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ORIGINAL STUDY

Role of progesterone and inhibin A in predicting the adverse outcome of pregnancy

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Abstract

Background: The prediction of future miscarriages in patients who have had a first-trimester abortion can be improved by measuring levels of inhibin A and progesterone. Pregnancy outcomes can be improved by using this important information to direct clinical treatment and care. **Objectives:** Progesterone and Inhibin A during the first trimester can be used to quickly and precisely detect pregnancy outcomes, improving prenatal services.

Methods: A total of 180 women from Badr City Hospital participated in the study, split up into two groups: group B contained 90 women who had undergone a first-trimester abortion, and group A comprised 90 well-being expectant mothers. The cases were carefully evaluated by comprehensive medical history, cervical-pelvic examinations, and transvaginal ultrasound. Enzyme-linked immunosorbent assay (ELISA) was used to measure the concentrations of progesterone and inhibin A in blood samples. The goal of the study was to compare the two groups' hormone levels.

Results: The findings of the study indicate that low progesterone levels, high diastolic blood pressure, previous abortions, and primigravida may independently contribute to the risk of abortion with odds ratios (95% confidence intervals), 0.895 (0.850–0.943), 1.123 (1.018–1.240), and 26.857 (8.769–82.250), respectively, with associated *P* values of less than 0.001, 0.021, and less than 0.001.

Conclusion: Pregnant females with high diastolic blood pressure and a history of previous abortion along with low levels of progesterone are at more risk of developing abortion in their first trimester of pregnancy. Inhibin A is another promising marker but needs more studies.

Keywords: Early marker, Inhibin A, Previous abortion, Progesterone

1. Introduction

In the first trimester of pregnancy, vaginal bleeding may indicate a threat of abortion, which can have a worse outcome on the women's health [1]. Measuring the level of the Human chorionic gonadotrophins (HCG) whether qualitatively or quantitatively is not enough for predicting adverse outcomes [2]. Pregnant females experiencing vaginal bleeding in their first trimester of pregnancy will need to do Ultrasound to assess fetus viability [3]. Progesterone, a sex steroid, prepares the endometrium for fertilized egg implantation and regulates immune responses by cytokines balance and

natural killer cell activity. It suppresses uterine contractions and enhances uteroplacental circulation [4].

The placenta produces inhibin A, which controls hormone levels during pregnancy. It affects trophoblast development and endometrial decidualization, which in turn affects fetal growth and the success of pregnancy. In the first trimester inhibin A levels peak, after which they stay constant and rise once again until the full term [5].

2. Aim

Improving prenatal care and finding early serum biomarkers, Progesterone, and Inhibin A.

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3. Patients and method

This cross-sectional study was conducted at Badr City Hospital, specifically in the Department of Gynecology and Obstetrics. A total of 180 women participated in the study, split into two groups: group B, which included 90 women who had had a first-trimester abortion, and group A, which included 90 healthy pregnant women. Women with first-trimester spontaneous abortions who were between the ages of 25 and 35 and had a BMI of 21–26 met the inclusion criteria. Medical disorders like type 2 diabetes, endometriosis, and Fibrosis were excluded.

A detailed medical history was obtained for each participant, which included information on menstrual history (last menstrual period, age at menarche, characteristics of menstrual cycles) and obstetric history (number of pregnancies, previous abortions, number of living children, and history of previous cesarean sections). To investigate the possibility of local factors contributing to vaginal bleeding, a pelvic and cervical examination was conducted using a speculum, allowing for assessment of cervical opening, and the presence of cervical erosion or other abnormalities.

This work was officially approved by an Ethics Committee (adapting the Declaration of Helsinki principles), and a knowledgeable written consent was signed by all participants before enrollment.

To accomplish the goals, the Logic 4c platform was used for the obstetric Trans Vaginal ultrasonography evaluation (TVS). A TVG examination was performed during the initial presentation, which occurred during the 5th or 7th week of pregnancy, in order to assess the fetus' viability and choose the best course of action. Based on the results of the inquiry, the cases were divided into two distinct groups (Figs 1 and 2).

All participants had withdrawn 5 mL of venous blood in a serum separator tube, in the 7th week of pregnancy. After being centrifuged at 3000 rotations

per minute (RPM), for a period of 10 min, they were refrigerated at -20° till time of their measurement.

