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COMPARISON OF ORAL VERSUS VAGINAL PROGESTERONE IN THE PREVENTION OF PRETERM LABOR AND ITS CORRELATION WITH CERVICAL LENGTH ON TRANSVAGINAL SONOGRAPHY

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Abstract

Background: *The prevention of preterm labor remains a major challenge in obstetrics due to its strong association with neonatal morbidity and mortality. Progesterone therapy is widely used in women at high risk, but the optimal route of administration—oral or vaginal—remains unclear.*

Objectives: *To compare the efficacy of oral versus vaginal progesterone in preventing preterm labor and to evaluate their correlation with cervical length measured via transvaginal sonography.*

Study Design & Setting: *This was a prospective, comparative observational study conducted at the Department of Obstetrics and Gynecology DHQ Teaching Hospital Mirpur AJK.*

Methodology: *A total of 150 pregnant women at 16–24 weeks of gestation with cervical length <25 mm on transvaginal ultrasound were enrolled and randomly allocated into two equal groups. Group A received oral progesterone (Dydrogesterone 10 mg twice daily) while Group B received vaginal progesterone suppositories (Micronized Progesterone 200 mg once daily). Cervical length was measured every two weeks. The primary outcome was the incidence of preterm labor before 37 weeks. Secondary outcomes included changes in cervical length and treatment tolerability.*

Results: *Preterm labor occurred in 28.0% of women in the oral group and 14.7% in the vaginal group (p = 0.046). Vaginal progesterone showed significantly better preservation of cervical length at 4 and 6 weeks. Compliance was good in both groups, with mild adverse effects varying by route.*

Conclusion: *Vaginal progesterone is more effective than oral progesterone in preventing preterm labor and maintaining cervical length in high-risk pregnancies.*

INTRODUCTION

Preterm labor (PTL), defined as the onset of labor before 37 completed weeks of gestation, remains a significant contributor to neonatal morbidity and mortality worldwide.[1] The World Health Organization (WHO) reports that approximately 15 million babies are born preterm each year, with complications of prematurity accounting for a substantial proportion of under-five deaths.[2,3] In developing countries like Pakistan, the burden is especially high due to limited access to specialized neonatal care. Preventing preterm labor is thus a critical goal in obstetric care, and numerous strategies have been explored, among which progesterone therapy has gained prominence for its ability to maintain uterine quiescence and support pregnancy continuation.[4,5]

Progesterone plays a pivotal role in maintaining pregnancy by inhibiting myometrial contractions, modulating inflammatory responses, and preserving cervical integrity. Supplementation of progesterone, especially in women at risk for PTL due to a history of preterm birth or shortened cervical length, has shown promise in prolonging gestation and improving neonatal outcomes.[6] However, the optimal route of administration—oral or vaginal—remains a topic of ongoing debate. Oral progesterone is convenient but may have lower bioavailability due to hepatic first-pass metabolism, while vaginal progesterone provides direct access to the uterus and cervix, potentially offering superior local efficacy with fewer systemic side effects.[7]

Transvaginal sonographic (TVS) measurement of cervical length (CL) has emerged as a reliable and non-invasive tool for predicting the risk of preterm labor. Studies have consistently demonstrated that a shortened cervix in the second trimester is a strong predictor of spontaneous PTL.[8,9] Combining progesterone therapy with cervical length monitoring allows for targeted intervention in high-risk pregnancies. However, the comparative effectiveness of oral versus vaginal progesterone in relation to cervical length dynamics remains inadequately studied, particularly in South Asian populations.[10,11]

This study aims to compare the efficacy of oral versus vaginal progesterone in preventing preterm labor and to correlate their effects with cervical length measured via transvaginal ultrasound. By evaluating changes in cervical length and the rate of preterm births in both groups, the study seeks to provide evidence-based guidance on the preferable route of administration in at-risk pregnancies. Additionally, exploring this correlation will help refine risk stratification and management strategies for women with a shortened cervix. Given the high stakes associated with preterm birth and the need for cost-effective, accessible interventions in resource-limited settings, our research addresses a critical gap. The findings have the potential to inform clinical guidelines, optimize the use of progesterone therapy, and ultimately contribute to reducing the incidence of preterm births and their associated complications.

MATERIALS AND METHODS

This comparative observational study was conducted in the Department of Obstetrics and Gynecology DHQ Teaching Hospital Mirpur AJK from October 2024 to March 2025, after approval from the institutional ethical review board. A total of 150 pregnant women who were at high risk for preterm labor were included in the study through non-probability consecutive sampling. The sample size of 150 was calculated using OpenEpi software by taking the frequency of preterm labor in high-risk pregnancies to be 20%, with a 95% confidence interval, 5% margin of error, and power of 80%.[15]

Women between 18 and 40 years of age, with singleton pregnancies, a gestational age between 16 and 24 weeks confirmed by ultrasonography, and a transvaginal cervical length of less than 25 mm were included. Women with multiple pregnancies, known uterine anomalies, vaginal bleeding, active labor, ruptured membranes, or any contraindications to progesterone therapy were excluded.

