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Maria Pekkola, Minna Tikkanen, Mika Gissler, Mikko Loukovaara, Jorma Paavonen and Vedran Stefanovic*

Delivery characteristics in pregnancies with stillbirth: a retrospective case-control study from a tertiary teaching hospital

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Abstract

Objectives: We compared delivery characteristics and outcome of women with stillbirth to those with live birth.
Methods: This was a retrospective case-control study from Helsinki University Hospital, Finland. The study population comprised 214 antepartum singleton stillbirths during 2003–2015. Two age-adjusted controls giving live birth in the same year at the same institution were chosen for each case from the Finnish Medical Birth Register. Delivery characteristics and adverse pregnancy outcomes were compared between the cases and controls, adjusted for gestational age.
Results: Labor induction was more common (86.0 vs. 22.0%, p<0.001, gestational age adjusted odds ratio [aOR] 35.25, 95% confidence interval [CI] 12.37–100.45) and cesarean sections less frequent (9.3 vs. 28.7%, p<0.001, aOR 0.21, 95% CI 0.10–0.47) among women with stillbirth. Duration of labor was significantly shorter among the cases (first stage 240.0 min [115.0–365.0 min] vs. 412.5 min [251.0–574.0 min], p<0.001; second stage 8.0 min [0.0–16.0 min] vs. 15.0 min [4.0–26.0 min], p<0.001). Placental abruption was more common in pregnancies with stillbirth (15.0 vs. 0.9%, p<0.001, aOR 8.52, 95% CI 2.51–28.94) and blood transfusion was needed more often (10.7 vs. 4.4%, p=0.002, aOR 6.5, 95% CI 2.10–20.13). The rates of serious maternal complications were low.
Conclusions: Most women with stillbirth delivered vaginally without obstetric complications. The duration of labor was shorter in pregnancies with stillbirth but the risk for postpartum interventions and bleeding complications was higher compared to those with live birth.

Keywords: adverse pregnancy outcome; congenital anomaly; delivery; placental abruption; stillbirth.

Introduction

Every year 2.6 million pregnancies worldwide end in stillbirth [1]. There is considerable variation in stillbirth rates worldwide. In 2015, counting stillbirths at or after 28 gestational weeks, six countries in Europe including Finland, had a stillbirth rate of less than 2/1,000 total births whereas the rates for Pakistan and 13 countries in sub-Saharan Africa were above 30/1,000 [2]. Regulations and reporting practices for late terminations vary also between European countries influencing remarkably reported national stillbirth numbers [3].

Stillbirth is always a family tragedy often stigmatized and insufficiently managed [4]. Despite the abundant literature on etiology, prevention, and emotional aspects of stillbirth, data concerning management of delivery in pregnancies with stillbirth are insufficient.

Earlier studies have shown that labor induction after stillbirth is common [5, 6], but the optimal management of delivery is not known. The American College of Obstetricians and Gynecologists (ACOG) recommends adjustment of the timing and mode of the delivery to gestational age, maternal obstetric history, and maternal preference [7].

Two recent studies reported a cesarean section rate between 8 and 17 percent [8–11], one of them showed that approximately 40% of primary cesarean sections and 80% of repeat cesarean sections were performed without a clear obstetric indication [9].

***Corresponding author: Vedran Stefanovic**, MD, PhD, Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, PO Box 140, 00029 Helsinki, Finland, Phone: +358504271230, E-mail: vedran.stefanovic@hus.fi
Maria Pekkola, Minna Tikkanen, Mikko Loukovaara and Jorma Paavonen, Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
Mika Gissler, THL, Finnish Institute for Health and Welfare, Helsinki, Finland; and Department of Neurobiology, Care Sciences, and Society, Karolinska Institute, Stockholm, Sweden

Ramirez et al. showed a high vaginal birth success rate after cesarean delivery (86.7%) and a low rate of uterine rupture (2.4%) in pregnancies with stillbirth [6]. Another US study reported a low rate of complications, although the rates for postpartum hemorrhage (10%), retained placenta (23%), blood transfusion (3%), and shoulder dystocia (4%) were higher compared to live births [10]. Abnormal presentation was more common among stillbirth deliveries [10, 11], whereas episiotomies and perineal lacerations were infrequent [10].

The aim of this study was to analyze delivery management and adverse pregnancy outcomes of women with antepartum singleton stillbirth in comparison to women with singleton live birth.

