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Route of Delivery in Women With Stillbirth: Results From the Stillbirth Collaborative Research Network

Annelee Boyle, M.D.¹, Jessica P Preslar, B.S.², Carol J R Hogue, Ph.D.², Robert M Silver, M.D.³, Uma M Reddy, M.D.⁴, Robert L Goldenberg, M.D.⁵, Barbara J Stoll, M.D.⁶, Michael W Varner, M.D.³, Deborah L Conway, M.D.⁷, George R Saade, M.D.⁸, Radek Bukowski, M.D. Ph.D.⁹, Donald J Dudley, M.D.¹, and for the Stillbirth Collaborative Research Network

¹Department of Obstetrics and Gynecology, University of Virginia School of Medicine, Charlottesville, VA

²School of Medicine and School of Public Health, Emory University, Atlanta, GA

³Department of Obstetrics and Gynecology, University of Utah School of Medicine, Salt Lake City, UT

⁴Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD

⁵Department of Obstetrics and Gynecology, Columbia University School of Medicine, New York, NY

⁶Department of Pediatrics and Dean's Office, UTHealth McGovern Medical School, Houston, TX

⁷Department of Obstetrics and Gynecology, University of Texas School of Medicine – San Antonio, San Antonio, TX

⁸Department of Obstetrics and Gynecology, University of Texas Medical Branch, Galveston, TX

⁹Department of Women's Health, University of Texas at Austin Dell Medical School, Austin, TX

Abstract

OBJECTIVE—To describe delivery management of singleton stillbirths in a population-based, multicenter, case series.

METHODS—We conducted a retrospective chart review of 611 women with singleton stillbirths at 20 weeks from March 2006 to September 2008. Medical and delivery information were abstracted from medical records. Both antepartum and intrapartum stillbirths were included; these were analyzed both together and separately. The primary outcome was mode of delivery. Secondary outcomes included induction of labor and indications for cesarean delivery. Indications

Corresponding author: Annelee Boyle, MD, Department of Obstetrics and Gynecology, University of Virginia Health System, P.O. Box 800712, Charlottesville, VA 22908-0712, Telephone: 434-924-9934, Fax: 434-982-0058, ab9cd@virginia.edu.

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for cesarean delivery were classified as obstetric (abnormal fetal heart tracing prior to intrapartum demise, abruption, coagulopathy, uterine rupture, placenta previa or labor dystocia) or non-obstetric (patient request, repeat cesarean delivery, or not documented).

RESULTS—Of the 611 total cases of stillbirth, 93 (15.2%) experienced cesarean delivery, including 43.0% (46/107) of women with prior cesarean and 9.3% (47/504) of women without prior cesarean. No documented obstetric indication was evident for 38.3% (18/47) of primary and 78.3% (36/46) of repeat cesarean deliveries. Labor induction resulted in vaginal delivery for 98.5% (321/326) of women without prior cesarean and 91.1% (41/45) of women with a history of prior cesarean, including two women who experienced uterine rupture. Among women with a history of prior cesarean delivery who had spontaneous labor, 74.1% (20/27) delivered vaginally with no cases of uterine rupture.

CONCLUSION—Women with stillbirth usually delivered vaginally regardless of whether labor was spontaneous or induced, or whether they had had a prior cesarean delivery. However, 15% underwent cesarean delivery, often without a documented obstetric indication.

Précis

In a population-based case series of women with stillbirth, 15% undergo a cesarean delivery, more than half of which had no documented obstetric indication.

INTRODUCTION

Stillbirth is defined in the United States as fetal death at or after 20 weeks of gestation, or in a fetus that weighs at least 350 grams if the gestational age is unknown¹. In the United States there are approximately 24,000 stillbirths yearly, a rate of 1 in 160 pregnancies². Despite the frequent occurrence of stillbirths, data to inform management of delivery are limited^{3,4}. Prior to the pharmaceutical use of oxytocin and prostaglandins for induction of labor, these pregnancies were usually managed expectantly. Approximately 75% of women who suffer stillbirth will enter spontaneous labor within 2 weeks of diagnosis⁵. However, with the widespread availability of oxytocin and prostaglandins, induction of labor soon after diagnosis of fetal death is now common^{3,4}. While many different induction regimens have been described^{6–15}, no method of induction has been studied rigorously. Furthermore, most data regarding method of induction have been extrapolated from induction of labor in pregnancies with a viable fetus or from termination of pregnancies in the second trimester^{16–19}. These circumstances are different from induction of a known stillbirth and may not be applicable.

