Haregewoin Mussie. Sisay Teklu. *Ethiop Med J, 2019, Vol. 57, No. 2*

ORIGINAL ARTICLE

INDUCED LABOR OUTCOME WITH OR WITHOUT CERVICAL RIPENING IN TERM PREMATURE RUPTURE OF MEMBRANES IN ETHIOPIA.

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ABSTRACT

Background: *Premature rupture of membranes (PROM), if not followed by natural labor or delivered within a limited period of time, will lead to complications such as the development of infections and a reduced volume of amniotic fluid. These complications will have negative maternal and perinatal health outcomes. Several factors affect the success of labor induction in women with term premature rupture of membranes.*

Objective: *This study compares the pregnancy outcome and success of induction of labor in women with term premature rupture of membranes and low BISHOP score, managed with direct oxytocin induction protocol and prostaglandin followed by oxytocin protocol.*

Methods: *A facility basedcomparative cross-sectional study design was used on cases of term premature rupture of membranes having a low BISHOP score in three teaching hospitals of Addis Abeba University. As both protocols are practiced in these hospitals, mothers managed with direct oxytocin induction protocol were compared with those managed with prostaglandin and oxytocin protocol for induction of labor.*

Results: *Out of the total 98 term premature rupture of membranecases with low BISHOP score included in the study, 49 mothers were managed with the direct oxytocin protocol while the remaining were managed with the prostaglandin and oxytocin protocol. Increased cesarean delivery due to failed labor induction and non-reassuring fetal heart pattern was observed usingthe direct oxytocin protocol group.*

Conclusion: *Prostaglandin cervical ripening reduces the burden of cesarean section in cases of term premature rupture of membranes with low BISHOP score.*

INTRODUCTION

Premature rupture of membranes (PROM) is defined as rupture of fetal membranes before the onset of labor. It occurs in 8-10% of all pregnancies and most often (80%), it occurs at term(1).

PROM at any gestational age is associated with a brieflatency period from membrane rupture to delivery. The latency period increases withdecreasing gestational age at membrane rupture. Women with term PROM who are followed expectantly will go into spontaneous labor and will deliver within 24, 48, and 72 hours of PROM in 70, 85 and 95 percent of cases respectively (2-5).

Chorioamnionitis is the most common maternal complication after PROM. Abruptio placentae can cause PROM or can occur subsequent to membrane rupture, and it affects 4% to 12% ofsuchpregnancies. Fetal complications after membrane rupture include infection and non-reassuring fetal heart rate pattern (NRFHRP) due to umbilical cord compression orplacental abruption. If the interval from leaking to delivery exceeds 18 hours, there is an increase in incidence of neonatal infections and admissions (6,7).

The recommended management strategy for a woman with PROM at term has changed considerably during the last several decades. Various pharmacological agents have been introduced to stimulate uterine contractions and for cervical ripening but only few have been scientifically evaluated. Intravenous oxytocin, mechanical methods and different preparations of prostaglandins have been used for inducing labor but the effectiveness of these agents varies.Intravenous oxytocin infusion has stood the test of time as a labor inducing agent. The advantages of misoprostol include effectiveness, low cost and ease of administration. The lower the pre-induction BISHOP score, the more time that will be required for the woman to go into active labor irrespective of the drug used (7).

The American College of Obstetricians and Gynecologists' Committee on Obstetric Practice recommends that the decision regarding management of term PROM should be direct induction. However for those mothers who decline induction, expectant management can be offered after counseling about the risks.

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During induction of labor with oxytocin, a sufficient period of adequate contractions (at least 12-18hours) should be allowed for the latent phase of labor to progress before diagnosing a case of failed induction and moving to caesarian section (8).

The Ethiopian national guideline recommends expedited delivery without delay in term PROM, and to consider induction, especially if the duration of PROM is more than 12-16hoursand if there is a favorable presentation of the cervix. If the cervix is unfavorable, prostaglandin cervical ripening is recommended (9).

