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COMPARATIVE STUDY OF VIT D LEVELS IN NORMAL PREGNANCY AND GESTATIONAL DIABETES MELLITUS AT TERM

Obstetrics & Gynaecology

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ABSTRACT

BACKGROUND: The increasing rates of overweight and obesity in the general population are undoubtedly contributing to the ongoing rise in the prevalence of GDM. GDM has serious adverse maternal and fetal outcomes like congenital anomalies, macrosomia, birth trauma, respiratory distress syndrome, jaundice and hypoglycemia. Placenta plays an important role in vitamin D metabolism during pregnancy and several interdependent risk factors that regulate vitamin D metabolism at the fetomaternal interface increase the risk of placental dysfunction that causes adverse pregnancy outcome. **MATERIAL AND METHODS**: The study was conducted in women at term pregnancy, diagnosed as GDM in DMCH Darbhanga, From 18 months duration. in pregnant patients who were admitted in labour room at Darbhanga medical college and Hospital Darbhanga Laheriasarai, Bihar. **CONCLUSION** :To conclude from this study Vitamin D deficiency is an independent modifiable risk factor associated with gestational diabetes mellitus.

KEYWORDS

Gestational Diabetes Mellitus, Vitamin D deficiency.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy[1].Depending on the geographical locations and diagnostic methods used, the prevalence of Gestational diabetes mellitus in India varies from 3.8 to 21% in different parts of the country[3].At any given point of time in India, it is estimated that about 4 million women are affected by GDM[4]. Differences in the prevalence rates across India could be attributed to differences in age, body mass index (BMI), socio-economic status of females and cultural differences as well. Different screening and diagnostic criteria could also be responsible for different prevalence rates. GDM could cause serious adverse maternal, fetal and neonatal outcomes like congenital anomalies, birth trauma, respiratory distress syndrome, macrosomia, neonatal jaundice and neonatal hypoglycemia. altered Vitamin D(VD) levels in GDM. Vitamin D deficiency is found in one billion of world population belonging to all ages and ethnic groups. Higher prevalence of vitamin D deficiency was seen in developing countries as well as some of the developed countries. Reduced vitamin D level based on low circulating 25-hydroxy-vitamin D (25OHD) concentration, has been described in pregnant women in several countries. Indian women are known to have Vitamin D deficiency(VDD)[5].Vitamin D deficiency in mothers during pregnancy period could cause adverse effects in the growing fetus such as low birth weight, poor postnatal growth, lower bone mineral content, impaired glucose homeostasis. Vitamin D metabolism during pregnancy is affected by placental function. Vitamin D metabolism at the fetomaternal interface are regulated by many interdependent risk factors that could increase the risk of placental dysfunction and thereby, could affect the outcome of pregnancy[7].Perinatal investigators studying GDM in animal models were fascinated on finding that pancreatic exocrine function and insulin sensitivity improves with vitamin D[8]. Low vitamin D levels have been associated with a wide range of adverse maternal and child health outcomes. One of them is gestational diabetes mellitus according to few studies. The increasing rates of overweight and obesity in the general population are undoubtedly contributing to the ongoing rise in the prevalence of GDM.

REVIEW OF LITERATURE

In normal pregnancy, hyperplasia of the insulin-secreting pancreatic beta cells, increase in secretion of insulin and an early increase in insulin sensitivity would shadow progressive insulin resistance. In contrast to this, hyperglycaemic state is seen in GDM due to failure by beta cell to compensate for the increased demand for insulin. GDM causes pancreatic β-cell dysfunction through autoimmune β-cell dysfunction, impairment in insulin secretion through highly penetrable genetic abnormalities, down regulation of insulin receptors all of which finally lead to insulin insufficiency[11].β-cell dysfunction that is associated with chronic insulin resistance and limitation in pancreatic β cell reserve results in hyperglycemia only when insulin secretion does not increase to match the increased insulin needs of late pregnancy[12]. Prevalence of GDM is found to be increased in Indian women due to increasing obesity, insulin resistance and better screening protocols. Even after pregnancy, insulin resistance may persist and can lead to development of DM in some women.