Patients were divided into two groups of 75 each. Group A received oral progesterone (Dydrogesterone 10 mg twice daily), while Group B was administered vaginal progesterone suppositories (Micronized Progesterone 200 mg once daily at bedtime). All patients were advised to take the treatment regularly until 36 completed weeks of gestation or delivery, whichever occurred earlier. Compliance was monitored through follow-up visits every two weeks.

Transvaginal sonography (TVS) was performed at baseline and then every two weeks to assess cervical

length using a high-frequency endovaginal probe. All sonographic measurements were conducted by the same experienced sonologist to ensure consistency. The primary outcome was the incidence of preterm labor, defined as spontaneous onset of labor before 37 completed weeks. The secondary outcome was the change in cervical length over the treatment period.

Data were collected using a structured proforma, including demographic information, obstetric history, gestational age, cervical length measurements, treatment compliance, and pregnancy outcomes. All data were analyzed using SPSS version 25.0. Mean and standard deviation were calculated for continuous variables, while frequencies and percentages were reported for categorical variables. The chi-square test was used to compare categorical outcomes between groups, and an independent t-test was used for continuous variables. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Table 1 shows the baseline demographic and clinical characteristics of the 150 participants, divided equally into oral and vaginal progesterone groups. The mean age of participants in the oral group was 28.4 ± 4.6 years, while in the vaginal group it was 29.1 ± 4.2 years (p = 0.328), indicating no significant age difference between groups. The mean gestational age at enrollment was similar across groups (20.2 ± 2.1 weeks in the oral group and 20.4 ± 1.9 weeks in the vaginal group; p = 0.521). Both groups were also comparable in terms of obstetric history, including gravida, parity, and history of previous preterm births, with p-values > 0.05. Baseline cervical length measured via transvaginal sonography was not significantly different between groups (22.4 ± 1.7 mm in the oral group vs. 22.6 ± 1.8 mm in the vaginal group; p = 0.451), suggesting both cohorts were clinically matched at the start of the study.

Table 2 presents the serial measurements of cervical length across different time points during progesterone therapy. While both groups started with similar baseline cervical lengths, over time the vaginal progesterone group demonstrated a more significant preservation and improvement in cervical length. After 2 weeks, the vaginal group had a cervical length of 22.8 ± 1.6 mm compared to 22.1 ± 1.6 mm in the oral group (p = 0.021). The difference continued to widen at 4 weeks (23.0 ± 1.5 mm vs. 21.8 ± 1.8 mm; p = 0.003) and at 6 weeks (23.1 ± 1.4 mm vs. 21.4 ± 2.1 mm; p = 0.001). These results from Table 2 suggest that vaginal progesterone was more effective in maintaining cervical length over time, a key indicator in the prevention of preterm labor.

Table 3 displays the pregnancy outcomes in terms of preterm labor incidence. The rate of preterm labor was significantly lower in the vaginal progesterone group (14.7%) compared to the oral progesterone group (28.0%), with a p-value of 0.046. Conversely, term deliveries were more common in the vaginal group (85.3%) than in the oral group (72.0%). These findings from Table 3 indicate a superior efficacy of vaginal progesterone in reducing the risk of preterm birth among high-risk women.

Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 150)

Variable	Oral Progesterone (n = 75)	Vaginal Progesterone (n = 75)	p-value
Mean Age (years)	28.4 ± 4.6	29.1 ± 4.2	0.328
Mean Gestational Age (weeks)	20.2 ± 2.1	20.4 ± 1.9	0.521
Gravida (≥2)	43 (57.3%)	40 (53.3%)	0.627
Parity (≥1)	38 (50.7%)	36 (48.0%)	0.740
Previous Preterm Birth	19 (25.3%)	21 (28.0%)	0.712
Baseline Cervical Length (mm)	22.4 ± 1.7	22.6 ± 1.8	0.451

Table 2: Cervical Length Change Over Time (mm)

Timepoint	Oral Progesterone (Mean ± SD)	Vaginal Progesterone (Mean ± SD)	p-value
Baseline (16–24 weeks)	22.4 ± 1.7	22.6 ± 1.8	0.451
After 2 Weeks	22.1 ± 1.6	22.8 ± 1.6	0.021
After 4 Weeks	21.8 ± 1.8	23.0 ± 1.5	0.003
After 6 Weeks	21.4 ± 2.1	23.1 ± 1.4	0.001

Table 3: Incidence of Preterm Labor (<37 Weeks)

