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POSSIBLE ASSOCIATION OF VITAMIN D LEVEL IN PREGNANCY AND GESTATIONAL DIABETES

***DR. BUSHRA J.AL-RUBAYAE**

Assist. Prof.,Medical College ; Obstetrics and Gynaecology Department; Babylon University, Iraq.

ABSTRACT

Gestational diabetes affects maternal, foetal and neonatal outcome if detected early lessen complications on the mother and her foetus. The objective of the study is to find any association between maternal serum 25-dihydroxyvitamin D in the first, second trimester of pregnancy and development of gestational diabetes. Our study included one hundred sixty- six pregnant women, Serum levels of 25-hydroxyvitamin D were measured with an automated chemiluminescence immunoassay in the first trimester and second trimester with oral glucose tolerance test between 24-28 weeks of pregnancy for screening gestational diabetes. From one hundred sixty-six pregnant forty-five women had low vitamin D level in the first trimester and in the second trimester, from these thirty-two pregnant developed gestational diabetes which followed for the rest of pregnancy. Low level of vitamin D in pregnancy may be associated with development gestational diabetes.

KEY WORDS: Gestational diabetes, vitaminD, 25(OH), vitamin D.

DR. BUSHRA J.AL-RUBAYAE
Assist. Prof.,Medical College ; Obstetrics and Gynaecology Department; B*abylon University, Iraq.*

***Corresponding author**

INTRODUCTION

Diabetes is a disorder of carbohydrate metabolism that necessities immediate changes in lifestyle. In its chronic forms, diabetes is associated with long-term vascular complications, including retinopathy, nephropathy, neuropathy and vascular disease. Approximately 650,000 women get delivery in England and Wales each year, and 2–5% of pregnancies involve women with diabetes. Approximately 87.5% of pregnancies complicated by diabetes are estimated to be due to gestational diabetes (which may or may not resolve after pregnancy), with 7.5% being due to type 1 diabetes and the remaining 5% being due to type 2 diabetes. The prevalence of type 1 and type 2diabetes is increasing. Type 2 diabetes is more in certain ethnic groups (including people of African, black Caribbean, South Asian, Middle Eastern and Chinese family origin)[1]. Maternal hyperglycaemia increases the risk of poor pregnancy outcome congenital abnormalities miscarriage, accelerated foetal growth, late stillbirth, birth trauma and neonatal hypoglycaemia also with maternal hyperglycaemia, later complications is more like risk of the baby developing obesity and/or diabetes in later life [2]. The management of diabetes and its complications in women who are planning to conceive and those who are already pregnant according to clinical guideline which include usual care during the antenatal, intra-partum and postnatal periods and additional care should be offered to women with diabetes and their newborn babies and those with gestational diabetes[1].There are risk factors for gestational diabetes to develop which include: Body mass index above 30 kg/m^2, previous macrosomic baby weighing 4.5 kg or above Previous gestational diabetes, family history of diabetes, family origin with a high prevalence of diabetes: South Asian, black Caribbean. Middle Eastern (Saudi Arabia, United Arab Emirates, Iraq, Jordan, Syria, Oman, Qatar, Kuwait, Lebanon or Egypt). Women with any one of the risk factors should be offered testing for gestational diabetes [1]. Screening for gestational diabetes using fasting plasma glucose, random blood glucose, glucose challenge test and urinalysis for glucose should not be performed [1].The two hour 75 g oral glucose tolerance test (OGTT) been used to test for gestational diabetes and diagnosis made using this criteria: plasma glucose greater than 5.1mmol/L fasting, 10.0mmol/Lat one hour or 8.5mmol/Lat two hours [2]. Women who have had gestational diabetes in a previous pregnancy should be offered early monitoring of blood glucose or an OGTT at 16–18 weeks, and a further OGTT at 28 weeks if the results are normal. Women with any of the other risk factors for gestational diabetes should be performed an OGTT at 24–28 weeks1.In most women, gestational diabetes will be controlled by changing diet and exercises, some women (10% - 20%) may need oral hypoglycaemic agents or insulin therapy if these are not effective in controlling gestational diabetes1.Hypoglycaemic therapy for women with gestational diabetes (which may include insulin and/or oral hypoglycaemic agents metformin and glibenclamide should be tailored to the glycaemia control of the woman [2].Vitamin D is not an essential nutrient. Essential means nutrients that are required for life, and must be supplied from an external source because they cannot be produced by our own bodies. In the presence of sunlight, humans can form enough vitamin D to support life, which makes vitamin D conditionally essential. The active metabolite, 1, 25-dihydroxyvitamin D, formed from 25-hydroxyvitamin D (25OHD), is involved in calcium balance and bone metabolism, acts as a transcription factor, and functions in glucose metabolism. Its level increase progressively from the first trimester and are increased by 100% during the third trimester relative to the non-pregnant women [3, 4]. There is increasing interest to find any relationship between vitamin D and GDM. Some studies have reported lower vitamin D levels in women with GDM[5,6] and other studies have demonstrated lower levels at 16 weeks gestation among women who experienced the development of GDM[7]. however, these results are controversial [8,9].The placenta plays an important role in vitamin D metabolism during pregnancy and several interdependent risk factors that regulate vitamin D metabolism at

the foetal-maternal interface increase the risk of placental dysfunction that causes adverse pregnancy outcome[10].