Materials and methods

This retrospective case-control study was conducted at the Department of Obstetrics and Gynecology, Helsinki University Hospital, Finland. The study population included all singleton antepartum stillbirths ≥22 + 0 gestational weeks or with a birth weight of ≥500 g during 2003–2015. Among 62,319 children born during the study period, 325 (5.2/1,000) were stillborn. Multiple pregnancies, intrapartum deaths, and stillbirths of unknown gestational age were excluded, leaving 214 antepartum singleton stillbirths for the final analysis (Figure 1). Two age-adjusted controls giving live birth in the same year at the same institution were chosen for each case from the Finnish Medical Birth Register kept by Finnish Institute of Health and Welfare (THL).

Data were collected from the hospital electronic records and included maternal baseline characteristics, obstetric-history variables, pregnancy-related risk factors, gestational age at delivery, duration and mode of delivery, pain management methods, delivery interventions, specific adverse pregnancy outcomes, sex and birth weight of the stillborn, and the length of hospital stay of the mother after delivery. Corresponding data of the control group were obtained from the Medical Birth Register.

Additionally, placental weight, blood loss during delivery, and the proportion of placentas with a single umbilical artery for both groups originated in the hospital database. ICD-10 codes for anomalies were obtained from the hospital database for the case women and from THL's Register of Congenital Malformations for the controls. The congenital anomalies among stillbirths and until the age of one year in live births were characterized as major or minor according to European surveillance of congenital anomalies (EUROCAT) classification [12].

Maternal baseline characteristics included body mass index before pregnancy, smoking after the end of first trimester of pregnancy, and assisted reproductive technology. Smoking was self-reported at the first visit (non-smokers, quitted smoking during the first trimester, continued smoking after the first trimester) to prenatal care and controlled at the following visits. Assisted reproductive technology included *in vitro* fertilization, intra-cytoplasmic sperm injection, insemination, and ovulation induction. Obstetric-history variables included the number of prior normal and complicated pregnancies comprising miscarriages, induced abortions, ectopic pregnancies, cesarean deliveries, and stillbirths.

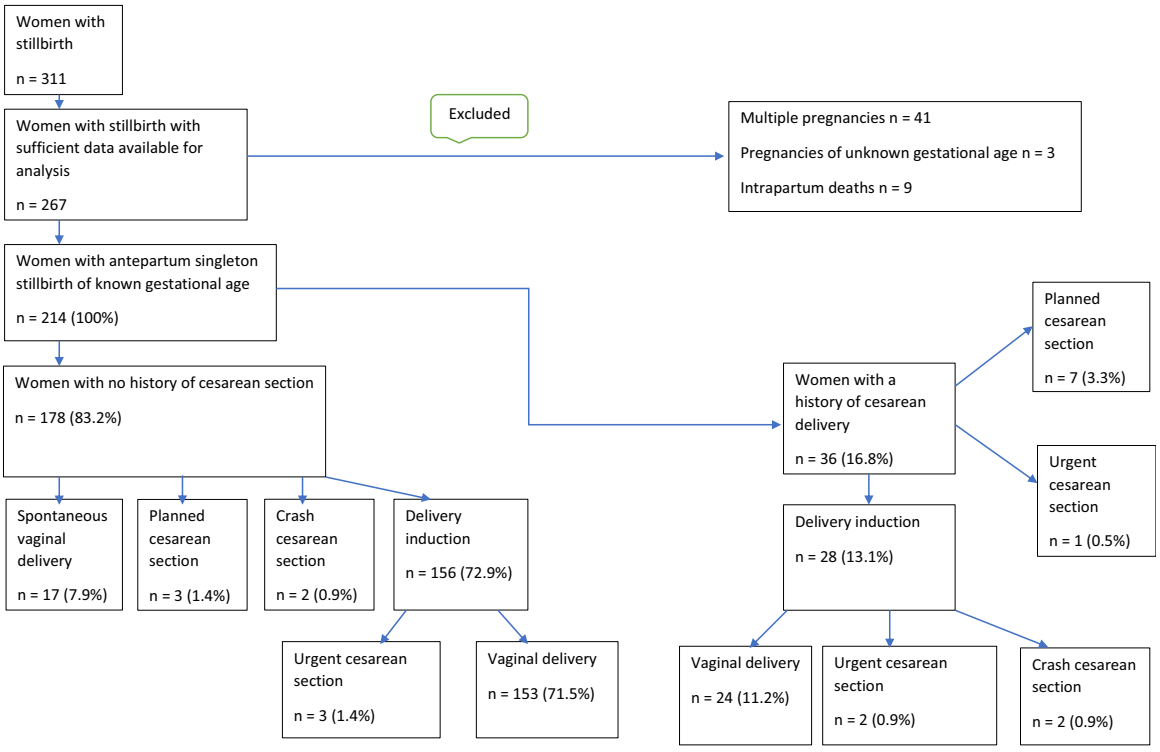

Figure 1: Flow chart of the study.

