First Trimester Placental Volume and Vascular Indices by 3D Ultrasonography and 3D Power Doppler in Pregestational Diabetic and Non-Diabetic Pregnant Patients

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ABSTRACT

Background: 3D power Doppler ultrasonography enables the quantitative analysis of the region observed through vascular indices as VI (vascularization index), FI (flow index) and VFI (vascularization flow index), which show the quantity of vessels, the local blood flow and their combination and placental volume. These indices can be calculated using VOCAL program. Aim of the Study: This study aimed at comparing placental volume and vascular indices using 3D ultrasonography and 3D power Doppler in pregestational diabetic and non-diabetic pregnant women at the first trimester (11th week and 13th week). Patients and Methods: This current study was conducted at Antenatal care Clinic in cooperation with "the feto-maternal Unit for ultrasound assessment", Ain-Shams University Maternity Hospital during the period between November 2015 and April 2017, on 46 women at the eleventh 11th week and thirteen 13th week of gestation. They were divided into two groups: Group (A) included 23 women with pregestational diabetes mellitus and group (B) included 23 non-diabetic pregnant women as a control group after respecting certain inclusion and exclusion criteria. Results: There was no statistically significant difference between pregestational diabetic and non-diabetic group as regard placental volume and vascular indices (VI, FI and VFI). Conclusion: There was no statistically significant difference as regard placental volume and vascular indices (FI, VI and VFI) in pregestational diabetic compared to non-diabetic pregnant patients at the first trimester of pregnancy especially with good glycemic control but changes may be present with poor glycaemic control. Recommendations: Further studies are recommend as regard evaluating placental volume and vascular indices (FI, VI and VFI) in pregestational diabetic at the second and the third trimester of pregnancy giving more time for the pathological effect of diabetes mellitus to appear. Keywords: first trimester placental volume, vascular indices, 3D ultrasonography, 3D power Doppler.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia and caused by defects in insulin secretion and/or insulin action (1). Diabetes mellitus is a major public health problem worldwide. Its prevalence has been used as one of the parameters in the assessment of the quality of health care by the world health organizations (WHO)(2). In 1842, an Austrian professor of mathematics and geometry Dr. Christian John Doppler first described in detail the effect that now bears the name. Satomura was the first describing clinical application of Doppler ultrasound technology in 1959 (3). The placenta is an essential link between the mother and the developing fetus, and histological studies have evidenced characteristic changes in the placental vascular structures of diabetic mothers(4). The umbilical artery was the first vessel studied by obstetric Doppler examination. Flow velocity waveforms from the umbilical artery represent the downstream or placental resistance to flow. Umbilical artery resistance decreases progressively throughout gestation, reflecting the increase and dilution in villous vascularization(5). Doppler US offers a unique non-invasive technology for investigating the circulatory system. Doppler ultrasound velocimetry has been extensively used to investigate fetal, feto-placental and utero-placental circulation. There is ample evidence associating abnormal Doppler findings with complication of pregnancy and an adverse perinatal outcome (6). The advent of three-dimensional (3D) power Doppler ultrasound has begun a new era in tissue and organ vascularization research. Therefore, we can calculate vascular indices using the specially designed VOCAL TM software(7). Doppler examinations of intra-placental blood circulation appear to be an efficient method for diagnosing and managing pregnancies complicated by fetal intrauterine growth restriction (IUGR), because the changes in maternal Doppler findings (i.e., uterine artery) and in fetal Doppler (i.e., umbilical artery) are secondary to the changes in the placental vascular tree(8).

Objective and non-invasive quantification of vascularization of a given tissue volume holds much promise, particularly because this method has proved to be highly reproducible between observers (thereby overcoming one of the main limitations of conventional Doppler ultrasound)(9).
Recent advances in ultrasonography was by combining 3D ultrasonography with power Doppler makes it possible to quantify Doppler signals in volumes obtained by 3D scanning and thus allows to assess the whole placental circulation, with this technique, it is possible to impair placental vascularization in different clinical conditions (16).

