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# Role of inhibin a and progesterone as prognostic indicators in patients with first trimester abortion

## Abstract

**Background**: measuring levels of inhibin A and progesterone can be helpful in predicting the risk of future miscarriages in patients with first-trimester abortion. This information can help guide clinical management and interventions to improve pregnancy outcomes. This study aimed to improve prenatal services via rapid accurate useful pregnancy diagnostic indicators inhibin A & progesterone in first trimester of pregnancy.

**Methods**: The study involved 180 women from Badr city Hospital, divided into two groups: Group A included 90 healthy pregnant women, while Group B included 90 who had experienced first-trimester abortion. The inclusion criteria were maternal age between 24-34 years and BMI of 20-25, and. The cases were documented with a complete history, pelvic and cervical examinations, and a transvaginal ultrasound. Blood samples were collected to analyze inhibin A and progesterone levels using ELISA and Sequential Chemiluminescence Immunometric Assay Method. The study aimed to compare the hormonal levels in the two groups.

**Results**: The study found that patients with a history of previous pregnancies and first-trimester spontaneous abortion may have a higher risk of experiencing the condition. The study suggests that Progesterone levels may be a more useful prognostic indicator However inhibin levels may not be a reliable prognostic indicator for predicting the risk of first-trimester abortion, but further research is needed to confirm this. The study highlights the importance of considering the pregnancies history and previous abortions when studying first-trimester abortion.

**Keywords:** Inhibin A, progesterone, prognostic indicators, first trimester abortion

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Ahmed Hassan,[1] Amany Seif Mohammed Soliman,[2] Yasmine Mohamed Amrous,[3] Shaimaa Belal[4]

[1]Assistant Professor of Obstetrics & Gynecology, Faculty of Medicine, Helwan University, Egypt
[2]M.B.B.CH, M. Sc., Faculty of Medicine, Cairo University 2013, Egypt
[3]Assistant Professor of Clinical and Chemical Pathology, Faculty of Medicine, Helwan University, Egypt
[4]Assistant professor of Obstetrics & Gynecology, Faculty of Medicine, Helwan University, Egypt

**Correspondence:** Ahmed Hassan, Assistant Professor of Obstetrics & Gynecology, Faculty of Medicine, Helwan University, Egypt, Email dra7mad7asa@icloud.com

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## Introduction

Early pregnancy failure is a common pregnancy complication whereby 15% to 20% of clinically recognized pregnancies end up as abortions. Historical definitions of early pregnancy failure include threatened abortion, incomplete abortion, complete abortion, inevitable abortion and missed abortion with the outcome of viable or nonviable pregnancy. In clinical practice, the time delay to distinguish viable from nonviable pregnancy is often distressing to patients and doctors.[1]

Spontaneous miscarriage is one of the adversarial pregnancy outcome That negatively impact the physician and the lady. Threatened abortion could be suspected if woman has vaginal bleeding in the first trimester of pregnancy[2] US and serum human chorionic gonadotropin (HCG), estrone, estradiol (E2), estriol, human placental lactogen, cortisol, urine HCG, progesterone and urine estrogen have a role in diagnosis of abortion.

Fifty percent of ladies who experience vaginal bleeding , their pregnancy will end in miscarriage.[3] Pregnancy tests are not always dependable as they may remain positive or unsure in up to forty percent of women for up to five days, even after end of pregnancy.[4]

Ultrasound might be precise in the diagnosis of in the first trimester but does not deliver information on the function of the trophoblast. Vaginal smears does not have a dependable prognostic value.[5]

Progesterone and human chorionic gonadotropin concentration measurement are used in assessing the proceedings during both normal and complicated pregnancies.[6]

In the hope that plasma progesterone estimation might be of diagnostic and prognostic value in complications of the first trimester of pregnancy (i.e., threatened abortion, missed abortion, and ectopic pregnancy).[7]

Inhibins are multifunctional molecules involved in the control of pituitary FSH secretion. A body of observational and experimental evidence from several species, including the human, supports the concept that inhibins are gonadal messengers that exert a physiological negative feedback control on FSH release at the pituitary gland. Apart from their essential role in the selective control of FSH secretion, inhibins are currently recognized as paracrine ovarian and testicular regulators and have multiple paracrine effects in the utero-placental unit, representing a promising marker for male and female infertility, gynecological and gestational diseases.[8]

Inhibins are glycoproteins produced by the granulosa and theca cells of the ovary and by the Sertoli cells of the testis. They are of great importance for the negative feedback control of pituitary gonadotrophin secretion. There are at least two active molecular forms in circulation, inhibin A and inhibin B, which are heterodimers made by an a subunit and either bA (inhibin A) or bB (inhibin B) subunits.[9]

We have aimed to improve prenatal services via rapid accurate useful pregnancy diagnostic indicators inhibin A & progesterone in first trimester of pregnancy.

