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Is Induction of Labor with Early Rupture of Membranes Associated with an Increased Rate of Clinical Chorioamnionitis?

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Abstract

Objective: The objective of this study was to determine if early rupture of membranes (ROM) in women undergoing induction of labor (IOL) at term is associated with an increased rate of clinical chorioamnionitis. **Study Design:** A retrospective cohort study was performed on women undergoing IOL. Early ROM was defined as ROM at a modified Bishop score less than 5, cervical dilation less than 4 cm, or cervical effacement less than 80%. The rate of clinical chorioamnionitis was compared between women with early and late ROM. **Results:** The rate of clinical chorioamnionitis was 8.6% (24/279). ROM at an effacement of less than 80% was associated with a rate of clinical chorioamnionitis of 15.4% (12/78) compared to 6.0% (12/201) at an effacement of equal to or greater than 80%, p = 0.017. The rate of cesarean delivery was higher for patients with early ROM by any definition: 32% compared to 17.5% by modified Bishop score (p = 0.031), 32.4% versus 18.2% by cervical dilation (p = 0.049), and 33.3% versus 14.9% by cervical effacement (p = 0.001). **Conclusions:** In patients undergoing IOL, early ROM may be associated with an increased rate of clinical chorioamnionitis when performed at a cervical effacement of less than 80% and an increased rate of cesarean delivery.

Keywords

Amniotomy, Cesarean Delivery, Chorioamnionitis, Induction of Labor, Intraamniotic Infection, Perinatal Infection, Rupture of Membranes, Term Pregnancy

1. Introduction

Clinical chorioamnionitis complicates about 1% - 4% of all deliveries [1] [2] [3].

It is an important source of maternal and perinatal morbidity and mortality worldwide and it is associated with an increase in the rate of cerebral palsy, periventricular leukomalacia, respiratory distress syndrome, neonatal sepsis, neonatal death, labor dystocia, cesarean delivery, endometritis, postpartum hemorrhage, maternal sepsis, and death [4]-[9]. Therefore, it is important that obstetric units attempt to reduce the incidence of clinical chorioamnionitis. The pathogenesis of chorioamnionitis is thought to be due to migration of cervicovaginal flora through the cervical canal. Cervical mucus and amniotic fluid and membranes act as natural barriers protecting against intrauterine infection.

Among other risk factors, patients undergoing induction of labor have an increased risk for chorioamnionitis compared to spontaneous labor [10]. This is of particular importance as the rate of labor induction in the United States continues to rise. In 2017, approximately 25.7% of births were induced [11]. Besides medical induction of labor using prostaglandins or oxytocin, mechanical methods including stripping of membranes, artificial rupture of membranes, transcervical balloons, and hygroscopic cervical dilators have been recognized methods for induction of labor, either isolated or in combination.

Studies have suggested that early amniotomy decreases the time to delivery [12]-[17]. Whether early amniotomy is associated with an increased rate of clinical chorioamnionitis is uncertain, as there are conflicting results in the literature. Some studies have demonstrated an increased rate of chorioamnionitis with early amniotomy during labor induction [16] [18]. In contrast, other studies have shown no change in the rate of clinical chorioamnionitis [14] [16] [19]. The purpose of this study was to determine if early rupture of membranes, artificial or spontaneous, in women undergoing an induction of labor at term may be associated with an increased rate of clinical chorioamnionitis.

2. Materials and Methods

This is a retrospective cohort study on women undergoing an induction of labor at term (37 0/7 weeks to 42 6/7 weeks) between January 1, 2015, and December 31, 2017, at University Hospital, Newark, New Jersey. Women presenting for induction of labor with cervical dilation greater than 4 cm, a modified Bishop score greater than 5, spontaneous or prelabor rupture of membranes, clinical chorioamnionitis, previous cesarean delivery, intrauterine fetal demise, immunodeficiency, or multiple gestation were excluded from the study.

A modified Bishop score was defined as a simplified Bishop score using only cervical dilation, cervical effacement, and fetal station. The modified Bishop score was performed visually during a vaginal speculum examination, and for fetal station visually as well as by abdominal palpation. Early rupture of membranes was defined as rupture of membranes at a modified Bishop score less than 5, cervical dilation less than 4 cm, or cervical effacement less than 80%. A diagnosis of clinical chorioamnionitis was made based on a maternal oral temperature greater than or equal to 102.2˚F (39˚C) once, or greater than or equal to

100.4˚F (38˚C) on two occasions 30 minutes apart, and one of the following: fetal tachycardia, maternal white blood cell count greater than 15,000/mm^3, or purulent/foul smelling amniotic fluid. This definition is in agreement with the American College of Obstetricians and Gynecologists [20].

