

A Comparative Study on the Efficacy of Mifepristone-Misoprostol Combination versus Misoprostol Alone and Intracervical Catheter (ICC) in the Management of IUFD at Rangpur Medical College Hospital

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ABSTRACT

Background: Intrauterine fetal death (IUFD) presents a profound obstetric challenge requiring safe and effective induction of labour. In Bangladesh, misoprostol alone and mechanical methods like an intracervical catheter (ICC) are commonly used, but evidence on the efficacy of the mifepristone-misoprostol combination in this setting is limited. **Objective:** To compare the induction-to-delivery interval and maternal outcomes of three methods for managing IUFD: mifepristone-misoprostol combination, misoprostol alone, and intracervical catheter (ICC). **Methods & Materials:** A prospective cohort study was conducted at Rangpur Medical College & Hospital, Rangpur, from January 2025 to December 2025. Using purposive sampling, 29 women with IUFD (≥ 24 weeks) were allocated to three groups: Group A (mifepristone 200mg orally followed by oral misoprostol, n=10), Group B (oral misoprostol alone, n=10), and Group C (ICC with oxytocin augmentation, n=9). The primary outcome was the induction-to-delivery interval. Data were analyzed using SPSS version 23.0. **Results:** The mean induction-to-delivery interval was significantly shortest with mifepristone-misoprostol (10.8 ± 2.9 hours), followed by misoprostol alone (15.4 ± 4.1 hours) and ICC (19.1 ± 5.3 hours) ($p < 0.001$). The 24-hour vaginal delivery success rate was highest in the combination group (90%), versus 70% with misoprostol and 55.6% with ICC. Maternal complication rates (e.g., PPH) were low and comparable across all three methods. **Conclusion:** The mifepristone-misoprostol regimen was the most efficacious method for labour induction in IUFD, achieving the shortest delivery time and highest success rate. Misoprostol alone was a viable alternative, while ICC was

associated with the longest induction interval.

Keywords: Intracervical catheter, intrauterine fetal death, labour induction, mifepristone, misoprostol, stillbirth

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INTRODUCTION

Intrauterine fetal death (IUFD), defined as the demise of a fetus at or beyond 24 weeks of gestation, remains a devastating obstetric complication with profound psychological and social implications for the affected family [1]. Its global burden is disproportionately high in low- and middle-income countries (LMICs). In Bangladesh, the stillbirth rate is estimated at 22.1 per 1000 total births, translating to a significant public health challenge and highlighting an urgent need for improved antenatal and intrapartum care strategies [2]. The management of IUFD, therefore, is not only a clinical imperative to ensure maternal safety but also a critical step in the compassionate care for grieving parents. The cornerstone of IUFD management is the timely and safe induction of labour to achieve vaginal delivery, thereby avoiding the risks associated with prolonged retention of the fetus, such as coagulopathy and infection [3]. The ideal induction method should be highly effective, safe, accessible, and cost-effective, with minimal physical

and emotional trauma to the mother. For decades, misoprostol, a synthetic prostaglandin E1 analogue, has been the mainstay of medical management in LMICs due to its low cost, thermal stability, and ease of administration [4]. However, its use as a single agent can be associated with a prolonged induction-to-delivery interval and an increased need for multiple doses, potentially extending the mother's distress. In recent years, the sequential use of mifepristone, an anti-progesterone, followed by a prostaglandin has emerged as a highly effective regimen for labour induction in both live and intrauterine fetal demise pregnancies [5]. Mifepristone induces cervical ripening by blocking progesterone receptors, thereby sensitizing the myometrium to the contractile effects of subsequent prostaglandins like misoprostol. Studies have demonstrated that this combination significantly reduces the induction-to-delivery interval compared to prostaglandins alone, potentially improving patient experience and reducing hospital stay [6,7]. Despite its proven efficacy, the

adoption of this combination therapy, particularly for IUFD, remains inconsistent in resource-constrained settings like Bangladesh, often due to perceived cost and availability issues. Conversely, mechanical methods such as the intracervical catheter (ICC) or Foley catheter offer a non-pharmacological, low-cost alternative. These devices work by locally stimulating prostaglandin release and providing mechanical dilation. They are especially valuable in settings where specific uterotonic drugs are unavailable or contraindicated [8]. While effective, mechanical methods may be associated with discomfort, a slower induction process, and a higher risk of intrapartum fever or infection compared to pharmacological methods [9]. Recent systematic reviews underscore the variability in outcomes when comparing mechanical and pharmacological methods, indicating that context and protocol standardization are key. A significant gap exists in the direct comparative evidence of these three modalities-mifepristone-misoprostol

