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S Shanthi
Associate Professor, Government Medical College & ESI Hospital, Coimbatore, Tamil Nadu, India

S Usha Rani
Professor, Institute of Obstetrics & Gynaecology, Egmore, Chennai, Tamil Nadu, India

J Arumaikannu
Assistant Professor, Institute of Obstetrics & Gynaecology, Egmore, Chennai, Tamil Nadu, India

Correspondence
S Shanthi
Associate Professor, Government Medical College & ESI hospital, Coimbatore, Tamil Nadu, India

Role of vitamin D in gestational diabetes mellitus

S Shanthi, S Usha Rani and J Arumaikannu

Abstract
Objective: To find the association between Vitamin D deficiency and GDM.
Methods: Prospective study included 50 women with GDM and 50 normoglycemic pregnant women. Serum Vitamin D level was estimated and correlation between low Vitamin D level and GDM was analysed statistically.
Results: Prevalence of Vitamin D deficiency was 56%.Vitamin D was not significantly decreased in GDM group. Obesity, advancing age were significant risk factors for GDM (p<0.05).Parity, bad obstetric history and weight of baby were comparable in both groups. 34(68%) GDM women needed insulin for glycemic control. 4 GDM women on insulin developed preeclampsia. Baby weighing >3.5Kg was significantly higher in women treated with insulin.
Conclusion: High prevalence of Vitamin D deficiency in pregnancy is not associated with the risk of GDM. Further trials are needed to document Vitamin D deficiency as risk factor for the occurrence of GDM.

Keywords: Gestational diabetes, vitamin D deficiency, insulin, T. Metformin

Introduction
Gestational Diabetes Mellitus (GDM) - glucose intolerance diagnosed initially at pregnancy is a major health hazard all over the world. Asian women are ethnically more prone to develop glucose intolerance compared to other ethnic groups [1]. Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women [2]. Intrauterine exposure to hyperglycemia during the critical period of fetal development programmes the development of pancreas negatively and affects the insulin secretory function and the offsprings are at high risk of developing glucose intolerance in their later life [3]. Diabetes in pregnancy is associated with serious complications for both the mother and child, adverse effects increase linearly with increasing maternal blood glucose [4]. Maternal risks associated with hyperglycemia in pregnancy are preeclampsia, hydramnios, obstructed labour, post partum hemorrhage and infections. Fetal risks include congenital anomaly, intra uterine death, shoulder dystocia, birth injuries, RDS, neonatal hypoglycemia and future obesity [5]. GDM is significant predictor of woman's predisposition to the development of future overt diabetes mellitus type 2 in later life [6]. Role of Vitamin D in bone mineralization and calcium homeostasis is well established [7]. In spite of being a tropical country most of the pregnant Indian women have Vitamin D deficiency. Recent evidences show that Vitamin D is involved in insulin secretion and insulin resistance [8]. Vitamin D deficiency is associated with increased risk for GDM [9]. Aim of this study is to compare Vitamin D status in pregnant women with or without GDM and to find out the association between Vitamin D deficiency and GDM.

Materials and Methods
Study Design: Prospective case control study done at Institute of Obstetrics & Gynaecology, Chennai from September 2016 to April 2017.

Subjects: 50 pregnant women diagnosed with GDM and 50 normoglycemic pregnant women (control) were included for the study and serum 25 (OH) Vitamin D concentration in these women were compared.

Exclusion Criteria: Women with Chronic hypertension, Renal disease, Hypothyroidism, Collagen vascular disease, Diabetes mellitus and multiple pregnancy were excluded.

