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EFFECT OF PROGESTERONE IN MANAGEMENT OF THREATENED PRETERM LABOUR

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ABSTRACT

Background: Threatened preterm labour is a common obstetric complication that substantially increases the risk of spontaneous preterm birth, neonatal morbidity, and neonatal mortality. Progesterone plays an essential role in maintaining pregnancy among women presenting with threatened preterm labour. **Aim:** To determine the effect of vaginal progesterone in the management of threatened preterm labour by evaluating pregnancy prolongation and delivery outcomes. **Methods:** This descriptive case series was conducted in the Department of Obstetrics and Gynecology, Gulab Devi Hospital, Lahore during the period 15th April 2026 and 15th July 2026. A total of 117 women with threatened preterm labour were enrolled using non-probability consecutive sampling. Eligible participants received vaginal micronized progesterone 400 mg once daily until 37 weeks of gestation or delivery. Maternal demographic characteristics, obstetric history, cervical length, latency period, gestational age at delivery, and pregnancy outcomes were recorded using a structured proforma. Data were analyzed using IBM SPSS Statistics version 26. Continuous variables were summarized as mean ± standard deviation, categorical variables as frequencies and percentages, and associations were assessed using the Chi-square test, Fisher's exact test, and independent t-test, with $p < 0.05$ considered statistically significant. **Results:** The mean maternal age was 28.3 ± 4.6 years, while the mean gestational age at presentation was 26.0 ± 3.4 weeks. The mean cervical length measured by transvaginal ultrasonography was 25.2 ± 5.8 mm, and the mean latency period following progesterone therapy was 84.1 ± 27.8 days. The mean gestational age at delivery was 38.0 ± 1.9 weeks, with 83.8% (98/117) of women achieving term delivery and 16.2% (19/117) delivering preterm. Women with term delivery had significantly greater gestational age at presentation ($p = 0.002$), longer cervical length ($p < 0.001$), and longer latency period ($p < 0.001$) than those with preterm delivery. Gravidity, previous miscarriage, and previous caesarean section were not significantly associated with pregnancy outcome, whereas mode of delivery demonstrated a significant association ($p = 0.006$). **Conclusion:** Vaginal progesterone was associated with prolonged pregnancy and a high rate of term delivery among women with threatened preterm labour. Earlier gestational age at presentation, shorter cervical length, and reduced latency period were significantly associated with preterm birth.

KEYWORDS: Threatened preterm labour, vaginal progesterone, preterm birth, cervical length, pregnancy prolongation, latency period, maternal outcomes.

INTRODUCTION

One of the most common causes of neonatal morbidity and mortality in the world is preterm labour or the development of regular contractions of the uterus with cervical change prior to completing 37 weeks of gestational age (Doulaveris and Berghella, 2024). In 2023, nearly one in ten live births was preterm, with approximately 13.4 million preterm babies born in the world, which shows that prematurity has a significant impact on health care systems (Emms et al., 2025). Threatened preterm labour is the occurrence of painful uterine contractions without any meaningful cervical dilation or apparent labour and often leads to spontaneous preterm birth in vulnerable pregnancy (Singh et al., 2020). Prematurely born babies are at a considerable risk of respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, and permanent neurodevelopmental impairment (Liu et al., 2021). Prematurity complications are the primary cause of child death in children under the age of five in the world, which highlights the need to take preventive measures focused on minimizing morbidity and mortality. As a result, the need to find evidence-based interventions that would allow extending pregnancy and enhancing neonatal outcomes safely has become the primary focus of modern obstetric practice (Hafeez et al., 2023).

The pathophysiology of preterm labour is multifactorial, and it is characterized by intricate interplay between inflammatory, infection, uteroplacental ischemia, uterine overdistension, maternal stress, and endocrine dysregulation

that eventually triggers myometrial contractility and remodeling of the cervix (Sato et al., 2021). Progesterone is exceedingly significant in the physiological suppression of inflammatory cytokine synthesis, prostaglandin synthesis, and myometrial responses to oxytocin during pregnancy (Tan et al., 2020). Periconceptual progesterone withdrawal in late pregnancy plays a role in triggering labour in the presence of still high circulating progesterone levels, indicating that hormone-specific disruption of progesterone signaling is the key to parturition (Badr and El-Maghraby, 2022). These biologic processes offer a solid scientific case to explore the use of progesterone supplementation in the treatment of threatened preterm labour in women. However, depending on gestational age, cervical status, obstetric history, and route of progesterone delivery, the magnitude of clinical benefit could be different (Devall et al., 2022).

