words: infants of diabetic mothers, gestational diabetes, deficiency.

Vitamin D is the most common nutritional deficiency and a public health issue worldwide, with the number of people affected by vitamin D deficiency or insufficiency reaching nearly 1 billion.[1,2] Various adverse fetal outcomes have been linked with Vitamin D deficiency during pregnancy including low birth weight, neonatal hypocalcaemia, abortions, impaired development and rickets.

Some previous studies have linked decreased Vitamin D levels with onset of GDM, so it was postulated that an infant of a diabetic mother may also have decreased levels of Vitamin D when compared to healthy mothers.

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Material and Methods

An institutional ethical and scientific committee approval for the research and the informed consent was taken before starting the study (Ref. INST.EC/EC/092/2015-16; dated 16/11/2015). An informed consent was taken before enrolling any of the mother-infant pair. The maternal sampling was done along with routine investigations and cord blood was taken from neonates to prevent unnecessary invasive pricks.

Mothers diagnosed with GDM were enrolled in the study. Any mother, who was on any drug affecting Vitamin D levels, or had history of thyroid disease, metabolic bone diseases or pre gestational type 1 or type 2 diabetes mellitus were excluded. Any neonates who were preterm or had low birth weight or multiple gestation were also excluded from the study.

Thirty consecutive, live born, healthy infants born to mothers with GDM were enrolled into study. A complete data sheet was prepared for both the mother and infant, including their anthropometric measurements and laboratory values including HbA1c and vitamin D levels. Thirty healthy age, weight and gestational age matched controls were enrolled as the control group.

The 75gm Glucose Tolerance Test was done to diagnose GDM. according to Carpenter and Couston guidelines.[3] Any mother with overt diabetes mellitus were excluded from the study.

The blood samples of mothers in both the cases and controls groups were collected at 37 weeks of gestation. After delivery, the cord blood sample of their newborns were collected. Measurement of the Vitamin D level was done using ELISA, via a commercially available kit.

For this study, we followed the US Endocrine Society guidelines for the vitamin D levels.[4] We took vitamin D levels less than 20ng/ml as deficiency, whereas, 21-29ng/ml was taken as insufficiency, >30ng/ml was considered sufficiency and >150ng/ml was considered toxicity. As the Endocrine society guidelines have been standardized for all ages and hold true for neonates as well, and the data was collected only for comparative analysis, for the purpose of this study, we used the same criteria for Vitamin D insufficiency and deficiency for both mothers and their neonates. Vitamin D levels of mothers and infants born to GDM mothers were compared to normal controls.

Statistical analysis

Descriptive statistics of the data collected were calculated and presented with suitable tables and diagrams. Quantitative variables such as age of mother, Vitamin D levels in mother and baby, period of gestation of baby, baby length, head circumference and weight were expressed in mean and standard deviation. Qualitative variables such as Vitamin D deficiency states in mother and baby, HbA1C levels was expressed in terms of percentage. Chi-square test was used for determination of age, weight and Body mass Index (BMI) of mother and birth weight of baby and association of HbA1C, maternal age with Vitamin D deficiency. Independent t test was used to determine difference in mean length of baby. After finding normality with Shapirowilk test, Mann-Whitney U test was used for comparison of Vitamin D levels in GDM and healthy mothers and Vitamin D levels in GDM babies and healthy babies. A p value of <0.05 was taken as significant.

Statistical analyses were performed using statistical software.

Results

Anthropometric data were taken and analysed for both cases and control groups (Table I). There was no statistically significant difference between the mothers of the cases or control groups on the basis of body weight or BMI. A significant difference was found in the ages (30 ± 4.3 years and 27.6 ± 4.5 years for cases and controls respectively; p value 0.034), as one mother in control group had age less than 20 years.

Among the neonates, no statistically significant difference was found on the basis of mean gestational age, birth weight, length or head circumference in either group. Majority of mothers in our cases (14; 46.67%) were managed with oral hypoglycemics, 12 (40%) were managed by diet modification alone while only 4 (13.33%) required insulin. Out of 30 mothers in the case group, 16 (53.3%) had HbA1c levels ≤6%.

