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Research Article

Evaluation of outcome of pregnancy in threatened abortion by serum progesterone levels

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ABSTRACT

Background: Early pregnancy maintenance depends on the progesterone production by the developing trophoblasts of the placenta and the corpus luteum of ovary. Threatened abortion has a psychological impact on patients so we need to have a tool that could predict the outcome of threatened abortion in advance. Serum progesterone level has shown to be a reliable marker of pregnancy outcome. The aim of the study was to assess the correlation between maternal serum progesterone level and pregnancy outcome in threatened abortion and to assess the role of maternal serum progesterone levels in the immediate diagnosis of pregnancy failure.

Methods: This observational study was conducted in the Department of Gynaecology and Obstetrics, Lalla Ded Hospital, Government Medical College, Srinagar over a period of 1 year in 100 women presenting with threatened abortion of less than 12 weeks of gestation, having spotting but without cervical dilatation.

Results: Mean maternal serum progesterone level in patients of threatened abortion who aborted was 21.5 ± 10.4 nanograms per millilitre and patients of threatened abortion who progressed normally to the period of viability had mean maternal serum progesterone level of 41.6 ± 10.8 nanograms per millilitre. Considering 24 nanograms per millilitre as cut off limit, 19% of patients of threatened abortion were having serum progesterone level of lesser than or equal to 24 nanograms per millilitre and 81% of patients of threatened abortion were having serum progesterone level of greater than 24 nanograms per millilitre.

Conclusions: Serum progesterone level is easy and reliable assay for determination of pregnancy outcome.

Keywords: Threatened abortion, Serum progesterone level, Period of viability

INTRODUCTION

Threatened abortion is a clinical dilemma for the obstetrician regarding the outcome of pregnancy. Threatened abortion is a clinically descriptive term applied to women who are less than 20 weeks of gestation having vaginal spotting or bleeding, closed cervical os and possibly mild uterine cramps.¹ It may progress to a term viable pregnancy or may result in incomplete, complete, missed or septic abortion.

Threatened abortion is the most common complication of pregnancy in the first half of gestation.² Threatened abortion is such an event during pregnancy which needs meticulous attention to fulfill the purpose of healthy baby from healthy mother. It occurs in about 20% of early pregnancies.³ Most of these pregnancies continue to term with or without treatment. Spontaneous abortion occurs in less than 30% of the women who experience threatened abortion.²

Steroidal hormones especially oestrogen and progesterone play a crucial role in the maintenance of pregnancy. Oestrogen causes hypertrophy and hyperplasia of the uterine myometrium, thereby increasing the accommodation capacity and blood flow of the uterus. Progesterone in conjunction with oestrogen stimulates growth of uterus, causes decidual changes of the endometrium required for implantation and it inhibits myometrial contraction. Progesterone maintains uterine quiescence by stabilizing lysosomal membranes and inhibiting prostaglandin synthesis.⁴ It has been aptly called as hormone of pregnancy because it helps in preparing the endometrium for embryo implantation and facilitating the endometrial development. It has a critical role in the very survival of pregnancy.⁵

Progesterone is produced by the corpus luteum of ovary in the normal menstruating women and to a lesser extent by the adrenal cortex.⁶ Corpus luteum maintains its capacity to synthesise the progesterone throughout pregnancy but at approximately 7th week of gestation its functional ability markedly decreases at the start of luteoplacental transition.⁷ During the follicular phase of cycle serum progesterone remains low. Following Luteinizing hormone (LH) surge and ovulation, luteal cells in the ruptured follicle produces progesterone in response to LH. During luteal phase progesterone level rises rapidly to a maximum of 10-20 ng/ml at day 5-7 following ovulation. During the luteal phase, progesterone transforms oestrogen primed endometrium from proliferative to secretory state.⁸ When conception occurs the levels of serum progesterone are maintained at mid-luteal levels by corpus luteum until 6th week. After that placenta becomes the main source of progesterone and level rises from 10-50 ng/ml in the first trimester to approximately 50-280 ng/ml in the third trimester.^{6,7,9}

If the amount or timing of progesterone release or the response of the endometrium to its stimulation is inadequate, the embryo fails in its attempt to achieve successful implantation resulting in infertility or spontaneous abortion. Serum progesterone is the reflection of the progesterone production by the corpus luteum which is stimulated by a viable pregnancy.¹⁰ It has been advocated as the main hormone balancing and inhibiting the stimulatory effect of oestrogen until last few weeks of pregnancy.⁶ As a result measurement of serum progesterone has been advocated as an early marker of detecting abnormal pregnancy.

