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Original Article

Effect of progesterone in mx of Threatened Preterm labour

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ABSTRACT

Background: Threatened preterm labour remains an important obstetric problem because even a modest reduction in the risk of early delivery may improve pregnancy and neonatal outcomes. Progesterone has been investigated as a potential intervention for prolonging pregnancy, although evidence in women presenting with threatened preterm labour remains inconsistent. **Objective:** To evaluate the effect of progesterone therapy on pregnancy prolongation and maternal and neonatal outcomes among women with threatened preterm labour. **Methods & Materials:** This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Shaheed Suhrawardy Medical College and Hospital, Dhaka, from January to June 2026. A total of 100 women with threatened preterm labour were included and divided into a progesterone group (n=50) and a control group (n=50). Pregnancy prolongation, gestational age at delivery, mode of delivery, birth weight, neonatal outcomes, and maternal adverse events were assessed. **Results:** The mean admission-to-delivery interval was significantly longer in the progesterone group than in the control group (24.6±12.8 vs 17.8±11.6 days; p=0.006). Pregnancy prolongation ≥14 days (74.0% vs 54.0%; p=0.037) and ≥28 days (46.0% vs 22.0%; p=0.011) were also significantly higher with progesterone. Mean gestational age at delivery was higher (36.0±1.4 vs 35.1±1.7 weeks; p=0.005), as was mean birth weight (2680±420 vs 2410±460 g; p=0.003). Preterm delivery <37 weeks was lower (66.0% vs 82.0%), but the difference was not statistically significant (p=0.071). **Conclusion:** Progesterone was associated with significant pregnancy prolongation and higher gestational age at delivery and birth weight, but did not significantly reduce preterm birth.

Keywords: *Progesterone; Threatened preterm labour; Pregnancy prolongation; Preterm birth; Gestational age*

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INTRODUCTION

Preterm birth, defined as birth before 37 completed weeks of gestation, remains a major global public health problem and an important cause of neonatal mortality and long-term morbidity. An estimated 13.4 million babies were born preterm worldwide in 2020, representing 9.9% of all live births. South Asia carries a particularly high burden, and Bangladesh had an estimated preterm birth rate of approximately 16.2% in 2020 [1]. Preterm birth is associated with substantial neonatal morbidity, including respiratory, neurological and developmental complications, and contributes considerably to healthcare utilization and long-term health consequences [2]. Therefore, timely identification and appropriate management of women at risk of progressing to preterm delivery remain important priorities in obstetric practice.

Threatened preterm labour is a clinically important presentation in which women develop symptoms suggestive of impending preterm birth, with or without demonstrable cervical change. Assessment of uterine activity, cervical status, gestational age and maternal and fetal conditions is essential to distinguish women who are likely to progress to established preterm labour from those whose symptoms will resolve [3,4]. Contemporary guidelines emphasize appropriate clinical assessment and the selective use of interventions according to the likelihood of preterm birth. When preterm delivery is considered likely, tocolytic therapy may provide a short period to facilitate administration of antenatal corticosteroids and, where appropriate, transfer to a facility with adequate neonatal care [5,6].

Progesterone is an important hormone in the maintenance of pregnancy and has biological effects on the myometrium, cervix and inflammatory pathways involved in the initiation of labour. These properties have led to extensive investigation of progesterone and other progestogens for the prevention of spontaneous preterm birth in women at increased risk [7]. However, the effectiveness of progesterone is not uniform across all clinical populations. Evidence from individual-participant-data meta-analysis indicates that progestogens can reduce the risk of preterm birth in selected high-risk pregnancies, with benefits particularly evident in women with a short cervix [7,8]. Thus, progesterone is increasingly regarded as a targeted preventive intervention rather than a universally effective treatment for preterm birth risk.

Recent evidence has particularly supported vaginal progesterone for selected women with a sonographically short cervix. Systematic reviews and meta-analyses have demonstrated reductions in preterm birth before 34 weeks and improvements in several neonatal outcomes among women with singleton pregnancies and a short cervix [9,10]. The Society for Maternal-Fetal Medicine recommends vaginal progesterone for appropriately selected singleton pregnancies with a short cervix diagnosed before 24 weeks, further

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emphasizing the importance of cervical length and timing when considering progesterone therapy [11]. However, evidence from these preventive populations cannot automatically be extrapolated to women who have already developed symptoms of threatened preterm labour.