Methods: Informed consent obtained. Data regarding age, socio-economic class, educational status, parity, H/o abortion, body mass index were recorded. At 20-24 weeks of gestation GDM screening was done with oral glucose challenge test (75 gm-2 hrs) irrespective of the fed status and venous plasma glucose of ≥ 140 mg/dl was considered as diagnostic of GDM. Venous blood samples for 25(OH) Vitamin D estimation were collected after 12 hr overnight fasting, protected from light, centrifuged and stored at - 20 ^{0} C until analysis. 25(OH) Vitamin D estimation was done using Chemiluminiscent Immunoassay (CLIA).Value of 25(OH) Vitamin D ≤ 20 ng/ml was the cut off to define Vitamin D deficiency. Details regarding previous H/o GDM, family H/o diabetes mellitus, previous pregnancy outcome were recorded. Thorough clinical examination and BP monitoring done. Treatment used for glycemic control and birth weight of the baby were noted. Data were expressed as percentage and Pearson χ^2 was used to analyse the statistical significance of the parameters compared.

Results

Patients who had BMI > 25 had higher incidence of GDM when compared to control group (p<0.05). 94 % of the women were between 20 to 30 years in the control group and 30 % of the GDM patients were > 30 years of age. Elderly women had higher incidence of GDM which was statistically significant (p<0.05). No statistical difference was noted between the two groups with respect to parity, BOH, education and socio-economic status (p>0.05). 28 % in GDM group and 10 % in the control group had baby weight > 3.5 kg (p>0.05) (Table-1). Prevalence of Vitamin D deficiency was 56% (GDM-26 %, control-30 %) in our study. Vitamin D deficiency was comparable in both GDM and control groups. There was no statistical correlation with Vitamin D deficiency and occurrence of GDM (p>0.05). (Table-2) Family h/o DM and previous h/o GDM were not significantly associated with risk of GDM (p=1). 4 GDM women developed preeclampsia subsequently (Table-3). But GDM women treated with insulin had significantly more heavier babies (Table-4). 12 women with GDM were managed with meal plan and 34 needed insulin for glycemic control. There was no correlation between Vitamin D value and the need for insulin (Table-5).

Table 1: Maternal characteristics

Maternal characteristics		GDM cases (N=50)	Controls (N=50)	χ2	P value
Age(years)	20-25	12(24%)	25(50%)		
	26-30	23(46%)	22(44%)		
	31-35	9(18%)	2(4%)		
	>35	6(12%)	1(2%)	12.61	0.005
Pre pregnancy BMI(kg/m2)	18.5-24.9	6(12%)	18(36%)		
	25-29.9	28(56%)	18(36%)		
	≥30	16(32%)	14(28%)	8.30	0.015
Gravida	primi	21(42%)	28(56%)		
	multi	24(48%)	20(40%)		
	BOH	5(10%)	2(4%)	2.64	0.26
Education standard	<12	15(30%)	18(36 %)		
	≥12	35(70%)	32(64%)	0.40	0.52
Socio economic status	High	11(22%)	8(16%)		
	Low	39(78%)	42(84%)	0.58	0.44
Weight of Baby	2.5-3 kg	12(24%)	18(36%)		
	>3-3.5 kg	24(48%)	27(54%)		
	>3.5 -4 kg	10(20%)	4(8%)		
	>4 kg	4(8%)	1 (2%)	5.74	0.12

Table 2: Vitamin D level

Vitamin D (ng/ml)	GDM		Controls	
	No. of cases	Median (range)	No. of cases	Median (range)
<20(deficient)	26(52%)	5.32 (3-9.18)	30(60%)	10.31 (3-19.5)
>20(normal)	24(48%)	39.65 (20.48-61.39)	20(40%)	36.8 (20.02-65.13)

χ2=0.64; p=0.42; Risk ratio = 0.86. 95% CI (0.61-1.22)

Table 3

	GDM cases No.	Control No.	P value
Previous H/o GDM	10	1	
Family H/o GDM	6	0	
Preeclampsia	4	1	0.82