After identification of the subjects meeting inclusion criteria, maternal demographics including age, gravidity, parity, body mass index (BMI), weight, and gestational age were collected. Details pertaining to the induction, including induction agents used, the modified Bishop score at time of admission, cervical dilatation and effacement at time of admission, and presence of group B streptococcal (GBS) infection were also collected. The number of vaginal examinations and time from admission to delivery and from rupture of membranes to delivery were recorded. Maternal outcomes, including the presence of clinical chorioamnionitis and mode of delivery, as well as neonatal outcomes (APGAR scores, birth weight) were collected and compared. The primary outcome was the rate of clinical chorioamnionitis among all women with early versus late rupture of membranes. Secondary outcomes included mode of delivery, rate of clinical chorioamnionitis among nulliparous women, and rate of clinical chorioamnionitis among multiparous women undergoing early compared to late rupture of membranes.

Statistical analysis was performed using Fisher's exact test for categorical variables, and a Shapiro-Wilk Normality and Mann Whitney U test for continuous variables. Median and interquartile ranges were reported for continuous variables. A p value of less than 0.05 was considered statistically significant.

3. Results

There were 632 women undergoing induction of labor at term during the study, 279 of which met the inclusion criteria. Of the 279 women, 24 (8.6%) developed clinical chorioamnionitis. Demographics, induction characteristics, maternal, and neonatal outcomes of the cohort are listed in **Table 1**. The median age was 27 years. The median body mass index was 33 kg/m^2. 23.7% of patients were GBS positive. Most women received misoprostol and oxytocin (79.6% and 82.8%, respectively) during the induction. Vaginal delivery was achieved in 79.9% of women in the cohort.

Those who developed clinical chorioamnionitis were younger, of lower parity, lower weight, delivered at later gestational ages, and had a lower modified Bishop score, and lower cervical effacement at the time of rupture of membranes. They had more cervical examinations and a longer time from admission to delivery and from rupture of membranes to delivery. Women with clinical chorioamnionitis also had a higher cesarean delivery rate (**Table 2**). No difference in the rate of clinical chorioamnionitis was found when stratifying by month and year of delivery (data not shown).

There was a higher rate of clinical chorioamnionitis in those with rupture of membranes at a cervical effacement less than 80% compared with greater than or

Table 1. Characteristics of induction cohort.

Characteristic	Value (N = 279)
Demographics	
Age (years)	27 (22 - 33)
Parity	1 (0 - 2)
Gestational age (days)	278 (268 - 286)
Body mass index (kg/m^2)	33 (30 - 38)
Weight (kg)	87 (75.5 - 102)
GBS positive	23.7% (66)
Induction characteristics	
Dilation at admission (cm)	1 (0 - 2)
Effacement at admission (%)	0 (0 - 50)
Modified Bishop score at admission	1 (0 - 2.5)
Dilation at ROM (cm)	5 (4 - 8)
Effacement at rupture of membranes (%)	90 (70 - 100)
Modified Bishop score at ROM	7 (5 - 8)
Time from admission to delivery (h)	22.5 (15 - 33.25)
Time from ROM to delivery (h)	4.5 (1.5 - 8)
Vaginal exams from admission to delivery	6 (4 - 8)
Vaginal exams from ROM to delivery	2 (1 - 3)
Misoprostol use	79.6% (222)
Oxytocin use	82.8% (231)
Transcervical balloon catheter use	21.2% (59)
Dinoprostone use	5.0% (14)
Artificial ROM	59.9% (167)
Maternal and neonatal outcomes	
Clinical chorioamnionitis	8.6% (24)
Spontaneous vaginal delivery	75.6% (211)
Operative vaginal delivery	4.3% (12)
Cesarean delivery	20.1% (56)
Birth weight	3306 (2925 - 3600)
APGAR score at 1 min	9 (8 - 9)
APGAR score at 5 min	9 (9 - 9)

Data are reported as median (interquartile range) or % (n). ROM = rupture of membranes.

equal to 80% (15.4% versus 6.0%, p = 0.017). This difference was found in all women and in nulliparous women, but it was not significant in multiparous women. There was no difference in the rate of clinical chorioamnionitis based on the modified Bishop score or cervical dilation (Table 3).

