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CLINICAL ARTICLE

# Labor induction outcomes in third-trimester stillbirths

Lori M. Gawron *, Jessica W. Kiley

*Department of Obstetrics and Gynecology, Section of Family Planning and Contraception, Northwestern University Feinberg School of Medicine, Chicago, USA*

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ABSTRACT

*Objective:* To describe the management of third-trimester stillbirth at a single institution, stratifying induction intervals and adverse outcomes by method. *Methods:* Women diagnosed with fetal demise at 28 weeks or later and admitted to an academic hospital between January 2007 and September 2010 were identified. A chart review extracted demographics, history, induction method, delivery interval, and adverse outcomes. *Results:* Seventy-four women were included, with a median gestational age of 35.5 weeks (range, 28–40 weeks). Ten women had undergone at least 1 prior cesarean. Induction methods included misoprostol alone or for cervical ripening; oxytocin and amniotomy; transcervical Foley catheter; and mifepristone. Overall, 88% of patients delivered within 24 hours; median time to fetal delivery was 11 hours 20 minutes (range, 7 minutes to 57 hours 12 minutes). Adverse outcomes included intrapartum fever and postpartum hemorrhage. In total, 98% of patients, including those with prior cesarean, had a successful vaginal delivery. *Conclusion:* Regardless of third-trimester induction method for management of stillbirth, the majority of women experience safe delivery within 24 hours. The descriptive data imply that misoprostol-only inductions might confer the shortest induction intervals; however, further prospective trials are needed to identify the optimal misoprostol regimen for women with third-trimester stillbirth.


## 1. Introduction

In the USA, more than 25 000 stillbirths occur annually at 20 weeks or later, with half diagnosed at 28 weeks and beyond [1]. The ideal induction method for third-trimester stillbirth has not been determined. The Practice Bulletin on stillbirth management by the American College of Obstetricians and Gynecologists recommends that, "After 28 weeks gestation, induction of labor should be managed according to usual obstetric protocols" [2].

Prior to 28 weeks of gestation, vaginal misoprostol—alone or with mifepristone—is the recommended induction method over oxytocin [3] or other routes of misoprostol administration [4], owing to safety profile and shortest induction-to-delivery time, yet it remains poorly studied in the third trimester. Only 3 of the 38 trials included in a recent Cochrane review included third-trimester patients [3–6]. A wide range of doses, variation of route of delivery, poor documentation of gestational ages, and mixed indications for delivery in published trials make a standard third-trimester misoprostol regimen difficult to identify [7–14]. Furthermore, publication bias probably obscures analysis of adverse outcomes; complications including hemorrhage, infection, retained placenta, and uterine rupture may be underreported.

The medical literature also lacks data on management of patients with prior cesarean delivery who present with a third-trimester stillbirth. A recent study of 209 third-trimester stillbirths with prior cesarean reported a 2.4% overall uterine rupture rate for all management options [15]. The 2 misoprostol studies that included women with prior cesarean were inconclusive on adverse outcomes, as the majority of participants were less than 28 weeks pregnant [12,16]. Use of a transcervical Foley catheter for cervical ripening in third-trimester patients with prior cesarean has been found to have a uterine rupture rate consistent with that of spontaneous labor [17].

In order to expand upon current literature and identify future research initiatives, a review at a single institution was undertaken. The aim of the present study was to describe management of third-trimester fetal demise through comparison of induction methods by delivery interval and adverse outcomes. A secondary aim was to assess induction methods and adverse outcomes among women with prior cesarean delivery presenting with third-trimester fetal demise.

## 2. Materials and methods

A retrospective chart review was conducted following approval and waiver of consent from Northwestern University Institutional Review Board. The Northwestern Enterprise Data Warehouse was queried for all women aged 18 years and older who were diagnosed with a third-trimester stillbirth and admitted to Northwestern Prentice Women's Hospital, Chicago, USA, between January 1, 2007, and September 30, 2010. Obstetric providers during the study period consisted of 122

* Corresponding author at: Department of Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, 680 North Lake Shore Drive, Suite 1015, Chicago, IL 60611, USA. Tel.: +1 312 695 4373; fax: +1 695 0014.
*E-mail address:* lgawron@northwestern.edu (L.M. Gawron).