Vitamin D levels for the cases and controls are given in Table II. All (100%; n= 30) of the GDM mothers and infants born to them had Vitamin D deficiency (serum values <20ng/ml). In control group of mothers, 13(43.33%) were deficient, 14(46.66%) were insufficient and only 3(10%) had normal Vitamin D levels. Among their healthy infants (n= 30), 20(66.67%) were deficient, 8(26.67%) were insufficient, while only 2(6.67%) had normal levels of Vitamin D.

Table I. Mean anthropometric measurements of mothers and infants.

	Cases	Controls	p value
Mean age of mother (years)	30.0 ± 4.3	27.6 ± 4.5	0.034
Mean weight (kg) of mother	67.3 ± 8.44	64.1 ± 8.61	0.151
Mean body mass index (kg/m^2) of mother	27.4 ± 3.19	26.5 ± 3.54	0.328
Mean gestational age(days)	268.9 ± 6.70	268.9 ± 9.07	0.987
Mean birth weight of neonate (kg)	3.1 ± 0.36	3.2 ± 0.41	0.343
Mean length(cms) of neonate	49.2 ± 1.3	48.9 ± 0.99	0.378
Mean head circumference of neonate (cms)	34.0 ± 0.83	33.9 ± 0.86	0.432

Table II. Comparison of vitamin D levels in GDM mothers and their newborns with healthy controls.

Mothers	Median [IQR] (ng/ml)	p value	Mann Whitney U
Cases	10.5[8.17-14.32]	0.000	9.00
Controls	21.9[20.03-28.42]		
Neonates	**Median [IQR] (ng/ml)**	**p value**	**Mann Whitney U**
Cases	8.9[6.73-10.80]	0.000	14.50
Controls	17.9[15.15-21.80]		

Lowest value of Vitamin D level in the mothers was 2.21 ng/ml and in the neonates, the level was 4.31 ng/ml.

However, the median values of the Vitamin D levels of the two groups had a very significant difference. In the mothers, the median value among cases was 10.5 (8.17-14.32) ng/ml, which was significantly lower than the median value 21.9 (20.03-28.42) ng/ml in controls. In the neonates, the median value in the case group was 8.9 (6.73-10.8) ng/ml as compared to 17.9 (15.15-21.80)ng/ml in the control group. The p value for both groups was 0.000 which was highly significant.

The individual mother-neonate pair showed a moderate to high level of positive correlation in their serum Vitamin D levels in both the cases and control (Fig. 1). However, this correlation appears more in cases than that of controls. Hence, it can be inferred that there was a significant positive correlation, i.e. with a decrease in Vitamin D levels of mothers a corresponding decrease in Vitamin D levels of their neonates can be expected. We did not get any positive correlation between maternal HbA1C levels and their neonate's vitamin D levels.

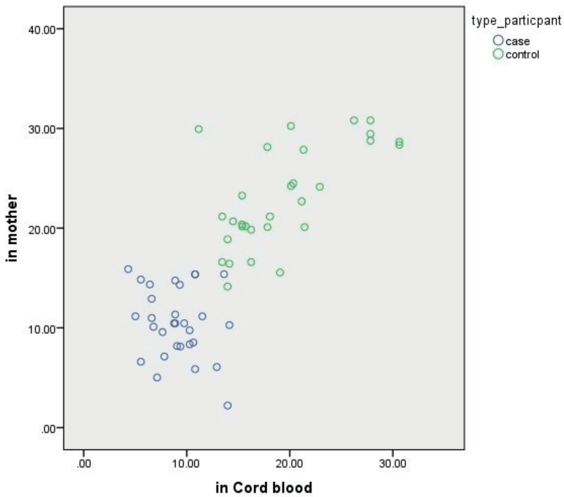

Fig. 1. The distribution scatter plot of the vitamin D levels in the mother with vitamin D levels in the infant. Pearson's correlation was carried out and coefficient was found to be 0.79.