Outcome	Oral Progesterone (n = 75)	Vaginal Progesterone (n = 75)	p-value
Preterm Labor	21 (28.0%)	11 (14.7%)	0.046
Term Delivery	54 (72.0%)	64 (85.3%)	

Table 4: Compliance and Adverse Effects

Variable	Oral Progesterone (n = 75)	Vaginal Progesterone (n = 75)	p-value
Good Compliance	68 (90.7%)	71 (94.7%)	0.341
Mild Nausea	12 (16.0%)	4 (5.3%)	0.037
Vaginal Discharge (Non-infective)	1 (1.3%)	6 (8.0%)	0.049

DISCUSSION

Preterm labor remains a leading cause of neonatal morbidity and mortality globally, especially in low-resource settings. Progesterone therapy is commonly used to prevent preterm birth in high-risk pregnancies.[12] Two main routes—oral and vaginal—are employed, but their comparative efficacy remains debated.[13] Vaginal progesterone is thought to act more directly on the uterus and cervix, potentially improving outcomes. Transvaginal sonographic measurement of cervical length is a key predictor of preterm labor risk.[14] This study compares oral versus vaginal progesterone and their impact on cervical length and preterm birth prevention.

The current study demonstrated that vaginal progesterone was significantly more effective than oral progesterone in preventing preterm labor, with a preterm birth rate of 14.7% in the vaginal group compared to 28.0% in the oral group (p = 0.046). Additionally, the vaginal group showed better preservation of cervical length over the treatment period, with a mean cervical length of 23.1 ± 1.4 mm at six weeks versus 21.4 ± 2.1 mm in the oral group (p = 0.001). These findings are consistent with the results reported by Fayyaz et al. (2022), where the efficacy of vaginal progesterone was 63.33% in preventing preterm birth, though it was lower than the 93.33% observed in the cervical cerclage group (p = 0.0001). While our study did not include cerclage as a comparator, our results support the efficacy of vaginal progesterone as a preventive strategy.

Similarly, Bangash et al. (2025) reported that in their meta-analysis, both vaginal progesterone and cervical cerclage significantly reduced the risk of preterm birth and associated perinatal morbidity when compared with no intervention. Their adjusted indirect meta-analysis showed no significant difference between the two interventions, suggesting that clinical decisions should consider patient preference, cost, and adverse event profiles. This aligns with our findings where vaginal progesterone showed high compliance (94.7%) and minimal side effects, supporting its practical usability in resource-limited settings.

In our study, the mean maternal age in the vaginal progesterone group was 29.1 ± 4.2 years, closely matching the age ranges reported by Bangash et al. (2025) and Hafeez et al. (2022), which were 26–33 years and 29.6 ± 5.44 years, respectively. The similarity in demographic characteristics strengthens the external validity of our findings. Hafeez et al. also demonstrated superior efficacy of vaginal progesterone (90.5%) compared to oral nifedipine (73.0%) in delaying preterm labor (p = 0.011),

further reinforcing the role of vaginal progesterone in high-risk pregnancies. Additionally, Qamar et al. (2020) reported similar effectiveness between vaginal progesterone (86.3%) and cervical cerclage (84.9%) in preventing preterm labor in women with a short cervix. These results are congruent with our study, which showed favorable outcomes with vaginal progesterone. The mean gestational age at recruitment in their study (21.46 ± 1.52 weeks for the vaginal group) was comparable to our study (20.4 ± 1.9 weeks), supporting methodological consistency. On the other hand, while Amiri et al. (2025) focused on the impact of COVID-19 on pregnancy outcomes, including preterm birth, their findings highlight the importance of timely and preventive strategies such as progesterone therapy, which our study directly addresses. Although their emphasis was broader and pandemic-specific, it underscores the critical need for ongoing research in the domain of preterm labor prevention. Collectively, the current study supports the growing body of evidence that vaginal progesterone is an effective, non-invasive intervention for women with short cervical length and risk of preterm labor. Compared to oral progesterone, it offers superior cervical length preservation and a lower incidence of preterm birth with good compliance and minimal side effects. These findings advocate for the routine use of vaginal progesterone in high-risk pregnancies, especially where cervical cerclage may not be feasible or preferred.

This study used a well-matched sample with consistent inclusion criteria and a standardized sonographic protocol. Regular follow-up allowed for dynamic assessment of cervical length over time. It compared two commonly used progesterone routes in a high-risk population. However, the study was limited by its single-center design and relatively short duration. Blinding was not feasible, which may introduce observer bias. Long-term neonatal outcomes were not assessed.

CONCLUSION

Vaginal progesterone was more effective than oral progesterone in maintaining cervical length and reducing preterm birth rates. Both routes were well tolerated with different side-effect profiles. Vaginal administration may be the preferred option in preventing preterm labor in high-risk pregnancies.

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