The relationship of Taq I(rs731236) polymorphism in vitamin D receptor gene besides gestational diabetes mellitus in Iraqi prenatal women

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Abstract
Gestational diabetes is a temporary rising of blood sugar levels in a pregnant female with no history of diabetes before gestational, it caused by not enough insulin in the locale of insulin resistance. Vitamin D receptor (VDR) gene variants play a critical role in some endocrinal disorders. The determination of this study is to observe the association of Taq I (rs731236) SNP in the VDR with gestational diabetes mellitus. Fifty females with gestational diabetes and fifty apparently healthy controls female determined their genotype by using Tag-man genotyping assay. The results show no significant variances in the frequency percentage of TT, TC and CC genotypes between the patients and apparently healthy women (22% vs 26%, 42%vs44% and 36% vs 30%, respectively). The frequency of the T allele was 0.86 inpatients and 0.96 in control, while the rate of recurrence of the C allele was 1.14 inpatients and 1.16 in control. In conclusion, our data suggest that a not significant association between VDR TaqI (rs731236) gene polymorphisms besides the GDM at the studied loci. Therefore, involves further trainings as a possible genetic danger marker for other gene polymorphism.

Keywords: Polymorphism, Gestational diabetes mellitus (GDM), Vitamin D receptor (VDR) gene

How to cite this article: Abdulkhaliq RJ, Farhan SH, Al Khateeb HM (2020): The relationship of Taq I(rs731236) polymorphism in vitamin D receptor gene besides gestational diabetes mellitus in Iraqi prenatal women, Ann Trop Med & Public Health; 23(S18): SP231833. DOI: http://doi.org/10.36295/ASRO.2020.231833

Introduction
Gestational diabetes mellitus (GDM) is a predominant and possibly severe disorder that might lead to adversative properties in both neonates and mothers (WHO, 1999). It is connected through preeclampsia, developed macrosomia and cesarean rates (Suohonem et al., 2000; Metzger et al., 2002). The treatment and detection of this condition decrease the dangers for the babies as well as for the mothers (Falavigna et al., 2012; Hartling et al., 2013).

Although the threats of difficulties in the occurrence of Gestational diabetes mellitus are well recognized, there is significant controversy concerning its diagnosis (Waugh. 2010). Gestational Diabetes mellitus can be apointer of increased danger of type 2 DM in the post-delivery historical. Gestation is a state-run of insulin resistance. These Hormones concealedvia the placenta, as well as progesterone, corticotrophin-releasing hormone, growth hormone, and placental lactogenic, all action to raise insulin resistance in the mothers, helping to make sure the acceptable source of nutrients toward the evolving fetus (Butte et al., 2000). Everywhere the mother has an inadequate pancreatic purpose to survive through this cumulative insulin resistance in diabetes follows.

Vitamin D3isplayavitalpart in a metabolism including calcium-phosphate homeostasis and directive of insulin secretion by the pancreas (Pittas et al., 2007). Around studies found that deficiency of vitamin D3 could cause insulin resistance (Wehr et al., 2009). Vitamin D3 is the central ligand for vitamin D3 receptor [VDR] which remains a member of the nuclear receptor family of transcriptional factors (Bollay, 2007). The mechanism of its function is a corresponding work with a retinoid X receptor by making a heterodimer distributed through the tissue and when vitamin D3 binds with the complex causing transcription to many genes (Haussler et al., 2011).

In current years, numerous polymorphisms, for example (FokI & BsmI), require been designated in the VDR genes that stay capable to modify the action of VDR proteins (Filus et al., 2008). Around of the added polymorphisms in the VDR gene recognizedvia allelic deviation in constraint enzyme locations are EcoRV, Tru9I,Apal, and TaqI. Wholly these are situated between exons 9 and 8excepting that FokI in exon 2. FokI
polymorphism has remained revealed toward have practical character in transcriptional stimulation of VDR gene (Whitfeld et al., 2001). The goal of this study existed to examine whether the genotype besides allele frequency of rs731236 on the VDR gene are related through the risk of GMD.

Material and methods
The present scholarship included one hundred pregnant women fifty women (n=50) with Gestational diabetes mellitus during the second-trimester suffering from hyperglycemia were discussed to Obstetrics also Gynecology Department of AL –Elwiya Education Hospital. Excluded standards patients were also fifty women (n=50) without infection and without Gestational Diabetes Mellitus from self-administered questionnaires was collected. Each patient was examined physically by a specialist and all information related to this research was obtained. The fasting serum glucose ranged between 90 and 380 mg/dl. The years of these patients reached between 30-38 ages throughout the period starting from January to June through 2019.

Samples collection
venous blood was draw Five milliliter from each patients then reserved at the period of diagnose by means of sterile reusable syringes, (three ml) of blood located nowin a white cylinder per gel mass and left-hand to position for one hour at room heat for mass creation, for serum assembly, the tube centrifuged designed for 20 minutes at 3500 revol per minute (rpm). At that time the serum extracted by expending a Pasteur pipette besides distributed into a sterilized Eppendorf tube thenput in storage at -20 C° till used. The concrete work was complete according to the directions of constructors of HbA1C (Crystal Chem USA) kit and Blood Sugar Test Kit. While two ml of blood testers were transported to di-potassium ethylene diamine tetra acet acid (K2EDTA) tube for the extraction of DNA. The DNA was extracted by using a kit (Quick-gDNA ™ Blood MiniPrep, Zymo research /USA), Nanodrop was used to assessment the purity then the concentration for DNA testers. Genotyping analysis was performed using Real-Time PCR, custom TaqMan fluorescent oligonucleotide probes and primers for examined SNP rs731236 in exon9 (T>C) were prepared and stored lyophilized at 20°C (ordered from integrated DNA technologies /USA). Taq man SNP genotyping analyzeby using real-time thermocycler allowing to the protocol optional by the manufacturer. There were two study groups in the current study, the first group of patients included: pregnant females in the second trimester with Gestational diabetes mellitus. The second was the control group: pregnant women also in the second trimester without Gestational Diabetes Mellitus.