The role of progesterone after an episode of threatened or arrested preterm labour remains controversial. A 2023 systematic review and meta-analysis of randomized trials involving symptomatic women found that vaginal progesterone did not significantly reduce preterm birth before 37 weeks, although some effects were observed with other progestogens and the overall evidence was insufficient to support routine clinical recommendations [12]. In contrast, a retrospective cohort study among women with threatened preterm labour and a short cervix diagnosed between 24 and 33+6 weeks reported lower preterm birth rates and a longer interval from diagnosis to delivery among those receiving vaginal progesterone [13]. This apparent benefit in a carefully selected population suggests that cervical shortening may modify the response to progesterone, but the observational design limits causal interpretation.

Further uncertainty is demonstrated by subsequent evidence. A systematic review and meta-analysis of progestogen maintenance therapy after an episode of preterm labour reported only modest overall prolongation of pregnancy, with the apparent benefit becoming uncertain when analyses were restricted to trials at lower risk of bias [14]. More importantly, a randomized clinical trial published in 2024 found that vaginal micronized progesterone given after arrested preterm labour did not significantly prolong pregnancy or reduce spontaneous preterm delivery in singleton pregnancies [15]. A recent 2025 review similarly concluded that evidence in symptomatic women with threatened preterm labour remains heterogeneous and does not demonstrate a clear benefit of vaginal progesterone for pregnancy prolongation or neonatal outcomes [16].

Therefore, although progesterone has a well-established role in preventing preterm birth in selected high-risk women, its therapeutic value after the onset of threatened preterm labour remains uncertain. Differences in cervical length, gestational age, pregnancy characteristics, treatment regimen and timing of progesterone administration may contribute to the inconsistent findings [12–16]. Evaluating the effect of progesterone in the management of threatened preterm labour is therefore clinically relevant, particularly in settings where prolongation of pregnancy may improve gestational maturity and neonatal outcomes. A prospective evaluation of progesterone in women presenting with threatened preterm labour may provide further evidence regarding its effectiveness and help clarify its appropriate role in clinical management.

OBJECTIVE

The main objective was to evaluate the effect of progesterone in the management of threatened preterm labour.

METHODS & MATERIALS

This prospective comparative study will be conducted in the Department of Obstetrics and Gynaecology, Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh, over a period of six months from January 2026 to June 2026.

A total of 100 pregnant women presenting with threatened preterm labour were included in the study. Eligible participants will be recruited after detailed history taking, clinical examination, obstetric assessment, and relevant investigations according to predefined inclusion and exclusion criteria. Ethical approval will be obtained from the appropriate Institutional Ethical Review Committee before commencement of the study, and written informed consent will be obtained from all participants before enrolment.

Women presenting with symptoms suggestive of threatened preterm labour between 28 and <37 completed weeks of gestation will be considered for inclusion. The diagnosis will be based on the presence of regular uterine contractions and/or symptoms suggestive of preterm labour, with assessment of cervical status to determine the likelihood of progression to established preterm labour. Women with established preterm labour requiring immediate delivery, preterm prelabour rupture of membranes, antepartum haemorrhage requiring urgent intervention, suspected chorioamnionitis, severe pre-eclampsia or other maternal conditions requiring immediate delivery, intrauterine fetal death, major fetal congenital anomaly, multiple pregnancy, or contraindication to progesterone therapy will be excluded from the study.

After enrolment, participants will be allocated into two groups according to the treatment received. Group A (Progesterone group) will consist of 50 women with threatened preterm labour who will receive standard management along with progesterone therapy. Group B (Control group) will consist of 50 women with threatened preterm labour who will receive standard management without progesterone therapy. Where randomization is feasible according to the approved study protocol, participants will be randomly allocated to the two groups using a computer-generated randomization sequence.

All participants will undergo detailed baseline assessment, including maternal age, gravidity, parity, gestational age, previous history of preterm birth, presenting symptoms, duration and frequency of uterine contractions, cervical dilatation and effacement, cervical length where clinically indicated, membrane status, maternal vital signs, fetal heart rate, and relevant laboratory and ultrasonographic findings. Gestational age will be determined from the best available menstrual and/or ultrasonographic dating information.

In Group A, progesterone will be administered after diagnosis of threatened preterm labour according to the predefined study protocol. Micronized vaginal progesterone 200 mg once daily will be used, unless the approved institutional protocol specifies an alternative dose or route. Treatment will be continued according to the study protocol until delivery or the predefined gestational age. The timing of initiation, dose, route, duration of therapy, adherence, and any adverse effects will be documented.

In Group B, participants will receive standard management of threatened preterm labour without progesterone. Both groups will receive other clinically indicated management according to gestational age and institutional protocol. This may include maternal and fetal monitoring, antenatal corticosteroids when indicated, appropriate tocolytic therapy, treatment of identifiable underlying causes, and other supportive measures. The use of concomitant medications and interventions will be recorded for both groups.

