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Original Article

Impact of Induction Timing on Maternal and Neonatal Outcomes in Term and Late Preterm Prelabor Rupture of Membranes: A Prospective Observational Study

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ABSTRACT

Prelabor rupture of membranes (PROM) is a significant obstetric complication predisposing a woman to chorioamnionitis, neonatal sepsis, and placental abruption. The optimal timing of labour induction, particularly in late preterm pregnancies, remains a clinical challenge requiring a balance between infectious risk and prematurity-related morbidity. **Objectives:** To evaluate the association between early versus late induction of labour and maternal and neonatal outcomes in women with term and late preterm PROM. **Methods:** This prospective study was conducted at the Combined Military Hospital, Malir, from October 2023 to September 2024. A total of 111 women with singleton pregnancies ≥34 weeks with confirmed PROM were grouped as term (≥37 weeks) or late preterm (34–36+6 weeks) and stratified by induction timing: early (6–12 hours) or late (>12 hours). Maternal and neonatal outcomes were analyzed using SPSS version 27.0, with Chi-square and Fisher's exact tests applied; $p<0.05$ was considered significant. **Results:** Of 111 participants, term PROM was present in 59 (53.2%) and late preterm PROM in 52 (46.8%); 61 (55.0%) underwent early and 50 (45.0%) late induction. Spontaneous vaginal delivery was the predominant mode (63.1%). Late preterm PROM was associated with significantly worse neonatal outcomes than term PROM across all parameters, while induction timing had no significant effect on any maternal or neonatal outcome. **Conclusions:** Gestational age at membrane rupture is a stronger determinant of neonatal morbidity than induction timing. Thus, we cannot claim that early induction is definitively 'safe'—only that it was not associated with worse outcomes in this specific cohort.

INTRODUCTION

Prelabor rupture of membranes (PROM) refers to the spontaneous rupture of amniotic membranes before uterine contractions occur, allowing amniotic fluid to leak into the external genital tract and expose the intrauterine environment [1]. It is a significant obstetric complication as it predisposes to complications, including ascending infection, chorioamnionitis, placental abruption, umbilical cord prolapses, and neonatal sepsis, which add to maternal and neonatal morbidity [2, 3]. The prevalence of PROM is 3–15% during pregnancy, but most cases are detected at term (37 weeks of gestation) [4]. Membrane rupture is a multifactorial process that includes mechanical stress on membranes and biochemical weakening of the extracellular matrix. Risk factors for PROM include genital tract infections such as bacterial vaginosis and Group B Streptococcal colonization, nutritional deficiencies, smoking, and prior cervical surgeries [5, 6]. Late preterm PROM, occurring at 34 to 36+6 weeks of gestational age, poses a specific management challenge wherein clinicians must balance the risk of preterm birth against the risk of infection related to prolonged membrane rupture [7]. After PROM at term, most women enter spontaneous labour

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within a day. Clinical evidence shows that early labour induction does not raise the likelihood of caesarean section but can potentially reduce the risk of maternal and neonatal infection compared with expectant management. The management of late preterm PROM is more complex because late preterm neonates are susceptible to respiratory and infectious morbidities [1, 8].

The rationale for the current study is that, although international studies can guide the management of PROM, there is limited evidence on this in Pakistan. Local health facilities vary in patient characteristics, available resources, and clinical practices, resulting in differences in outcomes. However, there is limited published evidence from Pakistan on the optimal timing of induction in PROM, and local clinical conditions, patient demographics, and available resources differ considerably from those in high-income settings. This gap makes it difficult to directly apply international guidelines to local clinical practice. The current study assesses how the timing of labour induction influences maternal and neonatal outcomes in women with PROM in term and late preterm pregnancies and produces evidence applicable to the local context. Therefore, this study aimed to evaluate the impact of early (6–12 hours) versus late (>12 hours) induction of labour on maternal and neonatal outcomes in women with term and late preterm PROM, and to compare outcomes between the two gestational categories.