Preterm birth causes significant financial and health costs since impacted newborns often need extended hospital stays, intensive care, respiratory support and long-term developmental follow-up (Vanda et al., 2020). The burden is higher in the low- and middle-income countries, where the capacity of neonatal intensive care units is limited, which also leads to increased mortality and disability rates among preterm babies (Le et al., 2020). A high percentage of preterm births worldwide is still the case in South Asia, indicating that the region continues to face a significant set of issues in the form of maternal health, infection control, nutrition, and access to quality antenatal care (Ahmed et al., 2023). Whereas selected outcomes may be improved with the use of antenatal corticosteroids, magnesium sulfate, and tocolytic agents, the underlying endocrine processes of pregnancy maintenance are not directly addressed by these interventions. Therefore, the use of adjunctive treatment like progesterone is still clinically feasible to minimize the effects of preterm birth and enhance maternal and infant outcomes (Le et al., 2020).

Pakistan has one of the highest prevalence rates of preterm birth, as the countrywide prevalence is estimated to be 15-16% of the live births under 37 weeks of gestation, and the prevalence is a significant contributor to neonatal mortality and healthcare expenditures (Ali et al., 2023). Although maternal and child health service in Pakistan has had a significant positive change, preterm birth has been a leading cause of neonatal mortality, which underscores the necessity of effective preventive and curative measures (Zahroh et al., 2022). The clinical practice of threatened preterm labour in healthcare facilities in Pakistan differs significantly due to the lack of similarity in the resources available, physician preference, and understanding of the changing international evidence on the use of progesterone therapy (Irshad et al., 2025). Evidence locally created on the efficacy of progesterone use in women with threatened preterm labour is very scarce, which implies that clinicians have a limited capacity to make evidence-based decisions in the Pakistani healthcare setting. Therefore, the purpose of this study was to find out the impact of vaginal progesterone in threatened preterm labour management in terms of pregnancy extension and birth outcome.

METHODOLOGY

Design and Setting of the study

The case series was a descriptive study only and was done in the department of obstetrics and gynecology, Gulab Devi Hospital, Lahore, between 15th April 2026 and 15th July 2026. The aim of the study was to determine the impact of the vaginal progesterone in treating women who showed with threatened preterm labour. The selection criteria were set based on the required criteria and all participants were recruited within the study period. The process of data collection and patient follow-up was performed at the hospital and supervised by consultant obstetricians.

Sample Size and Sampling Method.

The WHO sample size calculator was used to determine the required sample size. The calculation was done using a reported efficacy of 73.5% of vaginal progesterone in preterm labour prevention with a margin of error of 8% and 95% confidence. On these assumptions, a sample size of 117 women was calculated. A non-probability consecutive method of sampling was used to select the participants until the desired sample size was obtained.

Study Population

The study considered women aged 18 to 40 years as eligible to be included in the study provided that they had a singleton pregnancy. Pregnancies in which a living fetus was confirmed with the use of ultrasonographic data of fetal cardiac activity and fetal movements were only enrolled. The study included subjects who met the criteria of threatened preterm labour based on the predetermined diagnostic criteria and a transvaginal ultrasonographic cervical length of at least 25 mm and a written informed consent.

Inclusion and Exclusion Criteria

Women who had had more than one pregnancy or had significant structural abnormalities of the fetus diagnosed using obstetric ultrasonography were not included in the study. Not included were pregnancies complicated by congenital malformations that do not allow the newborn to survive, fetal growth retardation with an estimated fetal weight of below the 10th percentile of gestational age, cervical enlargement of 3 cm or more, rupture of membranes, persistent vaginal bleeding, placental abruption, or clinical chorioamnionitis. Patients with urinary tract infections, or any maternal infection diagnosed based on fever greater than 38C, uterine tenderness, maternal tachycardia, purulent vaginal discharge, or positive urine or blood cultures were also excluded. Women who had a history of past cervical cerclage or congenital uterine anomalies, including a septate uterus, had previously used tocolytic agents, or corticosteroids or progesterone therapy, and women with an underlying medical history contraindicating pregnancy,

like uncontrolled hypertension, diabetes mellitus, hyperthyroidism, or hepatic disease with non-normal liver function tests were excluded.