In a prior study, cesarean delivery was the route of delivery in 9.5–11.3% of women suffering stillbirth²⁰. However, little data are available regarding indications for cesarean and there is scant data to inform clinical decision-making regarding route of delivery and method of induction^{20,21}. Thus, the purpose of our study is to describe delivery management of singleton stillbirths in a large population-based, multicenter, case series.

MATERIALS AND METHODS

We conducted a secondary analysis of 611 women with singleton stillbirths at 20 weeks of gestation enrolled in the Stillbirth Collaborative Research Network from March 2006 to September 2008²². This study was conducted at 59 hospitals to ensure access to at least 90% of all deliveries in 5 geographically defined catchment areas (Rhode Island and selected counties in Massachusetts, Georgia, Texas and Utah). All hospitals received institutional review board approval. Participants in the Stillbirth Collaborative Research Network study underwent a standardized protocol including maternal interview, medical record abstraction, placental pathology, bio-specimen testing and, post-mortem examination²³. All participants gave informed consent (and assent if applicable). The University of Virginia institutional review board approved this secondary analysis (IRB-HSR 18443).

To be included in the Stillbirth Collaborative Research Network study women had to be at least 13 years of age, a resident within one of the geographic catchment areas, and be identified for participation prior to hospital discharge²³. Women were excluded if incarcerated or if informed consent (and assent if applicable) could not be obtained²³. For this secondary analysis, multiple gestations (with demise of one or more of the fetuses) were also excluded, as management in those situations had to take into account the surviving fetuses.

Medical and delivery information from the maternal interview and medical record were abstracted by one of the authors (AB, JPP, or DJD) for all patients. The primary outcome was route of delivery. Secondary outcomes included induction of labor, methods of induction, and indications for cesarean delivery, which were classified as obstetric [abnormal fetal heart tracing (prior to intrapartum demise), abruption, coagulopathy, uterine rupture, placenta previa or labor dystocia] or non-obstetric (patient request, repeat cesarean delivery, or not documented). Both antepartum and intrapartum stillbirths were included; these were analyzed both together and separately. Chi-square or t-test was used to compare characteristics of women with and without a prior cesarean delivery. A p-value <0.05 was considered statistically significant. Data are presented with the 95% confidence interval (CI) for sample proportions and means.

Multivariable logistic regressions were then performed separately to model the odds of cesarean delivery for intrapartum and antepartum stillbirths using variables that were significantly associated (p<0.05) in the bivariate analyses. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Table 1 shows the characteristics for our study population. The average age was 27.2 years and the average pre-pregnancy BMI was 27.7 kg/m². About half of the women (46.2%) were nulliparous and 76.3% began prenatal care during the first trimester. Women represented diverse racial and ethnic backgrounds; 35.9% were non-Hispanic white, 21.5% were non-Hispanic black, and 35.7% were Hispanic. Educational attainment was at least high school for 76.1%, and 46.6% had some college or more. Medical complications were relatively

common, with 5.1% of participants having pre-gestational diabetes and 4.3% developing gestational diabetes. Pre-gestational hypertension was noted in 8.0% of participants and another 8.0% of participants developed gestational hypertension, preeclampsia, or eclampsia. Compared to women with no history of previous cesarean, those with a previous cesarean were older, had a higher BMI, and were more likely to have diabetes or hypertension (all $p < 0.05$).

Of the 611 total cases of stillbirth, 15.2% (95% CI: 12.4%–18.0%) of women ($n = 93$) experienced cesarean delivery, including 9.3% (95% CI: 6.8%–11.8%) of women without prior cesarean (47/504) and 43.0% (95% CI: 33.6%–52.4%) of women with prior cesarean (46/107). Women with primary cesarean delivery had no documented obstetric indications in 38.3% (95% CI: 9.7%–66.9%) (18/47) of cases. Among women who underwent repeat cesarean delivery, 78.3% (95% CI: 66.4%–90.2%) (36/46) had no obstetric indication, including 35 for whom the only documentation was repeat procedure.

