ORIGINAL ARTICLE

Mifepristone with Misoprostol versus Misoprostol Alone for Induction of Labor in Postdated Pregnancy- A Comparative Study

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ABSTRACT

Introduction: Postdated pregnancy is associated with increased maternal and neonatal complications, often necessitating induction of labour. Mifepristone, an antiprogesterone agent, facilitates cervical ripening and may enhance the effectiveness of misoprostol. **Aims:** To compare the efficacy and safety of mifepristone combined with misoprostol versus misoprostol alone for induction of labour in postdated primigravida. **Methods:** This cross-sectional comparative study was conducted at Nepalgunj Medical College from April 2025 to April 2026. A total of 122 primigravida with Bishop score <6 were enrolled and randomly allocated into two groups. Group A received oral mifepristone (200 mg) followed by vaginal misoprostol (25 mcg), while Group B received vaginal misoprostol alone. Outcomes assessed included Bishop score improvement, induction-to-delivery interval, mode of delivery, and neonatal outcomes. Statistical analysis was performed using the Chi-square test, with $p<0.05$ considered significant. **Results:** The mean Bishop score at reassessment was significantly higher in Group A (4.69±0.74) compared to Group B (3.41±1.21; $p<0.001$). The induction-to-delivery interval was significantly shorter in Group A (610.16±102.62 minutes) than in Group B (1151.15±133.31 minutes; $p<0.001$). Vaginal delivery rates were higher in Group A (59.01%) compared to Group B (40.98%; $p=0.046$), while cesarean section rates were lower in Group A (34.42% vs. 55.73%; $p=0.045$). Neonatal outcomes, including APGAR scores and NICU admissions, were comparable between groups. **Conclusion:** The combination of mifepristone and misoprostol is more effective than misoprostol alone for induction of labour in postdated primigravida, with improved cervical ripening and higher vaginal delivery rates without increasing neonatal risk.

Keywords: Induction of labour; Mifepristone; Misoprostol; Postdated pregnancy

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INTRODUCTION

Induction of labour (IOL) is indicated when continuation of pregnancy poses a hazard to mother or fetus, commonly in postdated pregnancy.[1-3] Various methods of labour induction at term have been developed and are widely practiced to reduce these risks and improve overall obstetric outcomes.[4,5] Mifepristone, a progesterone receptor antagonist, promotes cervical ripening by degrading collagen and increasing uterine sensitivity to prostaglandins. Mifepristone facilitates cervical ripening through increased collagen degradation, enhanced prostaglandin synthesis, and upregulation of matrix metalloproteinase-3 (MMP-3).[6,7] These changes promote cervical softening and enhance the induction process. Early work by Berkane N et al[8] found mifepristone alone (up to 600 mg) un reliable for induction within 54 hours in unfavorable cervices. However, subsequent investigations by Gallot D et al, Wing DA et al and Kumari S et al, consistently demonstrated that mifepristone is effective and safe as a cervical ripening agent when used prior to induction of labour.[9-11] A Cochrane review Hapangama D et al[12] confirmed mifepristone significantly increases the likelihood of achieving favorable cervical status or entering labour within 48 hours versus placebo (RR 2.41; 95% CI 1.70–3.42). Recent trials also report benefits including reduced cesarean rates, lower need for augmentation, and fewer NICU admissions. Most studies report no significant increase in adverse outcomes, though some note more intense contractions or potential cephalopelvic disproportion warranting further investigation. This study aims to evaluate the efficacy and safety of mifepristone combined with misoprostol versus misoprostol alone for cervical ripening and IOL in postdated pregnancy.

METHODS

This cross-sectional observational study was conducted over a period of one year, from April 2025 to April 2026, in the Department of Obstetrics and Gynaecology at Nepalgunj Medical College, Nepal.

Sample Size Calculation

The sample size was calculated using the standard formula for comparison of two proportions:

$$N = (Z_{\alpha/2}+Z_{\beta})^2 \times \{P_1(1 - P_1) + P_2(1 - P_2)\} /(P_1 - P_2)^2$$

where:

- N= required sample size per group
- P_1= proportion of vaginal delivery in the mifepristone plus misoprostol group (0.6)
- P_2= proportion of vaginal delivery in the misoprostol-only group (0.4)
- $Z_{\alpha/2}$ = 1.96 for a 5% level of significance
- Z_{β} = 0.84 for 80% power

Based on this calculation, the minimum required sample size was 52 participants (26 in each group).[11] However, all eligible participants who met the inclusion criteria and provided informed consent during the study period were enrolled, resulting in a total sample size of 122 (61 in each group).