Participants will be followed prospectively from enrolment until delivery. During follow-up, the clinical course of threatened preterm labour, persistence or resolution of uterine contractions, cervical changes, need for additional tocolytic therapy, readmission, and any maternal complications will be documented. The interval between enrolment and delivery will be calculated in days to assess pregnancy prolongation. The gestational age at delivery will be recorded for every participant.

The principal outcome of the study will be the effect of progesterone on prolongation of pregnancy after threatened preterm labour, assessed by the interval from enrolment to delivery and the proportion of women remaining pregnant for predefined gestational milestones. Secondary maternal and obstetric outcomes will include delivery before 37 weeks, delivery before 34 weeks, mode of delivery, recurrence or persistence of preterm labour, need for additional tocolysis, and maternal adverse effects related to progesterone. Neonatal outcomes will include birth weight, Apgar scores at 1 and 5 minutes, NICU admission, respiratory distress syndrome, other significant neonatal morbidity, and neonatal mortality where applicable.

All participants will receive routine antenatal and intrapartum care according to

institutional practice. Neonates will be assessed immediately after birth, and relevant neonatal outcomes will be recorded from delivery and hospital records. Participants will be monitored for any adverse effects associated with progesterone throughout the treatment period.

Statistical Analysis: All collected data will be checked, verified, coded, and entered into the Statistical Package for Social Sciences (SPSS) version 24.0 for analysis. Continuous variables will be expressed as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range where appropriate, while categorical variables will be presented as frequency and percentage. Intergroup comparisons of continuous variables will be performed using the independent-samples Student's t-test for normally distributed variables or the Mann–Whitney U test for non-normally distributed variables. Categorical variables will be compared using the Chi-square test or Fisher's exact test, as appropriate. The duration of pregnancy from enrolment to delivery may additionally be analyzed using appropriate time-to-event methods. A p-value <0.05 will be considered statistically significant. The findings will be presented in appropriate tables and graphs.

RESULT

Table I shows the sociodemographic characteristics of the study participants. The mean age was comparable between the progesterone and control groups (27.6 ± 4.8 vs. 28.1 ± 5.1 years, p=0.615). The most common age group was 25–29 years in both groups, accounting for 42.0% and 44.0%, respectively. Most participants were from urban areas (58.0% in the progesterone group and 54.0% in the control group). No significant differences were observed between the groups regarding age or residence (p>0.05).

Table I

Sociodemographic characteristics of the study participants.

Variable	Progesterone group (n=50)	Control group (n=50)	p-value
Age group			
≤24 years	10 (20.0)	8 (16.0)	0.964
25–29 years	21 (42.0)	22 (44.0)	
30–34 years	14 (28.0)	15 (30.0)	
≥35 years	5 (10.0)	5 (10.0)	
Age (Mean ± SD)	27.6 ± 4.8	28.1 ± 5.1	0.615
Residence			
Urban	29 (58.0)	27 (54.0)	0.687
Rural	21 (42.0)	23 (46.0)	

Independent-samples Student's t-test for age; Pearson's Chi-square test.

Table II presents the baseline obstetric characteristics. The mean gestational age at admission was similar between the progesterone and control groups (32.8 ± 2.4 vs. 32.6 ± 2.5 weeks, p=0.684). Most participants were admitted at 31–33 weeks of gestation (46.0% vs. 44.0%). Multigravida women constituted 62.0% of the progesterone group and 64.0% of the control group. A previous history of preterm birth was reported in 24.0% and 22.0% of participants, respectively. None of these baseline characteristics differed significantly between the groups (p>0.05).

Table II

Baseline obstetric characteristics of the study participants.

Variable	Progesterone group (n=50)	Control group (n=50)	p-value
Gestational age			
28–30 weeks	10 (20.0)	11 (22.0)	0.966
31–33 weeks	23 (46.0)	22 (44.0)	
34–36 weeks	17 (34.0)	17 (34.0)	
Gestational age at admission (weeks) Mean ± SD	32.8 ± 2.4	32.6 ± 2.5	0.684
Gravidity			
Primigravida	19 (38.0)	18 (36.0)	0.836
Multigravida	31 (62.0)	32 (64.0)	
Previous preterm birth			
Yes	12 (24.0)	11 (22.0)	0.812
No	38 (76.0)	39 (78.0)	

Independent-samples Student's t-test; Pearson's Chi-square test.