Rizzo et al. (11) investigated the placental volume and vascular indices using 3D ultrasonography & 3D power Doppler in pregestational diabetic mothers during the first trimester and concluded that placental vascular indices (VI, FI and VFI) are increased and are more evident in pregnancies with poor first trimester glycemic control. 3D ultrasound was patented by von Ramm and Stephen Smith (12) at Duke University in 1987. 3D ultrasound has the potential to provide improved visualization of the fetal anatomic morphology compared to the conventional 2D imaging. 3D ultrasound and power Doppler give a more objective and more detailed method of evaluating placental volume and its vascular network. The first placental volumes acquired via sonography were conducted by Brinkley et al. (13).

The Doppler parameters derived from 3D interrogation of the placenta are different, include the Vascularization index (VI) that characterizes vessels’ density, the flow index (FI) that characterizes blood flow intensity and the vascularization flow index (VFI) that evaluate simultaneously the vessels and perfusion (14).

The 3D power Doppler allows the assessment of the architecture of the placental tree (15). Utero placental and feto placental perfusion have been extensively studied throughout gestation and after delivery. Direct investigation of the perfusion of in-vivo placentae has become possible using three-dimensional (3D) power Doppler sonography (16).

3D power Doppler does not take long to consider the possibility of a quantitative vascular analysis of the region observed. This was analyzed through the vascular indices as VI (vascularization index), FI (flow index) and VFI (vascularization flow index), which show the quantity of vessels, the local blood flow and their combination (17).

The pre-determined area was formed of small pieces of volume named voxels. From then on, they were divided into gray voxels, pieces that compose the non colored part of the three-dimensional area with black and white tones, and colored voxels, formed by the colored part of this section, both measured in a scale of 0–100 (18). Nowadays, all these indices can be calculated in a pre-determined area, through a program that is followed in a series of three-dimensional ultrasound machines named VOCAL (virtual organ computer-aided analysis) (16).

The vascularization of the placenta was evaluated through these indices at specific locations, because the research of the placenta, at advanced gestational ages (first trimester excluded), is impossible due to their dimensions (19). Three-dimensional (3D) ultrasonography allows examiners to move from a 3D mental reconstruction of two-dimensional (2D) images to actual 3D visualization of anatomical structures (20).

Thus, sonologists are no longer constrained by limitations of static 2D images to establish a diagnosis, but can, instead, interact with volume data sets to examine anatomical structures of interest in planes of section other than the original acquisition planes (21).

Color and power Doppler techniques permit direct visualization of placental vascularity, allowing assessment of both the utero placental and feto placental circulations. Poor vascularity secondary to uterine scarring or large fibroids can lead to atrophy of the chorionic villi and corresponding compromise of fetal circulation (22).

AIM OF THE WORK

To compare placental volume and vascular indices (VI, FI and VFI) using 3D Ultrasonography and 3D Power Doppler in pregestational diabetic and non-diabetic pregnant patients at the first trimester (the eleventh 11th week and the thirteenth 13th week).

Patients and Methods

This case - control study was carried out at the Antenatal care Clinic in cooperation with "the feto-maternal Unit for ultrasound assessment", Ain-Shams University Maternity Hospital during the period between November 2015 and April 2017, on 46 women at the eleventh (11th) week and thirteenth (13th) week of gestation, divided into two groups:

- group (A) included 23 women with pregestational diabetes mellitus and group (B) included 23 non-diabetic pregnant women as a control group.

The study protocol and patient informed consent were declared for ethical and research approval by the Council of Obstetrics and Gynaecology Department, Ain Shams University.

Sample size justification

Sample Size was calculated using Power and Sample size calculation program at a confidence level of 95% and a power of 80% and based on a previous study carried out by Khaskhelli et al. (23), which found that placental size in control subjects was 499.6 cm³ while it was 975.0 cm³ in diabetic mothers, and the
difference between these two was -475.4±23.46
and accordingly we needed to study 23 patients
with Pre-gestational diabetes and 23 control
subjects (non-diabetic pregnant women) to be able
to reject the null hypothesis.

**Inclusion criteria**
- Singleton pregnancies.
- Confirmed pregestational diabetes mellitus by
  history and laboratory investigation (FBS - 2h
  PPBS - HbA1C).
- Absence of fetal structural or chromosomal
  anomalies.