Table 4: Treatment and weight of Baby

Weight of Baby	GDM			χ2	P value
	Meal plan	Metformin	Insulin		
2.5-3 kg	8(16%)	1(2%)	2(4%)		
>3-3.5 kg	3(6%)	2(4%)	19(38%)		
>3.5 -4 kg	1(2%)	1(2%)	9(18%)		
>4 kg	0(0%)	0(0%)	4(8%)	18.06	0.006

Table 5: Treatment of GDM cases

Treatment	Number	Percentage
Meal plan	12	24
Metformin	4	8
Insulin	34	68

Discussion

Positive correlation between age and GDM in our study is comparable to the report of Jain M *et al.* [10] (44 % >30 yrs). V.Seshiah *et al.* [11] also found significant linear trend for age. Correlation for GDM with age was also noted by others [12, 13]. BMI was higher in GDM women compared to control group. Similar result was reported by A Pleskacova *et al*. [14] and (71.9%) Jain M *et al* [10]. On the contrary J Muthukrishnan *et al* [15] did not find any association between BMI and GDM. Parity was not significantly associated with GDM in our study. Jain M *et al*. [10] reported primiparity (84.3%) as significant risk factor for GDM whereas V.Seshiah *et al.* [11] reported an increase in GDM prevalence proportion from 18.1% in primi to 25.8 % in gravida ≥ 4. A Pleskacova *et al.* [14] found significant association between previous H/o GDM and family H/o DM and occurrence of GDM. This association was not observed in our study. Birth weight of the baby was comparable in both groups. Balaji *et al*. [16] and Gayle *et al* [17] also found no statistically significant difference in birth weight between GDM and control. Jain M *et al*. [10] found significant negative correlation between fasting blood glucose and 25 (OH) D level. In our study we did not find any correlation between Vitamin D level and severity of GDM.

Prevalence of Vitamin D deficiency in our study is 56 % compared to (72.8%) Jain M *et al.* [10] and (94%) A Pleskacova *et al.* [14] We did not find any statistically significant difference in vitamin D levels between GDM women and controls. Some other published studies also report lack of association between Vitamin D levels in pregnancy and GDM. Ferrant *et al.* [18] found no association between maternal Vitamin D levels in 559 nondiabetic pregnant women from South India and risk of GDM. Makgoba *et al.* [19] found no statistically significant difference in Vitamin D levels between GDM and control in 248 British women. A Pleskacova *et al.* [14] also observed no correlation between Vitamin D levels and risk of GDM in the 76 Czech pregnant women analysed by them. Contrary to our study Maghbooli *et al.* [12] in a study of 741 Iranian women found statistical difference in Vitamin D levels between GDM and control groups. Zahur *et al.* [9] described significantly lower Vitamin D levels in 234 Turkish pregnant women with GDM compared to 162 controls. Jain M *et al.* [10] observed that maternal Vitamin D deficiency is associated with 11.5 times increased risk of GDM. Poel *et al.* [20] in a meta analysis of four out of seven observational studies have reported a high incidence of vitamin D deficiency in pregnant women with the risk of GDM with an odds ratio of 1.61. J Muthukrishnan *et al.* [15] in their study found that Vitamin D deficiency was significant in GDM women. But replacement of Vitamin D did not significantly improve the glucose intolerance in the GDM women.

Conclusion

Incidence of GDM is about 15% to 18% in India. The maternal and fetal complications associated with GDM are significant with long term morbidity. Vitamin D deficiency is associated with the risk of GDM in some studies. But prevalence of vitamin D deficiency is comparable in both GDM and normal pregnant women. Replacement of Vitamin D in GDM women did not significantly improve glucose intolerance. Race and ethnicity play a major role in occurrence of GDM and hypovitaminosis D. Hypovitaminosis D and GDM are more common in Asian women. So the cause-effect relationship of Vitamin D deficiency in the occurrence of GDM has to be well documented by further large double blind randomized control studies with women of all ethnic groups. Role of vitamin D supplementation in prevention of GDM to promote maternal and child health has to be explored and proved beyond doubt.

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethical committee

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