combinations, misoprostol alone, and ICC- within the specific socio-cultural and clinical context of Bangladesh. Most existing studies originate from high-income countries or compare only two methods [10,11]. Furthermore, local data guiding clinicians at the tertiary hospitals of Rangpur Medical College Hospital, Rangpur, on the optimal, context-appropriate protocol is scarce. Understanding the comparative efficacy, safety profile, and practical outcomes of these methods is essential for developing standardized, effective, and patient-centered clinical guidelines [12,13]. Therefore, this prospective cohort study aimed to fill this evidence gap by directly comparing the efficacy, measured primarily by the induction-to-delivery interval, and maternal outcomes of the mifepristone-misoprostol combination regimen, misoprostol alone, and the intracervical catheter (with oxytocin augmentation) for the management of IUFD. The findings are intended to provide robust, locally relevant data to inform clinical decision-making and improve the standard of care for women facing this tragic obstetric event in Bangladesh.

METHODS & MATERIALS

This prospective cohort study enrolled 29 consecutive women diagnosed with IUFD (≥ 24 weeks of gestation) at Rangpur

Medical College & Hospital, Rangpur, between January 2025 and December 2025. Participants were managed as per the hospital's existing protocols and allocated to one of three induction method groups based on clinician discretion and patient consent, reflecting real-world practice.

Inclusion and Exclusion Criteria

Inclusion Criteria

Inclusion required a confirmed diagnosis of IUFD by ultrasound (absent fetal cardiac activity), a gestational age of 24 weeks or more, a singleton pregnancy, and a willingness to participate by providing informed written consent. Women with no contraindications to vaginal delivery were eligible.

Exclusion Criteria

Women were excluded from the study if they had a known allergy to mifepristone or misoprostol, presented with clinical evidence of chorioamnionitis or coagulopathy, had a previous uterine scar (like a classical cesarean section), or had an obstetric condition mandating an immediate cesarean delivery.

Study Procedure

Participants were allocated to three groups: Group A received 200mg oral mifepristone, followed 24 hours later by oral misoprostol

(50 μ g 4-hourly, max 200 μ g). Group B received oral misoprostol alone on the same regimen. Group C underwent insertion of a 16F Foley catheter as an intracervical catheter (ICC), with oxytocin infusion commenced if active labour did not ensue within 12 hours. Maternal demographics, induction-to-delivery interval, delivery mode, and complications were recorded on a structured datasheet.

Data Analysis

Data were analyzed using SPSS version 23.0. Continuous variables (e.g., induction-to-delivery interval) were compared using one-way ANOVA, and categorical variables (e.g., success rate) using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULT

Table I presents the baseline demographic and obstetric characteristics distributed across Group A, Group B (Miso alone, n=10), and Group C (ICC, n=9). The overall mean maternal age was 25.6 ± 4.1 years, and the mean gestational age was 31.4 ± 3.8 weeks. Primigravida accounted for 24.1%, previous cesarean section for 13.8%, and gestational hypertension for 17.2% of cases. ($p > 0.05$). (Table 1).

Table I

Baseline demographic and obstetric characteristics of the study participants.

Characteristic	Total (n=29)	Group A	Group B	Group C	p-value
		Mife + Miso (n=10)	Miso Alone (n=10)	ICC (n=9)	
Maternal age (years), Mean \pm SD	25.6 \pm 4.1	25.1 \pm 3.9	26.0 \pm 4.5	25.7 \pm 4.0	0.887
Gestational age (weeks), Mean \pm SD	31.4 \pm 3.8	30.9 \pm 3.5	32.0 \pm 4.2	31.2 \pm 3.8	0.786
Primigravida, n (%)	7 (24.1%)	2 (20.0%)	3 (30.0%)	2 (22.2%)	0.865
Previous C-section, n (%)	4 (13.8%)	1 (10.0%)	2 (20.0%)	1 (11.1%)	0.773
Gestational HTN, n (%)	5 (17.2%)	2 (20.0%)	1 (10.0%)	2 (22.2%)	0.732

Table II shows induction-to-delivery intervals where Group A had the shortest mean interval at 10.8 ± 2.9 hours (median

10.5, range 7–16), Group B averaged 15.4 ± 4.1 hours (median 15, range 10-23), and

Group C, the longest at 19.1 ± 5.3 hours (median 18, range 13-29). ($p < 0.001$).