**Exclusion criteria**
- Multifetal pregnancies.
- Women with other medical conditions eg.
  (chronic heart disease, chronic hypertension,
  chronic renal insufficiency and any other
  chronic illnesses) were excluded from the
  study.

All pregnant women included in the study underwent the following:

**History taking**

At the initial visit, a detailed history was
obtained including personal history and past
history concerning:
- 1st day of Reliable last Menstrual Period to
calculate gestational age according to
Naegle’s rule.
- Family history of DM.
- Any history suggestive of pregestational
diabetes as abortion, repeated, unexplained
IUFD or fetal macrosomia.
- History of chronic heart diseases, chronic
  hypertension, thyroid disease, chronic renal in
  sufficiency, hepatic disease, thrombophilia
  and systemic lupus erythematosus.

**Clinical examination**

Careful general clinical examination including
body weight, blood pressure, lower limb
edema, maternal body mass index and abdominal
examination.

**Laboratory investigations**

Including FBS, 2hPPBS, HbA1C, CBC, liver
(ALT-AST and albumin) and renal (s.urea
and creatinine) function tests and urine analysis.

**Specific investigations**

At the first trimester of gestation (11th
week and 13th week), we calculated placental
volume by 3D ultrasonography and calculated
vascularization index, flow index and
vascularization flow index by 3D power Doppler,
the machine used in the study was
VolusonE6BT12(general electric) with convex
probe-RAB -6 D curved array.

A Voluson E6BT12 ultrasound machine
equipped with a 4-MHz to 8-MHz trans-
abdominal transducer was used for 3D volume
scanning during a period of maternal apnea and
fetal rest. The entire view of the placenta was
identified by two-dimensional ultrasound, and the
volume box was adjusted to include the entire
placenta. The angle of volume acquisition varied
from 45–90° according to placental size. The
volume acquisition was obtained in ‘maximum’
quality and its duration was between 10 and 15
second. For posteriorly and laterally located
placentas, a slight lateral inclination of the
transducer was performed to acquire the entire
placenta. The same pre-established instrument
settings were used in all the cases (power 96%;
frequency low; quality normal, density 6,
ensemble 16; balance 150; filter 2; smooth 3/5;
pulse repetition frequency 0.9 kHz, gain _0.2). All
placental volumes were acquired, which were
aware of diabetic condition of the mother but
blind of the metabolic control condition.
Successful recordings of placental volume were
obtained in all the cases.

Placental volumes were stored and later analyzed
off-line by using the Virtual Organ Computer-
aided Analysis (VOCAL) of 3D view software
with a 15° rotation step. Vascularization index
(VI), flow index (FI), and velocity flow index
(VFI) were calculated.

**Statistical analysis**

- Qualitative data was presented as numbers and
  percentages while quantitative data was
  presented as Mean and standard deviation.
- Comparison between the means of two
  independent groups was performed using
  independent t-test.
- Comparison between numbers and percentages
  was performed using chi-square test, if 25% of
  the cells or more expected frequency less than
  5 Fisher Exact test was used.
- Differences were considered to be statistically
  significant if p-value <0.05.
- Statistical analysis was undertaken using
  SPSS(statistical program for social science).

**RESULTS**

The current study was conducted on 46
women (23 pregestational diabetic and 23 non-
diabetic) attending the antenatal care clinic in
cooperation with the "feto-maternal unit for
ultrasound assessment" Ain-Shams University
Maternity hospital during the period between
November (2015) and April (2017) to calculate
placental volume and vascular indices at the first
trimester of gestation (the 11th week and 13th week)
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by 3D power Doppler ultrasonography after respecting certain inclusion and exclusion criteria.

**Table (1):** Comparison between Diabetic and Non-Diabetic women as regard VI at the eleventh 11th week.

<table>
<thead>
<tr>
<th>U/S Indices (VI)</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>12.1359</td>
<td>2.62390</td>
<td>-1.494</td>
<td>0.142</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>17.6987</td>
<td>2.62361</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VI= Vascularization index

\( p>0.05 \) ➔ Non-Significant

\( p<0.05 \) ➔ Significant

\( p<0.001 \) ➔ Highly Significant

Table (1) shows that the mean VI at the eleventh 11th week in Diabetic group (12.1359 ± 12.62390) was higher than non-diabetic group(17.6987 ± 12.62361); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard VI at the eleventh 11th week (\( P>0.05 \)).