Delivery interventions recorded were induction of labor (amniotomy, oxytocine, and prostaglandin use), episiotomy, manual removal of the placenta, curettage, suturing of third or fourth degree perineal tear, and blood transfusion during labor or during the hospital stay after labor. Delivery diagnoses recorded as ICD-10 codes included placenta previa, placental abruption, eclampsia, fetal malpresentation, and shoulder dystocia.

Statistical analyses

Data were analyzed with IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). Comparisons between women with stillbirth and live birth were evaluated with the Chi-square test or Fisher's exact test for categorical variables. Normally distributed continuous variables were analyzed by Independent-samples t-test and other continuous variables by Mann–Whitney U-test. A p-value of <0.05 denoted statistical significance. Conditional logistic regression was used to compare categorical variables between stillbirths and live births with and without adjustment for gestational age.

Ethical approval

The Ethics Committee of Helsinki and Uusimaa Hospital district approved the study with the permission number 92/13/03/03/2014. THL allowed the use of their health register data by permission number THL/278/5.05.00/2016.

Results

Women with stillbirth were more often multiparous and had more often a history of stillbirth compared to the women with live birth. Other variables between the groups were comparable (Table 1).

Labor induction was more common among women with stillbirth compared to controls. Prostaglandin, vaginal or peroral misoprostol, was used more often for induction of labor in pregnancies with stillbirth. Amniotomy and oxytocin for induction or augmentation of labor were more commonly used in deliveries with live birth. When adjusted for gestational age, the difference for amniotomy and oxytocin use was not significant (Table 2). Only one induction (0.5%) was performed by balloon catheter among the case women, whereas there were 14 balloon catheter inductions (3.3%) among control women with live birth (data not shown).

The gestational age was shorter among pregnancies ending in stillbirth. Both the first stage and the second stage of labor were shorter among women with stillbirth (Table 3). Vacuum extraction (VE) was performed in 3 (1.4%) deliveries with stillbirth, whereas 38 (8.9%) women in the control group had VE (p<0.001) performed (data not shown).

Table 1: Maternal baseline characteristics and obstetric-history variables.

	Stillbirth n=214	Live birth n=428	p-Value
Age, mean ± SD[a]	32.1 ± 5.6	32.1 ± 5.6	1.00
BMI, median (IQR)	23.0 (20.35–25.65)	22.8 (20.25–25.35)	0.91
Smoking, n (%)[b]	25 (12.2)	40 (9.4)	0.28
Parity, n (%)			
0	99 (46.3)	196 (45.8)	
1–2	84 (39.3)	299 (46.5)	0.02
3 or more	31 (14.5)	33 (7.7)	
History of miscarriage, n (%)			
0	155 (72.4)	326 (76.2)	
1–2	53 (24.8)	94 (22.0)	0.50
3 or more	6 (2.8)	8 (1.9)	
History of induced abortion, n (%)			
0	182 (85.0)	378 (88.3)	
1–2	29 (13.6)	48 (11.2)	0.25
3 or more	3 (1.4)	2 (0.5)	
History of ectopic pregnancy, n (%)	2 (0.9)	5 (1.2)	1.00
History of stillbirth, n (%)	9 (4.2)	5 (1.2)	0.02
History of cesarean delivery, n (%)	36 (16.8)	70 (16.4)	0.88
ART, n (%)			
IVF/ICSI/FET	7 (3.3)	27 (6.3)	0.11
Insemination	2 (0.9)	3 (0.7)	1.00
Ovulation induction	6 (2.8)	17 (4.0)	0.45
Unspecified ART	7 (3.3)	22 (5.1)	0.28

SD, standard deviation; IQR, interquartile range; BMI, body-mass index; ART, assisted reproductive technology; IVF, *in vitro* fertilization; ICSI, intra-cytoplasmic sperm injection; FET, frozen embryo transfer. [a]Age adjusted. [b]Missing data: cases n=9, controls n=3.

Cesarean section was less frequent among the cases (Table 3). Crash cesarean sections were equally common (4 [1.9%] vs. 8 [1.9%]) but the rates of planned (10 [4.7%] vs. 54 [12.6%]) and urgent (6 [2.8%] vs. 61 [14.3%]) cesarean sections were significantly lower among women with stillbirth compared to controls (p<0.001).

