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Original article

Comparative Study of Color Doppler Imaging in Normal and Abnormal First Trimester Pregnancy

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ABSTRACT

Background: Color Doppler ultrasonography enables the non-invasive study of physiologic and pathophysiologic changes in the uterine and ovarian circulation in pregnant and non-pregnant women.

Aim of the work: To evaluate the potential value of color Doppler of the uterine artery, corpus luteum blood flow, and subchorionic blood vessels in abnormal first-trimester pregnancy.

Patients and methods: The study included 200 pregnant women in the first trimester in the antenatal care clinic of the Department of Obstetrics and Gynecology AL Azhar University [Assiut], divided into two groups; control group [100 cases] with normal pregnancy and study group [100 cases] which was further subdivided into threatened abortion [60 cases], blighted ovum [20 cases] and vesicular mole [20 cases].

Results: The uterine artery resistance index [RI] of the study groups was lower than the control group. The decrease was highly significant in the uterine artery RI of both threatened abortion and blighted ovum groups and significant in the vesicular mole group. Uterine artery pulsatility index [PI] showed a significant decrease in the study group compared with the control cases. There was a highly significant negative correlation between gestational age and both RI and PI of the study group's uterine artery. There was a higher prevalence of abortion in a group of threatened abortion compared to the control group.

Conclusion: The prevalence of pregnancy complications is increased in association with abnormal blood flow patterns of the early uteroplacental circulation. Doppler indices of the early gestation uteroplacental circulation have an important value in the threatened abortion follow up.

Keywords: Color Doppler; Waveform; Transvaginal; Ultrasonography; Pregnancy

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* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

According to the World Health Organization [WHO], "abortion is defined as loss of a pregnancy before 20 weeks of gestation" [1]. Doppler ultrasound supply is used to measure blood velocity and flow [2]. Different methods of Doppler are used in pregnancy: continuous-wave, pulsed-wave, color, and power Doppler flow [3]. Doppler ultrasound imaging can be used to assess the function of the uteroplacental and fetoplacental circulations. It enables the detection of blood flow in minute vascular branches of uteroplacental vessels [as radial and spiral network] that cannot be visualized with conventional real-time grayscale imaging [4]. That permits more understanding of hemodynamics, physiologic development, and pathophysiologic mechanisms associated with miscarriage [5].

It was found that the evaluation of fetomaternal circulation during early pregnancy gives data regarding the physiology and pathophysiology of early placentation [4]. The use of pulsed-wave Doppler ultrasonography has provided us the means for non-invasive uterine artery impedance assessment and may help identify women with recurrent miscarriage associated with impaired uterine perfusion [6]. The transabdominal/transvaginal Doppler ultra-sound examination is a non-invasive tool used to evaluate pregnancy's physiologic and pathologic blood flow characteristics. Observations that many complications of advanced pregnancy and postnatal life derived from early pregnancy events justifies the application of these technological advances to identify early pregnancy changes [7]. Elevated uterine artery resistance is associated with recurrent miscarriage. The use of Pulsed Doppler ultrasonography may give help in identifying patients with unexplained recurrent miscarriage who have impaired uterine circulation [8]. During Early pregnancy between the 5th and 7th weeks of gestation, the spiral artery resistance decreases and blood flow velocity increases; during that period, the uterine and arcuate artery's hemodynamics remains unchanged. In the uterine and arcuate arteries, a decrease in impedance and an increase in absolute velocities are detected after the 8th week

of gestation. The delay between changes in the spiral and uterine arteries may represent the magnitude of the increased placental volume and spiral arterial involvement, which is needed to affect uterine hemodynamics [9].

AIM OF THE WORK

The current work aimed to assess uteroplacental blood flow in early pregnancy abnormalities. Evaluate the potential clinical value of Doppler waveform analysis of uterine and subchorionic vessels in normal and abnormal early pregnancy.

PATIENTS AND METHODS

This study is a prospective cohort observational study that was done in the period between May 2019 to November 2019 at Al-Azhar University Hospitals Assiut Egypt [follow up of all patients finished in November 2019]. The study included 200 pregnant women coming to the Department of Obstetrics and Gynecology antenatal care clinic. The study includes women admitted to the hospital during the 6-12 weeks of gestation with the following inclusion criteria: age between 20-35 years old, women who had normal intrauterine pregnancies [confirmed by sonographic measurement], spontaneous conception, and agreement to sign the informed consent to participate in the study. Exclusion criteria: subjects were excluded from the study that have multiple pregnancies and uterine anatomic abnormalities. The selected patients were divided into two groups: The control group included 100 pregnant women with normal pregnancy without any medical or obstetric complications, and the study group included 100 pregnant women and was further subdivided into threatened abortion [60 cases], blighted ovum [20 cases] and vesicular mole [20 cases]. All patients of the study and control groups were subjected to full history taking, general examination, routine laboratory investigation as β -human chorionic gonadotropin [hCG], hemoglobin percentage [Hb%], rhesus [Rh] typing and fasting blood sugar determination, ultrasonographic examination, color Doppler study of the uterine artery, corpus luteum blood flow, and subchorionic blood vessels.