**Table (2):** Comparison between Diabetic and Non-Diabetic women as regard FI at the eleventh 11th week.

<table>
<thead>
<tr>
<th>U/S Indices (FI)</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>34.5942</td>
<td>9.65622</td>
<td>-2.004</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>40.7201</td>
<td>11.03053</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FI= Flow index

\( p>0.05 \) ➔ Non-Significant

\( p<0.05 \) ➔ Significant

\( p<0.001 \) ➔ Highly Significant

Table (2) shows that the mean FI at the eleventh 11th week in Diabetic group(40.7201 ± 11.03053) was higher than non-diabetic group(34.5942 ± 9.65622); however there is a statistically near significant difference between diabetic and non-diabetic women as regard FI at the eleventh 11th week (\( P>0.051 \)), may be large sample size show significant difference.

**Table (3):** Comparison between Diabetic and Non-Diabetic women as regard VFI at the eleventh 11th week.

<table>
<thead>
<tr>
<th>U/S Indices (VFI)</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>6.5221</td>
<td>1.19599</td>
<td>-0.384</td>
<td>0.703</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>7.7670</td>
<td>2.36749</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VFI= Vascularization Flow index

\( p>0.05 \) ➔ Non-Significant, \( p<0.05 \) ➔ Significant, \( p<0.001 \) ➔ Highly Significant

Table (3) shows that the mean VFI at the eleventh 11th week in Diabetic group(7.7670 ± 2.36749) was higher than non-diabetic group(6.5221 ± 14.19599); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard VFI at the eleventh 11th week (\( P>0.05 \)).

**Table (4):** Comparison between Diabetic and Non-Diabetic women as regard Placental volume at the eleventh 11th week.

<table>
<thead>
<tr>
<th>U/S Indices (Placental volume/cm3)</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>27.5304</td>
<td>7.45907</td>
<td>0.132</td>
<td>0.895</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>26.9004</td>
<td>4.74398</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( p>0.05 \) ➔ Non-Significant

\( p<0.05 \) ➔ Significant

\( p<0.001 \) ➔ Highly Significant

Table (4) show that the mean Placental volume at the eleventh 11th week in Diabetic group(26.9004 ± 14.74398) was lower than non-diabetic group(27.5304 ± 17.45907); however there is a
Table (5): Comparison between Diabetic and Non-Diabetic women as regard VI at the thirteenth 13\textsuperscript{th} week.

<table>
<thead>
<tr>
<th>U/S Indices</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>Non-diabetic</td>
<td>16.3664</td>
<td>4.17095</td>
<td></td>
<td>0.968</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>16.5110</td>
<td>3.81227</td>
<td>-0.040</td>
<td></td>
</tr>
</tbody>
</table>

VI=Vascularization index

*p* > 0.05 ➔ Non-Significant, *p* < 0.05 ➔ Significant, *p* < 0.001 ➔ Highly Significant

Table (5) shows that the mean VI at the thirteenth 13\textsuperscript{th} week in Diabetic group (16.5110 ± 9.81227) was slightly higher than non-diabetic group (16.3664 ± 14.17095); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard VI at the thirteenth 13\textsuperscript{th} week (*P* > 0.05).

Table (6): Comparison between Diabetic and Non-Diabetic women as regard FI at the thirteenth 13\textsuperscript{th} week.

<table>
<thead>
<tr>
<th>U/S Indices</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FI</td>
<td>Non-diabetic</td>
<td>40.2874</td>
<td>7.52382</td>
<td>-0.562</td>
<td>0.579</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>42.5189</td>
<td>7.47494</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FI=Flow index

*p* > 0.05 ➔ Non-Significant, *p* < 0.05 ➔ Significant, *p* < 0.001 ➔ Highly Significant

Table (6) shows that the mean FI at the thirteenth 13\textsuperscript{th} week in Diabetic group (42.5189 ± 7.47494) was higher than non-diabetic group (40.2874 ± 17.52382); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard FI at the thirteenth 13\textsuperscript{th} week (*P* > 0.05).