Figure 1 shows the flow chart of the study with proportions of vaginal and cesarean deliveries among women with stillbirth by delivery history. Among the 36 women with stillbirth and prior cesarean section, 18 (50.0%) delivered by cesarean section; 7 (19.4%) had planned, 3 (8.3%) urgent, and 2 (5.6%) crash cesarean sections. The trial-of-labor rate among these women was 80.6% (29/36), and the vaginal-birth-after-cesarean-delivery (VBAC) success rate was 82.7% (24/29). The delivery was induced in 77.8% (28/36) of the patients with prior cesarean delivery. There was one uterine rupture in this group.

Table 2: Labor induction or augmentation.

	Stillbirth n=214	Live birth n=428	p-Value	OR with 95% CI	For gestational age adjusted OR (95% CI)
Induction total, n (%)	184 (86.0)	94 (22.0)	<0.001	21.79 (13.91–34.13)	35.25 (12.37–100.45)
Prostaglandin	151 (70.6)	63 (14.7)	<0.001	13.89 (9.33–20.66)	12.05 (5.57–26.08)
Amniotomy, n (%)	71 (33.2)	186 (43.5)	0.012	0.65 (0.46–0.91)	1.22 (0.74–2.02)
Oxytocin, n (%)	86 (40.2)	228 (56.3)	<0.001	0.59 (0.42–0.82)	0.94 (0.56–1.58)

OR, odds ratio; CI, confidence interval.

Table 3: Selected delivery characteristics.

	Stillbirth n=214	Live birth n=428	p-Value	OR (95% CI)	For gestational age adjusted OR (95% CI)
Gestational age at the time of delivery, median (IQR)	31.86 (26.34–37.38)	39.71 (38.71–40.71)	<0.001		
Duration of labor in vaginal births, median (IQR)					
First stage, min	240.0 (115.0–365.0)	412.5 (251.0–574.0)	<0.001		
Second stage, min	8.0 (0.0–16.0)	15.0 (4.0–26.0)	<0.001		
Cesarean section, n (%)	20 (9.3)	123 (28.7)	<0.001	0.26 (0.15–0.42)	0.21 (0.10–0.47)
Management of pain in vaginal births, n (%)[a]					
Epidural	108 (55.7)	293 (96.1)	<0.001	0.05 (0.03–0.10)	0.86 (0.39–1.93)
Spinal	5 (2.6)	19 (6.2)	0.33	0.40 (0.15–1.08)	0.29 (0.05–1.60)
Epidural-spinal	1 (0.5)	5 (1.6)	0.41	0.31 (0.04–2.68)	0.76 (0.06–10.33)
Paracervical block	1 (0.5)	10 (3.3)	0.01	0.15 (0.02–1.2)	
Pudendal block	3 (1.5)	7 (2.3)	0.49	0.67 (0.17–2.62)	0.47 (0.02–10.64)
Nitrous oxide	83 (42.8)	249 (81.6)	<0.001	0.17 (0.11–0.25)	0.50 (0.26–0.98)
Peroral analgetics	139 (71.6)	108 (35.4)	<0.001	4.61 (3.12–6.81)	3.48 (1.76–6.88)
Non-medical analgesia	6 (3.1)	53 (17.4)	<0.001	0.15 (0.06–0.36)	0.24 (0.06–1.01)
Episiotomy in vaginal births n (%)[a]	12 (6.2)	91 (29.8)	<0.001	0.16 (0.08–0.29)	0.16 (0.06–0.43)
Weight of newborn, g, (median [IQR])	1,473.0 (505.0–2,441.0)	3,473.5 (3,101.5–3,845.5)	<0.001		
Newborn sex, n (%)			0.12		
Male	109 (50.9)	210 (49.1)			
Female	103 (48.1)	218 (50.9)			
Undetermined	2 (0.3)	0 (0.0)			
Placental weight, g (median [IQR])[b]	400.0 (231.5–568.5)	590.0 (490.0–690.0)	<0.001		
Blood loss, mL, (median [IQR])[b]	300.0 (150.0–450.0)	400.0 (250.0–550.0)	<0.001		
Single umbilical artery, n (%)[b]	9 (4.4)	1 (0.3)	0.001		
Length of hospital stay, days (median [IQR])	2.0 (1.0–3.0)	3.0 (1.5–4.5)	<0.001		

OR, odds ratio; CI, confidence interval; IQR, interquartile range; g, grams; mL, milliliters. [a]n (cases) = 194, n (controls) = 305. [b]Missing data: weight of placenta n (cases) = 28, n (controls) = 50; blood loss (cases) = 28, n (controls) = 50; single umbilical artery n (cases) = 8, n (controls) = 52.