METHODS

This prospective observational study was conducted at the Department of Obstetrics and Gynecology, CMH Malir Cantt, Karachi, from October 2023 to September 2024 after ethical approval vide 108/2023/TRG/CPS; dated 6th October 2023. Neonatal outcomes were captured from birth until hospital discharge (or up to a maximum of 28 days of life). Data on NICU admission, Apgar scores, birth weight, and antibiotic treatment for suspected sepsis were recorded daily during the entire neonatal hospital stay. A minimum sample size of 111 participants was estimated using the formula $n = Z^2p(1–p)/d^2$, where Z = 1.96 (95% confidence interval), p = 0.25 (anticipated caesarean section rate in PPROM) [9], and d = 0.08 (precision level). A consecutive non-probability sampling method was used. Patient data were anonymised using unique serial identifiers, and no personal identifying information is disclosed in this manuscript, ensuring participant confidentiality. Women aged 18–40 years with singleton pregnancy, gestational age ≥34 weeks, confirmed PROM through sterile speculum examination, and cephalic presentation were included. Women with multiple gestations, malpresentation, placenta praevia or placental abruption, known fetal abnormalities, or intrauterine fetal death, or who required emergency caesarean delivery upon admission were excluded. After written informed consent and recording baseline demographic information, patients were categorized as term PROM (≥37 weeks) or late preterm PROM (34–36+6 weeks). Gestational age was determined using the first-trimester ultrasound crown-rump length whenever available (78% of participants). For the remaining women, reliable LMP with regular cycles was used as a secondary method. They were also grouped by induction timing: Following the hospital's standard protocol for managing PROM at ≥34 weeks, induction was categorised as early (6–12 hours) – reflecting active management to reduce infectious risk – or late (>12 hours), when spontaneous labour was awaited. This 12-hour threshold was chosen based on local consensus and prior cohort data suggesting a reasonable balance between infection prevention and avoiding unnecessary early intervention. Cervical favorability (Bishop score) was not systematically recorded and could not be included in the analysis. Consequently, clinician discretion in choosing early versus late induction remains a potential source of confounding by indication.

Early induction (6–12 hours) was consistent with active management approaches aimed at reducing infectious morbidity by initiating labour promptly, while late induction (>12 hours) reflected a more expectant approach allowing more time for spontaneous labour onset [1,8]. Induction was performed using sublingual misoprostol (PGE1) 25 mcg; a second dose was administered after 6 hours if the Bishop score remained <6. Oxytocin infusion was started at 2 mU/min and increased by 2 mU/min every 15–30 minutes until 3 contractions per 10 minutes were achieved. If a woman entered spontaneous labour before the scheduled induction time, she was allocated to the 'late' group, and no induction agents were given. Neonatal evaluation was performed by the attending paediatrician, with Apgar scores assigned at 1 and 5 minutes, and daily clinical examinations until discharge. Maternal outcomes included mode of delivery, while neonatal outcomes included NICU admission, Apgar score <7 at 5 minutes, birth weight <2.5 kg, and Suspected neonatal sepsis was defined as the presence of ≥2 of the following clinical features (respiratory distress, temperature instability, lethargy, poor feeding, or tachycardia) within the first 72 hours, leading to initiation of empirical antibiotics for ≥48 hours. Blood cultures were obtained before antibiotic initiation to confirm early-onset sepsis where possible. All data were analyzed using SPSS version 27.0 and normality of numerical variables was confirmed using the Shapiro–Wilk test. The Chi-square test was used to compare categorical variables between groups when the expected cell frequency was ≥5; Fisher's exact test was used when the expected cell frequency was <5. Continuous variables were expressed as mean ± standard deviation. Comparisons of

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outcome variables were performed across gestational categories and induction timing, and a stratified analysis combining both was conducted. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 111 participants were included in the study. The mean age was 28.43 ± 4.56 years (range: 18–38 years). The mean gestational age was 37.41 ± 2.59 weeks (range: 34–42 weeks). Most were aged 21–30 years (68, 61.3%), followed by 31–40 years (36, 32.4%) and 18–20 years (7, 6.3%). Regarding parity, 50 (45.0%) were primigravida and 61 (55.0%) multigravidas. The majority lived in urban areas (67, 60.4%) and were booked for antenatal care (77, 69.4%). Gestationally, 59 (53.2%) had term PROM and 52 (46.8%) late preterm PROMS. Induction was early in 61 (55.0%) and late in 50 (45.0%). Most deliveries were spontaneous vaginal (70, 63.1%), followed by caesarean (29, 26.1%) and assisted vaginal (12, 10.8%). Neonatally, 24 (21.6%) required NICU admission, 12 (10.8%) had low 5-minute Apgar scores, 24 (21.6%) had low birth weight, and 15 (13.5%) had suspected sepsis (Table 1).