Antepartum stillbirth was diagnosed in 509 women, while 102 women had an intrapartum stillbirth. Among women with an antepartum stillbirth, the overall cesarean delivery rate was 16.1% (82/509, 95% CI 12.9%–19.3%) and cesarean delivery rate for stillbirths at 24 weeks' gestation or more was 21.3% (81/381, 95% CI 17.2%–25.4%). Of the 81 women who delivered by CD in this group, 28 (34.6%, 95% CI 24.2%–45.0%) had an obstetric indication, and 53 (65.4%, 95% CI 55.0%–75.8%) did not. The primary cesarean rate for all antepartum stillbirths was 9.3% (39/419, 95% CI 6.5%–12.1%), while the repeat cesarean rate for all antepartum stillbirths was 47.8% (43/90, 95% CI 37.5%–58.1%). The primary cesarean rate for antepartum stillbirths at 24 weeks' gestation or more was 12.3% (39/317, 95% CI 8.7%–15.9%) while the repeat cesarean rate for antepartum stillbirths at 24 weeks' gestation or more was 65.6% (42/64, 95% CI 54.0%–77.2%). Among women with an intrapartum stillbirth, the overall cesarean delivery rate was 10.8% (11/102, 95% CI 4.8%–16.8%). The primary cesarean rate for intrapartum stillbirths was 9.4% (8/85, 95% CI 3.2%–15.6%), while the repeat cesarean rate for intrapartum stillbirths was 17.7% [3/17, we were unable to estimate CI using normal approximation ($n \cdot p < 5$)]. The indications for cesarean delivery among the 11 women with intrapartum stillbirth were abnormal fetal heart tracing prior to intrapartum demise (7), abruption (3), and repeat cesarean (1).

Among women without previous cesarean delivery, vaginal delivery occurred for 321 of 326 (98.5%, 95% CI 97.1%–99.8%) women who underwent induction, and for 136 of 143 (95.1%, 95% CI 91.6%–98.6%) women who presented in labor. Those presenting in labor who had a cesarean had either labor dystocia ($N=2$) or were noted to have abnormal fetal heart rate tracings, delivered via emergent cesarean, and were then diagnosed with intrapartum stillbirth ($N=5$).

For women with a history of previous cesarean who underwent induction, 91.1% (41/45, 95% CI 82.8%–99.4%) delivered vaginally. Of the 4 women with prior cesarean who underwent induction but ultimately delivered via cesarean the indications were “failed induction” for 2 and uterine rupture for 2. Both of the women who experienced uterine rupture had had only 1 prior cesarean. In the first case, the woman had 2 vaginal deliveries prior to her cesarean delivery. She presented at 37 weeks' gestation with fetal death. Her

cervical examination at entry was 2 cm dilation with 50% effacement. In addition, her fetus was noted to have anencephaly. Oxytocin induction was employed for an unknown amount of time. Whether the uterine rupture was diagnosed prior to laparotomy is not clearly described in the medical records. In the second case, the patient was at 22 weeks' gestation and underwent misoprostol induction. Uterine rupture was then diagnosed clinically and confirmed radiologically. She then had a laparotomy. Unfortunately the clinical records for these two women were incomplete and we could not obtain any other records, though neither woman appeared to have had a hysterectomy. The other 43 women with a history of previous cesarean who underwent induction and did not have uterine rupture included 21 with 1 prior cesarean, 8 with 2 prior cesareans, 1 with 3 prior cesareans, 1 with 4 prior cesareans, and 12 with an undocumented number of prior cesareans.

For women with a history of previous cesarean who presented in labor, 74.1% (20/27, 95% CI 56.8%–91.4%) delivered vaginally with no cases of uterine rupture. Reasons for cesarean delivery included labor dystocia (N=2), abruption (N=1), and emergent cesarean delivery for abnormal fetal heart rate tracing resulting in an intra-partum stillbirth (N=4). These 27 women included 10 with 1 prior cesarean, 7 with 2 prior cesareans, 3 with 3 prior cesareans, and 7 with an undocumented number of prior cesareans.

Gestational age was positively associated with the rate of cesarean delivery; the cesarean delivery rate was 0.9% [we were unable to estimate CI using normal approximation ($n \cdot p < 5$)] at less than 24 weeks, 8.6% (95% CI 2.9%–14.3%) at 24–27 weeks, 14.3% (95% CI 6.8%–21.8%) at 28–31 weeks, 35.4% (95% CI 25.0%–45.8%) at 32–35 weeks, and 30.2% (95% CI 22.6%–37.8%) at 36 weeks' gestation and above. Gestational age was associated with mode of delivery for intrapartum deaths, but not for antepartum deaths. At less than 24 weeks' gestation, 1 of 85 women with intrapartum stillbirth underwent cesarean delivery, while after 24 weeks' gestation 10 of 17 women with intrapartum stillbirth underwent cesarean delivery. These associations are depicted in the logistic regression analysis (Table 2). Controlling for prenatal care entry, and compared with gestational age <24 weeks, intrapartum deaths at 24–31 weeks were 19 times as likely to be delivered by cesarean [adjusted odds ratio (aOR)=18.91, 95% Confidence Interval (CI) 1.14–312.4, $p=0.040$] and for gestational age of 32+ weeks, were 467 times as likely (aOR=466.6, 95% CI 27.08–8040.4, $p<0.0001$). However, for antepartum stillbirths (Table 3), when controlling for gestational diabetes, prior history of cesarean increased the odds almost 10-fold among multiparous women [aOR = 9.57, 95% CI 4.86–18.83, $p<0.0001$]. Conversely, when controlling for prior pregnancy and prior cesarean, there is an increased odds of cesarean delivery of approximately 5-fold for women with gestational diabetes versus no diabetes (aOR=4.73, 95% CI 1.84–12.18, $p=0.001$).