MATERIALS AND METHODS

It's a cross sectional study to show the relationship between vitamin D status during pregnancy and gestational diabetes, it involved one hundred sixty-six pregnant women attended Babylon Maternity & Paediatric Teaching Hospital during the period from January 2013 till January 2014.Their ages between (20 – 31) years old at 10 -13 weeks of gestation with uncomplicated singleton pregnancy, no history of diabetes or gestational diabetes, miscarriage or any complications. After taking the consent of the pregnant to participate in the study after explaining to them and ethical committee approval of the study then history taken, including maternal age. Gestational age was calculated according to the last menstrual period and was confirmed by ultrasonic examination during the first trimester in ninety percent of the pregnant and in ten percent there is difference so we depend on ultrasound, anthropometric measures were done, Body Mass Index calculated as weight (kg) /height squared(m2) then venous blood samples were aspirated and centrifuged then measured 25 hydroxy vitamin D at 10 -13 weeks of gestation and at 24 -28 weeks of gestation.The measurement of 25(OH)D level been performed with an automated chemiluminescence immunoassay (CLIA) [11], an automated electrochemiluminescent immunoassay (ECLIA) from Roche Diagnostics. Clinical categories of vitamin D status: Deficiency less than20 nanogram/millilitre(ng/ml) equal to less than 50 nanomol/litre(nmol/L) Insufficiency 20-30ng/ml equal to 50-74nmol/l Sufficient 31-100ng/ml equal to 75-250nmol/l[12] , forty five women with low vitamin D of whom, thirty-two pregnant had vitamin D level less than 20ng/ml , thirteen of them their level between 20-30 ng/ml ,thirty-two of them developed gestational diabetes and one hundred twenty-one pregnant with sufficient level of vitamin D regarded as control group, and all been assessed for gestational diabetes at 24 -28 weeks of gestation by 75-g fasting oral glucose tolerance test (OGTT) to determine normal glucose tolerance or GDM according to criteria of the International Association of the Diabetes and Pregnancy Study Groups (fasting glucose ≥ 5.1 mmol/L; 1 hour post-OGTT glucose ≥ 10.0 mmol/L; 2-h post-OGTT glucose ≥8.5 mmol/L) [2]. We classified pregnant with a normal glucose screening as having normal glucose tolerance and women with at least two abnormal results on the fasting glucose tolerance test as having GDM.All pregnant women been followed during pregnancy, those with gestational diabetes some controlled by diet alone or necessity for oral hypoglycaemic drugs or insulin with diet Mode of delivery in those with gestational diabetes operative delivery for twenty-two pregnant and ten by vaginal delivery, all healthy babies admitted to intensive neonatal care unit.Statistical analysis were done using SPSS version 15.0 for Windows (statistical Package for Social Science,Inc.,Chicago,IL, USA).Descriptive analysis was used to show frequencies, percent, the mean and standard deviation of variables. The significance of difference between mean and values was determined by Student T-Test .The probability P value less than 0.05significant.

RESULTS

Demographic distributions of women according to definite characteristics were shown in Table (1) the mean differences of age, the range of age (20 – 31) years old and BMI (20-26). The overall mean age of patients was (25.28± 2.27) years old; those with gestational diabetes their mean age 25.50± 2.87 years old and for the remaining non diabtic pregnant (25.23± 2.13) years old. Regarding parity ninety-two (55.4%) pregnant were Para one and seventy –four pregnant were Para two (44.6%).The overall mean BMI of pregnant was (22.42± 1.48) kg/m^{2}and majority(96.5%) of patients had normal weight, there were no significant mean differences of pregnant women age or BMI by gestational diabetes. The results for vitamin D were observed as follows from one hundred sixty - six pregnant forty-five pregnant with low vitamin D, thirty-two developed gestational diabetes the mean differences of vitamin D in 1st and^{2nd} trimester between pregnant women with and without gestational diabetes (16.69± 2.44)(28.70± 5.16),(17.31± 2.70) and(29.23± 4.93)respectively. There were significantly low

vitamin D readings for pregnant women with gestational diabetes in 1st trimester as well as 2nd trimester, P value < 0.001Table (1) shows the mean differences of age, BMI, vitamin D in 1st and 2nd trimester between pregnant women with and without gestational diabetes