Vitamin D is a fat soluble vitamin. It is a derivative of cholesterol which is present naturally in many food products like fish liver oil, fish-Tuna, egg yolks, cheese and mushroom. Best source of vitamin D are fatty flesh fish and fish liver oil. When exposed to ultraviolet rays, it is produced endogenously. Calcitriol synthesis in the kidney is tightly regulated by parathyroid hormone. It is biologically inert and activation is by hydroxylation. Vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) are two major forms of vitamin D. vitamin D deficiency include aging, obesity, limited sun exposure, regular use of sunscreens, dark skin, extensive clothing and malabsorptive syndromes (like cystic fibrosis, cholestatic liver disease, inflammatory bowel disease, short gut syndrome).

MATERIAL AND METHODS

The study was conducted in women at term pregnancy, diagnosed as GDM in DMCH Darbhanga, From 18 months duration. in pregnant patients who were admitted in labour room at Darbhanga medical college and Hospital Darbhanga Laheriasarai, Bihar.

INCLUSION CRITERIA

CASES: Age : 18-35yrs of age Singleton

Term gestation

Gestational diabetes mellitus. for GDM at 24-28 weeks of gestation with a 75-gm oral glucose challenge test.

EXCLUSION CRITERIA

Patients with any other co-morbidities affecting vitamin D levels like Diabetes mellitus (Type I, Type II). Chronic renal disease.

Fat malabsorption. Gastric bypass surgery. Hepatic dysfunction.

Estimation

The study population was screened based on the inclusion and exclusion criteria. They were categorized into cases and controls. A blood sample was collected from each subject by venipuncture for determination of serum 25 OHD (Serum 25hydroxyl vitamin D) and was sent to the laboratory.

STATISTICALANALYSIS

Statistical analysis of association of vitamin D in GDM and controls were compared and was studied by odds ratio with 94% confidence interval, Student t test and chi square test and results were tabulated and analysed.

OBSERVATION AND RESULTS

There were 60 subjects recruited for the study. 30 cases and 30 controls.

Comparision of age between cases and controls

AGE * GROUP Crosstabulation					
			Group		Total
			Control	Case	
AGE	<25	Count	9	6	15
		% within GROUP	30.0%	20.0%	25.0%
	25-30	Count	14	16	30
		% within GROUP	46.7%	53.3%	50.0%
	30-35	Count	7	8	15
		% within GROUP	23.3%	26.7%	25.0%
Total	Count	30	30	60	
	% within GROUP	100.0%	100.0%	100.0%	
Chi-Square Tests					
Pearson Chi-Square		Value	df	Asymp. Sig. (2- sided)	
		.800	2	.670	

Comparison of BMI between cases and controls.

			Group		Total
			Control	Case	
BMI	<18.5	Count	1	1	2
		% within GROUP	3.3%	3.3%	3.3%
	18.5-24.9	Count	18	7	25
		% within GROUP	60.0%	23.3%	41.7%
	25-29.9	Count	9	16	25
		% within GROUP	30.0%	53.3%	41.7%
	>=30	Count	2	6	8
		% within GROUP	6.7%	20.0%	13.3%
Total		Count	30	30	60
		% within GROUP	100.0%	100.0%	100%

There was statistically significant difference in BMI when compared between cases and controls(p value-0.032). Higher number of patients(60%) were in the normal range of BMI in control group whereas, higher number of GDM patients i,e 53% and 20% were found to be overweight and obese respectively compared to controls and this difference was statistically significant.

Comparison of mean serum vitamin D levels between cases and controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	t	p value
VITAMIN D	Control	30	20.376	5.137565	0.937987	2.946	0.005
	Case	30	15.68267	7.054254	1.287925		

Mean serum Vitamin D in controls was 20.37±5.13ng/ml and in cases was 15.68±7.05ng/ml. Mean serum Vitamin D level in cases (GDM patients) is significantly lesser than, mean serum vitamin D level of controls (normoglycemic patients)(p value 0.005).

Primigravidas have significantly higher Vitamin D deficiency in the cases(87%) compared to controls(36%) with p value of 0.026. Higher proportion of women having vitamin D deficiency was found in primigravida in comparision to multigravida in GDM group.