Table (7): Comparison between Diabetic and Non-Diabetic women as regard VFI at the thirteenth 13\textsuperscript{th} week.

<table>
<thead>
<tr>
<th>U/S Indices</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VFI</td>
<td>Non-diabetic</td>
<td>8.1196</td>
<td>2.54738</td>
<td>0.571</td>
<td>0.572</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>7.0832</td>
<td>2.35210</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VFI= Vascularization Flow index

*p* > 0.05 ➔ Non-Significant, *p* < 0.05 ➔ Significant, *p* < 0.001 ➔ Highly Significant

Table (7) shows that the mean VFI at the thirteenth 13\textsuperscript{th} week in Diabetic group (7.0832 ± 4.35210) was lower than non-diabetic group (8.1196 ± 7.54738); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard VFI at the thirteenth 13\textsuperscript{th} week (*P* > 0.05).

Table (8): Comparison between Diabetic and Non-Diabetic women as regard Placental volume at the thirteenth 13\textsuperscript{th} week.

<table>
<thead>
<tr>
<th>U/S Indices</th>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Independent sample t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placental volume/cm\textsuperscript{3}</td>
<td>Non-diabetic</td>
<td>54.4592</td>
<td>7.84787</td>
<td>0.457</td>
<td>0.650</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>52.0443</td>
<td>7.95270</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p* > 0.05 ➔ Non-Significant, *p* < 0.05 ➔ Significant, *p* < 0.001 ➔ Highly Significant

Table (8) shows that the mean Placental volume at the thirteenth 13\textsuperscript{th} week in Diabetic group (52.0443 ± 17.95270) was lower than non-diabetic group (54.4592 ± 17.84787); however there is a statistically insignificant difference between diabetic and non-diabetic women as regard Placental volume at the thirteenth 13\textsuperscript{th} week (*P* > 0.05).

**DISCUSSION**

The current study was conducted at the antenatal care clinic in cooperation with "the feto-maternal Unit for ultrasound assessment", Ain-Shams University Maternity Hospital during the period between November (2015) and April
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(2017), included 46 pregnant women subdivided into two groups
Group (A) 23 Pregestational Diabetic women
Group (B) 23 Non – Diabetic pregnant women

To compare placental volume and vascular indices (VI, FI and VFI) between the two group at the first trimester of gestation (the eleventh 11th week and the thirteenth 13th week) Using 3D ultrasonography and 3D power doppler.

The results of this study showed that there is no statistically significant difference between pregestational diabetic and non-diabetic group as regard maternal age, parity number, of abortions, gestational age, placental volume and vascular indices (VI and VFI only) except FI which showed near statistical significance value(P>0.051), may be larger sample size would show significant difference.

A prospective case-control study conducted by Gonzalez et al. (24) on pregnant women with pregestational DM and singleton pregnancies at the eleventh 11th week and the thirteenth 13th week of gestation subdivided into 69 women with pregestational DM (44 with type I DM and 25 with type II DM) and the control group comprised 94 pregnant women, showed that no statistical as regard age, parity and placental volume except for vascular indices, (VI,FI and VFI) were significantly reduced among the diabetic group in contrast to the results of this study. The difference may be attributed to the larger sample size in this study (163 women) and the diabetes mellitus control of the patients, including HbA1Cof the other study (60 women had HbA1C more than 7%), but all patients in the current study had HbA1C less than 7% (well-controlled).

Montlår et al., (25) conducted a study between 2011 and 2013 to evaluate the vascular indices (VI, FI and VFI)at the first trimester of pregnancy. The pregnancies were divided into two groups: I. non-pathological control group (n=113) and II. case group comprising pregnancies complicated by two subgroups of diabetes mellitus (n=99): II.a Type I DM (n=43) and II.b) GDM (n=56).

