

## Early Threatened Miscarriage: Can Single Serum Progesterone Levels Provide Insight into Pregnancy Outcome?

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### ABSTRACT

**Introduction:** Around 20-25% of pregnant women experience vaginal bleeding in the first 20 weeks, with about 50% leading to miscarriage. Progesterone, a key pregnancy hormone, may reduce the risk of spontaneous pregnancy loss. Accurate prediction of pregnancy continuation is vital for appropriate care. This study assesses the role of a single serum progesterone measurement during threatened miscarriage in predicting pregnancy outcomes. It also examines the relationship between pregnancy continuation, maternal age, gestational age, symptoms, and risk factors.

**Methods:** Conducted at the Institute of Obstetrics and Gynecology in Chennai, India, the study included 160 pregnant women ( $\leq 12$  weeks gestation) with bleeding. Sociodemographic data, clinical history, and blood samples for serum progesterone and hemoglobin levels were collected and analyzed.

**Results:** Participants had an average age of  $26.7 \pm 3.5$  years, with 76.40% aged 20-30 years. First-time mothers comprised 47.75%. Common symptoms were vaginal bleeding and spotting. Anemia was observed in 22.47% of participants. Majority of participants had serum

progesterone levels exceeding 20 ng/ml. Higher serum progesterone levels significantly correlated with continued pregnancy, while hemoglobin, body mass index, and pregnancy outcomes showed no significant associations.

**Conclusion:** Serum progesterone levels are promising for diagnosing viable pregnancies conveniently and cost-effectively during threatened miscarriages.

**Keywords:** Pregnancy, Threatened Abortion, Progesterone, Female, Gestational Age

## **INTRODUCTION**

Elevated maternal blood progesterone levels have been empirically linked to a decreased risk of experiencing spontaneous pregnancy loss. In general, when progesterone levels fall below the threshold of 20 nmol/l (equivalent to 6 ng/ml), this condition is found to possess a robust positive predictive value for the unfortunate outcome of a miscarriage. Conversely, when progesterone levels surpass 60 nmol/l (equivalent to 19 ng/ml), there exists a strong association with a viable, ongoing pregnancy [1-4]. This scientific insight underscores the significance of monitoring progesterone levels during pregnancy, especially when complications arise.

Adding to the complexity of pregnancy, the risk of miscarriage tends to rise with maternal age. This is particularly distressing for expectant mothers, as the loss of a pregnancy at any stage can be an emotionally harrowing experience. Hence, it becomes paramount to swiftly identify any potential issues and initiate appropriate interventions to enhance the prospects of a healthy pregnancy outcome [5].

In light of these considerations, the present study undertakes the task of assessing a single blood progesterone measurement precisely at the moment when a threatened miscarriage is suspected. The objective is to discern whether the pregnancy is likely to persist and develop positively or if it faces a heightened risk of termination. By doing so, this research endeavor

endeavors to contribute to the early identification of pregnancy risks and to facilitate timely interventions that can significantly impact the well-being of both the mother and her prospective child.

The present study was undertaken with several key objectives in mind. Firstly, it aimed to investigate the role of a single serum progesterone measurement conducted on the day when a threatened miscarriage is diagnosed, with the specific goal of predicting whether the pregnancy would continue or not. Secondly, the study sought to delve into the relationship between the continuation of pregnancy in instances of early threatened miscarriage and various risk factors, including anemia, as assessed through hemoglobin levels, and the mother's body mass index. Furthermore, this research endeavor also aimed to explore the potential role of progesterone supplementation as a means to address and manage threatened miscarriages. The outcomes observed in the study were expected to shed light on the effectiveness of such supplementation in improving pregnancy outcomes in cases where miscarriage was initially threatened. These multifaceted objectives collectively formed the foundation of the study, providing valuable insights into the factors influencing pregnancy continuation and offering potential strategies for enhancing maternal and fetal well-being in challenging situations like threatened miscarriages.

## **MATERIAL AND METHODS**

This study was conducted at a Medical College in India. The research took place over the duration of one and a half year.

