Sumer Journal for Pure Science (ISSN: 2790-7031)
SJPS 2024 (August), Vol. 3, No. 1, p.p.: 48-55

Studying the Effect of Vitamin D3 and Other Biochemical Parameters in Gestational Diabetes Mellitus with Thyroid Disorder

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Abstract

Diabetes and hypothyroidism are the two most common endocrine opathies during pregnancy. this study aimed to study the effect of vitamin D3 and some biochemical parameters among study groups. The subject of this study divided to (30) GDM with hypothyroidism ,(30) GDM without hypothyroidism , and compared with (30) control, the age of the participants ranged (30-43). There was a highly significant increase at $p<0.01$ of FBS,PPFG, and HOMA-IR among study groups (GDM with hypothyroidism (G1), GDM without hypothyroidism (G2), control (G3), and a significant study f HbA1C and insulin level $p<0.05$ among study groups. There was a significant decrease at $p<0.05$ of FT3,FT4, and a significant increase at $p<0.05$ TSH among study groups. Significant increase vitamin D3 among study groups , there was a significant decresd of Ca between GDM with hypothyroidism vs control and a significant increase of ALP in GDM with and without hypothyroidism vs control . Conclusion: Vitamin D3 deficiency with high levels of sugar and insulin resistance in pregnant diabetic women with hypothyroidism and pregnant diabetic women without hypothyroidism leads to complications of early onset of diabetes mellitus in the pregnant mother The lowering secretion of the thyroid gland, and thus the mother and her child become risk indicator for many other diseases, the first of which is heart disease.

Keywords: Gestational Diabetes Mellitus, Hypothyroidism, Lipid profile, Insulin Resistance, Vitamin D3.

دراسة تأثير نقص فيتامين دي وبعض المتغيرات الكيموحياتية لدى النساء السكري الحوامل و المصابات بخلل الغده الدرقية

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الخلاصة

يعد مرض السكري وقصور الغدة الدرقية من أكثر أمراض الغدد الصماء شيوعًا أثناء الحمل. هدفت هذه الدراسة إلى دراسة تأثير فيتامين دي الثلاثي وبعض المتغيرات البيوكيميائية لدى مجموعات الدراسة. قسمت هذه الدراسه الى (30 من نساء المصابات بسكر الحمل مع قصور الغدة الدرقية ، 30 من نساء المصابات بسكر الحمل بدون قصور الغدة الدرقية و30 من الاصحاء) ،تراوحت الفئة العمرية بين (30-43)سنه. كانت هناك زيادة معنوية عالية عند ($p<0.01$) من سكر الدم الصائم و سكر الدم العشوائي و مقاومه الانسولين بين مجاميع الدراسة نساء المصابات بسكر الحمل مع قصور الغدة الدرقية (المجموعه الاولى) و نساء مصابات بسكر الحمل بدون قصور الغدة الدرقية (المجموعه الثانيه) ووالاصحاء (المجموعه الثالثه) و.زياده معنويه لـ الهيموغلوبين المعسل ومستوى الأنسولين ($p<0.05$)بين مجموعات الدراسة ، كان هناك انخفاض معنوي عند ($p<0.05$) من ثلاثي يود الثايرونين الحر ,رباعي يود الثايرونين الحر ، وزيادة معنوية عند ($p<0.05$) الهرمون المحفز للغده الدرقيه بين مجموعة الدراسة ، وزيادة ملحوظة في فيتامين دي الثلاثي بين مجاميع الدراسة ، انخفاض معنوي لمستوى الكالسيوم بين نساء مصابات بسكر الحمل مع قصور الغدة الدرقية مقابل السيطرة وزيادة كبيرة في الفوسفاتيز القاعدي لدى النساء المصابات بسكر الحمل مع أو بدون قصور الغدة الدرقية مقابل مجموعه الاصحاء الاستنتاج: نقص فيتامين دي الثلاثي مع ارتفاع مستويات السكر ومقاومة الأنسولين لدى النساء الحوامل المصابات بداء السكري و المصابات بقصور الغدة الدرقية والنساء الحوامل المصابات بداء السكري غير المصابات بقصور الغدة الدرقية يؤدي إلى مضاعفات الظهور المبكر لمرض السكري لدى الأم الحامل ، وانخفاض إفراز الغدة الدرقية ، وبالتالي يصبح الأم وطفلها خطرًا مؤشر للعديد من الأمراض الأخرى ، أولها أمراض القلب.

