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OUTCOME OF INDUCING WOMEN APPEARING AT TERM WITH PREMATURE RUPTURE OF MEMBRANES (PROM) SOONER (BEFORE 6 HOURS) VS LATER (AFTER 12 HOURS)

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ABSTRACT

Objectives: To compare the outcomes of inducing women who appear at term with premature rupture of membrane (PROM) sooner (before 6 hours) and later (after 12 hours).
Study design: Randomized controlled trial
Place and duration of study: Department of Obstetrics & Gynecology, MCH Unit II, Pakistan Institute of Medical Sciences, Islamabad from July 2023 to June 2024.
Methods: A total of 140 women aged 18-42 years, parity <5, presenting at gestational age >37 weeks and reported with PROM were enrolled in this study and divided in to 2 equal groups.
In group A, patients were given induction of labor immediately after presentation (within 6 hours) while in Group B patients were given induction of labor late (after 12 hours) by instillation of 3mg tablet PGE_2 (dinoprostone) in the posterior fornix.
The comparison of outcomes between the 2 methods was done by applying chi-square test and independent t-test where p-value ≤0.05 was considered statistically significant.
Results: The Mean±SD of age in this study was 27.84±5.66 years. The results of the study outcomes show that there was significantly less PROM to delivery interval (13.96±5.83 Vs 24.40±7.59 respectively, p=0.00), significantly more spontaneous delivery (70% Vs 50% respectively, p= 0.04) in Group A compared to Group B. The results of neonatal outcomes show significantly better APGAR score at 1 min (7.16±1.07 Vs 6.84±0.68 respectively, p=0.04) as well as at 5 min (7.89±1.46 Vs 7.45±1.01 respectively, p=0.04) and thereby significantly less number of neonates to be admitted in NICU (25.7% Vs 51.43% respectively, p=0.03) in Group A compared to group B.
Conclusion: For women presenting at term with PROM, sooner inductions are more effective than later inductions by providing better maternal and neonatal outcomes.

Keywords: At term, Induction of labour, Maternal outcomes, Neonatal outcomes, Premature rupture of membrane.

INTRODUCTION

Premature rupture of membranes (PROM) is the rupture of amniotic sac before the labor actually begins. PROM complicates 5-10% of pregnancies. Among term PROM cases, 60-70% progress to spontaneous labor within 24 hours, with an additional 20-30% initiating labor within 72 hours.[1]
Membrane rupture is precipitated by multiple factors culminating in expedited membrane weakening. This process is attributed to elevated local cytokine levels, dysregulation in the balance between matrix metalloproteinases and their tissue inhibitors, enhanced collagenase and protease activity, and various elements contributing to increased intrauterine pressure.[2]
Numerous studies have shown that the length of PROM increases the risk of newborn sepsis and chorioamnionitis. Pregnancies complicated by PROM were linked with a greater risk of intrauterine infection in addition to an elevated risk of newborn infections.[3] Shortening the duration between PROM onset and parturition correlates with reduced incidence of maternal infections. [4]
Due to this link of PROM with higher rates of labor induction, fetal distress, maternal infections, and cesarean deliveries, there is increased risks of maternal and fetal morbidity and mortality. PROM thereby remains among the most challenging issues in obstetrics.[5,6]
In managing PROM cases, the primary clinical decision revolves around deciding the time of labor induction. Multiple studies demonstrate improved outcomes with labor induction versus expectant management for PROM occurring after 37 weeks' gestation.[7] Preliminary research also indicates that inducing labor during a prolonged latent period in cases of PROM might help to prevent the necessity for a cesarean section (CS). Current protocols for PROM management advocate immediate labor induction with oxytocin.[8]
A notable clinical discussion, however, still persists for the exact timings of labor induction in women reported with PROM and having unfavorable cervical conditions especially for women who are nulliparous. [7,8] In this context, a consensus protocol for labor induction in healthy, term gravidas with potential for vaginal delivery remains elusive and enhanced clinical data is requisite for optimal PROM management to ensure favorable maternal and neonatal outcomes.[9,10]
Modified Bishop Score (MBS) has been used effectively to evaluate the induction efficacy. Maternal assessment for uterine activity and cervical status via MBS is performed prior to induction initiation and subsequent dose administration. A Bishop score < 6 indicates an unfavorable cervix, necessitating cervical ripening or induction with intravaginal PGE2. A Bishop score > 7 is considered favorable, permitting amniotomy and oxytocin-induced labor. A Bishop score > 8 signifies a ripened cervix with high probability of spontaneous labor onset.[8]
This study was therefore designed to evaluate the outcomes of inducing women who appear at term with PROM sooner (before 6 hours) vs later (after 12 hours) in terms of better maternal and neonatal outcomes. The results of this study will help our obstetricians to make the decision of opting for labour induction in cases where women appear at term with PROM in our local population and with our current health facilities.