The inclusion criteria for participants in the study were as follows: pregnant women in the early stages of their pregnancy, specifically those at or below 12 weeks of gestation, and who were carrying a singleton intrauterine pregnancy while experiencing complaints of vaginal bleeding or spotting.

The inclusion criteria were as follows: pregnant women who had progressed beyond 12 weeks of gestation, those with inevitable miscarriages, cases of ectopic pregnancy, multiple pregnancies, molar pregnancies, pregnancies resulting from artificial reproductive techniques, individuals with anomalous uteruses, and those with multiple fibroids complicating pregnancy, except for the subserosal type.

The research methodology involved recruiting pregnant women who met the inclusion and exclusion criteria and sought medical attention at the antenatal outpatient department or casualty. Informed consent was obtained from these individuals. Subsequently, a comprehensive examination, encompassing general, systemic, and obstetric assessments, was conducted. Ultrasonological assessments were also employed to ascertain the viability of the pregnancy.

For the purposes of the study, 3 ml of venous blood were collected from pregnant women who were experiencing threatened abortion. From these blood samples, serum progesterone and hemoglobin levels were assessed. The measurement of serum progesterone levels was carried out using a competitive binding immune enzymatic assay.

Following admission, patients were evaluated and treated in accordance with established protocols. Subsequently, these patients were closely monitored and followed up until they reached 20 weeks of gestation. The data collected during this period allowed for a comparison and statistical analysis of patients with viable fetuses and those who experienced miscarriages, with particular attention to their serum progesterone levels obtained on the first day of admission.

## **RESULTS**

In the present study, majority (76.40%) of the participants were in the age group between 20-30 years of age. The mean age of the study participants was  $26.7 \pm 3.5$  years. Among the study

participants, approximately 20.79% had a history of previous lower segment cesarean section (LSCS). Primi mothers, on the other hand, made up 47.75% of the study population. A history of previous normal delivery was observed in around 18.54% of the study participants, while approximately 12.92% of the study population had a documented history of previous abortion. The predominant presenting symptom within the study population was bleeding or spotting per vaginum, which was reported by 46% of the total study participants. 22.47% participants were having Anaemia (Table 1).

**Table 1: Clinical and demographic parameters in study participants**

<b>Parameter</b>	<b>n</b>	<b>%</b>
<b>Age Group</b>		
20 years	19	10.67
20-30 years	136	76.40
>30 years	23	12.92
Total	178	100.00
<b>Obstetric History</b>		
Previous Normal delivery	33	18.54
Previous LSCS	37	20.79
Previous Abortion	23	12.92
Primigravida	85	47.75
Total	178	100.00
<b>Gestational Age</b>		
> 8 weeks	51	28.65
≤ 8 weeks	127	71.35
Total	178	100.00
<b>BMI Group</b>		
Underweight	28	15.73
Normal	99	55.62
Overweight	37	20.79
Obese	14	7.87
Total	178	100.00
<b>Chief Complaints</b>		
Bleeding Per Vaginum	81	45.51
Bleeding Per Vaginum + Lower Abdominal Pain	13	7.30
Spotting Per Vaginum + Lower Abdominal Pain	2	1.12
Spotting Per Vaginum	82	46.07
Total	178	100.00
<b>Comorbidities</b>		
Anemia	40	22.47
Type 2 DM and GDM	1	0.56

Hypothyroidism	10	5.62
Consanguineous marriage	6	3.37
Chronic Hypertension	2	1.12
Cardiac Disease	4	2.25
Seizure Disorder	3	1.69

In our current study, the majority of participants exhibited normal hemoglobin levels. Mild anemia, as determined by their hemoglobin values, was observed in around 19.10% of the study participants. Among the study population, approximately 2.25% were found to have moderate anemia, while a smaller proportion, approximately 1.12%, had mild anemia (Table 2).

**Table 2: Hemoglobin levels among study participants**

Hemoglobin Level	n	%
Normal	138	77.53
Mild Anemia	34	19.10
Moderate Anemia	4	2.25
Severe Anemia	2	1.12
Total	178	100.00

In our study, the majority of participants exhibited serum progesterone levels exceeding 20 (approximately 58.8%), whereas around 30% of the study participants had serum progesterone levels below 10. Furthermore, we observed that approximately 28.65 % of the participants had serum progesterone levels falling within the range of 10 to 20 (Table 3).