1. Introduction

Gestational diabetes mellitus (GDM), which is classified as a state of hyperglycemia that is diagnosed during pregnancy, is the most common medical problem during pregnancy. Over 15% of pregnancies worldwide have GDM, leading to roughly (18.5) million births annually [1, 2]. GDM also increases the chance of adverse effects such cardiovascular disease, obesity, and impaired glucose metabolism, which lead to type 2 diabetes (T2DM) in both the mother and the kid [3, 4]. It is important to pay more attention to and spread knowledge of the rising frequency of GDM since it has serious economic consequences [5]. The pathogenesis of GDM is still unknown despite extensive research, and the findings to date point to a complicated process of interplay between various genetic, metabolic, and environmental variables [6]. The cornerstones of treating GDM include a proper diet and increased physical exercise, and when these are insufficient, medication, typically insulin treatment, is utilized.

Oral hypoglycemic drugs, mostly metformin and glibenclamide, are also utilized in developing countries [7]. Proper GDM prevention and treatment are necessary to limit the morbidity, complications, and financial effects of GDM that harm society, households, and people [8]. Pregnancy is a typical time to see two of the most prevalent endocrine disorders: thyroid dysfunction and gestational diabetes (GDM). Changes in glucose metabolism and insulin resistance (IR) have been linked to aberrant thyroid function. Thyroid hormones are recognized to be crucial for the metabolism of glucose. As a result, it has been proposed that thyroid dysfunction contributes to the aetiology of GDM. Pregnancy-related abnormal thyroid function may have an impact on the mother's glucose homeostasis. This process involves multiple mechanisms: decrease in the half-life of insulin and a rise in GLUT-2 content on the hepatocyte membrane due to endogenous thyroid hormone synthesisReduced hepatic glucose synthesis, delayed peripheral glucose absorption, and peripheral glucose assimilation are all linked to hypothyroidism. This leads to with decreased insulin resistance and peripheral glucose utilization [9].

Cholecalciferol, another name for vitamin D3, can be broken down to form 25-hydroxyvitamin D3. Sunlight and diet are two ways to supplement vitamin D3. Because vitamin D acts as a hormone and influences many different bodily systems, it serves a number of vital roles in the body. One of the most important global public health problems is vitamin D insufficiency. Around 1 billion people globally are thought to have inadequate amounts of vitamin D in their blood [10]. As a micronutrient, vitamin D is correlated with GDM and several harmful effects for both mothers and babies. According to certain research [11, 12], pregnant women consume much more vitamin D than non-pregnant women do in order to sustain the development of the fetal bones. This can result in general vitamin D insufficiency or even deficiency in women after delivery. Pregnant women with GDM are at a high risk for vitamin D deficiency. Vitamin D should be taken as supplementary to help prevent vitamin D insufficiency during pregnancy [13]. this study aimed to study the effect of vitamin D3 and other clinical l parameters among study groups.

2. Patients and Methods

Sixty voluntaries women with gestational diabetes patients were divided in two groups (GDM with hypothyroidism (G1=30), GDM without hypothyroidism (G2=30), and compared with control (G3=30)), age ranged (30-43)years . This study was done in Al-Alawi Maternity

Hospital, Baghdad, Iraq. Using an automated analyzer, the levels of FBG and the lipid profile (cholesterol, triacylglycerol, HDL, and LDL), calcium (Ca) and Alkaline phosphates (ALP) were determined cobas /Germany . Utilizing (Bio-Rad) (VARIANT), the HbA1c% was calculated. Free software can be downloaded from: http://www.dtu.ox.ac.uk/HOMA.calculater/download.php to calculate HOMA-IR. DRG Company used ELISA Kits to determine insulin. Through the use of minividas kits provided by Bio Meriux-France, the levels of vitamin D3, TSH, FT4, and FT3 were measured.

3. Statistical Analytic

For the data analysis, the SPSS program in version 20.0 was employed. The variance was analyzed in one direction to compare group differences. A 0.05 p-value was considered significant.

4. Results

As shown in Table (1): there was a highly significant increased at $p<0.01$ of FBS,PPFG, and HOMA-IR among study groups (GDM with hypothyroidism (G1), GDM without hypothyroidism (G2), control (G3), and a significant increase of HbA1C and insulin level $p<0.05$ among study groups (GDM with hypothyroidism (G1), GDM without hypothyroidism (G2), control (G3).