Studies conducted in maternity hospitals in the United Kingdom and Egypt have suggested that misoprostol may be more effective in cases of an unfavorable cervix(7).Similarly, a Nigerian study has shown that the mean time interval from induction to vaginal delivery was significantly shorter in the misoprostol arm (504 minutes) compared to the oxytocin arm (627 minutes). The caesarean section rate of 18.1% among the misoprostol arm was also significantly lower than the 41.4% recorded in the oxytocin arm (p=0.002). Among patients with a Bishop score greater than 6, there were no statistically significant differences between the two groups in the outcomes measured (10). A further study which used data derived from a term PROM study compared all maternal and neonatal treatment costs associated with oxytocin induction versus other treatment alternatives, including expectant management or induction with prostaglandins. In all the economic models used, the study found that induction with oxytocin had the lowest cost (11).

Althoughthe national guideline recommends priming in situations of term PROM with unfavorable /low Bishopscore (< 6), the management of term PROM in the Ethiopian setting remains haphazard, with different practices in different institutions. For instancein the three teaching hospitals of Addis Abeba University, one hospital was using the direct induction with oxytocin irrespective of the Bishop score, while in the other two hospitals, pre induction priming was being practiced.

The purpose of this study was to compare the pregnancy outcome and route of delivery incases of term PROM with an unfavorable BISHOP score managed using two different induction protocols and to recommend a uniform protocol fora resource-limited setting such as Ethiopia.

PATIENTS AND METHODS

A cross sectionalcomparative study design was used in three teaching hospitals of Addis Abeba University (AAU) to compare the pregnancy outcomes and mode of delivery of cases of term PROM having an unfavorable/low BISHOP score. In all of the cases, there was to be induction of labor. The three teaching hospitals included in the study were Black Lion Hospital (BLH) of AAU, Ghandi Memorial Hospital (GMH)and Zewditu Memorial Hospital (ZMH). Since both direct oxytocin and prostaglandin with or without oxytocin protocols are practiced according to physicians' preference in these institutions, randomization was not done. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the College of Health Sciences of AAU and from the Research Committee of the Department of Obstetrics and Gynecology of the School of Medicine of AAU. Information about the study was provided to all participants.

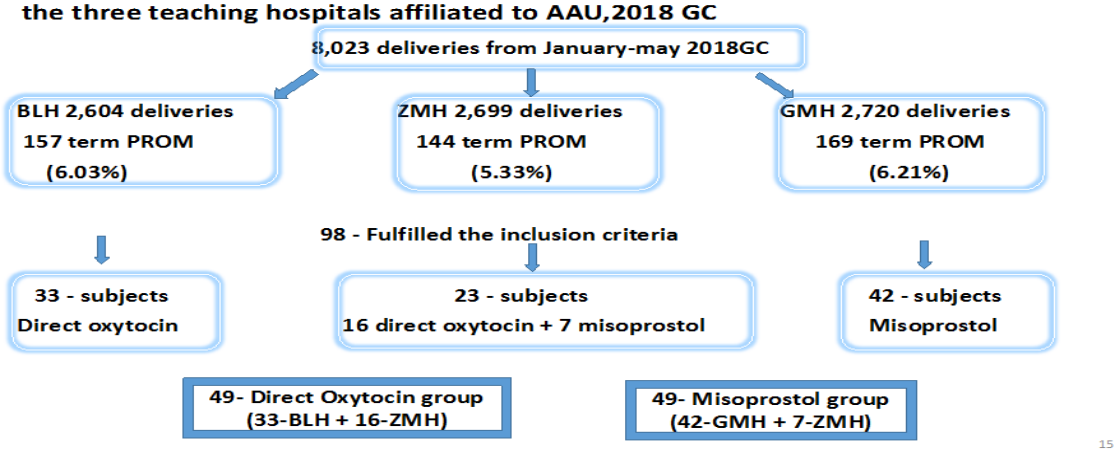
All who fulfilled the inclusion criteria and consented to participate in the studywere included in the study. Enrollment of study subjects continued until the desired sample size was achieved. Sample size was determined using EpiInfo 7 StatCalc, based on estimates obtained from a multicenter comparative cross sectional study conducted in Nigeria (10), with 95% confidence interval and 80% powerof the test to detect a difference between the groups. Assumptions were as follows: a ratio of exposed to unexposed of 1, caesarean section rate of 18.1% among the misoprostol arm and 41.4% in the oxytocin arm and adjusting sample size for a 10% non-response rate.Under these conditions, the minimal sample size calculated was 44 each for the prostaglandin group and the direct oxytocin group.