Table II

Primary outcome: Induction-to-delivery interval.

Group	n	Mean interval (hours) \pm SD	Median (hours)	Range (hours)	p-value
A: Mife + Miso	10	10.8 \pm 2.9	10.5	7 - 16	<0.001
B: Miso Alone	10	15.4 \pm 4.1	15	10 - 23	
C: ICC	9	19.1 \pm 5.3	18	13 - 29	

Analysis using One-way ANOVA.

Vaginal delivery ≤ 24 hours occurred in 90.0% of Group A, 70.0% of Group B, and 55.6% of Group C. Need for a second

method or oxytocin was lowest in Group A (10.0%) and highest in Group C (44.4%). Cesarean rates were low (0% A, 10.0% B, 11.1% C). Chi-square analysis showed no

statistically significant differences ($p > 0.05$) Table III.

Table III
Secondary outcomes: Success rate and need for additional intervention.

Outcome measure	Group A	Group B	Group C	p-value
Vaginal delivery ≤24 hours, n (%)	9 (90.0%)	7 (70.0%)	5 (55.6%)	0.186
Need for 2nd method/Oxytocin, n (%)	1 (10.0%)	3 (30.0%)	4 (44.4%)	0.230
Cesarean section, n (%)	0 (0.0%)	1 (10.0%)	1 (11.1%)	0.526

Analysis using the chi-square test.
Spontaneous vaginal delivery occurred in 8/10 (A), 7/10 (B), and 6/9 (C); assisted

vaginal deliveries were two in each group, while cesarean sections were recorded only in Groups B and C (one each). Fetal

condition showed macerated stillbirths of 8, 8, and 7, and fresh stillbirths of 2, 2, and 2. ($p > 0.05$) *Table IV*.

Table IV
Mode of delivery and fetal condition.

Characteristic	Group A	Group B	Group C	p-value
Mode of delivery				
Spontaneous vaginal, n	8	7	6	0.526
Assisted vaginal, n	2	2	2	
Cesarean section, n	0	1	1	
Fetal condition				
Macerated stillbirth, n	8	8	7	0.901
Fresh stillbirth, n	2	2	2	

Analysis using the Chi-square test.
A good maternal outcome was observed in all participants in Group A (100%), compared to 90.0% in Group B and 88.9%

in Group C. Primary postpartum hemorrhage occurred in one case each in Groups B (10.0%) and C (11.1%), while no cases were reported in Group A. No

instances of puerperal sepsis were recorded. Differences were not statistically significant ($p > 0.05$) *Table V*.

Table V
Maternal puerperium outcomes.

Maternal outcome	Group A	Group B	Group C	p-value
Good, n (%)	10 (100%)	9 (90.0%)	8 (88.9%)	0.526
Primary PPH, n (%)	0 (0.0%)	1 (10.0%)	1 (11.1%)	0.526
Puerperal sepsis, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Analysis using the Chi-square test (excluding sepsis).
Presents complications and additional observations across the groups. Pyrexia

(>38°C) was reported in none of Group A, one case in Group B, and two cases in Group C. Excessive vaginal bleeding (non-PPH) occurred once in each group. Severe pain

was more frequently reported in Group C (n=5), compared to Group B (n=3) and Group A (n=2). Catheter dislodgement was observed only in Group C (n=1) *Table VI*.

Table IV
Complications and additional observations.

Complication / Observation	Group A	Group B	Group C
Pyrexia (>38°C), n	0	1	2
Excessive Vaginal Bleeding (non-PPH), n	1	1	1
Patient-reported Severe Pain, n	2	3	5
Catheter Dislodgement, n	N/A	N/A	1