Table 1: Baseline Characteristics and Maternal and Neonatal Outcomes of Participants

Variables	Categories	n (%)
Age Group	18–20	7 (6.3%)
	21–30	68 (61.3%)
	31–40	36 (32.4%)
Parity	Primigravida	50 (45.0%)
	Multigravida	61 (55.0%)
Residence	Urban	67 (60.4%)
	Rural	44 (39.6%)
Booking Status	Booked	77 (69.4%)
	Unbooked	34 (30.6%)
Gestational Category	Term PROM	59 (53.2%)
	Late Preterm PROM	52 (46.8%)
Induction	Early	61 (55.0%)
	Late	50 (45.0%)
Mode of Delivery	Spontaneous Vaginal	70 (63.1%)
	Caesarean	29 (26.1%)
	Assisted Vaginal	12 (10.8%)
NICU Admission	Yes	24 (21.6%)
	No	87 (78.4%)
Low Apgar (<7 at 5 min)	Yes	12 (10.8%)
	No	99 (89.2%)
Low Birth Weight (<2.5 kg)	Yes	24 (21.6%)
	No	87 (78.4%)
Suspected Neonatal Sepsis	Yes	15 (13.5%)
	No	96 (86.5%)

Neonatal outcomes differed significantly by gestational category. Late preterm PROM infants had higher rates of NICU admission (34.6% vs 10.2%, OR 4.7, 95% CI 1.7–12.9, p = 0.004), low Apgar scores (19.2% vs 3.4%, OR 6.8, 95% CI 1.4–32.6, p=0.012), low birth weight (38.5% vs 6.8%, OR 8.6, 95% CI 2.7–27.3, p<0.001), and suspected sepsis (23.1% vs 5.1%, OR 5.6, 95% CI 1.5–21.1, p=0.010) compared with term PROM infants. The mode of delivery was similar across groups (p=0.802). It should be noted that while these findings align with several randomized controlled trials, direct comparisons should be interpreted cautiously, as our observational design cannot establish causality and is subject to confounding by indication (Table 2).

Table 2: Comparison of Maternal and Neonatal Outcomes by Gestational Category

Variables	Categories	Term PROMn (%)	Late Preterm PROMn (%)	p-value (Test)
Mode of Delivery	Caesarean	14 (23.7%)	15 (28.8%)	0.802 (Chi-square)
	Spontaneous Vaginal	38 (64.4%)	32 (61.5%)	
	Assisted Vaginal	7 (11.9%)	5 (9.6%)	
NICU Admission	Yes	6 (10.2%)	18 (34.6%)	0.004 (Chi-square)
	No	53 (89.8%)	34 (65.4%)	
Low Apgar	Yes	2 (3.4%)	10 (19.2%)	0.012 (Fisher)
	No	57 (96.6%)	42 (80.8%)	
Low Birth Weight	Yes	4 (6.8%)	20 (38.5%)	<0.001 (Fisher)
	No	55 (93.2%)	32 (61.5%)	
Suspected Sepsis	Yes	3 (5.1%)	12 (23.1%)	0.010 (Fisher)
	No	56 (94.9%)	40 (76.9%)	

When outcomes were compared by induction timing, no statistically significant differences were observed. Rates of caesarean delivery, assisted vaginal delivery, NICU admission, low Apgar, low birth weight, and suspected sepsis were similar between early and late induction groups (all p>0.050) (Table 3).