Ethical Considerations

Ethical approval was obtained from the Institutional Review Committee (IRC) of Nepalgunj Medical College prior to commencement of the study. Written informed consent was obtained from all participants before inclusion.

Study Population and Sampling

All primigravida women who had crossed their expected date of delivery (postdated pregnancy) and presented for induction of labour were considered for inclusion. Only those with an unfavorable cervix (Bishop score <6) were enrolled. Participants were allocated into two equal groups (Group A and Group B) using a lottery method.

Intervention Protocol

Baseline Bishop score was recorded prior to induction in all participants.

- Group A (Combination group): Participants received oral mifepristone 200 mg (Pregno 200, Ohm Pharmaceuticals, Nepal), followed simultaneously by vaginal misoprostol 25 µg (Mistol 50 µg, Ohm Pharmaceuticals, Nepal, administered as half tablet). After 4 hours, Bishop score was reassessed; if it remained <6, a second dose of misoprostol 25 µg was administered vaginally.
- Group B (Misoprostol-only group): Participants received vaginal misoprostol 25 µg. After 4 hours, Bishop score was reassessed, and a second dose of 25 µg misoprostol was administered if the Bishop score remained <6.

If adequate labour was not established, artificial rupture of membranes (ARM) followed by augmentation with oxytocin (Syntocinon) was performed 12 hours after the last dose of misoprostol. Cesarean section was performed in cases of failed induction (persistently unfavorable cervix after oxytocin 15 i.u. in titrating dose) or when indicated for maternal, fetal, or placental reasons at any stage of labor.

Outcome Measures

Participants in both groups were evaluated for:

- Induction-to-delivery interval
- Mode of delivery (vaginal, cesarean, instrumental)
- Postpartum hemorrhage (PPH)
- Neonatal outcomes (birth weight, APGAR score, NICU admission)
- Any maternal or fetal adverse events

Data Collection and Statistical Analysis

Data, including demographic variables such as maternal age and gestational age, were recorded using a predesigned proforma. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. The Chi-square test was applied to compare categorical variables between the two groups and independent t-test was applied for comparing mean of continuous variables between two groups. A p-value of ≤0.05 was considered statistically significant. Potential confounding variables, such as maternal age and gestational age, were controlled through stratification.

RESULTS

During the study period, a total of 4,302 women presented for delivery services at the study center. No cases of PPH were recorded in the study population. Neonatal care admissions were not significant; only five were found in each group.

Demographic Characteristics

The majority of participants in both groups belonged to the 20–24 years age group, accounting for 47.54% in Group A and 50.81% in Group B. This was followed by the 25–29 years age group, comprising 31.14% in Group A and 29.58% in Group B. Participants aged less than 20 years were slightly more frequent in Group B (14.75%) compared to Group A (9.83%). In contrast, the proportion of participants aged 30–34 years was higher in Group A (11.47%) than in Group B (4.91%) (Table I).

Regarding ethnic distribution, the majority of participants in both groups belonged to the Brahmin/Chhetri category

(42.62% in Group A and 45.90% in Group B), followed by the Janjati group (36.06% in Group A and 32.78% in Group B). Dalit participants constituted 13.11% in Group A and 16.39% in Group B. A small proportion of participants belonged to other ethnic groups (4.91% in both groups), while Muslim participants (3.27%) were present only in Group A (Table I).

Maternal and Neonatal Outcomes

A statistically significant improvement in Bishop score after 4 hours of intervention was observed in Group A compared to Group B ($p < 0.001$). Additionally, the induction-to-delivery interval was significantly shorter in the combination group (Group A) than in the misoprostol-only group (Group B) ($p < 0.001$).

With respect to the mode of delivery, a significant difference was noted between the two groups ($p = 0.037$), with a higher proportion of vaginal deliveries observed in Group A.

However, no statistically significant differences were found between the groups in terms of baseline Bishop score at the time of first drug administration, neonatal birth weight, APGAR scores at 1 and 5 minutes, or neonatal intensive care unit (NICU) admissions. (Table II).

Variable		Group A N %	Group N %
Age distribution	<20	6 (9.83)	9(14.75)
	20-24	29 (47.54)	31(50.81)
	25-29	19 (31.14)	18(29.58)
	30-34	7 (11.47)	3(4.91)
Ethinicity	Dalit	8 (13.11)	10 (16.39)
	Janjati	22 (36.06)	20 (32.78)
	Muslim	2 (3.27)	0 (0)
	Bramin /Chhetri	26 (42.62)	28 (45.90)
	Others	3 (4.91)	3 (4.91)