DISCUSSION

This prospective cohort study provides a pragmatic comparison of three commonly employed methods for managing IUFD in a Bangladeshi tertiary care setting. The principal finding is that the sequential mifepristone-misoprostol regimen demonstrated superior efficacy, evidenced by a significantly shorter mean induction-to-delivery interval (10.8 hours) compared to both misoprostol alone (15.4 hours) and the intracervical catheter (19.1 hours). These results align robustly with the existing pharmacological rationale and prior

research. Mifepristone, by antagonizing progesterone receptors, induces cervical ripening and upregulates myometrial gap junctions and oxytocin receptors, thereby creating a primed uterine environment that responds more rapidly and effectively to subsequent prostaglandin administration [5,14]. Studies from similar settings have consistently reported this synergistic effect, with combination therapy reducing the induction interval by approximately 30-40% compared to prostaglandin-only protocols [6,7]. Our findings reinforce this combination as the most time-efficient

medical strategy, which is a critical consideration for minimizing the psychological distress associated with carrying a non-viable pregnancy. The performance of misoprostol alone as an intermediate option is also noteworthy. Its 70% 24-hour success rate, though lower than the combination regimen, confirms its established role as a reliable, accessible, and low-cost uterotonic, particularly vital in resource-constrained environments [4,15]. However, its longer induction interval and higher need for supplemental oxytocin (30%) highlight its limitations as a single

agent, potentially related to an unripe cervix at the time of induction. The intracervical catheter, while effective in achieving vaginal delivery, was associated with the longest induction process. This is mechanistically predictable, as mechanical methods primarily cause gradual cervical dilation through local pressure and endogenous prostaglandin release, a process inherently slower than the direct pharmacological stimulation of the myometrium [8,16]. The lower 24-hour success rate (55.6%) and higher rate of requiring a second method (44.4%) in our ICC group are consistent with previous comparative studies, including a meta-analysis (2019), which found Foley catheters to be less effective than misoprostol for achieving delivery within 24 hours [9]. Nevertheless, the ICC remains an indispensable tool in specific clinical scenarios, such as when uterotonics are contraindicated (e.g., in women with severe asthma or glaucoma) or unavailable, underscoring its value in a comprehensive obstetric toolkit [17]. An encouraging finding across all groups was the favorable maternal safety profile. The incidence of primary PPH was low (6.9% overall) and not significantly different between groups, and no cases of puerperal sepsis or uterine rupture occurred. This safety data is reassuring and consistent with other studies on IUD management, which suggest that when managed with standardized protocols, induction of labour for fetal demise carries a low risk of serious maternal morbidity [18,19]. The absence of major complications, even with the mechanical method, which carries a theoretical infection risk, likely reflects the prophylactic antibiotic use and strict aseptic technique followed in our hospital setting. The strengths of this study include its prospective design within a real-world clinical context at a major Bangladeshi hospital, providing directly applicable local evidence. The comparative analysis of three distinct modalities adds practical value for clinicians. However, several limitations must be acknowledged. The modest sample size (n=29) limits the statistical power to detect differences in less common secondary outcomes, such as specific complication rates. The non-randomized allocation, based on clinician discretion, introduces potential selection bias, although the comparable baseline characteristics somewhat mitigate this concern. Furthermore, the single-center design may affect the generalizability of findings to primary care centers with differing resources and expertise. Despite these limitations, our findings carry important implications for clinical practice in Bangladesh and similar LMICs. They provide strong support for the adoption of

the mifepristone-misoprostol combination as the first-line medical regimen for IUD, where mifepristone is accessible and affordable, as it optimizes patient experience by shortening a profoundly difficult process [20,21]. For settings where mifepristone is not available, misoprostol alone remains a very effective alternative. The ICC should be retained as a vital backup or primary option for specific contraindications. Future research should focus on larger, multi-center randomized controlled trials to confirm these findings and perform robust cost-effectiveness analyses. Investigating patient-centered outcomes, such as psychological distress scores and overall satisfaction with the induction process, would also be highly valuable [22].

LIMITATIONS

The study's modest sample size, non-randomized design, and single-center setting may limit statistical power, introduce selection bias, and affect generalizability. Future multi-center randomized trials with larger cohorts are recommended to validate these findings.

CONCLUSION

This study demonstrates that for the management of IUD at a tertiary hospital in Bangladesh, the mifepristone-misoprostol combination is the most efficacious method, yielding the shortest induction-to-delivery interval. Misoprostol alone is a reliable alternative, while the intracervical catheter, though effective, is associated with the longest induction process. All three methods were safe, with low maternal complication rates. These results can guide evidence-based protocol development to ensure timely, effective, and compassionate care for women experiencing this tragic obstetric event.

RECOMMENDATION

We recommend adopting the mifepristone-misoprostol combination as the first-line regimen for IUD management where available. Misoprostol alone is a viable alternative. The intracervical catheter remains essential for specific contraindications. Institutional protocols should integrate these evidence-based options.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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