METHODS

This randomized controlled trial was conducted at the Department of Obstetrics & Gynecology, MCH Unit II, Pakistan Institute of Medical Sciences, Islamabad from 1st of July 2023 to 30th of June 2024 over a period of 1 year.
Sample size was calculated as per following assumptions:
alpha = 5 (two-sided), power=90
Mean recruitment to delivery intervals after PROM in the induction group =11.5±5
Mean recruitment to delivery intervals after PROM in the expected group =14.7±5.2. [11]
n2/n1 = 1, Estimated sample size: n1 = 66, n2 = 66.
A total of 140 women aged 18-42 years, parity <5, presenting at gestational age >37 weeks (on LMP) and reported with PROM were enrolled in this study through consecutive sampling and equally divided in to 2 groups through lottery method.

Exclusion criteria was set as women with placental abruption (on ultrasound), preeclampsia (BP≥140/90mmHg with proteinuria >+1) and eclampsia (BP≥140/90mmHg with convulsions). Women with reported allergy to dinoprostone were also excluded.
In group A, patients with unfavorable MBS were given induction of labor immediately after presentation (within 6 hours) by instillation of 3mg tablet PGE_2 (dinoprostone) in the posterior fornix.
In group B, patients with unfavorable MBS were given induction of labor late (after 12 hours) by instillation of 3mg tablet PGE_2 (dinoprostone) in the posterior fornix.
All the demographics were recorded for each patient in both the groups. Clinical parameters including duration of PROM, maternal conditions, MBS, chorioamnionitis and uterine contractions were also assessed at the time of inclusion in the study and then were monitored continuously during the study period. All the data was recorded on predesigned proforma.
After assessment, labor was accelerated by augmenting with oxytocin in patients who had a favorable cervix and normal fetal heart rate patterns but experiencing suboptimal contractions. Patients were monitored in the labor room until both the fetus and placenta were delivered.
A maximum of 2 doses of 3mg tablet PGE2 (dinoprostone) 6 hours apart, if needed, were placed per vagina in both groups.

The outcomes assessed included duration from premature rupture of membranes till delivery of fetus and placenta, mode of delivery, incidences of caesarean sections (CS), any incidence of maternal infection, APGAR score of neonates at 1 minutes and at 5 minutes and neonate admission to NICU. (A neonate was admitted to NICU if Apgar score at 5 minute was <7. The infection was determined if there was increased total leukocyte count (TLC) >16*10^9/L and raised C-reactive proteins (CRP) >7mg/L.)
The approval of conducting the study was received from institutional ethical approval committee.
Patients were enrolled after taking written informed consent for participation in the study.
The analysis of data was conducted utilizing SPSS version 25. Mean± standard deviation was used to describe continuous variables including age, gestational age, body mass index (BMI), PROM to delivery interval, and APGAR score. Frequency and percentages were applied to present categorical variables like parity, mode of delivery, and admission in neonatal intensive care unit (NICU) admission.
The significance of difference in outcomes between the 2 groups was done by applying chi-square test and independent t-test where p-value ≤0.05 was considered statistically significant.

RESULTS:
The Mean±SD of age in this study was 27.84±5.66 years with an age range of 18-42 years. Mean gestational age of overall study population was 38.79±1.02 weeks. The details of demographics and clinical findings are shown in Table-I.

Table-I: Group wise demographics and clinical findings n=140

Demographics and clinical findings		**Group A n=70**	**Group B n=70**
Age (Mean±SD) years		28.81±5.89	26.87±5.29
Gestational age (Mean±SD) weeks		38.73±1.05	38.84±1
BMI		26.07±2.76	25.84±2.6
Nulliparous n (%)		7 (10)	9 (13)
Parity	**1 n (%)**	34 (48.6)	32 (45.7)
	2 n (%)	16 (22.9)	18 (25.7)
	3 n (%)	9 (12.9)	6 (8.6)
	4 n (%)	4 (5.7)	5 (7.1)

The results of study maternal outcomes show that there was significantly less PROM to delivery interval in Group A compared to Group B. Moreover, significantly more women had spontaneous delivery in Group A compared to Group B. There was no incidence of infection recorded in both the groups as shown in Table-II.

Table-II: Maternal Outcomes n=140

Maternal Outcomes		**Group A n=70**	**Group B n=70**	**p-value**
PROM to delivery interval (Mean±SD) hours		13.96±5.83	24.40±7.59	0.00
Mode of delivery	**Spontaneous n (%)**	49 (70)	35 (50)	0.04
	Instrumental n (%)	4 (5.7)	10 (14.3)	
	CS n (%)	17 (24.3)	25 (35.7)	
Parameters for infection	**TLC (Mean±SD)10^9/L**	12.81±4.29	12.24±3.34	0.38
	CRP (Mean±SD) mg/L	1.96±0.19	1.98±0.13	0.47

The results of neonatal outcomes of the study show that the neonates in Group A had significantly better APGAR score at 1 min as well as at 5 min. Similarly, significantly less number of neonates had to be admitted in NICU in Group A compared to group B as shown in Table III.