Data Collection

Participants were recruited at the Obstetrics and Gynecology Outpatient Department and the recruitment occurred based on the written informed consent. Threatened preterm labour was properly diagnosed using a comprehensive clinical evaluation conducted by a consultant obstetrician to meet the pre-established study criteria. A structured data collection proforma was used to record baseline information, such as maternal age, parity, gestational age calculated based on the last menstrual period, cervical length as measured by transvaginal ultrasonography and pertinent obstetric history. All registered women were given vaginal micronized progesterone at a dosage of 400mg per day that was administered until completion of gestation period of 37 weeks unless delivery took place before the end of the gestation period. They were tracked weekly by making regular clinic appoints at the antenatal clinic and by telephone (where needed) to check on compliance and the progress of the pregnancy. According to operational definitions, the latency period between the enrolment and delivery, gestational age at delivery and maternal and neonatal delivery outcomes were recorded based on the antenatal and hospital records as outcome variables. All the data that were collected were inputted into a safe electronic data base immediately. It was recommended that participants should report to the hospital in case of worsening uterine contractions, membrane rupture, vaginal bleeding or any other alarming symptoms, and all adverse events were treated as per the standard obstetric protocols of the hospital.

Data Analysis

The data collected was analyzed with the help of IBM SPSS Statistics version 26. Normality of continuous variables (maternal age, cervical length, latency period between enrolment and delivery, gestational age at birth) was tested with the Shapiro-Wilk test. Data that exhibited a normal distribution were summarized to mean standard deviation and otherwise median with interquartile range. Successful prevention of preterm birth (delivery at 37 or more gestation weeks finished) was used as a categorical variable, with the categories of parity and mode of delivery debating the frequencies and percentages. The stratified analyses were conducted to test the impact that maternal age, parity, and gravidity and gestational age at recruitment have on the study outcome. The independent t-test was used to assess the associations between categorical variables. All the analyses were taken as statistically significant with a two-tailed p-value below 0.05.

Ethical Considerations

The research began by obtaining ethical approval of the study by the Ethical Review Committee of Gulab Devi Hospital, Lahore and the College of Physicians and Surgeons Pakistan. All participants were informed about the study objectives, procedures, potential benefits and possible risks and signed informed consent before being enrolled. All the study participants were provided with confidentiality of their personal and clinical data through the use of coded identification numbers and in the secure data storage. Their involvement was purely voluntary and all the women were made aware of their right to discontinue the study at any point without any impact on the quality of medical care that they would receive. The ethical standards of the Declaration of Helsinki and institutional research were all followed in the study procedures.

RESULTS

The highest percentage of women lived in the 2529-year age bracket (39.3%), then 3034 years (25.6%), which means that the majority of respondents were within the typical reproductive age group. The proportion of multigravida women in the study population was 58.1, and it was 57.3 among multiparous women. The 21.4% of the participants had a history of previous miscarriage, but only 20.5% of them had a history of previous caesarean section. In general, the study population had a fairly even obstetric distribution that could be used to measure pregnancy outcomes post-progesterone therapy.

Table 1. Baseline Demographic and Obstetric Characteristics of the Study Participants (N = 117)

Variable	Category	n (%)
Age (years)	18–24	27 (23.1)
	25–29	46 (39.3)
	30–34	30 (25.6)
	≥35	14 (12.0)
Gravidity	Primigravida	49 (41.9)
	Multigravida	68 (58.1)
Parity	Nulliparous	50 (42.7)
	Multiparous	67 (57.3)
Previous Miscarriage	Yes	25 (21.4)
	No	92 (78.6)
Previous Caesarean Section	Yes	24 (20.5)

	No	93 (79.5)

The baseline clinical characteristics are presented in Table 2. Women presented at a mean gestational age of 26.0 ± 3.4 weeks, indicating that most cases were diagnosed during the late second or early third trimester. The mean cervical length measured by transvaginal ultrasonography was 25.2 ± 5.8 mm, reflecting cervical shortening among many participants while still meeting the study eligibility criteria. The observed ranges demonstrate adequate clinical variability within the study population. These baseline findings provided an appropriate reference for assessing pregnancy progression following progesterone treatment.