Serum progesterone is a vital marker for the diagnosis of luteal phase deficiency. Measurement of serum progesterone in the first trimester has been shown to be a reliable predictor and effective tool for the diagnosis of patient with threatened abortion.¹¹ Decreased maternal serum progesterone in presence of detectable levels of HCG is highly suggestive of threatened abortion regardless of gestational age.^{12,13} The value of maternal serum progesterone has been studied by many investigators and it has been established that maternal

serum progesterone level is of great help in differentiating between viable and nonviable pregnancy.¹⁴

Maternal serum progesterone assay in cases of threatened abortion has a prognostic value.¹⁵ Majority of women who have defective ovum or in whom threatened abortion results in complete abortion have serum progesterone levels of less than 20 nanograms per millilitre irrespective of gestational age in the first trimester and those patients with threatened abortion whose pregnancy continues usually have higher than 20 nanograms per millilitre maternal serum progesterone levels. Maternal serum progesterone level is a suitable marker to estimate the final outcome of pregnancy with threatened abortion.¹⁶ Maternal serum progesterone assay in first trimester of pregnancy is safe, non-invasive and affordable. Considering the psychological impact of abortion, we need such a technique to predict the outcome of pregnancy in threatened abortion. Also, by adopting this technique, it has been demonstrated that institutions may improve the outcome of patients with threatened abortion. Looking at the large number of patients of threatened abortion attending our hospital, it became imperative to carry out this study and know its efficacy.

Aims and objective

1. To assess the correlation between maternal serum progesterone level and pregnancy outcome in threatened abortion.
2. To assess the role of maternal serum progesterone levels in the immediate diagnosis of pregnancy failure.

METHODS

This observational study was conducted in the Department of Gynaecology and Obstetrics, Lalla Ded Hospital, Government Medical College, Srinagar over a period of 1 year in 100 women presenting with threatened abortion of less than 12 weeks of gestation, having spotting but without cervical dilatation.

Exclusion criteria

1. Those pregnant women having spotting but with cervical dilatation.
2. Those patients who have already received HCG or progesterone.
3. Pregnant women with spotting over 12 weeks of gestation.
4. Patients having molar pregnancy.
5. Pregnant women with spotting but non-viable pregnancy.
6. Extra-uterine pregnancy.
7. Pregnant women with spotting but who are diagnosed to have other cause of bleeding like cervical polyp or erosion.

Patients coming with the symptoms of threatened abortion were admitted. Detailed history was taken and complete general physical examination was done. After that patients were subjected to gentle per speculum and per vaginal bimanual examination. All routine investigations including complete blood counts, blood grouping, liver function, kidney function, thyroid function, serum electrolytes and coagulogram were done. Urine sample was collected for human chorionic gonadotropin estimation. Ultrasonography was done to know the foetal viability and gestational age. Blood sample for maternal serum progesterone levels was collected before starting any hormonal treatment and then patients were treated as per protocol of our hospital.

Estimation of serum progesterone levels

Mechanism: Progesterone in the sample binds to the anti-progesterone: alkaline phosphatase conjugate. An aliquot of the reaction mixture is transferred to the fiber matrix and the fluorescent product is measured by the MEIA optical system.

Reagent: AxSYM progesterone reagent and specimen diluents

Serum sample: 2 ml of blood was collected in clot activated coated tubes (serum sample is required). Then serum sample was centrifuged for 10 minutes at a speed of 1500 rotations per minute. The sample was kept in a sample cup. Then sample was subjected to AxSYM machine containing progesterone kit. After 15 minutes, the results were displayed.

Statistical analysis

Data was described as mean ± standard deviation and percentage. Critical difference of interval variants among metric variables was analyzed by student’s t-test. Non metric variables were analyzed by Mann Whitney ‘U’ test, Fissure’s exact test and the chi-square analysis. Besides relative risk was evaluated. Statistical Package for Social Sciences (SPSS), Java stat and Microsoft excel software was used for data analysis.

RESULTS

Maximum number of the patients (50%) were in the age group of 25-29 (Table 1).

Table 1: Age distribution.

Age (years)	N	%
20 to 24	6	6.0
25 to 29	50	50.0
30-34	34	34.0
35-39	10	10.0
Mean ± SD	29.2 ± 3.6	(22,39)

Maximum number of the patients (52) were having gravidity of >3 (Table 2).