To achieve the objectives of the studyand factoring in a 10% non- response rate, the minimum sample size required was 49 for each of the two groups, totaling 98. Data was analyzed using SPSS version 23 statistical software. All cases of term PROM who fulfilled the inclusion criteria and who were managed in these hospitals from January to May 2018 were included until the desired sample size was reached.

Inclusion criteria

Singleton term pregnancy (37-42 weeks of gestation) with PROM confirmed by sterile speculum examination, no evidence of infection, cephalic presentation, unfavorable Bishop score (≤6),absence of labor or non-reassuring fetal heart rate pattern (NRFHRP), no known hypersensitivity to prostaglandins and no contraindications for induction of labor.

Figure 1. Schematic presentation of sampling procedure in patients with term PROM in the three teaching hospitals affiliated to AAU,2018 GC



Data was collected using a pretested questionnaire prepared in English. The data was collected by trained midwives, interns and residents after the mother who fulfilled the inclusion criteria was admitted to the labor ward and her consent was obtained.

Operational definitions

Gestational age: the age of the fetus counting from the last normal menstrual period.

Term PROM: a rupture of fetal membranes after 37 completed weeks of gestation. Prolonged PROM is rupture of membranes for more than 12 hours.

Latency period: the interval between the rupture of membranes until delivery.

Cervical priming: softening of the cervix prior to the onset of uterine contractions using either pharmacologic or mechanical methods.

Induction of labor: the artificial stimulation of uterine contractions before the spontaneous onset of true labor at 28 or more weeks of gestation to achieve vaginal delivery.

Failed induction with oxytocin: failure to achieve adequate uterine contractions after 12 to 18 hours of oxytocin administration and use of the maximum dose for at least 6-8 hours.

Failed induction with misoprostol: when a total of five doses or a cumulative dose of 200ug fail to initiate good uterine contraction.

RESULTS

The mean age of study participants was26.7 years (SD± 0.919), most were married with a monthly family income of 3000-5000 birr (114.3-187.5 in USD). Forty-nine women were in the direct oxytocin group and an equal number of women were assigned to the prostaglandin protocol. From the prostaglandin group, 25 needed additional oxytocin during labor induction. (Table1)

Most women in the study were nulliparous, gestational age of 39-40 weeks and six days and the mean duration of ROM was 24.4 hours(SD±16.1). The mean BISHOP score was 4.4(SD± 1.539) in the oxytocin arm and 3(SD± 1.757)in the misoprostol arm. BISHOP score at the time of admission to the labor ward showed a statistically significant association with the success of vaginal delivery, (p value=0.045, Adjusted OR 0.56 (95% CI 0.38-0.83) (Table 2).

The most commonly used route for misoprostol administration was vaginal, which happened in 31 of 49(63.3%) cases. A twenty-five microgram dose was used in all subjects. Forty-four out of 49 mothers (89.8%)received only one dose of misoprostol; 21 of them received misoprostol only while 23 women were in the subgroup who received misoprostol followed by oxytocin. The reason for oxytocin use after misoprostol was prolonged latent phase of first stage of labor (LFSOL) in15 out of 25(60%) the women.

The direct oxytocin group hada mean induction to delivery time interval of 681.65±345.5 minutes, mean established labor to delivery time interval of 466.1±209.6 minutes and a Cesarean section rate of 40.8% (20 out of 49 cases). The misoprostol group had a caesarian section rate of 16.3% (8 out of 49 cases). In the subgroup analysis of the misoprostol group, those women who received misoprostol only, had a mean induction todelivery time of 745.2±310.6 minutes and an established labor until delivery time of 574.6±310.6 minutes, compared to the group who required oxytocin after misoprostol. In the latter groupa mean induction until delivery time was 1,112.8±462.6minutes and the established labor until delivery time was 827±513.9minutes. (Table 3)

Table 1. Socio-demographic profiles and pregnancy outcome of induced labor in term PROM in three teaching hospitals of Addis Abeba, Ethiopia, 2018.