## Methodology

In this comparative-cross sectional study, we collected cases from the Department of Gynecology and Obstetrics at Badr city Hospital. Our study involved a total of 180 women, who were divided into two groups: Group A, comprising 90 healthy pregnant women and Group B, comprising 90 women who had experienced first-trimester abortion.

The study's inclusion criteria were as follows: women who had experienced first-trimester spontaneous abortion, with maternal age ranging from 24 to 34 years and a BMI of 20-25. Exclusion criteria included medical disorders such as diabetes mellitus and hypertension, as well as congenital uterine malformations or large fibroids distorting the cavity.

## Methods

A comprehensive record of each participant's medical history will be thoroughly documented, including personal details such as menstrual history (L.M.P, menarche, nature of menses), obstetric history (parity, abortion, living children, and previous sections).

To rule out any potential local causes of vaginal bleeding, such as cervical erosion, a pelvic and cervical examination using a speculum will be performed, which allows for the determination of whether or not the cervix is open. A thorough evaluation will be conducted to exclude the possibility of other potential general sources of bleeding prior to proceeding with treatment.

The obstetric ultrasound evaluation (TVS) will be performed using the Logic 4c platform to achieve the objectives. At the time of the initial presentation (5th to 7th week of pregnancy), a transvaginal ultrasonographic scan will be conducted to determine the viability of the fetus and take appropriate action. After the investigation is completed, the cases will be separated into two distinct groups based on the findings: the group that failed to continue and the group that succeeded in continuing (Figure 1) (Figure 2).

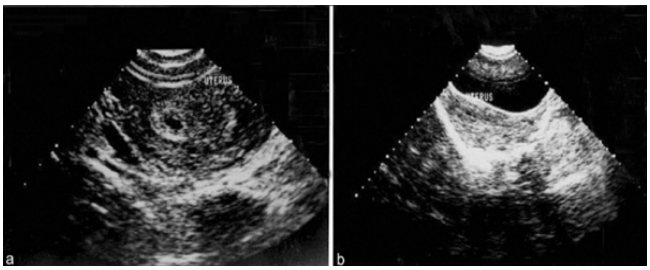

**Figure 1** Diagnosis-Normal early pregnancy. (a) (TVS)-Shows a single Intrauterine gestation sac. (b) (TAS)-Does not show any intrauterine gestation sac.

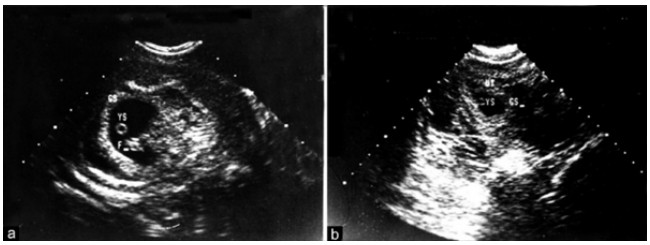

**Figure 2** Diagnosis-Normal early pregnancy. (a) (TVS)-Shows a single Intrauterine gestation sac with a double decidual sac sign, embryo with FHM, yolk sac. (b) (TAS)-Shows a single Intrauterine gestation sac with a double decidual sac sign, no embryo visualized, yolk sac present.

For the purposes of this study, the patients will be split into two groups: group A, which will consist of ninety healthy pregnant women in their first trimester, and group B, which will include ninety women who have experienced a naturally occurring miscarriage during the first trimester. Both groups will be matched in terms of patient numbers. Upon enrollment, all participants will undergo a venous blood draw of five milliliters at the 7th week of pregnancy, regardless of their group assignment. These samples will be centrifuged for ten minutes at a speed of 3,000 revolutions per minute and subsequently transported to the laboratory for further testing. All serum samples will be stored at -70 degrees Celsius until hormonal analysis is conducted. No preservatives will be added to the samples prior to testing.