Table 1- Clinical study (Mean±SD) among study groups

parameters	GDM with hypothyroidism (G1)	GDM without hypothyroidism (G2)	control (G3)	G1 vs G2	G1 VS G3	G2 VS G3
FBS mg/dL	255.0 ± 25.10	171.11 ±13.0	80.13 ±9.11	0.01	0.01	0.01
PPBS mg/dL	306.21± 15.20	252.5± 15.19	166.22± 8.32	0.01	0.01	0.01
HBA1C%	9.23± 1.42	6.03± 1.33	4.82± 1.30	0.05	0.05	0.05
Insulin ng/mL	17.21± 3.12	14.35± 2.51	9.11± 2.25	0.05	0.05	0.05
HOMA- IR	5.92± 198	3.08± 1.29	1.51± 0.65	0.05	0.01	0.01

NS, no significance differences. *$p<0.05$ is significant.**$p<0.01$is highly statistically significant

In Table(2), there was a significant increase in results at $p<0.05$ of TC, TG and LDL-C between GDM with hypothyroidism vs control and GDM without hypothyroidism vs control.

Table2- Lipid profile levels among study groups

parameters	GDM with hypothyroidism (G1)	GDM without hypothyroidism (G2)	control (G3)	G1 vs G2	G1 VS G3	G2 VS G3
TC mg/dL	273.0± 18.32	221.11.0± 13.41	180.32± 13.25	N S	0.05	0.05
TG mg/dL	180.0± 11.12	160.0± 8.98	120± 8.34	N S	0.05	0.05
HDL-C mg/dL	40.31± 3.19	48.32± 2.44	55.42± 3.25	N S	0.5	N S
LDL-C mg/dL	118.61± 10.62	105± 8.32	77.69± 11.32	N S	0.5	0.05

NS, no significance differences. *p<0.05 is significant.**p<0.01is highly statistically significant.

There was a significant decrease at p<0.05 of FT3,FT4, and a significant increase at p<0.05 TSH among study group(GDM with hypothyroidism (G1), GDM without hypothyroidism (G2), control (G3) in table (3).

Table3- Hormone profile levels among study groups

parameters	GDM without hypothyroidism (G1)	GDM without hypothyroidism (G2)	Control (G3)	G1 vs G2	G1 VS G3	G2 VS G3
FT3 mMole/L	1.26± 1.55	3.12± 1.39	5.68±1.32	0.05	0.05	N S
FT4 mMole/L	3.56± 1.30	9.45± 1.40	11.15±2.23	0.05	0.05	0.05
TSH uU/l	13.20± 5.41	5.61± 1.77	3.44±1.23	0.05	0.01	0.05

NS, no significance differences. *p<0.05 is significant.**p<0.01is highly statistically significant.

There was a significant increase in vitamin D3 among study groups GDM with hypothyroidism (G1), GDM without hypothyroidism (G2), control (G3).While there was a significant decresd of Ca between GDM with hypothyroidism vs control and a significant increase of ALP in GDM with and without hypothyroidism vs control in table (4)

Table 4- Vitamin D3, Ca, and ALP levels among study group

parameters	GDM without hypothyroidism (G1)	GDM without hypothyroidism (G2)	Control (G3)	G1 vs G2	G1 VS G3	G2 VS G3
D3 level ng/mL	14.13±2.33	27.33±3.24	38.81±3.42	0.05	0.01	0.05
Ca mg/dL	7.32±0.07	8.01±0.08	9.11±1.09	N S	0.05	N s
ALP mg/dL	124.1±10.12	106.80±8.42	76.70±8.34	N S	0.05	0.05

NS, no significance differences. *p<0.05 is significant.**p<0.01is highly statistically significant.

5. Discussion

The two endocrinopathies that affect pregnant women most frequently are diabetes and hypothyroidism. Both diseases have been linked to a number of pregnancy issues that can damage the mother and the newborn [14]. Insulin resistance (IR) and variations in glucose metabolism are both related to abnormalities in thyroid function. Our research produced a number of intriguing findings. First, we found that the risk of acquiring SGH was raised by both hereditary thyroid pathology and hereditary diabetes mellitus [9]. These findings suggest potential genetic overlap between thyroid disease and problems of glucose metabolism. These hypotheses were made in the prospective population-based cohort research in Rotterdam, which found that higher TSH levels are linked to a higher chance of developing thyroid problems and diabetes [15]. Pregnancy causes physiological changes in fat metabolism that boost the creation of lipid profiles. The synthesis of lipids in the liver may be increased by elevated estrogen levels and insulin resistance in pregnant women [16].