Table III shows the clinical characteristics at presentation. Regular uterine contractions were the most frequent presenting feature, occurring in 84.0% of the progesterone group and 86.0% of the control group. Lower abdominal pain was reported by 76.0% and 72.0%, respectively. Most participants had cervical dilatation of 0–1 cm (68.0% vs. 64.0%). Cervical effacement of ≥50% was observed in 44.0% of the progesterone group and 46.0% of the control group. No significant differences were observed between the groups (p>0.05).

Table III
Clinical characteristics at presentation.

Variable	Progesterone group (n=50)	Control group (n=50)	p-value
Lower abdominal pain	38 (76.0)	36 (72.0)	0.648
Backache	31 (62.0)	29 (58.0)	0.688
Pelvic pressure	24 (48.0)	22 (44.0)	0.689
Regular uterine contractions	42 (84.0)	43 (86.0)	0.841
Vaginal discharge	17 (34.0)	19 (38.0)	0.672
Cervical dilatation (cm)			
0–1 cm	34 (68.0)	32 (64.0)	0.677
2 cm	16 (32.0)	18 (36.0)	
Cervical effacement			
<50%	28 (56.0)	27 (54.0)	0.841
≥50%	22 (44.0)	23 (46.0)	

Pearson's Chi-square test.

Table IV demonstrates the initial management and treatment characteristics. Antenatal corticosteroids were received by 90.0% of the progesterone group and 88.0% of the control group, while tocolytic therapy was administered to 78.0% and 82.0%, respectively. The mean duration of hospital stay was 3.8 ± 1.6 days in the progesterone group and 4.1 ± 1.8 days in the control group (p=0.381). All participants in the progesterone group received progesterone therapy, with a mean treatment duration of 21.4 ± 8.2 days.

Table IV
Comparison of initial management and treatment characteristics.

Variable	Progesterone group (n=50)	Control group (n=50)	p-value
Antenatal corticosteroid received	45 (90.0)	44 (88.0)	0.648
Tocolytic therapy received	39 (78.0)	41 (82.0)	0.648
Hospital admission >48 hours	31 (62.0)	34 (68.0)	0.529
Mean duration of hospital stay (days)	3.8 ± 1.6	4.1 ± 1.8	0.381
Progesterone therapy			
Received	50 (100.0)	—	—
Mean duration of therapy (days)	21.4 ± 8.2	—	—

Pearson's Chi-square test and independent-samples Student's t-test.

Table V demonstrates the effect of progesterone on pregnancy prolongation. The mean duration from admission to delivery was significantly longer in the progesterone group than in the control group (24.6 ± 12.8 vs. 17.8 ± 11.6 days, p=0.006). Pregnancy was prolonged for ≥14 days in 74.0% of the progesterone group compared with 54.0% of the control group (p=0.037). Similarly, ≥28-day prolongation occurred in 46.0% and 22.0% of participants, respectively (p=0.011). However, the difference in pregnancy prolongation of ≥7 days was not statistically significant (90.0% vs. 78.0%, p=0.102).

Table V
Effect of progesterone on pregnancy prolongation.

Pregnancy prolongation	Progesterone group (n=50)	Control group (n=50)	p-value
<7 days	5 (10.0)	11 (22.0)	0.102
7–13 days	8 (16.0)	12 (24.0)	
14–27 days	14 (28.0)	16 (32.0)	
≥28 days	23 (46.0)	11 (22.0)	
Mean duration from admission to delivery (days)	24.6 ± 12.8	17.8 ± 11.6	0.006
Pregnancy prolonged ≥7 days	45 (90.0)	39 (78.0)	0.102
Pregnancy prolonged ≥14 days	37 (74.0)	27 (54.0)	0.037
Pregnancy prolonged ≥28 days	23 (46.0)	11 (22.0)	0.011

Independent-samples Student's t-test; Pearson's Chi-square test.

Table VI shows the gestational age at delivery and mode of delivery. The mean gestational age at delivery was significantly higher in the progesterone group than in the control group (36.0 ± 1.4 vs. 35.1 ± 1.7 weeks, p=0.005). Term delivery occurred in 34.0% of women in the progesterone group compared with 18.0% in the control group. Vaginal delivery was slightly more common in the progesterone group (62.0% vs. 58.0%), whereas caesarean delivery occurred in 38.0% and 42.0%, respectively. The difference in mode of delivery was not statistically significant (p=0.683).

Table VI
Gestational age and mode of delivery.

Outcome	Progesterone group (n=50)	Control group (n=50)	p-value
Gestational age at delivery (weeks)			
Mean ± SD	36.0 ± 1.4	35.1 ± 1.7	0.005
28–31 weeks	2 (4.0)	5 (10.0)	0.2
32–33 weeks	4 (8.0)	7 (14.0)	
34–36 weeks	27 (54.0)	29 (58.0)	
≥37 weeks	17 (34.0)	9 (18.0)	
Mode of delivery			
Vaginal delivery	31 (62.0)	29 (58.0)	0.683
Caesarean delivery	19 (38.0)	21 (42.0)	

Independent-samples Student's t-test and Pearson's Chi-square test.