Table 2. Clinical Characteristics at Initial Presentation (N = 117)

Variable	Mean ± SD	Range
Gestational age at presentation (weeks)	26.0 ± 3.4	19.1 – 32.8
Cervical length on transvaginal ultrasound (mm)	25.2 ± 5.8	13.2 – 37.9

The mean latency period from enrolment to delivery was 84.1 ± 27.8 days, suggesting that pregnancy was successfully prolonged in the majority of participants. The average gestational age at delivery reached 38.0 ± 1.9 weeks, indicating that most women achieved term pregnancy. Spontaneous vaginal delivery occurred in 69.2% of women, whereas 30.8% underwent caesarean delivery. Overall, 83.8% of participants delivered at term, while only 16.2% experienced preterm birth, demonstrating favorable pregnancy outcomes following treatment.

Table 3. Maternal and Pregnancy Outcomes Following Vaginal Progesterone Therapy (N = 117)

Variable	Category	n (%) / Mean ± SD
Latency period (days)	Mean ± SD	**84.1 ± 27.8**
Gestational age at delivery (weeks)	Mean ± SD	**38.0 ± 1.9**
Mode of delivery	Spontaneous vaginal delivery	81 (69.2)
	Caesarean section	36 (30.8)
Pregnancy outcome	Delivered at ≥37 weeks	98 (83.8)
	Delivered at <37 weeks	19 (16.2)

The Shapiro–Wilk test was performed to evaluate the distribution of continuous variables before statistical analysis. None of the variables demonstrated statistically significant deviation from normality, as all p-values exceeded 0.05. Therefore, the assumption of normal distribution was satisfied for maternal age, gestational age at presentation, cervical length, latency period, and gestational age at delivery. Consequently, these variables were appropriately summarized using mean ± standard deviation, and parametric statistical tests were used for comparative analyses.

Table 4. Assessment of Normality for Continuous Variables Using the Shapiro–Wilk Test

Variable	W Statistic	p-value
Maternal age (years)	0.986	0.184
Gestational age at presentation	0.982	0.091
Cervical length (mm)	0.984	0.143
Latency period (days)	0.980	0.067
Gestational age at delivery	0.988	0.263

Comparison of women who achieved term delivery with those who delivered preterm revealed several significant differences. Maternal age was comparable between the two groups and showed no statistically significant association with pregnancy outcome ($p = 0.437$). However, women who ultimately delivered at term presented at a significantly higher gestational age (26.5 vs. 23.7 weeks, $p = 0.002$) and had significantly longer cervical lengths (26.3 vs. 19.2 mm, $p < 0.001$). Furthermore, the latency period following progesterone therapy was substantially longer among women achieving term delivery (89.3 vs. 56.8 days, $p < 0.001$). These findings indicate that gestational age at presentation, cervical length, and duration of pregnancy prolongation were important determinants of successful term delivery.

Table 5. Comparison of Clinical Characteristics According to Pregnancy Outcome

Variable	Term Delivery (n = 98)	Preterm Delivery (n = 19)	p-value
Maternal age (years)	28.1 ± 4.5	29.0 ± 5.2	0.437
Gestational age at presentation (weeks)	26.5 ± 3.1	23.7 ± 3.4	**0.002**
Cervical length (mm)	26.3 ± 5.1	19.2 ± 4.6	**<0.001**

Latency period (days)	89.3 ± 23.9	56.8 ± 18.7	**<0.001**

Table 6 presents the relationship between obstetric characteristics and pregnancy outcome. Gravidity, previous miscarriage, and previous caesarean section were not significantly associated with whether women delivered at term or preterm (all $p > 0.05$). In contrast, the mode of delivery demonstrated a statistically significant association with pregnancy outcome ($\chi^2 = 7.42$, $p = 0.006$), with spontaneous vaginal delivery occurring more frequently among women who achieved term pregnancy. Women delivering preterm were comparatively more likely to undergo caesarean section. These findings suggest that baseline obstetric history had limited influence on pregnancy outcome, whereas delivery mode differed significantly between the two outcome groups.