Characteristics		Drugs used to induce labor		Total N=98(%)
		Direct oxytocin N=49	Misoprostol N=49	
Age (years)	15-19	2	1	3 (3.1%)
	20-24	13	16	29(29.6%)
	25-29	24	16	40(40.8%)
	30-34	8	13	21(21.4%)
	35-39	2	3	5(5.1%)
Religion	Orthodox	21	24	45(46%)
	Muslim	20	15	35(35.7%)
	Protestant	8	10	18(18.3%)
Marital status	Single	1	1	2(2%)
	Married	47	48	95(97%)
	Divorced	1	0	1(1%)
Educational status	College or university	6	13	19(19.4%)
	High school	20	22	42(42.9%)
	Primary education	15	12	27(27.6%)
	Able to read and write	7	0	7(7.1%)
	Unable to read and write	1	2	3(3%)
Occupation	Student	2	1	3(3%)
	Housewife	24	21	45(46%)
	Daily laborer	6	8	14(14.3%)
	Merchant	4	8	12(12.2%)
	Government employee	8	5	13(13.3%)
	Private employee	5	6	11(11.2%)
Monthly family income in Eth. birr	0-600	3	2	5(5.1%)
	601-1650	7	6	13(13.3%)
	1651-3200	15	16	31(31.7%)
	3201-5250	14	18	32(32.7%)
	5251-7800	6	6	12(12.2%)
	7801-10,900	1	1	2(2%)
	Over 10,900	3	0	3(3%)

There was one case with postpartum hemorrhage, managed medically after the mother was induced with direct oxytocin and then received a 4000gram vaginally.

Generally theaverage neonatal intensive care unit (NICU) stay was 5 days in both oxytocin and misoprostol groups.Twenty percent of neonates born fromthe direct oxytocin group and 31% from the misoprostol group were admitted to NICU. In the oxytocin induction group one neonate was kept for 21 days in the NICU before discharge.

There was also a case of a neonataldeath on the second day after delivery by cesarean section due to early onset neonatal sepsis (EONS). In the misoprostol group there was one neonatal death after a one-day stay in the NICU with a diagnosis of meconium aspiration syndrome and EONS after vaginal delivery.

Table 2: Obstetric variables, pregnancy outcome of induced labor in term PROM in three teaching hospitals of Addis Abeba, Ethiopia, 2018.

Variable		Drugs used to induce labor		Total N=98 (%)
		Direct oxytocin N=49	Misoprostol N=49	
Parity	Nulliparous	34	34	68(69.4%)
	Primiparous	8	10	18(18.4%)
	Multiparous	7	5	12(12.2%)
Place of ANC follow up	Health center	43	40	83(84.8%)
	Gov't Hospital	4	7	11(11.2%)
	Others	2	2	4(4%)
Gestational Age (weeks and days)	37-38 and 6	14	12	26(26.5%)
	39-40 and 6	22	22	44(44.9%)
	41-41and 6	13	15	28(28.6%)
ROM duration at admission	6-12 hours	4	0	4(4.1%)
	≥12-18 hours	18	21	39(39.9%)
	≥ 18-24 hours	13	11	24(24.5%)
	≥24-36 hours	4	9	13(13.2%)
	≥36-48 hours	4	3	7(7.1%)
	≥48-72 hours	3	4	7(7.1%)
	≥72 hours	3	1	4(4.1%)
BISHOP score at admission	0	0	2	2(2%)
	1	2	6	8(8.1%)
	2	7	16	23(23.5%)
	3	3	8	11(11.2%)
	4	10	3	13(13.3%)
	5	12	8	20(20.4%)
	6	15	6	21(21.5%)

Table 3. Intra-partum events, pregnancy outcome of induced labor in term PROM in three teaching hospitals of Addis Abeba, Ethiopia, 2018.

Variable		Drugs used to induce labor		Total N=98 (%)
		Direct oxytocin N=49	Misoprostol N=49	
Time interval from induction or priming untildelivery (minutes)	<360 minutes	8	1	9(9.2%)
	360-720 minutes	24	15	39(39.8%)
	721-1,080 minutes	11	18	29(29.6%)
	1,081-1,440minutes	5	11	16(16.3%)
	>1,440 minutes	1	4	5(5.1%)
Time interval from established labor untildelivery (minutes)	<360 minutes	18	12	30(30.6%)
	360-720 minutes	22	15	37(37.8%)
	721-1,080 minutes	9	14	23(23.4%)
	>1,080 minutes	0	8	8(8.2%)
Antibiotic prophylaxis	Ampicillin	40	32	72(73.5%)
	Ceftriaxone	9	15	26(26.5%)
Mode of delivery	Vaginal	29	41	70(71.4%)
	C/S*	20	8	28(28.6%)

*C/S: Cesarean section

Table 4: Neonatal outcome, pregnancy outcome of induced labor in term PROM in three teaching hospitals of Addis Ababa, Ethiopia, 2018.

