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Comparative Study between Corpus Luteum Changes in Normal Pregnancy and Threatened Abortion Using Transvaginal Color Doppler Sonography

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ABSTRACT

Background: Threatened abortion constitutes 15–20% of pregnancies and is one of the commonest gynecological emergencies. Transvaginal sonography seems more promising in evaluating the features of the Corpus luteum and therefor can predict pregnancy outcome.

Aim of work: The aim of our study is to compare the clinical and sonographic characteristics between women with threatened abortion compared to those with normal pregnancy using transvaginal color Doppler ultrasonography, to predict pregnancy outcome in first trimester threatened abortion pregnancies.

Patients and methods: This study a prospective cohort observational, was carried out on 200 pregnant women (divided into two groups). Group I: 100 pregnant women with normal pregnancy. Group II: 100 pregnant women with threatened abortion, in Al-Galaa Maternity Hospital.

Results: As regards the site, size and growth rate of C.L., there was no significant difference between normal pregnancy and threatened abortion. By T.V.S, 4 different patterns of C.L. could be identified: hypoechoic, thick walled cyst, complex cyst and simple cyst; and none of them was predictive of pregnancy outcome in threatened abortion. As regards resistance index of luteal blood flow, only resistance index increases significantly if abortion occurs; and so far, Doppler studies could serve as a predictive diagnostic tool in assessing C.L. function.

Conclusion: There is 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.

Keywords: Corpus Luteum, Normal Pregnancy, Threatened Abortion, Transvaginal Color Doppler Sonography.

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INTRODUCTION

Among different physiological factors responsible for initiating and maintaining pregnancy, corpus luteum plays a critical role in normal pregnancy. The corpus luteum produces several hormones, such as estradiol, progesterone, relaxin, inhibin A and B, as well as products such as cytokines and prostaglandins.¹

The synthesis of progesterone by corpus luteum is extremely important for the maintenance of normal

pregnancy in the first seven weeks. Similarly, the production of progesterone by the placental syncytiotrophoblast increases progressively during the first weeks of gestation, so that in eight and a half weeks the placenta and corpus luteum contribute in equal amounts of progesterone. However, from the eighth week, the placental contribution is sufficient to maintain gestation. Angiogenesis in the corpus luteum occurs under physiologic circumstances in each menstrual cycle and functionally is very important for maintenance of early pregnancy.² This role implies a potential correlation between abnormal function of corpus luteum and possible abnormal pregnancy including abortion.

The introduction of Doppler ultrasound in obstetrics has allowed evaluating hemodynamic characteristics of corpus luteum from the first trimester of pregnancy. For example, Kurjak et al in one of the

first studies using transvaginal pulsed-wave Doppler ultrasound in early pregnancies, identified the luteal flow characteristics in 75% of the patients.³

In fact, the use of transvaginal color Doppler sonography allows simple and precise recognition of an ovary with corpus luteum. Intensity of color corresponds with velocity of blood flow in newly formed intraovarian vessels. Color is an essential guide for pulsed Doppler exploration of such small and randomly dispersed vessels inside ovarian tissue. Without color flow, Doppler analysis would be time-consuming and potentially inaccurate. Using color Doppler sonography, it was feasible to distinguish the ovary containing an active corpus luteum from the inactive ovary. The technique is simple to use, and the results are displayed obviously.⁴

The RI of the corpus luteum vessels is apparently constant during the initial gestation, without significant changes. This can be explained by the absence of muscular tunica in the corpus luteum vessels, which provides minimal resistance, very full flow and inability to self-regulate. When compared to pathological pregnancies, RI is significantly higher in retained abortion and incomplete abortion than in normal pregnancies, and no statistical differences are found in cases of ectopic pregnancy, hydatidiform mole and anembryonic pregnancies.⁵ However, some more recent evidence reported non-significant difference in RI in threatened abortion when compared to normal pregnancy.⁶

The aim of our study is to compare the clinical and sonographic characteristics between women with threatened abortion compared to those with normal pregnancy using transvaginal color Doppler ultrasonography, to predict pregnancy outcome in first trimester threatened abortion pregnancies.

PATIENTS AND METHODS

This study was carried out on 200 pregnant women (divided into two groups): **Group I:** 100 pregnant women with normal pregnancy. **Group II:** 100 pregnant women with threatened abortion.

Prospective cohort observational study was done in the period between May 2019 to November 2019 at Al-Galaa Maternity Hospital and follow up of all patients finished in November 2019.

The study population includes women admitted to the hospital with 6-12 weeks of gestation with the following criteria:

Inclusion criteria: Age between 18-35 years old, women 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, molar pregnancy and uterine anatomic abnormalities.

Smoking.

Methods: Transvaginal ultrasound examination was carried out with a high color Doppler resolution transvaginal ultrasound, using standard techniques.