When comparing women with early versus late rupture of membranes based on cervical effacement, those with early rupture of membranes were at an earlier median gestational age, had a higher rate of oxytocin use, and a higher rate of transcervical balloon catheter use. In addition, more time elapsed for these women from admission and rupture of membranes until delivery and they had more cervical examinations (Table 4).

The rate of cesarean delivery was higher for women with early rupture of membranes by any of the definitions: 32% versus 17.5% based on modified Bishop

Table 2. Characteristics of women who developed clinical chorioamnionitis (cc).

Characteristic	Women with CC (N = 24)	Women without CC (N = 255)	p-Value
Demographics			
Age (years)	21.5 (19 - 28.3)	27 (23 - 33)	0.006
Parity	0 (0 - 0.25)	1 (0 - 2)	0.013
Gestational age (days)	282.5 (278 - 289)	277 (268 - 285)	0.016
Body mass index (kg/m^2)	32 (30 - 35.3)	34 (30 - 38.5)	0.156
Weight (kg)	79.5 (71.8 - 89)	88 (76 - 102.5)	0.048
GBS positive	12.5% (3)	24.7% (63)	0.216
Induction characteristics			
Dilation at admission (cm)	1 (0 - 1)	1 (0 - 2)	0.484
Effacement at admission (%)	0 (0 - 50)	0 (0 - 50)	0.412
Modified Bishop score at admission	1 (0 - 2)	1 (0 - 3)	0.317
Dilation at ROM (cm)	5 (4 - 6)	5 (4 - 8)	0.162
Effacement at ROM (%)	75 (50 - 100)	90 (70 - 100)	0.047
Modified Bishop score at ROM	6 (4 - 8)	7 (5 - 9)	0.047
Time from admission to delivery (h)	32.3 (24.5 - 41.8)	21.5 (14.75 - 31.5)	0.001
Time from ROM to delivery (h)	8.8 (6 - 14.9)	4 (1.5 - 7)	<0.0001
Vaginal exams from admission to delivery	9 (7 - 10)	6 (4 - 8)	<0.0001
Vaginal exams from ROM to delivery	3.5 (3 - 5)	2 (1 - 3)	<0.0001
Misoprostol use	79.2% (19)	79.6% (203)	1
Oxytocin use	91.7% (22)	82.0% (209)	0.393
Transcervical balloon catheter use	29.2% (7)	20.4% (52)	0.304
Dinoprostone use	4.2% (1)	5.1% (13)	1
Artificial ROM	58.3% (14)	60% (153)	1
Maternal and neonatal outcomes			
Spontaneous vaginal delivery	50% (12)	78% (199)	0.005
Operative vaginal delivery	4.2% (1)	4.3% (11)	1
Cesarean delivery	45.8% (11)	17.7% (45)	0.003
Birth weight	3477 (3296 - 3734)	3260 (2900 - 3598)	0.003
APGAR score at 1 min	8.5 (7 - 9)	9 (8 - 9)	0.084
APGAR score at 5 min	9 (8 - 9)	9 (9 - 9)	0.093

Data are reported as median (interquartile range) or % (n). ROM = rupture of membranes, CC = clinical chorioamnionitis.

Table 3. Rate of clinical chorioamnionitis (cc) with early vs late rupture of membranes.

Definition of ROM	Rate of CC with early ROM	Rate of CC with late ROM	p-Value
Modified Bishop score	**<5**	**≥5**	
All women (N = 279)	14% (7/50)	7.4% (17/229)	0.161
Nulliparous (N = 133)	25% (5/20)	11.5% (13/113)	0.148
Multiparous (N = 146)	6.7% (2/30)	3.5% (4/116)	0.603
Cervical dilation	**<4 cm**	**≥4 cm**	
All women (N = 279)	5.4% (2/37)	9.1% (22/242)	0.752
Nulliparous (N = 133)	4.7% (1/21)	15.2% (17/112)	0.304
Multiparous (N = 146)	6.3% (1/16)	3.9% (5/130)	0.508
Cervical effacement	**<80%**	**≥80%**	
All women (N = 279)	15.4% (12/78)	6% (12/201)	0.017
Nulliparous (N = 133)	27.6% (8/29)	9.6% (10/104)	0.027
Multiparous (N = 146)	8.2% (4/49)	2% (2/98)	0.095

ROM = rupture of membranes, CC = clinical chorioamnionitis.