They found no significant statistical difference as regard maternal age and gestational age, but showed that all three placental vascular indices (VI, FI and VFI) were significantly reduced among diabetic pregnant women as compared to the control group (p<0.001).In the above mentioned results, this difference may be attributed to the larger sample size (n 212) and the poor glycemic control (32 patient of type I DM and 15 patient of GDM had HbA1C more than 7%). Rizzo et al., (21) conducted a prospective observational study on 32 pregnant women with type I DM at the first trimester of gestation (eleventh 11th and thirteenth 13th week) to evaluate placental volume and vascular indices (VI, FI and VFI), they found that there was no significant statistical difference in the placental volume when compared to reference limits, this is in agreement with the results of the current study but 3D Doppler placental vascular indices were significantly higher in diabetic women (VIP=0.0012:FIP=0.0008VFI=0.0039) when compared to reference limits in contrast to the current study p-value>0.05, this difference may be attributed to the larger sample size and the glycemic state of the patients included in the study (9 patients had HbA1C more than 7%).

Raine-Fenning et al., (26) conducted a study on pregestational diabetic patients (n 220) at the first trimester (11weeks and 14 weeks). In contrast to the results of this study, they found that vascular indices (VI, VFI) increased while FI reached a peak with three vessels (uterine, middle cerebral. umbilical) and then decreased, this may be due to the larger sample, machine settings used (voluson 730), the poor glycemic state of patients (45 women had HbA1C more than 7%), moreover they measured vascular indices on three vessels (we used umbilical vessels only).

The results of this study were in agreement with a study conducted in Taipei Veterans General Hospital (Taiwan) on a total of 222 women with singleton pregnancy from the eleventh 11th week to the thirteenth 13th week. All the indices, including the mean gray value (MGV) showed no significant statistical difference. Although this study was conducted on a larger sample size, and measured the mean gray value (placental density) but the glycemic state of most of the patients were well – controlled (only 4 women had HbA1C more than 7%).

The results of the current study were in contrast to a case - control prospective study conducted by Pala et al. (27) aimed to measure placental volume and placental mean gray value in gestational diabetes mellitus (GDM) and healthy control patients using three-dimensional (3D) ultrasound and Virtual Organ Computer-aided Analysis (VOCAL) in 39 singleton pregnancies complicated by GDM and 42 healthy singleton pregnancies matched for gestational age, maternal age and parity. Placental volume was significantly larger in GDM (411.59 ± 170.82 versus 343.86 ± 128.94 cm3; p value = 0.046). This may be due to larger sample size and also the patient in the current study were well-known and controlled pregestational diabetic (not gestational diabetes mellitus). In agreement with the results of this study Salvesen et al. (28) conducted a cross-
sectional study on 65 well-controlled diabetic pregnancies. They found that the placental vascular indices (VI, FI and VFI) measured by 3D power doppler ultrasonography showed no statistical significant difference except when complicated with preeclampsia or fetal growth restriction (FGR).

In contrast to the results of the current study, Jauniaux and Burton (29) conducted a study on pregestational diabetic (n=66) at the first trimester, they found an increase in vascular indices (VI, FI and VFI), this may be due to poor glycaemic control (HbA1C >7% in 37 patients), in addition to the larger sample size.

In contrast to the results of this study another investigation was conducted by Hafner et al. (30) on pregestational diabetic (n=356), they found an increase in placental volume, this may be due to larger sample size and values were obtained at the first and the second trimester.

In contrast to the results of this study De Paula et al., (31) conducted a prospective study on pregestational diabetic (n=295), they found that placental volume and vascular indices (VI, FI and VFI) increased, this may be due to larger sample size, poor glycaemic control in addition to that values were calculated between 12th and 40 week of gestation (not only at the first trimester).

In contrast to the results of this study another study conducted by Odibo et al. (32) on pregestational diabetic (n=49), they found that there was statistically significant difference as regard placental volume and vascular indices (VI, FI and VFI), this may be due to higher mean age (over 33 years) in addition to poor glycaemic control (HbA1C >7% in 26 patients).

Martins et al., (33) conducted a study on pregestational diabetic patients (n=65) at the first trimester (11th and 13th week) to measure vascular indices (VI, FI and VFI) with 3D power Doppler ultrasonography which were significantly reduced in contrast to the results of the current study, this may be due to high body mass index (BMI) more than 30kg/m2 but our patients were with average BMI because (the values of vascular indices are affected by the depth between area of analysis and the probe).