Table 2: Gravidity status.

Gravidity	N	%
Primigravida	34	34
2 to 3	14	14
>3	52	52

Maximum patient (63%) were in rural group (Table 3).

Table 3: Demographic status.

Dwelling	N	%
Rural	63	63
Urban	37	37

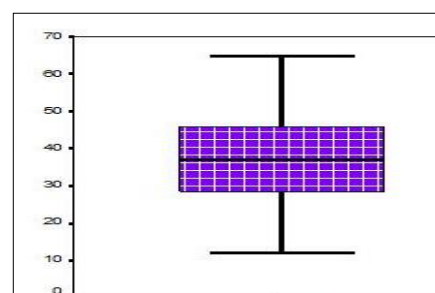


Figure 1: Maternal serum progesterone level (nanogram/ml).

Table 4: Serum progesterone level.

Outcome	Mean ± SD	p value
Aborted	21.5 ± 10.4 (12,46)	0.000 (significant)
Normal	41.6 ± 10.8 (21,65)	

Among patients of threatened abortion who aborted, mean maternal serum progesterone level was 21.5 ± 10.4 nanograms per millilitre and patients of threatened abortion who progressed normally to the period of viability had mean maternal serum progesterone level of 41.6 ± 10.8 nanograms per millilitre. Statistically the difference was significant with the p value of 0.000.

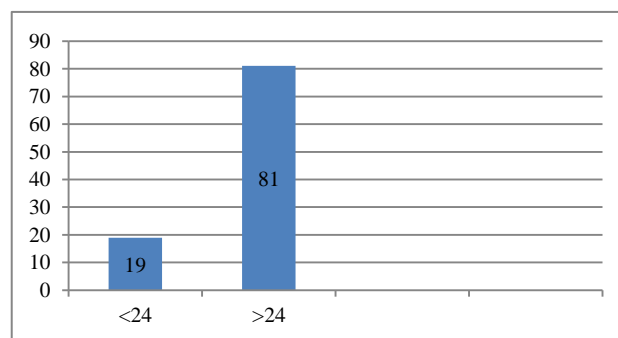


Figure 2: Maternal serum progesterone levels (nanograms/ml).

Considering 24 nanograms per millilitre as cut off limit, 19% of patients of threatened abortion were having serum progesterone level of lesser than or equal to 24 nanograms per millilitre and 81% of patients of threatened abortion were having serum progesterone level of greater than 24 nanograms per millilitre.

As shown in Figure 3 and Table 5, taking 24 nanograms per millilitre as cut off limit. 84.2% of patients of threatened abortion with maternal serum progesterone level of lesser than or equal to 24 nanograms per millilitre aborted while 15.8% of patients of threatened abortion with maternal serum progesterone level of lesser than or equal to 24 nanograms per millilitre continued to the period of viability. Among patients of threatened abortion with serum progesterone level of greater than 24 nanograms per millilitre, 6.2% of patients aborted while 93.8% of patients continued to the period of viability. Statistically the difference was significant with p value of 0.001. Relative risk was 13.6.

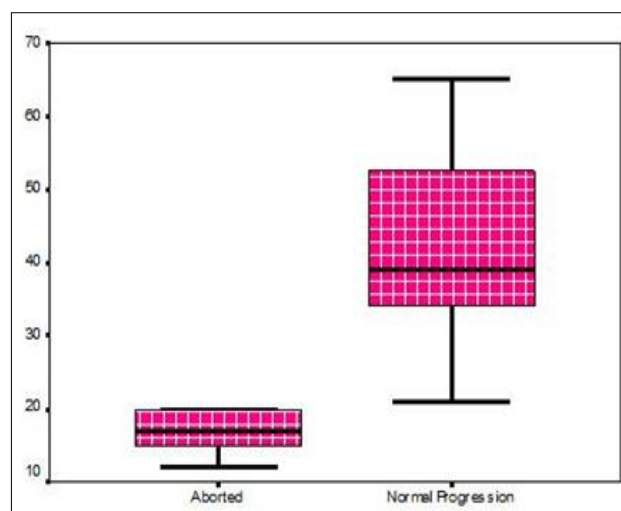


Figure 3: Maternal serum progesterone level in study group (ng/ml).

Table 5: Maternal serum progesterone level in study group (ng/ml).