Table 1
Possible Association of Vitamin D Level in Pregnancy and Gestational Diabetes

Variable	Groups	Mean ± SD	t	P value
Age	Diabetic Non-Diabetic	25.50± 2.87 25.23± 2.13	0.430	0.668
BMI	Diabetic Non-Diabetic	22.25± 2.02 22.46± 1.21	0.538	0.592
Vitamin D 1st Trimester	Diabetic Non-Diabetic	16.69± 2.44 28.70± 5.16	9.053	< 0.001*
Vitamin D 2ndTrimester	Diabetic Non-Diabetic	17.31± 2.70 29.23± 4.93	9.321	< 0.001*

t: Independent sample t-test to compare between two mean
****p value ≤ 0.05 is statistically significant***

Those thirty -two pregnant with gestational diabetes (71.1%) from forty –five pregnant with low vitamin D level, followed during the rest of gestation eight of them(25%) blood sugar controlled by diet, another nine(28.125%) blood sugar controlled by metformin and diet the rest fifteen(46.875%)necessities insulin for control blood sugar, all of them delivered at 38 weeks a live normal healthy babies thirteen males(40.62%) and nineteen(59.37%) females, twenty-two by elective C/S (68.75%)and ten(31.25%) by induction of labour alive healthy babies received by Paediatrician ,birth weight 3.36 ± 0.42 Kg and admitted for intensive neonatal care unit, neonatal body weight 3.20 ± 0.51Kg for control group which was statistically insignificant P value 0.53 as in Table (2).

Table 2
Gestational Diabetes Group (type of treatment, delivery, outcome)

Control of Gestational Diabetes		No.(T.32)	%
	Diet	8	25%
	Metformin	9	28.125%
	Insulin	15	46.875%
Mode of Delivery	Operative Delivery :	22	68.75%
	Vaginal Delivery:	10	31.25%
Outcome:			
	Male	15	40.62%
	Female	19	59.37%
Birth weight	3.36 +_ 0.42		

DISCUSSION

In this study, vitamin D level was lower in pregnant women with GDM compared with normal pregnant women. In addition, vitamin D deficiency was associated with an increased risk of GDM, which is consistent with results from other studies like Maghopooli,*etal* ,Clifton,*etal* and Zhang *etal* [5,6,7].However, several studies have reported no association

between vitamin D deficiency and GDM like Baker,*etal*and MakgobaM,*etal*[8,9].This difference between different studies could be due to variations in sampling time to measure vitamin D level. Serum vitamin D level increases 50-100% over the non-pregnant state through the second trimester and increases by 100% during the third trimester[13]. Based on the findings that vitamin D is produced by the placenta[14,15] and the fact that an increase in placental mass occurs with gestation, it is reasonable to suggest that placental production of vitamin D is the principal cause for the increase in vitamin D levels in late pregnancy. Vitamin D level was measured at term in another study by GeumJoonCho*,etal*, which showed lower level of vitamin D [16],and other studies reported lower vitamin D levels in pregnant women with GDM at the time of GDM screening (24-29 weeks' gestation)[5,6] which also seen in our study this mean that vitamin D has role in insulin secretion by the pancreas and pregnancy put a burden for its development. A single study by Zhang,*etal,* has demonstrated lower vitamin D levels at 16 weeks' gestation before the diagnosis of GDM [7]. Otherwise, studies by Baker,*etal* and Makgoba,*etal* reported no association measured and assessed vitamin D levels early in pregnancy (11-14 weeks' gestation) [8,9]. Farrant*et al,* studied 559 pregnant women in India and found no association between second trimester 25(OH)D levels and GDM [17].This can be explained that environmental factors play a role. This study showed vitamin D insufficieny is associated with an increased risk of gestational diabetes, and healthy average infants for gestational age which inconsistent with met analysis by Aghajafari F,*etal* [18] this is can be explained that early detection of the risky pregnant and timely diagnosis of gestational diabetes and follow up associated with good neonatal outcome and the possibility of transient morbidity in the baby during the neonatal period, which may require admission to the neonatal unit[19]. Regarding control of diabetes during pregnancy were by diet with insulin in around half of the cases and operative delivery in 68.75% of the diabetic women. Aghajafari F, *etal* found no increase in Caesarean section as mode of delivery [18]. Our study is limited because it's cross-sectional design. We checked vitamin D level in the first trimester before developing gestational diabetes which was low and from the same blood withdrawn for screening for gestational diabetes at (24- 28) weeks of gestation when developing gestational diabetes so unlikely hyperglycaemia is the cause for low vitamin D level. Although further studies will be necessary to show if vitamin D supplementation lessens the development of gestational diabetes so results in good maternal and foetal outcome In conclusion pregnant women with low level of vitamin D more prone to develop gestational diabetes and its complications causing adverse maternal and foetal outcome than healthy pregnant with normal vitamin D level.

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