Statistical examination
The Statistical Analysis System- SAS in 2012 database was used to disturb altered features in study limitations. The slightest important difference -F test (ANOVA) was used to a significant association between rates in this study. Chi-square examcastoff to insignificant associate genotype for separately of sample, (Odds ratio) and sureness intervals existed used to measure the risk or advantageous outcome of studied factors among groups (Elliott and Woodward, 2007).

Results
The total number of women was 100 (50 %) were normal pregnancy and (50 %) had gestational diabetes mellitus. The mean of age patients in the Group of the patient was not significantly (p>0.05) higher than the corresponding mean of control. The duration of pregnant (in the second trimester) in each group was approximately similar. While the Fasting blood glucose (mg/dl) amongst groups of the existent study was with the maximum level in a group of patients with gestational diabetes compared with the control groups without gestational Diabetes with high significance between different groups (p<0.001). The value for HbA1c in group of patient was (6.38 ± 0.22) mmol/mol, in control group was (1.79 ± 0.13) mmol/mol. The high level found in the group of gestational Diabetes compared to the control collection in pregnant healthy. There existed a significant variation at p < 0.001. As revealed in the table (1).

![Table (1): The characteristics of the study, the serum level of serum glucose and Hb1c concentration in the study groups.](http://doi.org/10.36295/ASRO.2020.231833)
The genotype results show that the TT, TC, and CC genotypes frequency percentage have non-significant difference noted between the control and patients, the frequency of T allele was 0.86 inpatients and 0.96 in control, while the frequency of C allele was 1.14 inpatients and 1.16 in control as exposed in table (2).

Table (2): The genotype results in the study groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Control</th>
<th>Aborted</th>
<th>( \chi^2 )</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>TT</td>
<td>13</td>
<td>26%</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>TC</td>
<td>22</td>
<td>44%</td>
<td>21</td>
<td>42%</td>
</tr>
<tr>
<td>CC</td>
<td>15</td>
<td>30%</td>
<td>18</td>
<td>36%</td>
</tr>
</tbody>
</table>

Allele frequency

<table>
<thead>
<tr>
<th>Allele</th>
<th>Frequency in Control</th>
<th>Frequency in Aborted</th>
<th>( \chi^2 )</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>0.96</td>
<td>0.86</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C</td>
<td>1.16</td>
<td>1.14</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

NS = non-significant

Discussion

The pathophysiology of gestational Diabetes mellitus is altered after diabetes mellitus (DM) in the common people. Nevertheless, gestational Diabetes mellitus may be an pointer of improved danger of non-insulin-dependent type 2 Diabetes M in the post-delivery period. Gestation is a state-run to resistance of insulin. Hormones secreted through the placenta, as well as progesterone, corticotrophin-releasing hormone, growth hormone, and placental lactogenic, totally doing to raise insulin resistance in the pregnant mothers, helping to certify the acceptable source of nutrients toward the evolving fetus [Butte et al., 2000]. Everywhere the mother ensures an inadequate pancreatic purpose to survive with this cumulative insulin confrontation in diabetes follows (Abdulkhaliq et al., 2019).

In difference, in type 2 diabetes mellitus, accumulative insulin resistance visibly is not facilitated through a placenta however rather via a complex relationship among genetic dispositions, reduced physical action, decrease vitamin D3, and obesity. Abdominal obese is metabolically dynamic, making hormones that stimulate insulin resistance, Tumor necrosis factor-alpha, Leptin is between the numerous adipocytes occupied in insulin resistance then following the change of type 2 diabetes mellitus [Li et al., 2009; Steppan et al., 2001]. Adipose cells, additionally, are understood to activate chronic infection, which in opportunity addstoward the improvement of insulin confrontation [Vandanmagsar et al., 2011].

This study revealed the relationship among TaqI in VDR gene polymorphism besides GDM, the result showed here was no significant alteration in genotype spreading GDM with control. TaqI established restriction piece measurement polymorphism is sited at the 3' finale of the VDR gene. The purpose of the TaqI- particularly per variable polymorphism is uncertain (Uitterlinden, 2004). It has been linked toward breast cancer danger (Guy, 2004), colorectal cancer (Yaylim-Eraltan, 2007), prostate cancer development (Xu, 2003), diabetes (Motohashi, 2003), PCOS (Mahmoudi, 2009; Ranjzad et al., 2011; Lerchbaum and Obermayer-Pietsch, 2012).

The study’s consequences agree with schoolwork on Turkish women with GDM (Apaydin et al., 2019, Dilmec F. et al., 2008) also a study on Polish population shows VDR gene polymorphisms did not constitute a risk factor for this case (Cyganek K et al., 2006). Other studied have detected a correlation between TaqI gene polymorphism with GDM. Mohammadnejad et al., (2012) described that the frequencies of VDR gene polymorphism increased in patients with GDM. Wang et al., (2012) found that BsmI polymorphism was linked with type I while TaqI associated with type II. In conclusion, the study doesn’t constitute TaqI polymorphism a pathological genetic marker for gestational diabetes and recommends screening more SNPs of VDR gene that may be related to gestational diabetes and non-agree through studies (Abdulkhaliq et al., 2019; Roua et al., 2019).

References