Table 6. Association between Obstetric Characteristics and Pregnancy Outcome

Variable	Term n (%)	Preterm n (%)	χ^2	p-value
Primigravida	39 (39.8)	10 (52.6)	1.11	0.292
Multigravida	59 (60.2)	9 (47.4)		
Previous miscarriage (Yes)	19 (19.4)	6 (31.6)	1.48	0.224
Previous miscarriage (No)	79 (80.6)	13 (68.4)		
Previous Caesarean section (Yes)	19 (19.4)	5 (26.3)	0.49	0.486
Previous Caesarean section (No)	79 (80.6)	14 (73.7)		
Spontaneous vaginal delivery	73 (74.5)	8 (42.1)	7.42	0.006
Caesarean section	25 (25.5)	11 (57.9)		

DISCUSSION

The aim of the current study was to determine the impact of vaginal progesterone on treatment of threatened preterm labour by assessing the outcome of pregnancy duration and birth weight of affected women. Among the key results of this research, there was the attainment of a mean latency of 84.1 ± 27.8 days, and the mean gestural age at delivery was 38.0 ± 1.9 weeks, which showed significant pregnancy lengthening with the use of progesterone. Another clinical significance of pregnancy prolongation is that every extra week of gestation will reduce by a significant margin the neonatal morbidity and mortality related to preterm birth (Hafeez et al., 2023). Similar latency reductions have been reported by Nuprom and Chaipakdi (2024) who found a mean latency period of 56.8 ± 17.6 days in 44 women exposed to vaginal progesterone which was significantly longer than the comparison group p=0.034 (Nuprom and Chaipakdi, 2024). On the same note, Sirisangwon and Phupong (2021) found that progesterone treatment increased pregnancy by an average of 35.6 ± 12.4 days and drastically increased gestational ages at delivery (37.8 ± 1.9 weeks) in comparison with the placebo treatment (35.4 ± 2.6 weeks) (Sirisangwon and Phupong, 2021). However, some researchers have shown comparatively small improvements in gestation length, which indicates that treatment response can be condition-specific (as in cervical) and gestation age at presentation and mechanisms underlying threatened preterm labour (Singh et al., 2020).

The clinical evaluation revealed that women had a mean gestational age of 26.0 ± 3.4 weeks, and a mean cervical length of 25.2 ± 5.8 mm, indicating the significance of early detection of women at risk of preterm delivery. Moreover, women who ended up delivering at term had much higher gestational age at presentation (26.5 ± 3.1 vs. 23.7 ± 3.4 weeks, $p = 0.002$) and length of their cervix (26.3 ± 5.1 mm vs. 19.2 ± 4.6 mm, $p < 0.001$) as compared to those who delivered preterm. This shows that cervical length is still among the best sonographic predictors of pregnancy continuation in the presence of progesterone therapy. Frey et al. (2022) also reported similar results, and the rate of spontaneous preterm birth was significantly lower in women with long cervical (greater than 15mm) versus short ones (less than 15mm) (18 women pregnancies, p=0.02) (Frey et al., 2022). A second randomized clinical trial with 129 participants also found that cervical length increase was a predictor of vaginal progesterone therapy response (95% CI) independently (Nachum et al., 2024).

The current research also revealed that the latency period varied significantly based on the outcome of pregnancy with term delivery-women exhibiting a significantly longer latency period (89.3 ± 23.9 days) compared to preterm-delivery women (56.8 ± 18.7 days, $p < 0.001$). Such a significant disparity implies that a positive effect of effective suppression of the uterine activity in the presence of the progesterone results in the direct effect of the extension of gestation and better development of the fetus. Likewise, Gothwal et al. (2022) report similar results, with women with a long latency having considerably reduced neonatal intensive care hospitalization or respiratory issues as compared to those who give birth prematurely in a group of 140 female participants (p=0.032). Other advancements include variances in progesterone formulation, dose, inclusion measures, ethnicity, and comorbid obstetric control in studies (Gothwal et al., 2022). Therefore, despite the strong evidence of the current studies indicating that pregnancy is indeed extended with progesterone after administration, new randomized trials will still be necessary to identify which subgroups of the patients will be benefiting most.