DISCUSSION

There was statistically significant difference in BMI when compared between cases and controls(p value-0.032). The BMI was found to be significantly higher among the GDM group when compared to normoglycemic mothers. Most of the patients(60%) belonged to the BMI range of 25-29.9 among the GDM patients whereas, higher number of controls (53%) belonged to lesser BMI range of 18.5-24.9. A study by Chu et al showed that unadjusted ORs of developing GDM among overweight, obese, and severely obese compared with normal-weight pregnant women were 2.14 (95% CI 1.82-2.53), 3.56 (3.05-4.21), and 8.56 (5.07-16.04) respectively. Though, some of the studies found comparable BMI in GDM patients and normoglycemic mother respectively, we found in our study that there was a statistically significant difference in BMI between case and controls. It is justified to have altered BMI since literatures already show that higher BMI is well correlated to GDM mothers. Decrease in the vitamin D concentrations are found in obese individuals. A study by Bodnar et al showed that lower levels of vitamin D is seen both in pregnant women and their neonates with prepregnancy obesity where, vitamin D deficiency was seen among 36% of women with a prepregnancy BMI of less than 25 and 61% of women who were obese (body mass index [BMI] ≥ 30) prior to pregnancy. the proportion of Vitamin D deficient primigravidas are comparatively higher in GDM group compared to control group. A study by Parlak et al showed Serum 25(OH)D3 concentrations in primigravida and multigravida were 3.71 ± 1.88 and 5.2 ± 3.4 ng/ml respectively, with a significant difference between them ($p < 0.05$).He inferred that the lower 25(OH)D3 levels may be explained by the main risk factor of lower socioeconomic class and avoidance of direct sun exposure.

There was statistically significant higher mean vitamin D level in controls when compared to GDM mothers group which were 20.37±5.13 ng/ml and 15.68±7.05ng/ml respectively. This difference in mean serum vitamin D levels was statistically significant with a p value of 0.005.Similiar studies also showed comparable results. A study by Jayaraman et al showed that serum 25-OH vitamin D levels were significantly lower in GDM (24.7 ±17.6) ng/ml versus normoglycemic (45.8 ± 28) group ($P = 0.0004$). He quoted that lack of physical activity could be the reason for GDM among Vitamin D deficient individuals which needs further study. He also quoted that frequency of GDM was not different in Vitamin D deficient individuals when compared to individuals with normal Vitamin D levels. A study by Jain et al showed that Vitamin D concentrations in women at the time of delivery remained almost half (48% lower) in women with GDM compared with controls (mean, 11.07± 3.021 ng/ml, and 95% CI, 9.9-12.16 ng/ml, vs 21.33 ± 14.40; 95%CI 19.20-23.46ng/ml;p<0.001 respectively. One of the study by Anna et al has found comparable serum Vitamin D levels at midgestation between cases and controls(47 GDM and 29 healthy controls). study the cut off for Vitamin D deficiency taken was 20 ng/ml according to criteria of ACOG (2011).Normal Serum Vitamin D level for some other studies have been taken as 50 ng/ml. In the present study, higher number of women having vitamin D deficiency was found in GDM group (70%) than controls(53.3%) but it wasn't statistically significant. A study by Cho GJ et al found that 27.5% of normal pregnant women and 85% of women with GDM had vitamin D deficiency, considering the serum 25(OH)D levels<20 ng/mL as deficiency. Serum levels of 25(OH)D were also found to be lower in women with GDM than normal pregnant women ($P < .01$) in this study. They attributed it to significantly higher production of CYP24A1 protein and messenger RNA expression in placental tissue from patients with GDM. He concludes that CYP24A1 catabolizes both 25(OH) D and bioactive 1,25 (OH)2 forms to inactive metabolites and hence, elevated levels of CYP24A1 in the placenta of GDM mothers may play a key role in producing Vitamin D deficiency in them.

CONCLUSION

Primigravida with GDM was found to have higher risk of developing Vitamin D deficiency. When vitamin D levels are considered for deficiency(<20 ng/ml) no statistically significant difference was found between cases and controls. Larger comparative studies is needed to establish a causative association between GDM and maternal vitamin D deficiency.

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