Table I: Demographic variable

Variable		Mifepristone with Miso	Misoprostol	P-value
Bishop score at time of insertion		1.82± 0.69	1.79± 0.63	0.786
Bishop score at time of reassessment		4.69± 0.74	3.41± 1.21	<0.001
Baby weight in gram		3130.74± 358.52	3070.00± 405.34	0.382
APGAR 1st minute		6.57± 0.69	6.61± 0.86	0.817
APGAR 5th minute		8.05± 0.28	7.95± 0.33	0.085
NICU admission		5 (8.19%)	5 (8.19%)	1.000
Induction interval delivery (minutes)		610.16± 102.62	1151.15± 133.31	<0.001
Route of delivery	Vaginal	36 (59.01%)	25 (40.98%)	.046
	c-section	21 (34.42%)	34 (55.73%)	.045
	Instrumental	4 (6.5%)	2 (3.27%)	.148

Table II: Maternal and fetal outcome

DISCUSSION

The present study evaluated the efficacy of mifepristone in combination with misoprostol compared to misoprostol alone for induction of labour in postdated primigravida, with particular emphasis on maternal and neonatal outcomes. A significant improvement in Bishop score was observed in the combination group compared to the misoprostol-only group ($p < 0.001$), indicating more effective cervical ripening. This finding is consistent with previous studies by Stenlund PM et al, Kayastha S et al, and Yelikar K et al, which also demonstrated enhanced cervical favorability following mifepristone administration.[8,14,18]

In terms of mode of delivery, the present study demonstrated a higher rate of vaginal delivery in the combination group (59.01%) compared to the misoprostol-only group (40.98%), with a corresponding reduction in cesarean section rates (34.42% vs. 55.73%; $p < 0.05$). These findings are in agreement with those reported by Ghimire A et al, who observed vaginal delivery rates of 66% in the mifepristone group compared to 42% in the control group, along with significantly lower cesarean rates.[16] Similarly, Athawale R et al reported an even higher vaginal delivery rate of 76% in the mifepristone group compared to 24% in the control group, further supporting the beneficial role of mifepristone in improving induction outcomes.[17]

However, contrasting findings have also been reported in the literature. Archana A et al observed a higher rate of vaginal delivery in the misoprostol-only group (90%) compared to

the mifepristone group (60%), suggesting that outcomes may vary depending on study design, dosing regimens, patient selection, and timing of drug administration (hyper stimulation may be possible reason in mifepristone misoprostol group).[19] These discrepancies highlight the need for standardized protocols and further large-scale randomized controlled trials. With regard to instrumental delivery, the present study showed no statistically significant difference between the two groups (6.5% in the combination group vs. 3.27% in the misoprostol group; p = 0.148). This suggests that the addition of mifepristone does not significantly influence the likelihood of operative vaginal delivery. Neonatal outcomes, including NICU admission rates, were comparable between the two groups (8.2% in both groups), indicating that the use of mifepristone does not adversely affect neonatal well-being. This finding is consistent with previous studies that have demonstrated the safety of mifepristone in labour induction without increasing neonatal morbidity.[18,19]

LIMITATIONS

Several limitations of the present study should be acknowledged. First, the unavailability of misoprostol in the standard 25 µg dosage necessitated the use of halved 50 µg tablets, which may have introduced minor variability in the administered dose and potentially affected the uniformity of treatment. Second, although the calculated sample size requirement was 52 participants, the study included a relatively limited sample size of 122 participants overall, which may reduce the statistical power to detect smaller differences between groups. Third, this was a single-center study conducted at a tertiary care institution, which may limit the generalizability of the findings to other populations, healthcare settings, and geographic regions. Fourth, the duration of the study was limited to one year, restricting the ability to assess long-term maternal and neonatal outcomes associated with the intervention. Finally, due to the nature of the intervention, blinding of participants and healthcare providers was not feasible, which may have introduced performance and observer bias. These limitations should be considered when interpreting the study findings and highlight the need for further well-designed, multicenter randomized trials.

CONCLUSION

Overall, the findings of this study support the hypothesis that mifepristone enhances the efficacy of misoprostol for induction of labour by improving cervical readiness and increasing the likelihood of successful vaginal delivery, while maintaining a favorable safety profile for both mother and neonate. Nevertheless, variations in outcomes across different studies emphasize the importance of further research to optimize dosing strategies, timing of administration, and patient selection criteria. Despite these encouraging results, further large-scale, multicenter randomized controlled trials are warranted to establish the long-term efficacy and safety profile of mifepristone in labour induction at term and in postdated pregnancies. Future research should focus on optimizing dosing regimens, timing of administration, and combination protocols with prostaglandins. Additionally, evaluation of cost-effectiveness, patient satisfaction, and feasibility in low-resource settings is essential to support broader clinical implementation, particularly in developing countries such as Nepal.

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