GE Voluson A6 equipped with a 5-MHz transvaginal probe. The high pass filter was set at 100 Hz and the spatial peak temporal average was 80 mW/cm² (according to the limits of security recommended by the American Food and Drug Administration for use in fetal medicine).

The ultrasonographic assessment was performed with the patient in the decubitus position.

A two-dimensional, B-mode scan was first performed to evaluate the state of the pregnancy and to determine the true gestational age. Normal pregnancy defined as an intrauterine gestational sac with live embryo (positive heart action) and crown-rump measurement correlated to menstrual age. Threatened abortion was mainly a clinical diagnosis (closed cervical os with vaginal bleeding) with sonographic findings of a prominent subchorionic anechoic area due to blood collection.

Corpus luteum blood flow was defined as random, usually semilunar in appearance, dispersed vessels with very prominent diastolic component of a cardiac cycle and consequently low impedance to blood flow.⁷

Endovaginal ultrasonography was done for 200 pregnant women starting at 6 weeks till 9 weeks menstrual age for evaluation of corpus luteum changes in normal pregnancy 100 cases and threatened abortion 100 cases as regard site, size, morphological type and growth rate (follow up after one week) as well as to evaluate the functional state by Doppler ultrasonography velocimetric analysis of CL blood flow (resistance index).

Follow up of the patients at 12 weeks GA to detect the outcome of pregnancy.

After identification of corpus luteum blood flow, pulsed Doppler sonographic sample volume was placed where highest intensity of color was visualized to obtain the flow velocity waveform, and results was applied for calculation the resistance index (RI) according to the following formula:

$$RI = \frac{S-D}{S}$$

Where RI is the resistance index, S corresponded to the peak systolic velocity and D corresponded to the peak diastolic velocity. RI of the corpus luteum vessels is considered as normal when less than 0.64.⁶

Statistical analysis: recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

-Independent-samples t-test of significance was used when comparing between two means.

-A one-way analysis of variance (ANOVA) when comparing between more than two means.

-Chi-square (χ^2) test of significance was used in order to compare proportions between qualitative parameters.

-The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the -Probability (P-value)

-P-value <0.05 was considered significant.

-P-value <0.001 was considered as highly significant.

-P-value >0.05 was considered insignificant.

RESULTS

Table (1) shows no statistically significant difference between study group and control group according to age (years) gestational age (days) and the location of corpora luteal.

Table (2) shows statistically significant difference between study group and control group according to resistance index at first visit.

Table (3) shows statistically significant difference between morphological appearance and resistance index at first visit and second visit in study group and no statistically difference in control group.

Table (4) shows no statistically significant difference between abortion group and continuing group according to diameter of CL at first visit and second visit in study group but shows statistically significant difference between abortion group and continuing group according to resistance index at second visit in study group.

Table (5) shows no statistically significant difference between abortion group and control

group according to diameter CL but shows statistically significant difference according to resistance index at first visit.

Table (6) shows no statistically significant difference between continuing group and control group according to diameter of CL but show statistically significant difference according to RI at first visit and second visit.

Table (7) shows statistically significant difference between study group and control group according to outcome after 12 weeks.

N.B. In study group, CL could not be seen in 20 cases but were added to the total outcome after 12 weeks of GA. In control group 10 cases were aborted after 12 weeks GA despite showing no signs of threatened abortion and they were included in control group from the beginning.

	Age (years) Mean±SD	Gestational age (days) Mean±SD	Location of corpora luteal		
			Right ovary	Left ovary	Not Seen
Study group (n=100)	27.91±5.10	51.47±4.43	42 (42%)	38 (38%)	20 (20%)
Control group (n=100)	27.09±5.06	51.33±4.96	45 (45%)	45 (45%)	10 (10%)
p-value	0.376	0.429	0.779		

p-value>0.05 NS;

Table 1: Comparison between study group and control group according to age (years), gestational age (days) and location of corpora luteal.

Resistance index	Study group (n=100)	Control group (n=100)	Mean Diff.	t-test	p-value
Resistance index V₁					
Mean±SD	0.54±0.12	0.46±0.04	0.080	2.524	0.024*
Range	0.42-0.88	0.42-0.57			
Resistance index V₂					
Mean±SD	0.62±0.09	0.63±0.06	0.010	0.488	0.263
Range	0.52-0.84	0.51-0.72			

t-Independent Sample t-test;

p-value>0.05 NS; **p-value* <0.05 S

Table 2: Comparison between study group and control group according to resistance index at first visit and second visit.