Serum Inhibin A was determined using an enzyme-linked immunosorbent test (ELISA) method kit that was purchased from Bioassay Technology Laboratory, Catalog EA0021HU, Zhejiang, China. Serum Progesterone was also measured by ELISA sandwich technique kit according to the manufacturer's instructions which was brought by Monocent, 9025 Eton Ave, Ste C, Ca91304, Canoga Park, USA.

3.1. Statistics

An extensive analysis of the data was conducted utilizing a variety of statistical techniques. To properly summarize the data, descriptive statistics were used, including the mean \pm standard deviation (\pm SD), median, range, frequencies, and percentages. A student *t*-test for independent samples was used to compare the study groups for numerical variables. Conversely, a Chi-square (χ^2) test was employed to compare categorical data; this test was used in cases when the anticipated frequency was less than 5. A multivariate logistic regression analysis was conducted to find independent predictors of abortion. Using a receiver operator characteristic analysis, the best cutoff values for progesterone and inhibin-A in predicting miscarriage were determined. When *P* values were less than 0.05, statistical significance was considered significant and less than 0.001 highly significant. IBM SPSS 22 (Statistical Package for the Social Science; IBM Corp, NY, USA) was used for all statistical analyses.

4. Results

On comparing age between two groups results showed matched groups as shown in (Table 1).

The Characteristics of pregnancy history data distribution were presented in (Table 2), where number of pregnancies was higher in group B 3.33 ± 1.03 than group A 2.69 ± 1.05 .

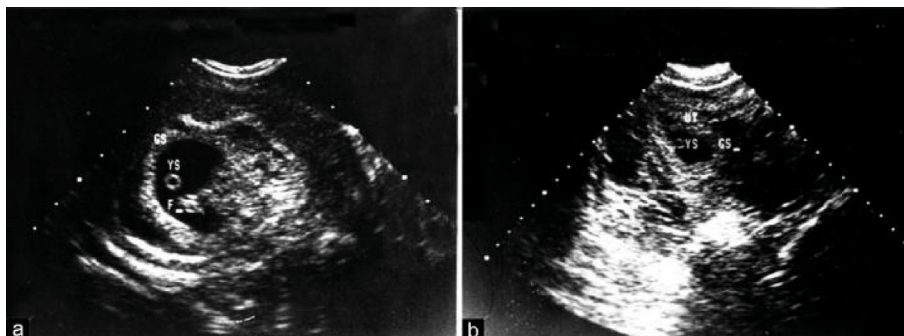


Fig. 1. Transvaginal Ultrasound, a: with gestational sac, b: without gestational sac.

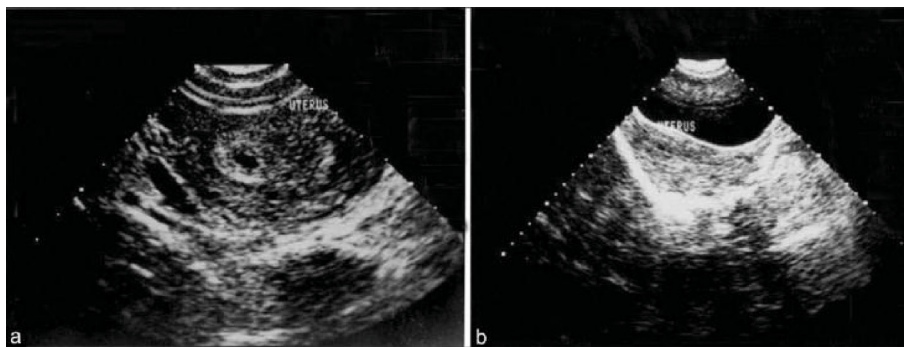


Fig. 2. Transvaginal ultrasound, a: with fetal heart rate and yolk sac, b: with a double decidual sac, no yolk sac, no embryo.

Table 1. Clinical data.

	Group A	Group B	P value	Statistically significant
AGE (Y)	29.36 ± 3.35	30.04 ± 2.94	0.1444	N. S
BMI (KG/M)	21.42 ± 1.32	24.92 ± 1.22	0.0089	Sig.
DBP (MM HG)	71.66 ± 5.12	77.98 ± 5.42		Sig.
SBP (MM HG)	113.7 ± 8.96	119.8 ± 6.91	<0.001	Sig.

All data presented in Mean ± SD.

BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 2. History of pregnancy.

