RENAL STIFFNESS ON PATIENTS WITH GESTATIONAL DIABETES

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ABSTRACT

Introduction: Gestational diabetes is defined as glucose intolerance first recognized in pregnancy. Oral glucose tolerance testing is the cornerstone in diagnosing gestational diabetes. In this study, we aimed to find a new method of diagnosis in addition to conventional diagnosed by 75 gr oral glucose tolerance testing.

Material and methods: 121 pregnant woman were included part in this study, forming two groups as gestational diabetic patients (51 patients) and control group (70 pregnant woman). Both kidneys are evaluated with B Mode Ultrasound and Colour Doppler Ultrasound mode by measuring resistive index for depiction of other renal pathologies. Stiffness of renal tissue determined by Acoustic Radiation Force Impulse (ARFI) technology utilized by two blinded radiology specialists.

Results: We were not able to find any correlation between gestational diabetes mellitus and resistivity index measurements (p>0.05). But a correlation between second hour glucose levels in oral glucose tolerance test and bilateral renal stiffness was found (p<0.05).

Conclusion: ARFI ultrasound may be a non-invasive technique in determining the course of the disease.

Keywords: Renal Stiffness, Gestational Diabetes, Acoustic Radiation Force Imaging, Ultrasound.

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Introduction

Diabetes is the most common complication of pregnancy. Depending on the time of diagnosis women with diabetes can be classified as pre-gestational or gestational diabetes. Gestational diabetes mellitus (GDM) is defined as glucose intolerance beginning during pregnancy with no known previous history⁽¹⁾. Prevalence of GDM is around 5-10%, with an increase about 40% between 1989 and 2004⁽²⁾.

Oral glucose tolerance testing (OGTT) is one of the most recommended ways of testing insulin tolerance of pregnant patient, who has not been diagnosed as diabetic prior to pregnancy, by American College of Obstetrics and Gynecology (ACOG) and other associations such as American Diabetes Association (ADA)^(3,4). Testing can be done either with one step testing approach as 75 gr OGTT testing or two step testing approach as initial 50 gr OGTT testing followed by a 100 gr OGTT if needed.

ARFI is an ultrasonography based technique of propagation of acoustic waves in attenuating tissues to establish values of elasticity. With increasing acoustic frequencies, the tissue does not respond fast enough to the transitions between positive and negative pressures and with this technique we have more valuable information about the stiffness of tissue applied to.

Our aim is to find correlation between renal elasticity and GDM screening results from 75 gr OGTT, to best of our knowledge this will be the first study done with 75 gr testing, to identify a different approach on GDM testing.

Material and methods: This was a prospective single blinded case-control study done on University Education and Research Hospital. On their 24-28th weeks of pregnancy, patients were asked to have an ARFI testing performed on their bilateral renal tissues. Patients with multiple pregnancies, patients with other systematic disorders such as pre-gestational diabetes, hypertension, rheumatological diseases are excluded from study. After approval from the Institutional Ethics Committee, and gathering written inform consent from volunteers, 121 pregnant woman were agreed to participate and consented appropriately.

GDM testing was done with 75 gr oral glucose solution. A diagnosis of GDM was established when any of the following results were obtained; fasting ≥92mg/dl (5.1mmol/L), 1 hour glucose level ≥180mg/dl (10.0mmol/L), 2 hour glucose level ≥153mg/dl (8.5mmol/L). Patients diagnosed GDM were initially and if possible treated only with nutritional therapy. If nutritional therapy was not effective or adequate for achieving the target glucose levels (fasting ≤95mg/dl, 1 hour ≤140mg/dl, 2 hour ≤120mg/dl) insulin therapy initiated with a consultation to endocrinologist specialist.

Two blinded radiologist, who are experienced more than ten years in field, participate in study doing the ARFI examination on the day of GDM testing. Radiologists were completely unaware of glucose testing result as sonographic examinations were performed in the second hour interval of OGTT process. The patients and control subjects underwent an ARFI examination using a commercial scanner (Siemens Acuson S3000™ 4 MHz (6C1) probe, Siemens Medical Solutions USA, Inc., Mountain View, CA, USA), which was performed by an US physician with three months of experience in ARFI elastography. Convex probe were used for colored doppler ultrasonography (CDU), ARFI and resistivity index (RI) measurements The patients were examined in the left and right lateral decubitus position with the left and right arm elevated above the head. Scanning was performed with minimal scanning pressure applied by the operator; the patients were asked to stop breathing to minimize motion. The operator positioned the probe over the following region of interest (ROI) box was used to acquire standard 1cm2 areas for ARFI measurement, on renal three regions (superior, middle, inferior) (Figure:1). Special attention was given for not having any vessel formation inside of ROI during the measurement. Mean of three measurements were calculated and used for statistical purposes.