Morphological appearance	R.I. (mean) study group		R.I. (mean) – control group	
	First Visit	Second Visit	First Visit	Second Visit
Hypo echoic	0.73±0.10	0.76±0.11	0.44±0.06	0.63±0.09
Thick walled cyst	0.52±0.07	0.61±0.09	0.46±0.08	0.64±0.11
Complex cyst	0.48±0.06	0.59±0.08	0.52±0.07	0.64±0.10
Simple cyst	0.60±0.08	0.57±0.08	0.46±0.06	0.59±0.08
ANOVA	7.203	5.053	3.919	0.881
p-value	0.007*	0.021*	0.236	0.463

Using: One Way Analysis of Variance; p -value <0.05 S;

Table 3: Comparison between morphological appearance and resistance index at first visit and second visit in study group and control group.

	Diameter of CL		Resistance index	
	Diameter of CLV1	Diameter of CLV2	Resistance index V1	Resistance index V2
Abortion group (n=40)	21.84±3.23	21.23±2.19	0.54±0.13	0.66±0.09
Continuing group (n=40)	21.93±4.22	23.23±3.53	0.54±0.12	0.58±0.07
Mean Diff.	0.090	2.010	0.010	0.080
t-test	0.062	1.172	-0.086	2.582
p-value	0.525	0.061	0.516	0.016*

t-Independent Sample t-test; p -value>0.05 NS;

Table 4: Comparison between abortion group and continuing group according to diameter and RI of CL at first visit and second visit in study group.

	Diameter of CL		Resistance index	
	Diameter of CLV1	Diameter of CLV2	Resistance index V1	Resistance index V2
Abortion group (n=40)	21.84±3.23	21.23±2.19	0.54±0.13	0.66±0.09
Control group (n=100)	21.22±3.43	21.38±3.14	0.46±0.04	0.63±0.06
Mean Diff.	0.620	0.150	0.080	0.030
t-test	0.758	0.659	2.906	1.143
p-value	0.331	0.487	0.007*	0.168

t-Independent Sample t-test; p -value>0.05 NS;

Table 5: Comparison between abortion group and control group according to diameter CL and RI at first visit and second visit.

	Diameter of CL		Resistance index	
	Diameter of CLV1	Diameter of CLV2	Resistance index V1	Resistance index V2
Continuing group (n=40)	21.93±4.22	23.23±3.53	0.54±0.12	0.58±0.07
Control group (n=100)	21.22±3.43	21.38±3.14	0.46±0.04	0.63±0.06
Mean Diff.	0.710	1.850	0.080	0.050
t-test	0.606	1.799	3.222	-2.723
p-value	0.322	0.061	0.003*	0.012*

t-Independent Sample t-test; p -value>0.05 NS;

Table 6: Comparison between continuing group and control group according to diameter of CL and RI at first visit and second visit.

Outcome after 12 weeks	Study group (n=100)	Control group (n=100)	χ^2	p-value
Continued pregnancy	50 (50%)	90 (90%)	9.481	0.013*
Missed abortion	27 (27%)	10 (10%)		
Complete and incomplete abortion	23 (23%)	0 (0%)		

χ^2 : Chi-square test; *p-value <0.05 S

Table 7: Comparison between study group and control group according to outcome after 12 weeks.

DISCUSSION

In present study, Endovaginal ultrasonography was done for 200 pregnant women starting at 6 weeks till 9 weeks menstrual age for evaluation of corpus luteum changes in normal pregnancy 100 cases and threatened abortion 100 cases as regard site size morphological type and growth rate (follow up after one week) as well as to evaluate the functional state by Doppler ultrasonography velocimetric analysis of CL blood flow (resistance index)

This was done to study CL changes by color doppler ultrasonography in early pregnancy to predict outcome of pregnancy in cases of threatened abortion.

Endovaginal ultrasonography examination was performed using GE Voluson A6 equipped with a 5-MHz transvaginal probe. At Al-Galaa Maternity Hospital & Al-Hussein University Hospital respectively.

The study revealed that corpus luteum detected in 170 cases (85%) and not detected in 30 cases (15%), (20 cases in study group and 10 cases in control group). This percentage is less than similar study by Frates et al.⁸ could identify 98% of corpus luteum and nearly similar to Ahmad et al.⁹ she could identify 90% of CL, while another study point to an average rate of detection about 82% by Valentin.¹⁰

It is possible that those patients in whom CL couldn't be identified represent the non-cystic corpora lutea in which the acoustic interface between luteal tissue and ovarian parenchyma wasn't visualized by our ultrasound.

It is also possible that they represent luteal tissue that regressed prematurely or never developed appropriately

As regard the site in normal pregnancy, the CL was situated in the right ovary in 45 cases (45%) and the left ovary in 45 cases (45%) and wasn't seen in 10 cases (10%)

In threatened abortion, it was situated in the right ovary in 42 cases (42%) and the left ovary in 38 cases (38%) and wasn't seen in 20 cases (20%). There was no significant difference between the site of corpus luteum in normal pregnancy and threatened abortion (p-value>0.05 NS). This is in contrast with Samsoie et al.¹¹, where they postulated that the corpus luteum was situated mainly in the right ovary in some abnormal pregnancies.