The protein under analysis is known as Inhibin A, and we will employ a two-site ELISA that has been validated for use with human serum Inhibin A to conduct the analysis. Additionally, to achieve our objective, we will use the Sequential Chemiluminescence Immunometric Assay Method to determine the overall level of progesterone in the sample.

## Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Because the groups are large enough, comparison of numerical variables between the study groups was done using Student *t* test for independent samples. For comparing categorical data, Chi-square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Multivariate logistic regression analysis was performed to test for the independent predictors for abortion. Accuracy was represented using the terms sensitivity, and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for progesterone and inhibin-A in predicting miscarriage. Two-sided *p* values less than 0.05 was considered statistically significant. IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows was used for all statistical analyses.

# Results

This study compares the demographic data of two groups of patients - Group A, consisting of healthy pregnant women in their first trimester of pregnancy, and Group B, consisting of women who experienced first-trimester abortion. The demographic data presented include age, BMI, and blood pressure measurements (systolic and diastolic) (Table 1).

**Table 1** Demographic data distribution

| | Group (A) N=90 | Group (B) N=90 | P value | Statistically significant |
|---|---|---|---|---|
| Age | | | | |
| Mean± SD | 29.36±3.35 | 30.04±2.94 | 0.1444 | N. S |
| Range (Min-Max) | 24-34 | 24-34 | | |
| BMI (kg/m2) | | | | |
| Mean± SD | 23.42±1.32 | 23.92±1.22 | 0.0089 | Sig. |
| Blood Pressure | | | | |
| SBP (mm Hg) | 114.5±9.36 | 120.5±7.11 | <0.0001 | Sig. |
| DBP (mm Hg) | 73.56±8.12 | 78.78±6.42 | | |

Statistical test used: Tow sample T-test & Chi-square test

P-value≤0.05 considered statistically significant (95% confidence interval).

Based on the Previous data, Group B had slightly higher blood pressure measurements compared to Group A. The mean systolic blood pressure (SBP) in Group B was 120.5 mm Hg compared to 114.5 mm Hg in Group A, while the mean diastolic blood pressure (DBP) in Group B was 78.78 mm Hg compared to 73.56 mm Hg in Group A, and the difference is statistically significant.

In terms of age and BMI, there were small differences between the two groups, with Group B having a slightly higher mean age (30.04 years) and a slightly higher mean BMI (23.92 kg/m$^2$) compared to Group A (mean age of 29.36 years and mean BMI of 23.42 kg/m$^2$).

However, these differences were within a narrow range, with both groups having a range of 24-34 years for age and a range of 24-34 kg/m$^2$ for BMI (Table 2).

**Table 2** Pregnancies history data distribution in all study population

| | Group (A) N=90 | Group (B) N=90 | P value | Statistically significant |
|---|---|---|---|---|
| Number of pregnancies | | | | |
| Mean± SD | 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%) | | |
| Statistical test used: Chi-Square test | | | | |
| p-value≤0.05 considered statistically significant | | | | |

Group B patients had a higher risk of experiencing first-trimester abortion. Patients who had previous pregnancies also had a higher risk (Table 3).

**Table 3** Cases history data distribution in all study populations

| | Group (A) N=90 | Group (B) N=90 | P value | Statistically significant |
|---|---|---|---|---|
| Primigravida | | | | |
| No | 77(85.56%) | 85(94.44%) | 0.047 | Sig. |
| Yes | 13(14.44%) | 5(5.56%) | | |
| Smokers | | | | |
| No | 87(96.67%) | 86(95.56%) | 0.9889 | N. S |
| Yes | 3(3.33%) | 4(4.44%) | | |
| History of preeclampsia | | | | |
| No | 87(96.67%) | 86(95.56%) | 0.9889 | N. S |
| Yes | 3(3.33%) | 4(4.44%) | | |
| Statistical test used: Chi-Square test | | | | |
| p-value≤0.05 considered statistically significant | | | | |

Smoking during pregnancy was low in both groups, with Group B having a slightly higher proportion of smokers. Both groups had a low proportion of patients with a history of preeclampsia, but Group B had a slightly higher proportion (Table 4).