Sonographic examination: Trans-abdominal

and transvaginal sonographic examinations were done and repeated every two weeks. Transvaginal ultrasound examination was carried out with a high color Doppler resolution transvaginal ultrasound, using standard machine [GE Voluson E6 equipped with a 4-9MHz transvaginal probe; or GE Voluson E6 equipped with a 2-5MHz transabdominal probe].

Color Doppler studies: The target vessels for this study were uterine arteries, corpus luteum blood flow, and subchorionic blood vessels. A two-dimensional, B-mode scan was first performed to assess the pregnancy state and to determine the accurate gestational age. Normal pregnancy is defined as an intrauterine gestational sac with the pulsating embryo and crown-rump measurement correlated to menstrual age.

[A] *The color Doppler technique of the uterine artery:* The main uterine artery was visualized at the level of the internal os it approaches the uterus laterally and curves alongside the uterine body. The uterine artery ipsilateral to the dominant ovary [i.e., ovary harboring the corpus luteum] was designated as the dominant uterine artery. In the transabdominal approach, the para-cervical site at the internal os level is preferred over the iliac crossover site as it is easier to obtain. In a prospective longitudinal study, Lefebvre and colleagues successfully obtained adequate Doppler signals from both the uterine arteries in all the cases at the para-cervical site at the os level, but only in about 60 % of the cases at the iliac crossover site^[10].

[B] *Color Doppler sonography of the sub-chorionic vessels:* The view usually assumed for Doppler study of the subchorionic vessels was a fundal transverse or slightly oblique view as most of the vessels in a posteriorly implanted ovum should lie in the posterior part of the decidua basalis. Doppler shift spectra from the subchorionic vessels were recorded from the intensively colored area on the border between the hyperechogenic choriodecidua and hypoechogenic myometrium^[11]. The mean resistance index was obtained for each ultrasound session.

[C] *Corpus luteum blood flow:* The ovary containing the corpus luteum was visualized by grayscale sonography. Then we demonstrate the

waveform, characteristic of corpus luteum blood flow in early pregnancy. In fact, the use of transvaginal color Doppler sonography allows simple and precise recognition of an ovary with corpus luteum. The intensity of color corresponds with the blood flow velocity in newly formed intraovarian vessels. Color is an essential guide for pulsed Doppler exploration of such small and randomly dispersed vessels inside ovarian tissue. Doppler analysis without color flow is considered time-consuming and potentially inaccurate, while by using color Doppler sonography, it was feasible to distinguish the ovary containing an active corpus luteum from the inactive ovary. The technique is very simple to use, and the results are displayed obviously by using a color map^[12].

Follow up: For control and threatened abortion groups, repeated follow-up by sonographic examination was performed, and they were divided into Cases who completed their pregnancy and cases that were aborted.

Statistical analysis: The present study's results were statistically analyzed using SPSS 22 [IBM, USA]. Quantitative variables were expressed as mean \pm standard deviation [SD] and qualitative variables as numbers and percentages. The Kolmogorov Smirnov test tested the normal distribution of the quantitative variables. Differences between independent groups were assessed by Student t-test for normally distributed quantitative variables. The P-value less than 0.05 was considered statistically significant.

RESULTS

There were statistically significant differences [$P < 0.05$] regarding results of uterine artery resistance index [RI] when we compared between cases and control groups at different gestational ages from 6-12 weeks [Table 1]. In addition, there were statistically significant differences [$P < 0.05$] regarding results of the uterine artery pulsatility index [PI] when we compared between cases and control groups at different gestational ages from 6-12 weeks [Table 2]. However, there was a non-significant difference between cases and controls regarding the corpus luteum blood flow resistance index [RI] and the subchorionic vasculature resistance index [RI]. Also, there was no significant difference between study and control groups

regarding subchorionic vasculature resistance index at gestational ages from [8-12 weeks]. The subchorionic vasculature resistance index decreases with advanced gestational ages from [8-12 weeks] [Table 4]. There was a significant

difference between aborted cases and cases that reached full term regarding uterine artery resistance index, but there was a non-significant difference regarding uterine artery PI and RI [Table 5].