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obstetricians (academic faculty and private-practice physicians), 22 midwives, and 55 residents and fellows. Exclusion criteria included gestational age less than 28 weeks, management via cesarean delivery without a trial of labor, and spontaneous labor without augmentation.

A detailed manual chart review was performed by a single reviewer (L.M.G.). Gestational age was based on best estimated due date from prenatal records or ultrasound biometry at the time of stillbirth diagnosis measuring 28 weeks or more. Data collected included patient demographics and obstetric history; gestational age; cervical exam and presence of contractions at admission; details of induction regimen; induction start time (defined as placement of cervical-ripening agent, amniotomy, or oxytocin initiation); fetal and placental delivery times; adverse outcomes; and total length of hospital stay.

Patients were stratified by induction method and a subgroup analysis was performed for patients with prior cesarean delivery. The primary outcomes were the proportion of patients delivered in less than 24 hours and the time from induction start to fetal delivery for each induction method. Secondary outcomes included any adverse outcomes, length of hospital stay, and choice of induction method and adverse outcomes in patients with prior cesarean delivery. Data were analyzed using an Excel spreadsheet (Microsoft, Redmond, WA, USA), and medians and ranges or proportions were reported as appropriate. As it was a descriptive study, no preliminary power analysis was completed.

## 3. Results

Seventy-four patients underwent trial of labor for third-trimester stillbirth during the study period. Median maternal age was 32.5 years (range, 17–43 years) and median gestational age was 35.5 weeks (range, 28-40 weeks). In total, 14% of the women had at least 1 prior cesarean delivery. Management included a range of induction methods: oxytocin and amniotomy (37.8%); misoprostol alone (23%); misoprostol for cervical ripening followed by oxytocin and amniotomy (18.9%); ripening with cervical Foley catheter followed by oxytocin and amniotomy (16.2%); amniotomy alone (2.7%); and mifepristone in an outpatient setting followed by labor without further augmentation (1.4%). Median cervical dilation at the start of induction was 1 cm (range, 0–4 cm), and 21.6% of patients reported contractions on admission for labor and delivery (Table 1).

Patients who received oxytocin and amniotomy were more likely to be older (median 36 years [range, 19–42 years]) and of a later gestational age (median 37 weeks [range, 28–40 weeks]) than women requiring cervical ripening or receiving misoprostol alone. Patients with uterine contractions on admission and a more favorable cervix were also more likely to receive oxytocin and amniotomy, or amniotomy alone over other induction methods (Table 1).

The misoprostol regimen varied by provider and no institutional standard was identified. In the misoprostol-only group, doses ranged from 25 μg every 6 hours to 400 μg every 4 hours; medications were administered buccally or vaginally. The total median dose was 400 μg (range, 25–1200 μg), and 52.9% of misoprostol-only patients had a change in dose or route during induction, based on clinical response. The misoprostol-only group was of the earliest median gestational age (32 weeks [range, 28–38 weeks]) and none of the patients in the group had a history of cesarean delivery (Table 1).

Patients who received misoprostol solely as a cervical-ripening agent prior to oxytocin and amniotomy also had varied regimens. The dose ranged from 25 μg every 4 hours to 200 μg every 6 hours, with a total median dose of 187.5 μg (range, 50–800 μg). Only one patient in this group had a change in misoprostol dose or frequency during ripening. One patient in the group had a prior cesarean (Table 1) and received 200 μg vaginally every 6 hours for 3 doses prior to oxytocin and amniotomy.