As regard sonographic morphological appearance. We could differentiate four types of corpora lutea. They are hypoechoic, thick walled cyst, complex cyst and simple cyst.

In normal pregnancy we detect the hypoechoic type in 23 cases (23%), thick walled cyst in 41 cases (41%), complex cyst in 13 cases (13%) and simple cyst in 13 cases (13%) and not seen in 10 cases.

In threatened abortion we detect the hypoechoic type in 10 cases (10%), thick walled cyst 30 cases (30%), complex cyst 33 (33%) cases and simple cyst 7 cases (7%) and not seen in 20 cases. There was no significant difference between the morphological appearance of corpus luteum between the two groups. This is in agreement with another two study by Frates et al.⁸ and Glock and Brumsted.¹² Pareja et al.¹³ founded that the most common morphologic types identified was the CL with the thick wall and dense hypoechoic center (48%), followed by CL looking hypoechoic (42.5%). The hypoechoic CL was more common among women who have aborted, but presented no significant difference compared to the other types.

As regard the size of CL, in normal pregnancy, the mean diameter ranged from 16-28 mm with mean of 21.22 ± 3.43 in the first visit, and ranged from 17-29 with mean of 21.38 ± 3.14 in the second visit.

In threatened abortion, the mean diameter ranged from 17-29 with mean of 21.88 ± 3.67 in the first visit, and ranged from 19-31 with mean of 22.23 ± 3.05 in the second visit. There was no significant difference in size (mean diameter) or growth rate of CL between the two group (p-value>0.05 NS). This agree with Glock et al.¹² that revealed lack of correlation between CL size or growth rate and steroid products. Also, Frates et al.⁸ found that CL size in pregnancies that survived the first trimester, similar to the size in those that spontaneously aborted during first trimester. This is in contrast with previous study by Pareja et al.¹³, when comparing the diameter and volume of the CL of normal pregnant women with those who aborted, found lower diameter and volume in cases of abortion.

As regard the Doppler velocimetric study in the CL, expressed as the resistance index or pourcelot index. In the first visit, the normal pregnancy R.I. ranged from 0.42-0.57 with mean of 0.46 ± 0.04 and in threatened abortion ranged from 0.42-0.88 with mean of 0.54 ± 0.12 with significant difference between the two group (*p-value <0.05 S)

In the second visit, the normal pregnancy R.I. ranged from 0.51-0.72 with mean of 0.63 ± 0.06 and in threatened abortion ranged from 0.52-0.84 with mean of 0.62 ± 0.09 with no significant difference between the two group (p -value > 0.05 NS). With increased R.I. in ovarian vasculature in both groups.

As regards resistance index of cl blood flow in threatened abortion group during the first visit the mean resistance index in aborted group was 0.54 ± 0.14 and in continued group was 0.55 ± 0.12 with no significant difference

In the second visit the mean resistance index in aborted group was 0.66 ± 0.09 and in continued group was 0.58 ± 0.07 with significant increase of R.I. in the aborted group. This study was in accordance with another two studies done by Alcazar¹⁴ and Durfee and Frates¹⁵, studies had demonstrated that RI and PI were significantly higher in patients of abortion R.I. is an indicator of blood circulation resistance. The smaller the RI value, the more abundant the blood flow.

Alcazar¹⁴ who found that no difference in the vessels of the corpus luteum in women with threatened abortion, but they found that a higher mean resistance index was observed in, inevitable abortion and missed abortion because luteal vascularization might be decreased in missed abortion but not in threatened abortion.

Ahmad et al.⁹ in a study of corpus luteum blood flow in normal and abnormal early pregnancy using 3D power Doppler ultrasound, seeking to define gestational CL sonographic parameters as morphology, size and volume, as well as evaluating the vascularity with color Doppler velocimetry, they found that, Detection of CL in this study was 100% among results reported in the literature, The morphology of the CL in early pregnancies is variable according to its echographically grayscale. In their study they found that the most common morphologic types were the hemorrhagic CL in 50% ($n = 18$) (18/36), The importance of the size of the CL is controversial and in their study the found lower volume in cases of abortion, concerning CL blood flow, the study found no association between the vascularization index (VI) 3D US of normal pregnant women and those who progressed to miscarriage.

CONCLUSION

There is no significant difference in site of corpus luteum between normal pregnancy and threatened abortion.

By transvaginal sonography, four different morphological types of corpus luteum could be identified: hypoechoic, thick walled cyst, complex cyst and simple cyst, with no functional or predictive significance of pregnancy outcome in either normal pregnancy or threatened abortion.

As regard the size and rate of growth of corpus luteum, there is no significant difference in normal pregnancy and threatened abortion.

There is 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.

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