**Table 4** Inhibin A and Progesterone levels in comparison in studied groups

| | Group (A) N=90 | Group (B) N=90 | P value | Statistically significant |
|---|---|---|---|---|
| Progesterone ng/L | | | <0.001 | S |
| mean±SD | 16.39±4.97 | 6.96±10.19 | | |
| median (minimum-maximum) | 15.35(10.1-34.3) | 2(0.3-44.2) | | |
| Inhibin A ng/L | | | 0.99 | N. S |
| mean±SD | 133.62±54.25 | 133.44±78.54 | | |
| median (minimum-maximum) | 117.65(16.6-249.6) | 113.7(42.9-611) | | |
| p-value≤0.05 considered statistically significant | | | | |

This Table 4 presents a comparison of Inhibin A levels and Progesterone levels between two groups: Group A and Group B. The mean Progesterone level in Group B was significantly lower than that of Group A (p<0.0001).

The mean Inhibin A levels in both groups were not significantly different (p=0.99) (Table 5).

**Table 5** The correlation coefficient between progesterone, clinical data, and Inhibin A in both Group A and Group B separately

| | Group A Progesterone n=90 | | Group B Progesterone n=90 | |
|---|---|---|---|---|
| | R | P value | R | P value |
| Age (Years) | -0.018 | 0.866 | -0.054 | 0.61 |
| BMI (Kg/m2) | 0.12 | 0.26 | -0.172 | 0.105 |
| SBP ( mmhg) | -0.207 | 0.051 | -0.016 | 0.881 |
| DBP (mmhg) | -0.255 | 0.015 | -0.029 | 0.79 |
| Number of pregnancies | 0.043 | 0.686 | 0.173 | 0.102 |
| Previous abortions | 0.119 | 0.262 | 0.034 | 0.75 |
| Primigravida | 0.033 | 0.754 | 0.026 | 0.807 |
| Smokers | -0.025 | 0.815 | 0.023 | 0.83 |
| History of preeclampsia | -0.029 | 0.789 | 0.166 | 0.118 |
| Inhibin A (ng/l) | 0.026 | 0.805 | 0.006 | 0.957 |

r, spearman's correlation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure

This Table 5 shows there is no significant correlation between progesterone (ng\l) and Age, BMI, SBP, DBP, number of pregnancies, previous abortions, primigravida, smokers, history of preeclampsia, and inhibin A in group B, while there was a statistically significant negative correlation between progesterone, and SBP and DBP in group A.

## Discussion

The occurrence of first-trimester abortion, defined as the loss of a pregnancy before the 12th week of gestation, is a common problem faced by many women worldwide. The causes of first-trimester abortion are multifactorial, ranging from genetic abnormalities to maternal medical conditions, such as thyroid disorders or diabetes. Accurate diagnosis and effective management of this condition are crucial, as it can have significant physical and emotional consequences for women.[10]

This study aimed to improve prenatal services via rapid accurate useful pregnancy diagnostic indicators inhibin A & progesterone in first trimester of pregnancy.

Our study compares the demographic data of two groups of patients - Group A, consisting of healthy pregnant women in their first trimester of pregnancy, and Group B, consisting of women who experienced first-trimester abortion. Group B had slightly higher blood pressure measurements compared to Group A. The mean systolic blood pressure (SBP) in Group B was 120.5 mm Hg compared to 114.5 mm Hg in Group A, while the mean diastolic blood pressure (DBP) in Group B was 78.78 mm Hg compared to 73.56 mm Hg in Group A, and the difference is statistically significant.

Several studies have investigated the relationship between demographic factors and the risk of first-trimester abortion. One study by Liu et al.[11] found that higher maternal age and higher BMI were associated with an increased risk of first-trimester abortion. Similarly, a study by Badr et al.[12] reported that maternal age and BMI were significant predictors of first-trimester abortion.[11,12]

In our results the higher mean blood pressure measurements in Group B may suggest an increased risk for these complications in this population. However, it is important to note that this study only

compared first-trimester healthy pregnant women to those who had experienced first-trimester abortion, and did not follow up with these patients to assess their pregnancy outcomes.

A study investigated the association between blood pressure and pregnancy outcomes in women with hypertensive disorders of pregnancy. The study found that higher blood pressure measurements were associated with a higher risk of adverse pregnancy outcomes, including preterm birth, fetal growth restriction, and stillbirth.[13]

Another study evaluated the relationship between maternal` blood pressure and fetal growth. The study found that higher maternal blood pressure in early pregnancy was associated with a lower birth weight and a higher risk of small-for-gestational-age infants.[12]

Our study shows in terms of age and BMI, there were small differences between the two groups, with Group B having a slightly higher mean age (30.04 years) and a slightly higher mean BMI (23.92 kg/m$^2$) compared to Group A (mean age of 29.36 years and mean BMI of 23.42 kg/m$^2$). However, these differences were within a narrow range, with both groups having a range of 24-34 years for age and a range of 24-34 kg/m$^2$ for BMI. The mean BMI of Group B is higher than Group A, and the difference is statistically significant.