Table [1]: The uterine artery resistance index [RI] in cases of normal pregnancy [control group] and cases of abnormal pregnancy [study groups] at different gestational weeks

	Normal Pregnancy		Abnormal pregnancy							
	Control group [n=100]		Threatened abortion [n=60]		Blighted ovum [n=20]			Vesicular mole [n=20]		
	$\bar{X}\pm SD$	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P
6-8 weeks	N = 32	N = 10	6.33	<0.05	N = 4	6.11	<0.05	N = 4	3.45	<0.05
	0.72±0.09	0.53±0.04			0.52±0.01			0.60±0.04		
8-10 weeks	N = 36	N = 30	5.04	<0.05	N = 10	4.5	<0.05	N = 10	4.01	<0.05
	0.69±0.04	0.58±0.04			0.55±0.03			0.57±0.03		
10-12 weeks	N = 32	N = 20	4.11	<0.05	N = 6	6.50	<0.05	N = 6	4.05	<0.05
	0.62±0.05	0.54±0.06			0.57±0.03			0.55±0.03		

Data expressed as mean [SD], range or frequency [percentage]. P value was significant if < 0.05.

Table [2]: Uterine artery pulsatility index [PI] in cases of normal pregnancy [control group] and cases of abnormal pregnancy [study groups] at different gestational weeks

	Normal pregnancy		Abnormal pregnancy							
	Control group [n=100]		Threatened abortion [n=60]		Blighted ovum [n=20]			Vesicular mole [n=20]		
	$\bar{X}\pm SD$	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P
6-8 weeks	N = 32	N = 10	7.46	<0.05	N = 4	5.67	<0.05	N = 4	5.6	<0.05
	1.73±0.09	1.59±0.12			1.32±0.10			1.49±0.11		
8-10 weeks	N = 36	N = 30	4.56	<0.05	N = 10	6.11	<0.05	N = 10	4.56	<0.05
	1.69±0.21	1.49±0.13			1.40±0.11			1.50±0.12		
10-12 weeks	N = 32	N = 20	5.59	<0.05	N = 6	5.67	<0.05	N = 6	5.01	<0.05
	1.66±0.15	1.41±0.12			1.39±1.16			1.44±0.11		

Data expressed as mean [SD], range or frequency [percentage]. P value was significant if < 0.05.

Table [3]: Corpus luteum blood flow resistance index [RI] and The subchorionic vasculature resistance index [RI] in the control group and the study groups.

	Normal pregnancy	Abnormal pregnancy [n=100]		
	Control group [n=100]	Threatened abortion [n=60]	Blighted ovum [n=20]	Vesicular mole [n=20]
Corpus RI				
$\bar{X}\pm SD$	0.49±0.09	0.51± 0.49	0.59±0.14	0.56±0.15
Range	[0.49-0.50]	[0.49-0.58]	[0.49-0.63]	[0.52-0.57]
t, p		1.22, >0.5 NS	1.50, >0.05 NS	1.50, >0.05 NS
Subchorionic RI [$\bar{X}\pm SD$]	0.51±0.11	0.53±0.18	0.50±0.10	0.51±0.13
Range	[0.23-0.81]	[0.11-0.83]	[0.45-0.83]	[0.39-0.78]
t, p		1.33, >0.05 NS	1.99, >0.05 NS	1.04, >0.05 NS

Data expressed as mean [SD], range or frequency [percentage]. P value was significant if < 0.05.

Table [4]: Subchorionic vasculature resistance index [RI] in cases of normal pregnancy [control group] and cases of abnormal pregnancy [study groups] at different gestational ages

	Normal pregnancy		Abnormal pregnancy							
	Control group [n=100]		Threatened abortion [n=60]		Blighted ovum [n=20]			Vesicular mole [n=20]		
	$\bar{X}\pm SD$	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P	$\bar{X}\pm SD$	t	P
6-8 weeks	N = 32	N = 10	1.20	>0.05	N = 4	2.11	>0.05	N = 4	1.09	>0.05
	0.46±0.03	0.45±0.11			0.47±0.12			0.415±0.12		
8-10 weeks	N = 36	N = 30	1.34	>0.05	N = 10	0.45	>0.05	N = 10	0.98	>0.05
	0.43±0.05	0.47±0.15			0.43±0.16			0.41±0.14		
10-12 weeks	N = 32	N = 20	1.29	>0.05	N = 6	0.90	>0.05	N = 6	0.85	>0.05
	0.41±0.05	0.44±0.12			0.43±0.13			0.47±0.12		

Table [5]: Comparison between Doppler indices of the two subgroups of threatened abortion cases [aborted cases versus cases reached full term]