DISCUSSION

More than 1 in 7 (15.2%) women with stillbirth were delivered by cesarean in this study, which is higher than the percentage (11.2%) in 2004 reported by Di Stefano et al using national U.S. data²⁰. These authors noted that cesarean deliveries for stillbirths increased 15% from 1995–2004²⁰. One reason for the higher percentage in our study may be that our patients delivered from 2006–2008 – an epoch with an even higher overall cesarean delivery

rate. Additionally, the other study was of a national data set, whereas our data are from 5 specified geographic regions of the country, such that our sample encompassed over than 90% of the stillbirths that occurred in each region. Since our data were collected from 59 hospitals, including academic and private settings in these 5 regions, we believe that our results reflect common obstetric practice and so we believe our data can be generalized nationally.

Cesarean deliveries were more common for antepartum than for intrapartum stillbirths. However, this is likely due to the considerable proportion of intrapartum stillbirths at less than 24 weeks of gestation. Indeed, an emergent cesarean delivery for abnormal fetal heart rate tracings, with the goal of preventing an intrapartum stillbirth, is appropriate when the fetus reaches a gestational age consistent with extrauterine viability. One reassuring finding is that compared to <24 weeks of gestation, those at 32+ weeks with an intrapartum stillbirth were 467 times more likely to undergo cesarean delivery. However, intrapartum stillbirths accounted for only 11.8% of all cesarean deliveries.

According to the American College of Obstetricians and Gynecologists, “Cesarean delivery for fetal demise should be reserved for unusual circumstances because it is associated with potential maternal morbidity without any fetal benefit³.” In a survey of members of the American College of Obstetricians and Gynecologists, Goldenberg et al found that 16% of respondents would deliver a stillbirth by repeat cesarean delivery²¹. In our study more than half of cesarean deliveries had no documented obstetric indication. Our study, Di Stefano’s study, and Goldenberg’s study all support increased provider education regarding the management of stillbirth. One argument for cesarean delivery for women with stillbirth is to spare a woman the psychologic effects of delivering a dead baby vaginally. However, data are insufficient to support the hypothesis that a cesarean delivery is psychologically protective. It is important to emphasize that hospitals with labor and delivery units should provide sensitive and supportive staff for women and families who suffer stillbirth.

A prior history of cesarean increased the odds of cesarean almost 10-fold among multiparous women. Most risks of trial of labor after cesarean are to the fetus (or neonate). Maternal risks include endometritis, blood transfusion, and scar dehiscence or rupture²³. However, a study of over 30,000 women with live births showed no increased risk of hysterectomy or maternal death with a trial of labor after cesarean compared to repeat cesarean delivery²⁴. In our series, 2 women suffered uterine rupture. Both cases occurred in women with a single prior cesarean, one of whom received misoprostol. However, given the gestational age (22 weeks) misoprostol was an appropriate choice³. Conversely, women with as many as 4 prior cesarean deliveries in our study had successful vaginal deliveries. Of note, neither woman who experienced uterine rupture in our series woman appeared to have had a hysterectomy.

Women were induced with multiple regimens including mechanical dilation, prostaglandin E1, prostaglandin E2, mifepristone, oxytocin, or a combination of methods. Given the retrospective nature of our study and small numbers in each group, we were unable to determine if one method of induction was superior to another. However, overall induction

success was 98.5% in those without a prior cesarean delivery indicating that many different regimens are likely effective.

Strengths of our study include a large number of women with stillbirth who were recruited from a diverse, population-based sample of hospitals from different regions of the country. Detailed data collection followed a standardized protocol. Weaknesses of our study include our reliance on the medical records and incomplete clinical data.