In terms of blood pressure, Skogsdal et al.[14] found that high blood pressure was associated with an increased risk of first-trimester abortion. This is consistent with our findings, which suggest that patients with first-trimester abortion have higher blood pressure measurements compared to healthy pregnant women. It is important to note that demographic factors are just one of many potential factors that can contribute to the risk of first-trimester abortion. Other factors, such as genetics, lifestyle factors, and medical conditions, may also play a role. Therefore, further research is needed to better understand the complex interplay between these factors and their impact on the risk of first-trimester abortion.[14]

Also, the results of this study are also consistent with previous research that has shown an association between higher BMI and pregnancy complications, such as gestational diabetes, preeclampsia, and preterm birth.[15] The higher mean BMI in Group B may suggest an increased risk for these complications in this population.[15]

Our study shows on the number of pregnancies and previous abortions highlight some interesting findings. Firstly, the number of pregnancies for Group B is slightly higher than Group A. However, the difference between the two groups is statistically significant, with Group B having a higher number of pregnancies.

One study conducted by Wang et al.[16] examined the relationship between RPL and subsequent pregnancy outcomes. The study found that women with a history of RPL had a higher risk of first-trimester abortion and other pregnancy complications compared to women without a history of RPL. The authors suggest that the increased risk of pregnancy loss in these women may be due to underlying genetic or immunological factors.[16]

Another study by Bush et al.[17] evaluated the role of progesterone supplementation in women with a history of RPL. The study found that progesterone supplementation significantly reduced the risk of first-trimester abortion in this population. The authors suggest that progesterone supplementation may help to support early pregnancy and prevent pregnancy loss in women with a history of RPL.[17]

Our study shows the majority of patients in Group B (86.7%) have a history of previous abortions, which is expected. On the other hand, 13.3% of cases in Group A have a history of previous abortions, which could be due to various factors such as age, medical conditions, or complications during a previous pregnancy. The difference in previous abortions between the two groups is statistically significant, further emphasizing the distinction between the two groups.

One study conducted by Skogsdal Y et al.[14] investigated the association between previous pregnancy outcomes and the risk of first-trimester abortion in subsequent pregnancies. The study found that women with a history of previous pregnancy loss were at increased risk of first-trimester abortion in subsequent pregnancies. The authors suggest that careful monitoring and early intervention may be needed to prevent pregnancy loss in this population.[14]

A study by Mirza FG et al.[18] evaluated the role of uterine abnormalities in the risk of first-trimester abortion. The study found that women with uterine abnormalities were at increased risk of first-trimester abortion. The authors suggest that early detection and management of uterine abnormalities may be important in preventing pregnancy loss in this population.[18]

Our study shows in terms of primigravida (first pregnancy), Group B had a higher proportion of patients who were not primigravida compared to Group A (94.44% vs. 85.56%). This suggests that patients who have had previous pregnancies may have a higher risk of experiencing first-trimester abortion.

Regarding smoking status, both groups had a low proportion of patients who reported smoking during pregnancy, with Group B having a slightly higher proportion of smokers (4.44%) compared to Group A (3.33%).

In terms of the history of preeclampsia, both groups had a low proportion of patients who reported a history of preeclampsia, with Group B having a slightly higher proportion of patients with a history of preeclampsia (4.44%) compared to Group A (3.33%).

A study by du Fossé et al.[19] investigated the risk factors associated with first-trimester abortion in Iranian women. They found that a previous history of miscarriage was a significant risk factor for first-trimester abortion. They also found that older maternal age and higher body mass index were associated with an increased risk of first-trimester abortion.[19]

Another study by Liu H, et al.[12] examined the risk factors for recurrent spontaneous abortion in Chinese women. They found that previous live births were protective against recurrent spontaneous abortion, while advanced maternal age and higher body mass index were associated with an increased risk of recurrent spontaneous abortion.[12]

A study by Kalantari N et al.[20] investigated the risk factors for spontaneous abortion in Iranian women. They found that a history of previous spontaneous abortion was a significant risk factor for future spontaneous abortion. They also found that older maternal age and higher body mass index were associated with an increased risk of spontaneous abortion.[20]

Our data presented in this section compare the levels of Inhibin A between the two studied groups. The mean Inhibin A level in Group A was 133.62±54.25, while the mean Inhibin A level in Group B was 133.44±78.54. The p-value of 0.99 indicates that there was relation difference in Inhibin A levels between the two groups. This finding suggests that Inhibin A levels may not be a useful prognostic indicator for predicting the risk of first-trimester abortion in patients.