Index		Aborted cases [n = 26]	Cases reached full term [n = 34]	T	P
I- Uterine artery					
RI	$\bar{X}\pm SD$	0.62±0.18	0.51±0.11		
	Range	[0.42-0.79]	0.50-0.59]	5.68	<0.001 HS
PI	$\bar{X}\pm SD$	1.69±0.11	1.60±0.21		
	Range	[1.22-1.32]	1.29-1.63]	3.11	<0.05 Sig.
II- Subchorionic vasculature RI					
RI	$\bar{X}\pm SD$	0.59±0.11	0.44±0.12		
	Range	[0.51-0.71]	[0.50-0.59]	1.56	>0.05 NS

Data expressed as mean [SD], range or frequency [percentage]. *P* value was significant if < 0.05.

DISCUSSION

This study was performed on 200 pregnant women in the first trimester. The selected patients age ranged from 20 to 30 years and had had at least one previously normal pregnancy and delivery. The menstrual age of the selected groups ranged from 6-12 weeks. The selected patients were divided into two groups, the control group consists of 100 cases of normal first-trimester pregnancy, and the study group consists of 100 cases of abnormal first-trimester pregnancy. The study group was subdivided into 60 cases of threatened abortion, 20 cases of blighted ovum, and 20 vesicular mole cases.

In our study, there was a statistically significant difference [$P < 0.05$] when we compare between cases of normal pregnancy [control group] and abnormal pregnancy [study groups] at different gestational ages from [6-12] as regards uterine artery [RI and PI] indices and this significant difference decrease with advancing gestational age from 6-12 weeks. Giacobbe et al.^[13] results were more or less similar to our results. They had found that uterine artery pulsatility and resistance indices were decreased with the advance of the gestational age in both controls and missed abortion groups. Pellizzari et al.^[14] had also found that uterine artery resistance index [RI] and pulsatility index [PI] decreased with gestational age in both normal and abnormal pregnancies, but this change was not statistically significant.

In our study, there is a nonsignificant difference in comparing corpus luteum blood flow resistance index [RI] between cases of normal pregnancy [control group] and abnormal pregnancy [study

groups] $P > 0.05$. Some evidence reported non-significant differences in The RI of the corpus luteum vessels in threatened abortion compared to normal pregnancy^[15].

In contradiction, Emad et al.^[16] In his study, there is a significant increase in resistance index of corpus luteum blood flow in cases of threatened abortion, which ended as missed, incomplete, or complete abortion compared to the continued or control cases.

In our study, in comparing subchorionic vasculature [RI] between the study and control groups, there was no significant difference [$P > 0.05$]. Alcazar et al.^[17] agree with our results they had found in their study that there was no significant difference in any Doppler indices of the spiral artery between the threatened abortion group and the normal early pregnant group. They found no apparent alteration in early uteroplacental circulation in patients with threatened abortion with a living embryo. They concluded that the use of color Doppler ultrasound does not help predict pregnancy outcome in these cases. Alfirevic and Kurjak^[18] agree with our results; they had been found in their study that the signals from subchorionic vasculature in pathologic intrauterine pregnancy showed slightly lower RI indices. However, the difference failed to reach a level of significance, Jauniaux et al.^[19] had found that the mean resistance index and pulsatility index of spiral arteries did not differ when we compare missed abortion with controls.

In our study, we had found that there was no significant difference [$P > 0.05$] when we compared the subchorionic vasculature resistance index [RI] between cases of normal pregnancy [control

group] and cases of abnormal pregnancy [study groups] at different gestational ages from [8-12 weeks]. Jauniaux et al.^[20] agree with our results. They found that subchorionic blood flow signals did not demonstrate any significant difference in RI and PI with advancing the abnormal early pregnant cases' gestational duration. On the other hand, they observe a significant difference in subchorionic vascular impedance of normal and anembryonic pregnancy.

In contradiction, Jaffe et al.^[21] had found in his study that means RI of the subchorionic space of the abnormal pregnancy compared with the control group by the ANOVA was statistically significant [$P < 0.05$] for gestational ages from "7-10" weeks but no significant differences for gestational age from 11-12 weeks.

Conclusion: Doppler indices of the uteroplacental circulation of early gestation have shown to be of important value in the follow-up of threatened abortion cases; both the uterine artery indices were significantly higher in aborted cases than cases reached full term. Abnormal blood flow patterns of the early uteroplacental circulation are associated with an increased prevalence of pregnancy complications. The subchorionic vasculature blood vessels and corpus luteum blood flow in early intrauterine pregnancy failure did not demonstrate clear cut results.

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None

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