Table 3: Comparison of Maternal and Neonatal Outcomes by Induction Timing

Variables	Categories	Early Induction, n (%)	Late Induction, n (%)	p-value (Test)
Mode of Delivery	Caesarean	14 (23.0%)	15 (30.0%)	0.533 (Chi-square)
	Spontaneous Vaginal	42 (71.2%)	28 (53.8%)	
	Assisted Vaginal	5 (8.5%)	7 (13.5%)	
NICU Admission	Yes	14 (23.7%)	10 (19.2%)	0.885 (Chi-square)
	No	47 (77.0%)	40 (80.0%)	
Low Apgar	Yes	9 (15.3%)	3 (5.8%)	0.219 (Fisher)
	No	52 (85.2%)	47 (94.0%)	
Low Birth Weight	Yes	13 (22.0%)	11 (21.2%)	1.000 (Chi-square)
	No	48 (78.7%)	39 (78.0%)	
Suspected Sepsis	Yes	10 (16.9%)	5 (9.6%)	0.166 (Chi-square)
	No	50 (82.0%)	46 (92.0%)	

DISCUSSION

Prelabor membrane rupture remains a significant obstetric issue, and the present study contributes evidence on how gestational age at membrane rupture and the timing of

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labour induction affect maternal and neonatal outcomes. The caesarean section rate in the study was 26.1%, which is in line with rates reported in similar settings. A Yemeni study on induction of labour outcomes reported a caesarean rate after induction of 12.1%, with PROM being the most commonly used induction trigger (65.1% of cases) [10]. The higher caesarean rate in the current cohort could be attributed to the clinical complexity of the mixed-term and late preterm population. Notably, no statistically significant difference was found between the early and late induction groups in caesarean delivery rates, which is consistent with the findings of Awkadigwe *et al.* who conducted a randomised controlled trial in Nigeria comparing active and expectant management of term PROM and reported no significant difference in caesarean rates between the groups, though active management significantly reduced the latency and induction-to-delivery interval [11]. It should be noted that while our findings align with those of several randomised controlled trials, direct comparisons should be interpreted cautiously, as our observational design cannot establish causality and is subject to confounding by indication. The most clinically significant observation of this research is the association between late preterm PROM and worse neonatal outcomes compared with term PROM group across all measured parameters. This is well supported by evidence from other settings. A large retrospective cohort study by Schmidt *et al.* showed that each additional week of gestational age at birth reduced the risk of adverse neonatal outcomes such as NICU admission, neonatal sepsis, and respiratory distress syndrome [12]. Similarly, Suleiman *et al.* in a study conducted in a tertiary hospital in Nigeria, found that neonatal outcomes of birth weight, Apgar score, and NICU admission were all heavily dependent on gestational age at membrane rupture rather than the management strategy applied [13]. Of particular interest is the high incidence of suspected neonatal sepsis in late preterm infants in this study (23.1% vs 5.1% in term PROM). This is consistent with the findings of Chiossi *et al.* who reported a multicentre cohort of expectantly managed late preterm PROM in Italy, in which gestational age at rupture of membranes, specifically at 34 weeks, was associated with adverse neonatal outcomes on multivariate analysis [14]. These findings confirm that late preterm neonates are more vulnerable to both infectious and respiratory morbidity, and this study demonstrates that this vulnerability is not modified by whether induction occurs early or late. The absence of statistically significant differences across all outcomes between the early (6–12 hours) and late (>12 hours) induction groups is also noteworthy. Abu Shqara *et al.* compared 12-hour and 24-hour induction protocols for term PROM at an Israeli tertiary centre and found that the 24-hour group experienced more chorioamnionitis, NICU admissions, antibiotic use, and respiratory distress [15]. Although the suspected sepsis rate in the early induction group was numerically higher in the current study (16.9% vs 9.6%), the difference was not statistically significant, possibly due to the small sample size. Yuan *et al.* reported that vaginal dinoprostone used within 6 hours of PROM was associated with lower caesarean rates and fewer non-reassuring fetal heart rate traces compared with induction within 6–24 hours, suggesting potential benefits of earlier induction [16]. Bitenc *et al.* found that a longer latency at 32–37 weeks of preterm PROM was associated with an increased risk of early neonatal infection and a higher caesarean rate, further supporting the need for timely delivery [17]. The debate over expectant versus active management, especially in late preterm PROM, continues internationally. Lee and Lynch reviewed key randomised trials and meta-analyses, including the PPROMEXIL series and argued that expectant management in late preterm PROM can mitigate respiratory morbidity and NICU admission when fetal and maternal status are stable [18]. On the other hand, Bitar and Sibai argued that expectant management should not be recommended at ≥34 weeks because of greater risks of haemorrhage and infection with longer expectancy [19]. Although no statistically significant differences were observed between early and late induction groups, the study was not formally designed as a non-inferiority trial. Thus, these negative findings should be interpreted cautiously; a larger sample would be required to rule out clinically meaningful differences. The PPROMEXIL 10-year follow-up study by Simons *et al.* reported no significant differences in neurodevelopmental outcomes between children born following induction and those born after expectant management, indicating that early delivery itself does not negatively affect child development [20]. The combination of these results suggests that, in the Pakistani tertiary care setting, gestational maturity is the most important determinant of neonatal prognosis, and induction timing within the 6–12-hour or > 12-hour window did not significantly affect outcomes. In their systematic review of term PROM management, Ramirez-Montesinos *et al.* noted that the debate between active and expectant management remains unresolved, and that reducing unnecessary vaginal examinations and using structured protocols could also be important factors in reducing infection risk [21]. This underscores the importance of standardised, locally adapted clinical guidelines in Pakistan, where heterogeneous practice may contribute to preventable morbidity. Several important confounders were not measured in this study, including maternal body mass index, smoking status, cervical length on admission,