	Group A (N = 90) [n (%)]	Group B (N = 90) [n (%)]	P value	Statistically significant
Number of pregnancies ^a	2.69 ± 1.05	3.33 ± 1.03	<0.001	Sig.
Previous abortions				
No	70 (77.78)	12 (13.3)	<0.001	Sig.
Yes	20 (22.22)	78 (86.7)		

^a Mean ± SD.

Table 3 represented primigravidae, smoking, and Preeclampsia history.

Table 4 presented a comparison of Inhibin A levels and Progesterone levels between two groups.

Factors predicting abortion in are presented in (Table 5).

The receiver operator characteristic curve for the validity of the progesterone measurement showed a significant area under the curve (AUC) = 0.836 (95%

CI: 0.765–0.908) ($P < 0.001$) at cut-off value 10.250 with sensitivity 78% and specificity 98% (Fig. 3).

5. Discussion

Early pregnancy loss, characterized by spontaneous termination of intrauterine pregnancy in the first trimester, presents complex challenges in diagnosis and management. Personalized

Table 3. Medical history.

	Group A (N = 90) [n (%)]	Group B (N = 90) [n (%)]	P value	Statistically significant
Primigravida				
No	76 (84.44)	85 (94.44)	0.039	Sig.
Yes	14 (15.55)	5 (5.56)		
Smokers				
No	89 (98.88)	84 (93.33)	0.867	N. S
Yes	1 (1.11)	6 (6.66)		
History of preeclampsia				
No	89 (98.88)	87 (96.66)	0.976	N. S
Yes	1 (1.11)	3 (3.33)		

Table 4. Level of inhibin A and progesterone.

	Group A	Group B	P value	Statistically significant
Progesterone ng/L ^a	16.39 ± 4.97	6.96 ± 10.19	<0.001	S
Inhibin A ng/L ^a	133.62 ± 54.25	133.44 ± 78.54	0.99	N. S

^a Mean ± SD.

Table 5. Factors predicting abortion.

	P value	OR	95%CI	
			Lower	Upper
Progesterone (ng/l)	<0.001	0.895	0.850	0.943
BMI (Kg/m ²)	0.782	1.053	0.732	1.513
SBP (mmhg)	0.603	0.978	0.900	1.063
DBP (mmhg)	0.021	1.123	1.018	1.240
Number of pregnancies	0.432	1.254	0.713	2.207
Previous abortions	<0.001	26.857	8.769	82.250

BMI, Body Mass Index; CI, confidence interval; DBP, Diastolic Blood Pressure; OR, odds ratio; SBP, Systolic Blood Pressure.

approaches are essential due to variations in manifestations and stages. Inadequate understanding of risk factors and failure to tailor management strategies to individual needs can lead to suboptimal care. Effective counseling skills and empathy contribute to improved patient outcomes by ensuring individualized care [6].

The BMI in the current study was higher in group B, 24.92 ± 1.22 kg/m compared with group A

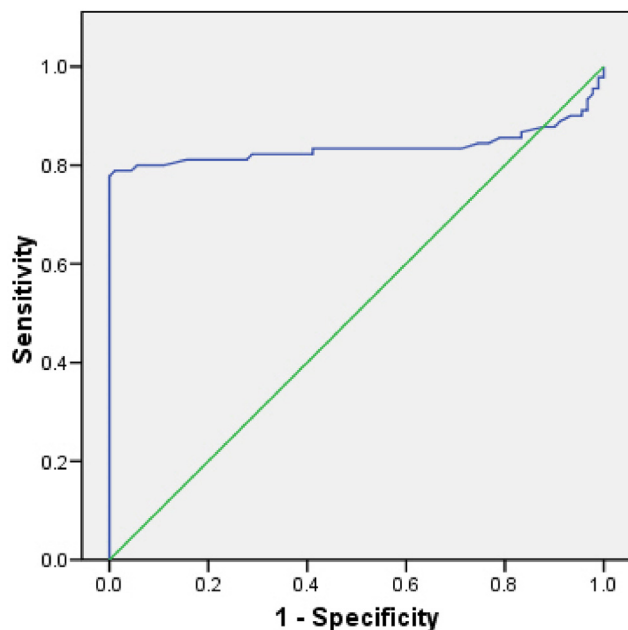
21.42 ± 1.32 with a statistical significance. The same was found in both diastolic blood pressure (DBP) and SBP, which had been in accordance with another study on pregnant females from Spain, suggesting that higher body mass index women are in more risk for spontaneous abortion with OR 4.02 (1.53–10.57) [7], and with another study done by Okoth and his colleagues concluding the increasing of developing diabetes (RR = 1.25, 95% CI: 1.15–1.36; P < 0.001) and hypertension (RR = 1.07, 95% CI: 1.02–1.12; P = 0.005) [8].