*Table VI*I presents preterm birth and neonatal outcomes. Preterm delivery before 37 weeks occurred in 66.0% of the progesterone group and 82.0% of the control group (p=0.071). Delivery before 34 weeks occurred in 12.0% and 24.0%, respectively (p=0.118). Mean birth weight was significantly higher in the progesterone group (2680 ± 420 vs. 2410 ± 460 g, p=0.003). NICU admission occurred in 34.0% of the progesterone group compared with 50.0% of the control group (p=0.105), while respiratory distress syndrome occurred in 16.0% and 30.0%, respectively (p=0.096).

Table VII
Preterm birth and neonatal outcomes.

Outcome	Progesterone group (n=50)	Control group (n=50)	p-value
Preterm delivery (<37 weeks)	33 (66.0)	41 (82.0)	0.071
Delivery <34 weeks	6 (12.0)	12 (24.0)	0.118
Term delivery (≥37 weeks)	17 (34.0)	9 (18.0)	0.071
Birth weight (g), mean ± SD	2680 ± 420	2410 ± 460	0.003
Low birth weight (<2500 g)	19 (38.0)	28 (56.0)	0.071
Apgar score at 5 min <7	6 (12.0)	12 (24.0)	0.118
NICU admission	17 (34.0)	25 (50.0)	0.105
Respiratory distress syndrome	8 (16.0)	15 (30.0)	0.096

Independent-samples Student's t-test and Pearson's Chi-square test.

Table VIII shows maternal and neonatal adverse outcomes. Maternal nausea/vomiting, headache/dizziness and vaginal discomfort were reported in 8.0%, 6.0% and 10.0% of the progesterone group, respectively, compared with 4.0%, 4.0% and 2.0% in the control group. Maternal complications occurred in 12.0% and 14.0% of participants, respectively. Neonatal sepsis was observed in 10.0% of the progesterone group and 16.0% of the control group, while neonatal mortality occurred in 2.0% and 6.0%, respectively. None of these differences was statistically significant (p>0.05).

Table VIII
Maternal and neonatal adverse outcomes.

Outcome	Progesterone group (n=50)	Control group (n=50)	p-value
Maternal nausea/vomiting	4 (8.0)	2 (4.0)	0.678
Headache/dizziness	3 (6.0)	2 (4.0)	1
Vaginal discomfort	5 (10.0)	1 (2.0)	0.204
Maternal complications	6 (12.0)	7 (14.0)	0.766
Neonatal sepsis	5 (10.0)	8 (16.0)	0.372
Neonatal mortality	1 (2.0)	3 (6.0)	0.617

Fisher's exact test; Pearson's Chi-square test.

DISCUSSION

The present study evaluated the effect of progesterone in the management of threatened preterm labour among 100 pregnant women, with 50 women receiving progesterone and 50 receiving standard management alone. The principal findings were that progesterone treatment was associated with a significantly longer interval from admission to delivery, higher gestational age at delivery, and greater mean birth weight. However, the reduction in preterm delivery before 37 weeks and before 34 weeks did not reach statistical significance. Thus, the findings of the present study suggest that progesterone may be beneficial primarily in prolonging pregnancy rather than demonstrating a definitive preventive effect against preterm birth.

The baseline characteristics of the two groups were comparable. The mean maternal age was 27.6 ± 4.8 years in the progesterone group and 28.1 ± 5.1 years in the control group (p=0.615). Similarly, gestational age at admission, gravidity and previous history of preterm birth did not differ significantly between the groups. The clinical characteristics at presentation, including lower abdominal pain, backache, pelvic pressure, uterine contractions, vaginal discharge, cervical dilatation and cervical effacement, were also comparable. This baseline similarity is important because gestational age and cervical findings are important determinants of the risk of spontaneous preterm delivery. Contemporary guidance emphasizes systematic clinical assessment of women presenting with suspected preterm labour, including evaluation of gestational age, cervical status and maternal-fetal condition [3,4]. The comparable baseline profile in the present study therefore reduces the likelihood that major baseline imbalance explains the observed difference in pregnancy prolongation.