Outcome	≤24		>24		p valve	RR (95%CI)
	n	%	n	%		
Aborted	16	84.2	5	6.2	p=0.001 (significant)	13.6 (6.6 to 23.6)
Normal	3	15.8	76	93.8		

DISCUSSION

Threatened abortion, a pregnancy complicated by vaginal bleeding and/or uterine cramps is one of the most common complication of pregnancy in the first half of gestation, occurring in about 20% of all clinically recognized pregnancies¹⁷ among which about 30% of patients abort at the end.⁵ From psychological perspective threatened abortion is a challenging dilemma and is a serious emotional burden for a woman so we need a marker to know its outcome. Attempts have been made from time to time to find out the diagnostic modality that could predict about the outcome of pregnancy and immediate diagnosis of pregnancy failure in threatened abortion. Hormone determinations have been used for such purpose¹⁷ among which maternal serum progesterone has been found to be a highly specific and sensitive biomarker of early pregnancy failure with good accuracy.

The present study was conducted in 100 women with threatened abortion of less than 12 weeks gestation. Patients were followed up to 20 weeks of gestation for pregnancy outcome in relation to maternal serum progesterone levels.

Majority of the patients were in the age group of 35-39 years (50%). Mean age being 29.2 ± 3.6 years and gravidity of greater than three. This observation was in

accordance to other studies where majority of the patients belonged to 21-30 years (58%)¹⁸ and gravidity of patients was greater than three.¹⁸ Majority of our patients (63%) belonged to rural area.

Mean maternal serum progesterone level of patients of threatened abortion who aborted was 21.5 ± 10.4 nanograms per milliliter and patients of threatened abortion who continued to the period of viability had levels of 41.6 ± 10.8 nanograms per milliliter. Statistically the difference was significant. This was comparable to other studies where mean serum progesterone level in patients who aborted was 20 nanograms per milliliter.¹⁶ In other studies also serum progesterone level was significantly low in patients who aborted.^{19,20}

In the present study, 24 nanograms per millilitre was taken as cut off value as with this value there was a clear demarcation in maximum number of patients into the groups who aborted and those who continued with pregnancy.

In the present study, 19% patients of threatened abortion had serum progesterone levels less than or equal to 24 nanogram/ml and 81% of patients were having levels more than 24 nanograms/ml.

84.2% of patients having serum progesterone level of less than or equal to 24 nanograms/ml aborted while as 15.8% continued till period of viability. Among patients with serum progesterone level greater than 24 nanogram/ml, 93.8% progressed to the period of viability and only 6.2% aborted. It was significant finding statistically and was comparable to other studies by Vahid Roudsari Fatimeh, Ayati S, Heydari F (2012)¹⁶ who in their study found that mean serum progesterone level in patient of threatened abortion was 24 nanograms per milliliter and in those patients who finally aborted mean levels were less than 20 nanograms per millilitre and those who progressed to the viability levels were 29 nanograms per milliliter. Similarly, in studies by Midha U, Narang APS, Sofat IB et al. (2002)²⁰ and Hanita O, Hanisah AH (2012)¹⁹ it was found that serum progesterone levels were significantly low (<20 ng/ml) in patients of threatened abortion who aborted while as in patients who progressed to viability levels were greater than 29 nanogram/ml. Maraghy MA, Lamiki H, Pinkert JH et al. (1978)²¹ studied about the predictive values of plasma progesterone levels in 70 patients of threatened abortion. It was found that no patient aborted whose plasma progesterone level remained above 35 nmol/l between 7 and 16 weeks of pregnancy, whereas if the plasma progesterone level was less than this, subsequent abortion always occurred.

In the present study, also, we found that maternal serum progesterone level in patients of threatened abortion who finally aborted was lower compared to the patients of threatened abortion who continued to the period of viability.

CONCLUSION

We concluded that serum progesterone levels were significantly low in majority of the patients who aborted and were normal in patients who progressed to period of viability. These results show that serum progesterone is a suitable, easy and affordable marker to estimate the final outcome of patients of threatened abortion. This assay can be used as an effective tool in counselling the patients of threatened abortion regarding the prognosis.

Abbreviation

HCG (human chorionic gonadotropin), LH (luteinizing hormone), MEIA (Microparticle Enzyme Immunoassay), ng/ml (nanogram/millilitre).

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Ethical approval: The study was approved by the institutional ethics committee

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