Statistical Package for Social Sciences (SPSS) v23.0 (IBM co. Chicago IL) was used for statistical analyses. Mann-Whitney U test, independent sample t test and Pearson correlation tests were used where appropriate. P value <0.05 considered statistically significant.



Figure 1: Renal ARFI measurement values in patients with gestational diabetes.

Results

Patients were divided into two groups. Patients with GDM referred as study group with 51 patients enrolled whereas patients with normal OGTT values referred as control group with 70 pregnant woman enrolled. The incidence of GDM in the whole group was found to be 23%. Mean age of study group was 32.60 and mean age of control group was 29.32 with a significant difference from study group (p<.05). Mean of characteristic properties were outlined in table 1 (Table 1).

Renal stiffness and renal resistivity index results of patients depending on their groups are listed at second hour in table 2. Mean renal stiffness for right and left kidney on study group and control group are 3.43 ± 0.88 , 2.86 ± 0.72 (right) and 3.52 ± 1.11 , 2.45 ± 0.92 (left) respectively. Significant difference were found between these two groups for both right and left kidneys (p=.003, p=.002) for the measurements of ARFI at second hours. Mean kidney tissue resistivity index values for right and left sides for study group and control group are $0.65 \pm$

0.06, 0.66 ± 0.05 (right) and 0.69 ± 0.04 , 0.67 ± 0.05 (left) respectively also with resistivity index there is no significant difference between these two values (p=.535, p=.412) at second hours.

When OGTT results are analyzed one by one for every hour and fasting values, there is found to be significant correlation between blood glucose level on second hour and bilateral kidney stiffness (p<0,05) (Table 2).

	Study Group n: 51	Control Group n:70	p value
Age	32.60 ± 4.71	29.32 ± 4.24	.013
Birth Weight (gr)	3350 ± 317	3169 ± 436	.143
Gestational Weeks at Birth	37.40 ± .828	38.06 ± 1.69	.125
Gravidity	1.38 ± .64	1.47 ± .60	.632
Parity	.27 ± .46	.28 ± .53	.931
Gestational Weeks at ARFI measurement	24.80 ± .775	24.88 ± 1.58	.852

Table 1: Comparing means of pregnancy relevant information for patient groups.

	Study Group n: 51	Control Group n:70	p value
Right Kidney Stiffness (m/sn)	3.43 ± 0.88	2.86 ± 0.72	0.003
Left Kidney Stiffness (m/sn)	3.52 ± 1.11	2.45 ± 0.92	0.002
Right Kidney Resistivity Index (m/sn)	0.65 ± 0.06	0.66 ± 0.05	0.535
Left Kidney Resistivity Index (m/sn)	0.69 ± 0.04	0.67 ± 0.05	0.412

Table 2: Mean renal stiffness values of both kidneys and resistivity index for both groups (second hour).

Discussion

The high prevalence of 24% for GDM is quite alarming considering the high risk for adverse pregnancy outcomes associated with diabetes in pregnancy^(5,6). A recent study from the geographically similar area found an incidence of 29.9% among pregnant population and they expressed the relation between higher prevalence of GDM with increasing age⁽⁷⁾. Our findings showed a significant age difference between patients with GDM and without, with an incidence of 23% in a relatively small population.

ARFI technology has been used for several years to evaluate the liver, thyroid, breast and renal tissues.

This technology has been proved to be safe for obstetric usage⁽⁸⁾. There are some reports presenting the use of ARFI in pregnant patient population with pre-eclampsia.

Abnormal glucose tolerance and collagen disorders are known causes of inflammatory changes in placenta^(9,10). Renal stiffness, which correlates well with renal fibrosis measured by ARFI elastography is a promising alternative imaging technology to biopsy⁽¹¹⁻¹⁴⁾. To our knowledge, there is no such study in patients with GDM so far.

Major limitations of our study is not having histopathological examination done for renal tissues and the number of patients is less than of the control group. Although in our study a correlation between second hour glucose level in OGTT and renal elasticity is found, it is inadequate to make a general statement. The renal stiffness is increasing on diabetes. ARFI ultrasound may be a non-invasive technique in determining the course of the disease. Future studies with a more patients are needed to assess to usage of ARFI in GDM patients for renal stiffness evaluation.

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