Neonatal outcome		Drugs used to induce labor		Total N=98
		Direct oxytocin N=49	Misoprostol N=49	
Neonatal Sex	Male	18	24	42(42.9%)
	Female	31	25	56(57.1%)
Birth weight	< 2500 grams	2	4	6(6.1%)
	2500-3999 grams	44	44	88(89.8%)
	>4000 grams	3	1	4(4.1%)
Gestation at birth	Early term	14	12	26(26.5%)
	Full term	22	22	44(44.9%)
	Late term	13	15	28(28.6%)
1st and 5th minute APGAR score	1-3	0	1	1(1.0%)
	4-6	1	0	1(1.0%)
	≥ 7	48	48	96(98.0%)
NICU admission	No	39	34	73(74.5%)
	Yes	10	15	25(25.5%)
NICU Diagnosis	EONS	9	14	23(92.0%)
	MAS	0	1	1(4.0%)
	Skull fracture	1	0	1(4.0%)
NICU stay in days	1 day	1	1	2(8.0%)
	2 days	3	1	4(16.0%)
	3 days	1	2	3(12.0%)
	4 days	0	2	2(8.0%)
	5 days	2	2	4(16.0%)
	6 days	2	3	5(20.0%)
	7 days	0	4	4(16.0%)
	21 days	1	0	1(4.0%)
Status of the neonate at the 7th post-delivery day	Discharged improved	8	14	22(88.0%)
	Still in NICU	1	0	1(4.0%)
	Dead	1	1	2(8.0%)

DISCUSSION

The study aimed to determine if there was a difference in mode of delivery, duration of labor and neonatal outcomes in women with prolonged term PROM and low BISHOP score, managed either with direct oxytocin or misoprostol induction protocols. There is evidence that use of misoprostol can shorten the duration of labor and also decrease the caesarian section rate.

In one Nigerian multicenter study, the mean induction to vaginal delivery interval was significantly shorter in the misoprostol arm (504 minutes) compared to 627 minutes in the oxytocin arm (p=0.005). The caesarean section rate of 18.1% among the misoprostol arm was also significantly lower than the 41.4% recorded in the oxytocin arm (p=0.002) (10). In conformity with the Nigerian study, our study revealed that direct oxytocin induction in cases of term PROM with an unfavorable BISHOP score increased the cesarean section rate (p value=0.001, AOR 10.217, 95% CI:2.723-38.329).

However, in contrast to the same Nigerian study, our study found that both the induction to delivery interval and the established labor to delivery interval was shorter for the direct oxytocin induction group. The most common indication for cesarean section in the direct oxytocin group in this study was failed labor induction which was observed in 11 out of 20 (55%) cases, followed by NRFHRP in 6 out of 20 (30%) cases, similar to the findings of a prospective study conducted in a university teaching hospital in Nepal where the leading indication was also failed induction (3).

Like the Nigerian study, this study did not identify intrapartum and postpartum maternal complications except one case of post partum hemorrhage (PPH) secondary to uterine atony which was managed medically in the oxytocin arm (10).This is in contrast to findings from a study conducted in Mizan-Aman hospital in southwestern Ethiopia which found an unfavorable maternal outcome in 22.2% of women (12).

In the oxytocin group, 10 of the 49(20.4%)and in misoprostol group,15 of the 49(30.6%) neonates were admitted to the NICU but there was no statistically significant difference in the need for NICU admission or duration of NICU stay between the two groups (p value=0.44 and AOR 1.53(95% CI: 0.52-4.50). However the admission rates in this study were higher than what was reported by investigators from a Canadian study (5,11).

Conclusion:
Prostaglandin cervical ripening reduces the high rate of cesarean section for failed labor induction in cases of term PROM with low BISHOP scores, without compromising maternal and perinatal outcomes. We recommend uniform prostaglandin cervical ripening practice in cases of term PROM with low BISHOP scores before oxytocin induction of labor, to be incorporated in the national treatment guideline. Further randomized control trials should be carried out to explore cost effective and safe cervical ripening methodsin cases of term PROM with low BISHOP scores which can be used in low resource settings like Ethiopia.

ACKNOWLEDGEMENTS

The authors would like to thank the teaching hospitals for granting permission to conduct the study, to the study participants, as well as to all who participated in data collection.

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