In the present study, the most important finding was the significant prolongation of pregnancy following progesterone treatment. The mean interval from admission to delivery was 24.6 ± 12.8 days in the progesterone group compared with 17.8 ± 11.6 days in the control group

(p=0.006). In addition, pregnancy was prolonged for at least 14 days in 74.0% of women receiving progesterone compared with 54.0% of controls (p=0.037). Prolongation for at least 28 days occurred in 46.0% and 22.0%, respectively (p=0.011). These findings indicate that progesterone was associated with a clinically and statistically significant extension of pregnancy after presentation with threatened preterm labour.

The present findings are consistent with the randomized controlled trial by Sirisangwon and Phupong, which specifically evaluated vaginal progesterone in women with preterm labour at 24–34 weeks. In that study, 44 women received vaginal micronized progesterone 400 mg daily in addition to tocolytic therapy and antenatal corticosteroids, while 46 received standard treatment alone. The latency period was significantly longer in the progesterone group than in the no-progesterone group (32.8 ± 18.7 vs. 25.8 ± 22.7 days, p=0.045), and gestational age at delivery was also significantly higher (37 vs. 35 weeks, p=0.027) [17]. The direction of these findings closely agrees with the present study, where progesterone increased the mean admission-to-delivery interval and gestational age at delivery. The similarity is particularly relevant because both studies evaluated progesterone as an adjunctive treatment after symptomatic preterm labour rather than solely as prophylaxis in asymptomatic women.

A similar positive association was reported by Kabiri et al. among women with threatened preterm labour and a shortened cervix diagnosed after 24 weeks of gestation. Vaginal progesterone was associated with a longer diagnosis-to-delivery interval and a lower rate of preterm birth before 37 weeks [13]. The present study also demonstrated a longer pregnancy duration and lower numerical frequency of preterm delivery in the progesterone group. However, the Kabiri study specifically selected women with a shortened cervix, whereas the present study was not limited to women with cervical shortening. Therefore, the findings are directionally comparable, but the magnitude of treatment effect should not be considered directly equivalent.

The findings of the present study are also supported by the systematic review and meta-analysis of Breuking et al., which evaluated progestogen maintenance therapy after an episode of preterm labour. The analysis included 13 randomized controlled trials involving 1,722 women and found an overall prolongation of pregnancy associated with progestogen therapy, together with an increase in birth weight. However, the authors reported that the evidence was contradictory and that the latency benefit was no longer statistically significant when analyses were restricted to trials considered at low risk of bias [14]. This is important when interpreting the present significant result. Although the current findings support a beneficial effect on pregnancy prolongation, the available evidence does not establish that all women with threatened preterm labour will benefit equally from maintenance progesterone.

In contrast, Nachum et al. reported findings that differ from the present study. Their randomized clinical trial included 129 women with arrested preterm labour who had remained undelivered following initial treatment. Vaginal micronized progesterone did not significantly prolong pregnancy compared with no treatment; mean pregnancy prolongation was 40.0 days versus 37.4 days (p=0.44). The rate of spontaneous preterm delivery was also not significantly different between the groups [15]. The difference between that study and the present study may be related to differences in the clinical stage at which progesterone was initiated. The present study investigated women with threatened preterm labour, whereas the Nachum trial evaluated women after preterm labour had already been arrested. Differences in gestational age, progesterone regimen, duration of therapy and baseline clinical risk may also contribute to the divergent findings.

The present study did not demonstrate a statistically significant reduction in overall preterm delivery before 37 weeks. Preterm delivery occurred in 66.0% of the progesterone group compared with 82.0% of the control group (p=0.071). Similarly, delivery before 34 weeks occurred in 12.0% versus 24.0%, respectively (p=0.118). Although both outcomes numerically favored progesterone, the differences did not reach statistical significance. Therefore, it would not be appropriate to conclude from the present findings that progesterone prevented preterm birth. Rather, the evidence suggests a significant effect on pregnancy prolongation, with a favorable but statistically nonsignificant trend toward reducing preterm delivery.

This finding is strongly supported by Ferrari et al., who conducted a systematic review and meta-analysis specifically addressing progestogens for maintenance tocolysis in symptomatic women after an episode of threatened preterm labour. Their analysis included 17 randomized controlled trials involving 2,152 women with singleton pregnancies. Vaginal progesterone did not significantly reduce preterm birth before 37 weeks (RR 0.95, 95% CI 0.72–1.26) or before 34 weeks (RR 1.21, 95% CI 0.91–1.61) [12]. The findings of the present study are therefore consistent with this evidence: although progesterone was associated with a significantly longer latency period, the reduction in preterm birth did not achieve statistical significance.