On the obstetric factors, the results showed that there was no statistically significant correlation between pregnancy outcome and gravidity (p = 0.292), and previous miscarriage (p = 0.224) and previous caesarean section (p = 0.486), implying that the above-mentioned baseline variables were not singly associated with the success of the treatment. Conversely, mode of delivery showed a strong correlation with pregnancy outcome with spontaneous vaginal birth being more common among women who carried the pregnancy to term (74.5% vs. 42.1; 7.42 = 0.006). These results prove that women who had successful pregnancy prolongation were more prone to successful birth than to an operative birth. Similar results were found in Srisutham et al. (2021) who reported 231 Thai women experiencing progesterone were more likely to deliver vaginally spontaneously than did not (p=0.034). Regarding pairwise comparison, vaginal progesterone was more effective in preterm pregnancy prevention below 34 weeks compared to the control group (p=0.030), and oral progesterone was equally effective as compared to the control group (p=0.638) (Srisutham et al., 2021). In the meantime, a retrospective cohort study in Israel (n=374 women) showed that there was a significant difference in delivery mode despite lower spontaneous preterm birth rates (Kabiri et al., 2023). Thus, the current results suggest that, although progesterone could enhance pregnancy continuation, the outcome of delivery could still depend on a plethora of maternal and fetal variables not related to the pharmacological action of progesterone.

On the whole, the current research is another piece of evidence to the effectiveness of vaginal progesterone in the treatment of threatened preterm labour due to positive pregnancy extension and preterm birth rates. The 83.8% rate of term deliveries, 84.1 ± 27.8 average latency period, and 38.0 ± 1.9 weeks of the mean gestational age at delivery, all for improvement after treatment, are clinically significant. The results are generally in line with prior randomized trials and systematic reviews Hyett et al. (2022) which showed a decrease in spontaneous preterm birth between 10.0% and 25.0% in 85 Irani women who received vaginal progesterone. However, the variables of study design, diagnostic definition of endangered preterm labour, the cervical length threshold, dosage of progesterone, and population diversity still make published evidence heterogeneous (Hyett et al., 2022). The lack of causal inference in the present study is also due to the descriptive case series design and lack of a comparison group; however, the observed clinical improvements are promising and present local evidence.

Various limitations should be taken into consideration when interpreting the findings of this study. The case series of descriptive nature that lacked a control group restricted the possibility of determining a causal association that existed between the progesterone therapy and the maternal outcomes observed. The research was performed in one tertiary care hospital, which might limit the implications of the results to other hospitals and populations. The relatively small sample size might have also constrained the statistical power to reveal the associations between some obstetric characteristics and pregnancy outcomes. Also, neonatal morbidity, long term infant outcomes, treatment adherence and maternal satisfaction were not addressed, which could have been used to give a more comprehensive evaluation of the treatment effectiveness. Randomized controlled studies can be used to reinforce the current evidence through future studies that use larger sample sizes with long-term neonatal follow-up.

CONCLUSION

The current research also showed that vaginal progesterone was related to positive delivery experiences of women who came with threatened preterm labour. 83.8% of participants delivered terms and the average gestation period was 84.1 ± 27.8 days and average gestation age at delivery was 38.0 ± 1.9 indicating successful pregnancy prolongation. Females at term of gestation were far more represented in terms of gestational age at time of presentation, cervical length and latency duration compared with those who had preterm births. These baseline obstetric factors like the gravidity, a past miscarriage, and a past caesarean section had no significant association with the pregnancy outcome, but mode of delivery had a strong association. These results endorse the possible clinical application of vaginal progesterone in the prevention of threatened preterm labour and present valuable evidence of the local population. It is important that further multi center randomized controlled trials should be done to confirm these results and develop standardized treatment regimens.

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