Discussion

In our study, we did not find any statistically significant difference between gestational age and anthropometry among the neonates of GDM and healthy controls. We believe the tight glycemic control achieved by the GDM mothers to be the reason behind this finding in our study. All the GDM mothers and their babies had

Vitamin D deficiency. In our study, although both cases and controls had a high number of participants with vitamin D deficiency, the mean value of Vitamin D levels in the GDM mothers was significantly lower than that of the controls. Similarly, the mean value of Vitamin D levels in GDM babies was significantly lower when compared to the controls. Individual mother-neonate pairs showed a high positive correlation, signifying the neonatal vitamin D levels to be directly influenced by the maternal levels. No correlation was found between the glycemic control of the mother and the neonatal vitamin D levels.

There have been many studies about Vitamin D deficiency among pregnant women and their cord blood, but no specific comparative studies between GDM and normal mothers has been published to our knowledge. Kumar et al.[5], studied 106 mother and cord blood samples for Vitamin D levels. They found majority of the mothers (70.7%) and neonates (83.01%) to have hypovitaminosis D. More neonates born to both mothers with hypovitaminosis D (93.3%) had low vitamin D levels than those born to mothers having normal Vitamin D (61.3%). Like our study, they also found a significant correlation between maternal and cord blood Vitamin D levels.

A similar study was done by Aly et al.[6], evaluating Vitamin D levels in 92 pregnant women at the end of the 3rd trimester and their newborns. Compared to pregnant women with adequate vitamin D levels, significantly higher number of women deficient in Vitamin D had infants with Vitamin D deficiency.Another study conducted by Rajoria et al.[7], on 250 pregnant patients and their newborns showed results similar to ours. Their maternal and cord blood samples also showed significant positive correlation (r= 0.90, p value <0.001).

A systemic review and meta-analysis noted that Vitamin D insufficiency was associated with high risk of GDM.[8] A previous meta-analysis done by Poel et al.[9] in 2012 also found a highly significant difference between the vitamin D levels in pregnant women with GDM compared to those without. The Vitamin D levels of diabetic pregnant women was significantly lower with a p value being 0.018. Similar results were also demonstrated by Soheilykhah et al.[10] in their case control study comparing GDM, Impaired Glucose Tolerant (IGT) women and normal women by their Vitamin D status. They found a 2.66 fold increased risk of Vitamin D deficiency in GDM group when compared to control. These all supported our results where all GDM mothers had Vitamin D deficiency and a mean Vitamin D levels significantly lower than the controls.

Triunfo et al.[11] in their paper have described lower circulating Vitamin D levels as a potential cause for development of gestational diabetes. They discussed the effect of Vitamin D on insulin sensitivity of tissues, genetic variations or polymorphisms of Vitamin D receptors and Vitamin D being an anti-inflammatory agent as potential causes for association of Vitamin D deficiency with GDM. These factors may explain the very significant difference found in the serum Vitamin D levels of pregnant women with and without GDM in our study.

We could not find any previously published articles about the Vitamin D deficiency in infants born to GDM mothers, despite extensive literature search. Our study shows that GDM is not only associated with significant Vitamin D deficiency in the mothers but also their neonates.

In a study done by Naik et al.[12], cord blood Vitamin D levels were estimated in 50 term healthy neonates. Majority of babies had values between 5 to 15ng/ml. This study showed that most of the neonates are born with deficient Vitamin D levels, even in tropical climates. Our study showed similar results where only two babies out of total 60 (3.33%), had normal vitamin D levels.

Our study was limited by the small sample size. Moreover, interventional studies are needed to evaluate the effect of maternal vitamin D supplementation on the neonatal levels.

The strong correlation between Vitamin D levels in mothers and their newborn indicate that adequate Vitamin D intake for pregnant women should be emphasized through maternal supplementation which might achieve the double effect of preventing Vitamin D deficiency in both mothers and children. GDM in mothers also seems to exacerbate the Vitamin D deficiency in their neonates. Hence, we conclude that all mothers should be recommended Vitamin D prophylaxis during pregnancy, but it should be specifically recommended for pregnant women with GDM.

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