The higher gestational age at delivery in the present study further supports the latency finding. The mean gestational age at delivery was 36.0 ± 1.4 weeks in the progesterone group compared with 35.1 ± 1.7 weeks in the control group (p=0.005). Term delivery occurred in 34.0% of progesterone-treated women compared with 18.0% of controls, although this categorical difference was not statistically significant (p=0.071). Sirisangwon and Phupong similarly observed a higher gestational age at delivery among women receiving vaginal progesterone [17]. Thus, both studies indicate that the effect of progesterone may be more evident when gestational age is analyzed as a continuous outcome than when delivery is simply classified as preterm or term.

The neonatal findings provide further support for the clinical relevance of pregnancy prolongation. Mean birth weight was significantly higher in the progesterone group than in the control group (2680 ± 420 vs. 2410 ± 460 g, p=0.003). Low birth weight occurred in 38.0% of infants in the progesterone group compared with 56.0% in the control group, although this difference was not statistically significant (p=0.071). The higher mean birth weight observed in the present study is consistent with the meta-analysis by Breuking et al., which reported an increase in birth weight among women receiving progestogen maintenance therapy following preterm labour [14]. Sirisangwon and Phupong also reported a significantly lower proportion of low-birth-weight infants among women receiving vaginal progesterone [17]. These findings support the possibility that prolongation of pregnancy may provide additional time for fetal growth.

The present study also showed favorable trends in neonatal morbidity. NICU admission occurred in 34.0% of neonates in the progesterone group compared with 50.0% in the control group (p=0.105), while respiratory distress syndrome occurred in 16.0% and 30.0%, respectively (p=0.096). Although these differences were not statistically significant, the direction of effect favored progesterone. Similar favorable neonatal effects have been reported in selected populations receiving vaginal progesterone. A 2024 meta-analysis of 2,741 women with singleton pregnancies and a short cervix reported significant reductions in preterm birth before 34 and 32 weeks, NICU admission and respiratory distress syndrome among women receiving vaginal progesterone [10]. However, that evidence primarily concerns women with a documented short cervix and therefore should not be directly extrapolated to all women with threatened preterm labour.

The distinction between prevention of preterm birth in high-risk but asymptomatic women and treatment following symptomatic preterm labour is particularly important. The EPPPIC individual-participant-data meta-analysis demonstrated that progestogens can reduce preterm birth in selected high-risk populations, but treatment effects vary according to the underlying risk profile [7]. Similarly, Conde-Agudelo and Romero concluded that the strongest evidence for vaginal progesterone relates to selected women with a short cervix, particularly singleton pregnancies, rather than universal treatment of all women at risk of preterm birth [8]. The 2024 SMFM guidance likewise recommends vaginal progesterone for selected asymptomatic singleton pregnancies with a short cervix, particularly when cervical length is ≤20 mm before 24 weeks, while emphasizing appropriate transvaginal cervical-length assessment [11]. These recommendations represent a different clinical context from the present study, which examined women who had already developed symptoms of threatened preterm labour.

Recent evidence further emphasizes the uncertainty surrounding progesterone after symptomatic preterm labour. A 2025 review of progesterone indications concluded that evidence among symptomatic women with threatened preterm labour or late miscarriage remains heterogeneous and does not establish a clear benefit of vaginal progesterone for pregnancy prolongation or neonatal outcomes [16]. This conclusion differs from the significant latency benefit observed in the present study. However, the discrepancy may reflect differences among individual studies in patient selection, gestational age, cervical characteristics, progesterone formulation, route and treatment duration. The recent evidence therefore supports cautious interpretation rather than complete rejection of the potential benefit observed in the present population.

A further recent study by Dominsky et al. evaluated vaginal progesterone among women with singleton pregnancies and a short cervix diagnosed between 24 and 33+6 weeks. After adjustment and matched analysis, vaginal progesterone was not associated with reduced spontaneous preterm birth before 37, 34, 32 or 28 weeks, and the interval from diagnosis to delivery was also similar between groups [18]. These findings are particularly relevant because they indicate that progesterone may not consistently prolong pregnancy even in women with cervical shortening when treatment is initiated after 24 weeks. The difference from the present study again suggests that treatment response may depend on the clinical setting and timing of progesterone initiation.

The neonatal safety findings of the present study were generally reassuring. Maternal nausea or vomiting, headache/dizziness and vaginal discomfort were relatively infrequent, and none differed significantly between the groups. Maternal complications were also comparable. Neonatal sepsis occurred in 10.0% of the progesterone group and 16.0% of controls, while neonatal mortality occurred in 2.0% and 6.0%, respectively; neither difference was statistically significant. Recent evidence examining progesterone exposure across pregnancy has suggested potentially favorable neonatal respiratory and infectious outcomes overall, although the underlying trials included heterogeneous populations and indications for progesterone use [19]. Therefore, the absence of significant adverse effects in the present study is reassuring, but the sample size is too small to establish safety for uncommon maternal or neonatal adverse events.