These modifications in fat metabolism point to a physiological change in pregnant women's bodies that prioritizes lipid metabolism over glucose metabolism. Pregnant women use lipids as a source of energy in order to preserve glucose for the growth and development of the fetus. Bile acids, steroid hormones, and embryonic cell membranes can all be produced thanks to lipids [17]. Early in pregnancy, there is an increase in blood lipid and lipid synthesis, which raises the blood levels of free fatty acids, particularly TG. Conversely, a rise in blood levels of free fatty acids can result in insulin resistance. Patients with type 2 diabetes also have aberrant lipid profile changes [18]. Negative pregnancy outcomes, such as miscarriage, premature birth, and gestational diabetes mellitus (GDM), have been linked to thyroid autoimmunity (TAI) and (subclinical) hypothyroidism (SCH). Two routes have been identified as connecting TAI and GDM. The cause of that heterogeneity was not stated, although it could be related to various definitions of thyroid dysfunction, modifications to the GDM diagnosis criteria (both prior to and following the International Association of Diabetes and Pregnancy Study Groups' criteria), or other factors [19].

When the predictive value of TSH was evaluated as a continuous variable without consideration for a pre-established normality threshold, different results were obtained. The majority of authors were unable to establish a direct, more relevant association between TSH readings and GDM risk, even after controlling for potential confounders [20]. However, other investigations demonstrated a direct, significant relationship between higher TSH values and GDM risk. Recent research has shown that even with a normal TSH, minute variations in circulating FT3 and FT4 may be associated with a higher prevalence of GDM. The link between low FT4 levels and high FT3 and, subsequently, a higher chance of developing GDM in late gestation, is the most frequently seen observation [21]. A recent meta-analysis further supported the negative correlation between FT4 levels and the risk of GDM. According to certain research, women with GDM have higher fasting glucose levels when the FT3 and FT3/FT4 ratio are present [22]. In healthy pregnant women without GDM, a lower FT4 may be associated with a worse metabolic profile, including an increase in BMI, OGTT glucose, HbA1c, fasting insulin, HOMA-IR, triglycerides, and placental weight [23].

This study demonstrates that vitamin D therapy may help decrease fasting plasma glucose and improve insulin resistance in pregnant women, despite a recent meta-analysis pointing out how the current randomized controlled trials (RCTs) are all of insufficient quality. Similar to this, it is currently not apparent how hypovitaminosis D or thyroid autoimmunity during pregnancy connect to one another [24]. Even though multiple studies show that non-pregnant

individuals with autoimmune thyroid disease had lower serum vitamin D levels than healthy controls, very few retrospective investigations have looked at the association between thyroid function and vitamin D deficiency during pregnancy [25, 26]. According to the findings of our study, women receiving vitamin D in the first trimester of their pregnancies had lower GDM levels than those receiving a placebo, and this difference was statistically significant [27]. Women with lower levels are 1.48 times more likely to develop gestational diabetes than those who took vitamin D ($P = 0.04$), according to research on low vitamin D levels in the first trimester and their association with an elevated risk of the condition.

ALP was also higher in study participants than in the other study groups. Alkaline phosphatase levels in diabetes have been observed in a small number of studies and have been linked to bone damage. In a case of gestational diabetes and hypertension complicating pregnancy, Heazell et al. (2006) described an extremely high elevation of the bone-specific isoenzyme of alkaline phosphatase during labor that resulted in an elevation of total serum alkaline phosphatase that wasn't consistent with placental origin [28]. In our investigation, there was no statistically significant difference between the two groups' serum ionized calcium levels, which were both within the normal range. In our study, females with GDM exhibited lower 25(OH)D levels, higher ALP levels, and more adiposity than participants in the control group. Although serum calcium levels were similar among research groups [29].

6. Conclusion

Vitamin D3 deficiency with high levels of sugar and insulin resistance in pregnant diabetic women with hypothyroidism and pregnant diabetic women without hypothyroidism leads to complications of early onset of diabetes mellitus in the pregnant mother. The lowering secretion of the thyroid gland, and thus the mother and her child become a risk indicator for many other diseases, the first of which is heart disease.

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