Table 4. Comparison of early and late rupture of membranes by effacement.

Characteristic	ROM at <80% cervical effacement (N = 78)	ROM at ≥80% cervical effacement (N = 201)	p-Value
Demographics			
Age (years)	28.5 (24 - 34)	26 (22 - 32)	0.082
Parity	1 (0 - 2)	0 (0 - 2)	0.070
Gestational age (days)	273 (266 - 283)	280 (270 - 287)	0.016
Body mass index (kg/m^2)	34 (30 - 39)	33 (30 - 38)	0.379
Weight (kg)	86.5 (77.3 - 106.8)	88 (75 - 102)	0.660
GBS positive	19.5% (15)	25.4% (51)	0.345
Induction characteristics			
Dilation at admission (cm)	1 (0 - 2)	1 (0 - 2)	0.119
Effacement at admission (%)	0 (0 - 50)	0 (0 - 50)	0.472
Modified Bishop score at admission	1 (0 - 2)	1 (0 - 3)	0.124
Dilation at ROM (cm)	4 (3 - 5)	6 (5 - 9)	<0.0001
Effacement at ROM (%)	50 (50 - 70)	100 (90 - 100)	n/a
Modified Bishop score at ROM	4 (3 - 5)	8 (7 - 9)	n/a
Time from admission to delivery (h)	29.5 (18 - 38.8)	21 (14 - 30.5)	0.001
Time from ROM to delivery (h)	7.8 (4.5 - 12.9)	3 (1 - 6.5)	<0.0001
Vaginal exams from admission to delivery	7 (5 - 9)	6 (4 - 8)	0.0003
Vaginal exams from ROM to delivery	3 (2 - 4)	2 (1 - 3)	<0.0001
Misoprostol use	79.5% (62)	79.6% (160)	1
Oxytocin use	93.5% (73)	78.6% (158)	0.002
Transcervical balloon catheter use	29.5% (23)	17.9% (36)	0.049
Dinoprostone use	6.4% (5)	4.5% (9)	0.545
Artificial ROM	62.8% (49)	58.7% (118)	0.587
Maternal and neonatal outcomes			
Clinical chorioamnionitis	15.4% (12)	6% (12)	0.017
Spontaneous vaginal delivery	64.1% (50)	80.1% (161)	0.008
Operative vaginal delivery	2.6% (2)	5.0% (10)	0.520
Cesarean delivery	33.3% (26)	14.9% (30)	0.001
Birth weight	3325 (2970 - 3567)	3283 (2885 - 3600)	0.704
APGAR score at 1 min	9 (8 - 9)	9 (8 - 9)	0.660
APGAR score at 5 min	9 (9 - 9)	9 (9 - 9)	0.787

Data are reported as median (interquartile range) or % (n). ROM = rupture of membranes.

score (p = 0.031), 32.4% versus 18.2% based on cervical dilation (p = 0.049), and 33.3% versus 14.9% based on cervical effacement (p = 0.001) (**Table 5**).

4. Discussion

Our data suggests that early rupture of membranes at a cervical effacement of less than 80% appears to be associated with an increased rate of clinical chorioamnionitis in patients undergoing an induction of labor at term. However, this association was present for nulliparous women only. There was also a significant increase in the rate of cesarean delivery in patients with early rupture of membranes in this cohort. Our findings suggest that rupture of membranes early in an induction process, particularly with long cervices, increases the risk of developing clinical chorioamnionitis. The 8.4% rate of clinical chorioamnionitis in

Table 5. Rate of cesarean delivery with early vs late rupture of membranes.