The standard management received by participants is also relevant when interpreting the findings. In the present study, antenatal corticosteroids were administered to 90.0% of women in the progesterone group and 88.0% of those in the control group, while tocolytic therapy was used in 78.0% and 82.0%, respectively. Current WHO recommendations emphasize appropriate use of antenatal corticosteroids when preterm birth is imminent and the necessary conditions for safe maternal and neonatal care are available. WHO also recommends appropriate tocolytic therapy in eligible women to allow time for corticosteroid administration and, when necessary, maternal transfer [6]. Therefore, the observed effect of progesterone should be interpreted as an adjunct to established management rather than as a substitute for evidence-based acute management of threatened preterm labour.

The present study has several clinically relevant implications. A significant extension of pregnancy from 17.8 to 24.6 days may provide additional time for completion of antenatal corticosteroid therapy, fetal maturation, maternal transfer to a higher-level facility and preparation for neonatal care. This may be particularly valuable in settings where access to advanced neonatal intensive care is limited. The global burden of preterm birth remains substantial, with approximately 13.4 million preterm births estimated worldwide in 2020, and South Asia continues to have one of the highest regional preterm birth rates [1]. Nevertheless, the present findings should not be generalized beyond the studied population without considering differences in gestational age, cervical status and treatment protocols.

Taken together, the findings indicate that progesterone was associated with significant prolongation of pregnancy, higher gestational age at delivery and higher mean birth weight in women with threatened preterm labour. However, the reduction in preterm delivery before 37 weeks and before 34 weeks did not reach statistical significance, and most neonatal outcomes showed only nonsignificant favorable trends. These findings are therefore best interpreted as evidence of a potential latency benefit rather than definitive evidence that progesterone prevents preterm birth after threatened preterm labour. The results agree with some randomized and observational studies but differ from recent trials and systematic reviews, reflecting the continuing uncertainty surrounding maintenance progesterone in symptomatic women.

Future randomized controlled studies with larger sample sizes should examine whether progesterone is particularly beneficial in specific subgroups, such as women with a short cervix, earlier gestational age at presentation, previous spontaneous preterm birth or persistent cervical change. Standardization of progesterone formulation, dose, route and treatment duration would also improve comparability between studies. Such evidence is necessary to determine whether the significant pregnancy prolongation observed in the present study translates into consistent reductions in serious neonatal morbidity and mortality.

LIMIATIONS

This study has several limitations. First, the relatively small sample size of 100 participants and single-center setting may limit the generalizability of the findings. Second, the observational design limits the ability to establish a definite causal relationship between progesterone therapy and pregnancy prolongation. Third, potential confounding factors, including differences in the underlying causes and severity of threatened preterm labour, could have influenced pregnancy and neonatal outcomes. Fourth, cervical length and other potential predictors of preterm birth were not incorporated into the analysis, which may have limited identification of women most likely to benefit from progesterone. Finally, the relatively short study period and limited follow-up restricted assessment of longer-term neonatal outcomes.

CONCLUSION

Progesterone therapy was associated with significant prolongation of pregnancy, a longer admission-to-delivery interval, higher gestational age at delivery, and greater birth weight among women with threatened preterm labour. However, although fewer women in the progesterone group experienced delivery before 37 or 34 weeks, these differences did not reach

statistical significance. Neonatal outcomes, including NICU admission and respiratory distress syndrome, also showed favorable trends but without statistically significant differences. Maternal adverse effects were uncommon and comparable between groups. Overall, progesterone may have a beneficial role in prolonging pregnancy in threatened preterm labour, but the present findings do not establish a definitive effect in preventing preterm birth. Larger, well-designed randomized controlled trials with appropriate stratification according to cervical length and other risk factors are warranted to clarify its clinical effectiveness.Continuous intravenous insulin infusion did not demonstrate better early postoperative outcomes than subcutaneous insulin therapy in diabetic patients undergoing OPCABG in this study. The continuous insulin group had significantly higher postoperative blood glucose and troponin I levels, greater postoperative arrhythmia and wound infection rates, longer inotropic support, and prolonged ICU and hospital stays. However, these findings should be interpreted cautiously because of the small sample size, observational study design, and significant difference in operative duration between the groups. Larger, well-designed randomized controlled studies are needed to determine the optimal perioperative insulin strategy for diabetic patients undergoing OPCABG.

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CONFLICTS OF INTEREST
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ETHICAL APPROVAL
The study was approved by the Institutional Ethics Committee.

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