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One study examined the levels of Inhibin A, as well as other biomarkers, in women who experienced first-trimester abortion compared to those who had successful pregnancies. The study found that Inhibin A levels were significantly lower in women who experienced first-trimester abortion.[13]

Another study investigated the utility of Inhibin A as a potential biomarker for predicting early pregnancy loss. The study found that Inhibin A levels were not significantly different between women with early pregnancy loss and those with ongoing pregnancies.[21]

Our data presented in this study compare the levels of Progesterone between the two studied groups. The mean Progesterone level in Group A was 16.4±4.97, while the mean Progesterone level in Group B was 6.96±10.19. The p-value of <0.001 indicates that there was a statistically significant difference in Progesterone levels between the two groups. This finding suggests that Progesterone levels may be a useful prognostic indicator for predicting the risk of first-trimester abortion in patients.

A study by Shimada et al.,[22] investigated the association between serum progesterone levels and first-trimester abortion. The study found that women with low serum progesterone levels were at a higher risk of first-trimester abortion. This supports your finding that progesterone levels may be a useful prognostic indicator for predicting the risk of first-trimester abortion.[22]

Another study by Ezoe et al.,[23] evaluated the predictive value of progesterone levels in the first trimester for adverse pregnancy outcomes, including miscarriage. The study found that low progesterone levels in the first trimester were associated with an increased risk of miscarriage. This supports your finding that progesterone levels may be a useful prognostic indicator for first-trimester abortion.[23]

A study investigated the relationship between serum progesterone levels and pregnancy outcomes in women undergoing IVF. The study found that low progesterone levels were associated with a higher risk of pregnancy loss. This finding supports your hypothesis that progesterone levels may play a role in predicting the risk of first-trimester abortion.[24]

A study by Tal R et al.,[25] found that Inhibin A levels were not significantly different between women with normal pregnancies and those who experienced early pregnancy loss.[25]

Another study by Sharma et al.,[26] found that Progesterone levels were significantly lower in women with first-trimester abortion compared to those with normal pregnancies.[26]

A study published in 2023 to elucidate the effects of multiple factors on spontaneous abortion, it conducted a multivariate logistic regression analysis, the study found that several factors were significantly associated with spontaneous abortion, including exposure to pollution (OR 1.347, 95%CI: 1.084-1.674), depression (OR 1.14, 95%CI: 1.055-1.232) and stress (OR 1,140, 95%CI: 1.053-1.233) (P<0.05). However, the relationship between BMI, number of abortions, diabetes, alcohol consumption, and spontaneous abortion was unclear (p>0.05).[27,28]

Multiple logistic regression was conducted in our study for the prediction of abortion within all participants, using Progesterone, SBP, DBP, Number of pregnancies, previous abortions, and Primigravida as confounders. Progesterone, DBP, Previous abortions, and Primigravida were significantly associated with abortion with an Odds ratio (95%CI), 0.895(0.850-0.943), 1.123(1.018-1.240), 26.857(8.769-82.250), 10.536(1.601-69.341) and P- Value <0.001. 0.021, < 0.001, and 0.014 respectively, considering as an independent risk factor for abortion.

## Conclusion

Our study suggest that progesterone levels may be more useful prognostic indicator for predicting the risk of first-trimester spontaneous abortion patients. The timing of progesterone measurement or the specific population being studied could impact the relationship between inhibin A levels and first-trimester spontaneous abortion. So further research may be necessary to confirm the results of the study.

The study's finding also suggests that inhibin A levels may not be a reliable prognostic indicator for predicting the risk of first-trimester spontaneous abortion patients. It is possible that the relationship between inhibin A levels and first-trimester spontaneous abortion could be impacted by other factors, such as the timing of inhibin A measurement or the specific population being studied, and further research may be necessary to validate these results.

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## Conflicts of interest

Authors declare that there is no conflict of interest.

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