In conclusion, women with stillbirth usually delivered vaginally regardless of whether labor was spontaneous or induced, or whether they had had a previous cesarean. However, cesarean delivery was utilized often in women with stillbirth, commonly without a documented obstetric indication. Our data supports recommendations to reserve cesarean delivery in stillbirth for exceptional circumstances.

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Table 1

Demographics

Characteristic	All women (n = 611)	No history of cesarean (n = 504)	History of cesarean (n = 107)	p-value
% Intrapartum Demise	102 (16.7%)	85 (16.9%)	17 (15.9%)	0.806
Maternal Age (years)	27.2±6.7	26.7±6.7	29.8±6.1	<0.001
Pre-pregnancy BMI* (kg/m ²)	27.7±7.3 Missing=26	27.2±7.3 Missing=21	30.3±7.0 Missing=5	<0.001
% Nulliparous	282 (46.2%) Missing=1	282 (56.1%) Missing=1	0%	n/a [†]
Gestational age (weeks)				0.7666
<24 weeks	213	175	38	
24–31 weeks	177	149	28	
31+ weeks	221	180	41	
Maternal race/ethnicity	Missing=1	Missing=1		0.238
Non-Hispanic white	219 (35.9%)	189 (37.6%)	30 (28.0%)	
Non-Hispanic black	131 (21.5%)	107 (21.3%)	24 (22.4%)	
Hispanic	218 (35.7%)	172 (34.2%)	46 (43.0%)	
Other	42 (6.9%)	35 (7.0%)	7 (6.5%)	
Maternal education level	Missing=47	Missing=41	Missing=6	0.451
Less than high school	135 (23.9%)	106 (22.9%)	29 (28.7%)	
High school or equivalent	166 (29.4%)	139 (30.0%)	27 (26.7%)	
Some college	263 (46.6%)	218 (47.1%)	45 (44.6%)	
Trimester of entry to prenatal care	Missing=52	Missing=47	Missing=5	0.101
No prenatal care	40 (7.2%)	34 (7.4%)	6 (5.9%)	
First	432 (77.3%)	360 (78.8%)	72 (70.6%)	
Second	81 (14.5%)	59 (12.9%)	22 (21.6%)	
Third	6 (1.1%)	4 (0.9%)	2 (2.0%)	
Diabetes	Missing=2	Missing=2		0.004
None	552 (90.6%)	464 (92.4%)	88 (82.2%)	
Pre-gestational	31 (5.1%)	21 (4.2%)	10 (9.4%)	
Gestational	26 (4.3%)	17 (3.4%)	9 (8.4%)	
Hypertension	Missing=47	Missing=37	Missing=10	0.027
None	474 (84.0%)	400 (85.7%)	74 (76.3%)	
Pre-gestational	45 (8.0%)	36 (7.7%)	9 (9.3%)	
Gestational	45 (8.0%)	31 (6.6%)	14 (14.4%)	

Data are mean ± standard deviation for age and BMI*; number (%) for others

* BMI = body mass index

[†] n/a = not applicable

Table 2

Logistic regression variables for intrapartum stillbirths

Characteristic	N vaginal delivery	N cesarean delivery	Unadjusted Odds Ratio	Adjusted Odds Ratio
Prenatal care				
1 st semester	61	6	Reference	Reference
2 nd semester	10	4	4.07 (0.97–17.01)	9.27 (0.63–135.4) *
3 rd semester or none	13	1	0.78 (0.09–7.06)	1.89 (0.03–107.8) *
Gestational age				
<24 weeks	84	1	Reference	Reference
24–31 weeks	5	2	33.60 (2.59–436.6)	18.90 (1.14–312.4) †
32+ weeks	2	8	336.0 (27.37–4124.5)	466.6 (27.08–8039.3) †

* Adjusted for gestational age

† Adjusted for prenatal care

Table 3

Logistic regression variables for antepartum stillbirths

Characteristic	N vaginal delivery	N cesarean delivery	Unadjusted Odds Ratio	Adjusted Odds Ratio
Parity and Previous cesarean				
Previous vaginal delivery	171	16	Reference	Reference
Nulliparous	209	23	1.18 (0.60–2.30)	1.26 (0.64, 2.50) *
Previous cesarean delivery	47	43	9.78 (5.06–18.89)	9.57 (4.86, 18.83) *
Diabetes				
No diabetes	392	61	Reference	Reference
Pre-gestational diabetes	20	10	3.21 (1.44–7.19)	2.45 (0.99–6.06) †
Gestational diabetes	14	11	5.05 (2.19–11.63)	4.73 (1.84–12.18) †

* Adjusted for diabetes

† Adjusted for parity and previous cesarean