Table-III: Neonatal outcomes n=140

Neonatal outcomes	**Group-A n=70**	**Group-B n=70**	**p-value**
Apgar score at 1 min (Mean±SD)	7.16±1.07	6.84±0.68	0.04
Apgar score at 5 min (Mean±SD)	7.89±1.46	7.45±1.01	0.04
NICU admission n (%)	18 (25.7)	36 (51.43)	0.03

Further evaluation on the reasons leading to CS in these patients showed that persistent non-reassuring cardiotocography (CTG) was the major cause. The details of causes leading to CS in both the groups are shown in Table-IV.

Table-IV: Indications of caesarean sections in study groups n=42

Indications of caesarean sections	**Group-A n=17**	**Group-A n=25**	**Total**
Persistent non-reassuring CTG n (%)	8 (19)	12 (28.6)	20 (47.6)
Failed induction n (%)	5 (12)	4 (9.5)	9 (21.4)
Chorioamnionitis n (%)	2 (4.8)	6 (14.3)	8 (19)
Meconium-stained liquor n (%)	2 (4.8)	2 (4.8)	4 (9.5)
Pathological CTG n (%)	0 (0)	1 (2.5)	1 (2.5)

DISCUSSION

The topic of induction of labor (IOL) in at term women presenting with PROM has been discussed in a number of international and national studies in view of different study outcomes, however, this discussion remains alive due to the importance of topic and variety of study outcomes.

A prospective study by Mukharya J on 200 term PROM patients compared early induction to expectant management. The expectant group had longer PROM-to-delivery intervals. Cesarean rates were higher in the induced group, while NICU admissions were more frequent in the expectant group. The study recommended earlier induction strategy for term PROM women to potentially reduce

cesarean rates in resource-limited settings.[12] Study conducted by Sheeraz S to compare the outcomes of earlier induction and expected management after the PROM at term reported that earlier management involving induction with prostaglandin E2 reduces the risk of maternal complications and lowers the rate of CS. The results were not, however, statistically significant in favor of earlier conduction.[13]

In comparison of earlier versus expectant management of fetomatenal outcomes in at term females reported with PROM, Zia MS shared that PROM to delivery interval was lower in active management group in comparison to expected management group (13.49 hours vs. 16.27 hours, p-value=0.002). This also led to shorter hospital stay for the women in active management group.[14] In a study conducted by Sohail A, comparing early versus late induction of labor (IOL) for PROM, early IOL demonstrated reduced maternal and fetal morbidity. Early IOL resulted in lower rates of chorioamnionitis (7% vs 18%), postpartum hemorrhage (8% vs 13%), neonatal sepsis (3% vs 10%), and poor APGAR scores (3% vs 12%). The study concluded that early induction in term PROM leads to better maternal and fetal outcomes. [15]

In a randomized controlled trial by Awkadigwe, the outcomes of active induction were compared with expected induction in at term PROM women. As per the results of this study, the active group showed significantly shorter mean latency periods (11.1 ± 7.3 h vs 8.8 ± 5.5 h) and recruitment to delivery intervals (14.7 ± 5.2 h vs 11.8 ± 5.0 h). Caesarean rates were lower in the expectant group (21% vs 30%), but difference was not significant. There was also no significant difference in delivery or neonatal complications. The study concluded that while both approaches had comparable outcomes, active management reduced induction to delivery intervals at statistical significance levels.[11] A meta-analysis by Bellussi F also narrates that early induction in post-PROM women at ≥36 weeks gestation reduces maternal chorioamnionitis, endometritis, neonatal sepsis, and NICU admissions compared to expectant management >24 hours. Prompt evaluation and induction within 6 hours of PROM symptoms was recommended to reduce morbidity without any evident harm.[16]

The Mean±SD of age in our study was 27.84±5.66 years with an age range of 18-42 years. The results of study outcomes show that there was significantly less PROM to delivery interval in Group A compared to Group B (13.96±5.83 Vs 24.40±7.59 respectively, p=0,00). Moreover significantly more women had spontaneous delivery in Group A compared to Group B (70% Vs 50%, respectively, p= 0.04). The results of neonatal outcomes of the study show that the neonates in Group A had significantly better APGAR score at 1 min (7.16±1.07 Vs 6.84±0.68, respectively, p=0.04) as well as at 5 min(7.89±1.46 Vs 7.45±1.01, respectively, p=0.04) compared to Group B. Similarly, significantly less number of neonates had to be admitted in NICU in Group A compared to group B (25.7% Vs 51.43%, respectively, p=0.03). These results are in line with the studies discussed above and provide evidence in favor of sooner (before 6 hours) induction compared to later (after 12 hours) induction.[11,12,13,14,15,16]

Our study's main limitation is small number of patients added from a single center. Future studies with multicenter design and larger number of patients will add up to this useful data for our obstetricians while making decision of induction in cases of PROM.

CONCLUSION

The results of this study conclude that for women presenting at term with PROM, sooner inductions (before 6 hours) provide better outcomes in terms of reduced PROM to delivery interval, more spontaneous vaginal deliveries, less CS deliveries, better APGAR score and less NICU admissions of neonates than later inductions (after 12 hours).

Disclaimer:
No

Conflict of interest:
No

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