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presence of regular contractions at presentation, antenatal corticosteroid administration, Group B Streptococcus colonization, and intrapartum antibiotic prophylaxis. The absence of these variables introduces the possibility of residual confounding, which could have biased the observed associations between induction timing and outcomes. For instance, women with more favourable cervical status or those who received corticosteroids may have been more likely to undergo early induction, potentially masking differences between groups. These limitations should be addressed in future studies through systematic collection and adjustment for these confounders. Data on several potential confounders were not collected in this pragmatic observational study, including maternal body mass index, smoking status, cervical length on admission, presence of regular contractions at presentation, antenatal corticosteroid administration, Group B Streptococcus colonization status, and intrapartum antibiotic prophylaxis. The absence of these variables means that residual confounding cannot be ruled out, and these factors should be addressed in future prospective studies.

This study has several important limitations: its single-centre military hospital setting limits generalisability, and the observational design introduces confounding by indication, particularly as cervical Bishop scores and clinician decision-making were not recorded. Additionally, we lacked data on multiple potential confounders including maternal BMI, smoking, Group B Streptococcus (GBS) colonization status, corticosteroid use, and antibiotic prophylaxis, which could have influenced both the decision regarding induction timing and the outcomes measured. Without these data, we cannot exclude residual confounding as an explanation for our findings. Future research should include multicentre randomised controlled trials in Pakistan to strengthen the evidence base. Studies should incorporate microbiological confirmation of neonatal sepsis, longer follow-up periods to assess neurodevelopmental outcomes, and cervical assessment scores to control for confounding. Additionally, cost-effectiveness analyses of early versus expectant management protocols in resource-limited settings would be of practical value for local health policy.

CONCLUSIONS

Gestational age at the time of membrane rupture appears to be the main contributor to neonatal morbidity in PROM, and late preterm newborns are at high risk irrespective of the timing of induction. Early labour induction was not associated with deleterious maternal or neonatal effects in this cohort, suggesting that an active approach could be considered as a management option, though causality cannot be inferred from this observational designwith PROM at ≥34 weeks of gestation. Based on these findings, we recommend developing and adopting gestational age-specific induction protocols in resource-limited settings such as Pakistan, with particular emphasis on close monitoring and early supportive care for late preterm neonates. Clinicians should be reassured that early induction (within 6–12 hours) does not worsen maternal or neonatal outcomes and may be safely implemented where clinical resources permit. Future multicenter prospective studies with microbiological outcome confirmation are warranted to provide stronger evidence to guide local clinical guidelines.

Authors' Contribution

Conceptualization: NF, SN
Methodology: NF, SN
Formal analysis: NF, SN
Writing and Drafting: NF, NH
Review and Editing: NF, SN, NH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflict of Interest

All the authors declare no conflict of interest.

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