Odeh et al., (34) conducted a case-control study at the first trimester aimed at measuring the placental volume and vascular indices (VI, FI and VFI), patients were classified into two groups (case=120 with pregestational diabetes) and (control=120), they found that there was no significant statistical difference as regard age, gestational age, (PV), (FI) and (VFI) in agreement to the current study except for (VI) which was significantly reduced, this may be due to poor glycaemic control (HbA1C >7% in 45 patient), in addition to the larger sample size.

Higgins et al., (35) conducted a prospective study on (10 women with Type I diabetes), (8 women with Type II Diabetes) and (10 non-diabetic women), aimed to measure the placental volume, length and surface area of placenta. They found that there was no significant statistical difference as regard placental volume (P=0.25) between diabetic and non-diabetic women. This was in agreement with the current study but vascular indices (VI, FI and VFI) were increased in diabetic group compared to non-diabetic women (P=0.002), although the small sample size in this study, the increased vascularization may be due to poor glycaemic control (2 women in type II DM with HbA1C >7% and 7 women in type I DM with HbA1C >7%).

The results of the current study were in agreement with a study conducted by De Paula et al., (36) (no significant statistical difference in VI, FI and VFI), where the entire placenta was identified as in the current study but were in contrast to a study conducted by Mercé et al. (37) which found an increase in VI, FI and VFI, this may be due to that they identified only a part of the placenta with the highest density of vessels, a technique called “vascular placental biopsy”, and also were in contrast to a study conducted by Guiot et al. (38) which found a decrease in VI, FI, and VFI, this may be due to the calculated vascular indices (VI, FI and VFI) in five constant region of the placenta.

The results of this study were in contrast to those of Yu et al. (39) Which revealed a decrease in vascular indices (VI, FI and VFI) measured at the first trimester on pregestational diabetic (n=7 type I DM=43 and type II DM=30), this may be due to higher mean age of patients (over 30 year) and vascular indices (VI, FI and VFI) were calculated for a fixed placental volume, in addition to the larger sample size.

The results of the current study were in contrast to those of a study conducted by Maly et al. (40), aimed to measure placental volume and vascular indices (VI, FI and VFI) in pregestational diabetic patients (n=10) compared to controls (n=13) at the first trimester, they found a decrease in placental volume and vascular indices, this may be due to the smaller sample size and poor glycaemic control (5 women had HbA1C >7%).

The results of the current study were in contrast to those observed by Lai et al. (41), and Negrini et al. (42) on pregestational diabetic (n=100), who found significant statistical difference as regard vascular indices (VI, FI and VFI), this difference may be attributed to the glycaemic state.
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(37 patient had HbA1C >7%), difference in the machine settings used (voluson730 expert), higher mean age of patients (over 32 year) and higher mean of parity (over 4).

The results of the current study were in contrast to The data of Hafner et al. (2008) on pregestational diabetic (n:88) Who measured placental volume not only at the first but also the second trimester, placental volume (PV) was significantly increased, this may be due to poor glycaemic control (56 patient with HbA1C>7%), the larger sample size and measurement of placental volume in the 2nd trimester. Finally, from most of the above studies we found that the distinct placental changes associated with diabetes mellitus depend on the gestational period. In early pregnancy, the high glucose level triggers vasculogenesis but vasculopathy is not present yet. In later stage of pregnancy the vasculopathy affects the blood flow in the placenta, especially in poor glycaemic control. Therefore, it is worth to display the usefulness of measuring vascular indices (VI, FI and VFI) and placental volume in pregestational diabetic at the first trimester was limited especially with good glycaemic control, also Differences in methodology of placental volume acquisition, machine settings, and sample sizes of the studies may contribute to the different results. In addition, the machine settings may influence the quantitative values obtained from 3D power Doppler interrogation of the placenta.

CONCLUSION

There was no statistically significant difference as regard placental volume and vascular indices (FI, VI and VFI) in pregestational diabetic compared to non-diabetic pregnant patients at the first trimester of pregnancy especially with good glycemic control but changes may be present with poor glycaemic control.

RECOMMENDATIONS

We recommend to conduct further studies as regard evaluating placental volume and vascular indices (FI, VI and VFI) in pregestational diabetic at the second and the third trimester of pregnancy giving more time for the pathological effect of diabetes mellitus to appear.

Flow index (FI) among vascular indices (VI and VFI) was near significant, so we also recommend a larger sample size in future studies.

REFERENCES