Our study reveals intriguing findings regarding the number of pregnancies. Group B exhibited a slightly higher number of pregnancies compared with group A, and this disparity was statistically significant, indicating a greater number of pregnancies in Group B. Additionally, a significant majority of patients in group B (86.7%) had a history of previous abortions, while only 13.3% of cases in group A had a similar history.

According to the research conducted by Dadheech *et al.* in 2021, a previous history of spontaneous abortion is linked to unfavorable outcomes in subsequent pregnancies. Such cases are associated with an elevated risk of abortion, preterm delivery, the necessity for caesarean sections, and fetal loss. However, these complications and fetal loss can be mitigated by timely patient booking and providing appropriate antenatal care [9].

The impact of uterine abnormalities such as intrauterine adhesions, polyps, and submucosal myomas can increase the risk of first-trimester abortion, authors recommended that early identification and appropriate management of uterine abnormalities could play a crucial role in preventing pregnancy loss in this specific cases [10,11].

ROC Curve



Diagonal segments are produced by ties.

Fig. 3. Progesterone receiver operator characteristic Curve.

Regarding primigravida, we found that group A, had a higher proportion in our study than group B (15.55% vs. 5.56%) with a statistical significance, suggesting that women who have been previously given birth may be less likely to have a first-trimester abortion. Which was in contrast to the study done by Sunil and Valsan whom found pregnant females with a history of abortion, women experiencing their first pregnancy, and those who have traveled may be more susceptible to experiencing an abortion. With odds ratio 3.5, 2.8, and 2.72, respectively [12].

We compared the levels of Inhibin A in the two groups, group B had an average of 133.44 ± 78.54 ng/l whereas group A had 133.62 ± 54.25 ng/l with *P* value of more than 0.05. This data raises the possibility that Inhibin A levels are not a reliable predictive factor for estimating a patient's likelihood of a first-trimester abortion.

In contrast, the study by Prakash *et al.*, Inhibin A and activin A was measured in the six week and repeated on the eighth week, for both of them they found their levels are lower in aborted female than live birth female, suggesting them as predicating marker for miscarriage [13]. While others had suggested high inhibin level can be related to adverse birth outcome (preterm delivery and gestational diabetes mellitus) [5].

The Progesterone levels in the current study showed a significant statistical difference, group A exhibited a mean Progesterone level of 16.4 ± 4.97 ng/l, whereas group B had a mean Progesterone level of 6.96 ± 10.19 ng/l. The *P* value of less than 0.001.

In similar to Deng *et al.*, a negative correlation between low serum progesterone and miscarriage (odds ratio [OR]: 0.97, 95% confidence interval [CI]: 0.95–0.98) [14]. Other emphasis the role of progesterone supplement as a protective treatment in threatened abortion [15–17].

Progesterone-mediated immunoregulation of cytokine for recurrent spontaneous abortion had been studied giving a promising result with its correlation with chlamydia infection and miRs upregulation [18].

In our study a logistic regression was done for progesterone for abortion with OR 0.895 (95% CI 0.850–0.943), and testing other confounding variables; high DBP OR 1.123 (95% CI: 1.018–1.240, *P* 0.021), previous abortions OR 26.857 (95%, CI: 8.769–82.250, *P* < 0.001) suggesting a high diastolic and with history of previous abortion can experience abortion in the first trimester and low serum progesterone level can be used as an early predicting marker. Which was similar to another study done by

Li J *et al.*, finding stress, pollution and depression other contributing factor in early abortion [19].

5.1. Conclusion

Pregnant females with high DBP and a history of previous abortion along with low levels of progesterone are at more risk of developing abortion in their first trimester of pregnancy. Inhibin A is another promising marker but needs more studies. Progesterone mediated immunoregulation of cytokines by miRs is a promising field of study.

Source(s) of support

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Presentation at a meeting

Nil.

Institutional review board (IRB) approval number

1-2022.

Conflicts of interest

There are no conflicts of interest.

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