Definition of ROM	Rate of CD early ROM	Rate of CD late ROM	p-Value
Modified Bishop score	**<5**	**≥5**	
All women (N = 279)	32% (16/50)	17.5% (40/229)	0.031
Nulliparous (N = 133)	60% (12/20)	27.4% (17/229)	0.008
Multiparous (N = 146)	13.3% (4/30)	7.8% (9/116)	0.469
Cervical dilation	**<4 cm**	**≥4 cm**	
All women (N = 279)	32.4% (12/37)	18.2% (44/242)	0.049
Nulliparous (N = 133)	38.1% (8/21)	31.3% (35/112)	0.613
Multiparous (N = 146)	25% (4/16)	6.9% (9/130)	0.038
Cervical effacement	**<80%**	**≥80%**	
All women (N = 279)	33.3% (26/78)	14.9% (30/201)	0.001
Nulliparous (N = 133)	62.1% (18/29)	24% (25/104)	<0.0001
Multiparous (N = 146)	16.3% (8/49)	5.2% (5/97)	0.033

CD = cesarean delivery, ROM = rupture of membranes.

this study is greater than the expected rate with spontaneous labor, in agreement with previous literature [16]. The rate of clinical chorioamnionitis and demographics of those diagnosed with clinical chorioamnionitis in this study are consistent with what has been reported previously. Prolonged rupture of membranes, prolonged duration of labor, and increased number of vaginal examinations were risk factors for the development of clinical chorioamnionitis in this study, also consistent with existing literature [21] [22]. However, there continues to be disagreement regarding the risk of clinical chorioamnionitis in women undergoing induction of labor with early amniotomy [15] [16] [18] [19] [23]. The likely causes of this discrepancy are the multiple confounding factors present in any labor induction, including the inherent patient risk of chorioamnionitis, different ripening agents used, labor management differences, use of oxytocin, departmental protocols, methodological limitations of studies, and definitions of early amniotomy. This study did not show a difference in clinical chorioamnionitis when early rupture of membranes was defined by cervical dilation or modified Bishop score. It did, however, show a significantly higher rate of clinical chorioamnionitis in women with early rupture of membranes when defined by cervical effacement of less than 80% at the time of rupture of membranes.

We believe those with rupture of membranes at a cervical effacement of less than 80% in our study had a higher rate of clinical chorioamnionitis for several reasons. Those with rupture of membranes after 80% effacement are more likely to be in the active phase of labor. Therefore, the duration from rupture of membranes to delivery is likely to be longer in those with amniotomy at less than 80% effacement. Women are also more likely to have increased cervical examinations and a longer duration of labor, as was demonstrated in our study. When stratified by parity, only nulliparous women had a higher rate of clinical chorioamnionitis when rupture of membranes occurred at less than 80% effacement. The high rate in nulliparous women of 27.6% (8/29) likely influenced the overall in-

creased rate seen in the entire cohort.

There was also an increase in the rate of cesarean delivery in women with early rupture of membranes by any of the three definitions. This has been demonstrated previously [15] [18] [24] [25]. This finding is important considering the increasing rate of labor induction in the United States, particularly in light of the findings of the ARRIVE Trial and the expected further increase in the induction rate [26].

Our study suggests that cervical effacement rather than cervical dilation should be considered when determining the optimal timing of amniotomy during induction of labor. We would suggest, based on our findings, if possible, to delay amniotomy and instead use additional ripening agents or oxytocin rather than rupturing membranes when cervical effacement is less than 80% to avoid increasing the risk of chorioamnionitis. We also suggest judicious use of early amniotomy, as it was associated with an increased risk for cesarean delivery. However, our findings in this retrospective study should be tested on a larger study population to further determine the risk for clinical chorioamnionitis based on the timing of rupture of membranes.

There are strengths and limitations of this study. Limitations include its retrospective nature, the overall small number of cases of clinical chorioamnionitis (24 total), and the lack of confirmation of histological chorioamnionitis on pathologic examination of the placenta. In addition, retrospective studies do not establish a cause-and-effect relationship between variables. Strengths include the multitude of variables assessed and the identification and acknowledgement of potential confounding factors associated with an increased clinical chorioamnionitis rate.

5. Conclusion

This study suggests that early rupture of membranes at a cervical effacement of less than 80% appears to be associated with an increased rate of clinical chorioamnionitis in nulliparous patients undergoing induction of labor at term. This study also demonstrates an increase in the rate of cesarean delivery in those with early rupture of membranes. With the known morbidities associated with chorioamnionitis and 1/3 of all U.S. deliveries being by cesarean, with well-documented morbidities associated with multiple repeat cesarean deliveries [27], we propose careful attention to the timing of amniotomy during term inductions of labor. We believe that perhaps, if possible, less aggressive early amniotomy may decrease the rate and morbidities associated with chorioamnionitis and cesarean delivery and improve maternal and neonatal health.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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