Median time from induction to fetal delivery was 11 hours 20 minutes (range, 7 minutes to 57 hours 12 minutes). The shortest median interval was found in the oxytocin and amniotomy group at 7 hours 44 minutes (range, 27 minutes to 18 hours 12 minutes), although these patients were more likely to be dilated and/or contracting on admission. The longest median intervals were in the cervical-ripening groups (Table 2). Fetal-to-placental delivery time did not differ significantly between induction methods. Four women required manual extraction of the placenta; the time to manual extraction ranged from 10 minutes to 40 minutes post-delivery. Only 1 woman required dilation and curettage for the placenta (>7 hours after fetal expulsion in a 34-week demise) (Table 3).

Adverse outcomes were identified, with intrapartum fever and postpartum hemorrhage the most frequent events. Intrapartum fever was more likely to occur in women who received misoprostol or underwent ripening with transcervical Foley. The 2 cases of endometritis occurred in the oxytocin and amniotomy group. Of the women with postpartum hemorrhage, only those diagnosed with disseminated intravascular coagulopathy (DIC) required transfusion (n = 5). The patients with DIC had an underlying etiology of placental abruption or prolonged stillbirth retention at the time of induction.

The 10 women with prior cesarean delivery were more likely to be parous and of an earlier gestational age (median 31 weeks [range, 28–38 weeks]), with a median induction interval of 16 hours 25 minutes (range, 27 minutes to 39 hours 59 minutes); 80% of these women delivered within 24 hours. One woman experienced postpartum hemorrhage but did not require transfusion. No uterine ruptures were identified. The only failed labor induction occurred in a woman with a history of 1 prior cesarean who arrested at 6 cm after a 16-hour induction with transcervical Foley catheter followed by oxytocin and amniotomy (Table 4).

## 4. Discussion

The present study involved the largest case series in the current literature—compiling outcomes for 74 patients, including 10 with at least 1 prior cesarean delivery. We aimed to define the “usual obstetric

**Table 1**
Patient characteristics stratified by induction method.[a]

| | All patients (n = 74) | Misoprostol only (n = 17) | Misoprostol + oxytocin + AROM (n = 14) | Cervical Foley + oxytocin + AROM (n = 12) | Oxytocin + AROM (n = 28) | AROM only (n = 2) | Mifepristone only (n = 1) |
|---|---|---|---|---|---|---|---|
| Maternal age, y | 32.5 (17–43) | 32 (21–41) | 31 (17–43) | 32.5 (24–35) | 36 (19–42) | 22.5 (22–23) | 26 |
| Parity | 0.5 (0–4) | 1 (0–4) | 0 (0–1) | 0.5 (0–2) | 1 (0–4) | 1 | 0 |
| Gestational age, wk | 35.5 (28–40) | 32 (28–38) | 34.5 (28–40) | 34 (29–38) | 37 (28–40) | 35.5 (33–37) | 29 |
| Twin gestation | 2/74 (3) | 1/17 (6) | 1/14 (7) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Prior cesarean | 10/74 (14) | 0 (0) | 1/14 (7) | 5/12 (42) | 4/28 (14) | 0 (0) | 0 (0) |
| Pre-eclampsia | 9/74 (12) | 1/17 (6) | 1/14 (7) | 3/12 (33) | 4/28 (14) | 0 (0) | 0 (0) |
| Placental abruption | 2/74 (3) | 1/17 (6) | 0 (0) | 0 (0) | 0 (0) | 1/2 (50) | 0 (0) |
| Contractions on admission | 16/74 (22) | 1/17 (6) | 0 (0) | 1/12 (8) | 11/28 (39) | 2/2 (100) | 0 (0) |
| Cervical dilation on first exam, cm | 1 (0–4) | 0 (0–3) | 0 (0–1) | 0 (0–1) | 2 (0–4) | 2.75 (2.5–3) | 2 |

Abbreviation: AROM, artificial rupture of membranes.
[a] Values are given as median (range) or number (percentage).