**Table 3: Serum Progesterone levels among study participants**

Serum Progesterone (ng/ml)	n	%
0 - 10	54	30.34
10 to 20	51	28.65
More than 20	73	41.01
Total	178	100.00

In our current study, approximately 66.29% of the study participants experienced a continued pregnancy, while the outcome of abortion was observed in approximately 33.71% of the study participants (Table 4).

**Table 4: Pregnancy Outcome among study participants**

<b>Pregnancy Outcome</b>	<b>n</b>	<b>%</b>
Abortion	60	33.71
Normal	118	66.29
Total	178	100.00

We examined the correlation between serum progesterone levels, hemoglobin levels, BMI, and the outcome of pregnancy. Our findings indicated a notable association between higher serum progesterone levels and the continuation of pregnancy. However, we did not observe a significant association between hemoglobin levels, BMI, and the outcome of pregnancy (Table 5).

**Table 5: Correlation between various parameters and Outcome of pregnancy**

	<b>Abortion (n=60)</b>	<b>Continue (n=118)</b>	<b>p Value</b>
<b>Hemoglobin Level</b>			
Normal	56	82	< 0.05
Mild Anemia	12	30	
Moderate Anemia	1	3	
Severe Anemia	1	1	
<b>BMI Group</b>			
Underweight	12	16	0.58
Normal	31	68	
Overweight	11	26	
Obese	6	9	
<b>Serum Progesterone</b>			
0 - 10	51	2	0.61
10 to 20	3	48	
More than 20	6	68	

## **DISCUSSION**

In our current research, the average age of the study participants was  $26.7 \pm 3.5$  years, with a significant majority falling within the 20-30 age group. This aligns with Dave et al.'s findings, where participants aged 21-25 constituted 48.8%, and those aged 26-30 accounted for 41.1% [6]. Similarly, Kadam et al. reported comparable results, with a mean age of 25.62 years and the majority of participants aged less than 25 years, which suggests a consistent age trend among antenatal mothers in various regions of India, possibly influenced by socio-cultural factors related to marriage [7].

Our study also revealed that primi-mothers made up 47.75% of the participants, which is in line with Dave et al.'s findings of 57.7% primi-mothers in their study. Kadam et al. and Srimathi J et al. also reported similar prevalence of primigravida mothers in their research [7, 8]. Furthermore, our results indicated that 66.29% of the study participants experienced continued pregnancies. Kadam et al. and Srimathi J et al observed a similar outcome, with 70% of their participants having viable pregnancies [7, 8].

In our study, the most common presenting symptoms were bleeding vaginum and spotting per vaginum, each accounting for about 46% of the total study population. This finding is consistent with Kadam et al.'s study conducted in Delhi, and and Srimathi J et al which also identified bleeding per vaginum as the most common presenting symptom [7].

Regarding serum progesterone levels, the majority of our participants had levels exceeding 20 ng/ml. Importantly, our research demonstrated that participants with elevated serum progesterone levels had significantly lower miscarriage rates compared to those with lower levels. This is in line with a meta-analysis conducted by Verhaegen et al. [9], which emphasized the importance of serum progesterone measurements in predicting fetal viability when ultrasound findings are inconclusive. They suggested that serum progesterone values below 3.2



to 6 ng/mL indicated a non-viable pregnancy. In our study, the cutoff for serum progesterone was set at 15 ng/ml, with observed sensitivity at 93.4% and specificity at 87.4%.

Furthermore, studies conducted by Al Jufairi et al., Phipps et al., and Elson et al. have also highlighted the significance of serum progesterone level estimation in early pregnancy as an effective indicator for pregnancy outcomes [10-12].

## **CONCLUSION**

In summary, our study findings support the notion that serum progesterone levels can serve as a valuable diagnostic tool for assessing the viability of pregnancies. Employing serum progesterone measurements at a single time point not only streamlines the diagnostic process but also offers a cost-effective alternative, thus relieving patients of the burden of more cumbersome procedures. Furthermore, there is a need for further research to explore the potential of serum progesterone levels as a screening tool in pregnancy assessment.

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