Epidural anesthesia, nitrous oxide use, and non-medical analgesia were more common in vaginal deliveries with live birth but when adjusted for gestational age the difference was not significant. Peroral analgetics were more often given to women with stillbirth. Spinal and epidural-spinal anesthesia and pudendal and paracervical block were used for analgesia equally commonly. Episiotomy was performed more often among controls with live birth (Table 3).

The birth weight was significantly lower among stillborns compared to liveborns. The placentas of stillborns were smaller and single umbilical artery was more common compared to controls. Blood loss was greater among live births. Mothers of live newborns stayed longer as inpatients than mothers of stillborns (Table 3).

Breech presentation was more common in pregnancies with stillbirth but after adjustment for gestational age the difference was not significant. Rates of other malpresentations were equal. Shoulder dystocia, grade 3–4 perineal tear, and eclampsia were few. On the other hand, manual removal of the placenta and curettage were performed more often in stillbirths, but when adjusted for gestational age, the difference was not significant. Placental abruption was more frequent in pregnancies with stillbirth (Table 4).

Blood transfusion was needed more often among women with stillbirth (Table 4). Blood transfusion was performed due to severe bleeding in 11 (5.1%) cases with placental abruption; in three of these cases the delivery was complicated by disseminated intravascular coagulopathy (DIC). Neither placental abruptions nor DIC occurred among controls receiving blood transfusion. The main reasons for blood transfusion among live births were severe bleeding at cesarean section or due to retained placenta.

Three women in the stillbirth group needed laparotomy after the delivery (two laparotomies after vaginal birth, one re-laparotomy after planned cesarean section and supravaginal uterine amputation). In addition, one uterine rupture occurred during an attempt of VBAC. After delivery by cesarean section, hysterectomy was performed. There was only one re-laparotomy after cesarean section in the control group. Resuscitation of the mother was necessary in two stillborn deliveries, one after abruption-related severe hemorrhage and another after amniotic fluid embolism. Both mothers were resuscitated successfully.

Major congenital anomalies were significantly more common in pregnancies with stillbirth while minor anomalies were observed more frequently in liveborns (Table 4).

Discussion

Our main finding was that most women with stillbirth delivered vaginally without obstetric complications. As anticipated, labor induction was more common among cases compared to women with live birth. Also, cesarean delivery was less common compared to the controls. The gestational age at the time of delivery and the duration of labor were shorter among cases compared to controls. Placental abruption and blood transfusion were more

Table 4: Adverse pregnancy and delivery outcomes.

	Stillbirth n=214	Live birth n=428	p-Value	OR (95% CI)	For gestational age adjusted OR (95% CI)
Malpresentation, n (%)					
Breech presentation	37 (18.8)	15 (3.5)	<0.001	5.76 (3.08–10.76)	2.02 (0.73–5.56)
Other malpresentation	9 (4.5)	19 (4.4)	0.95	0.95 (0.42–2.13)	0.80 (0.22–2.98)
Shoulder dystocia, n (%)	0 (0.0)	2 (0.5)	0.56		
Manual removal of placenta, n (%)	15 (7.0)	8 (1.9)	0.001	3.96 (1.65–9.49)	1.47 (0.43–4.95)
Curettage, n (%)	15 (7.0)	11 (2.6)	0.007	2.86 (1.29–6.33)	1.58 (0.48–5.28)
Grade 3–4 perineal tear, n (%)	0 (0.0)	1 (0.2)	1.00		
Need for blood transfusion, n (%)	23 (10.7)	19 (4.4)	0.002	2.59 (1.38–4.87)	6.50 (2.10–20.13)
Eclampsia, n (%)	1 (0.5)	0 (0.0)	0.33		
Placental abruption, n (%)	32 (15.0)	4 (0.9)	<0.001	18.64 (6.50–53.46)	8.52 (2.51–28.94)
Uterine rupture, n (%)	1 (0.5)	0 (0.0)	0.34		
Peripartum hysterectomy, n (%)	2 (0.9)	0 (0.0)	0.11		
Maternal resuscitation, n (%)	2 (0.9)	0 (0.0)	0.11		
Newborn congenital anomaly, n (%)[a]			<0.001		
Major	35 (19.3)	20 (4.7)		2.58 (1.39–4.78)	2.51 (1.09–5.78)
Minor	5 (2.8)	33 (7.7)		0.29 (0.11–0.74)	0.17 (0.04–0.78)

OR, odds ratio; CI, confidence interval. [a]Missing data: newborn congenital anomaly, n (stillbirths) = 33.

common among cases with stillbirth. Also, manual removal of placenta and curettage were more often necessary in stillbirth deliveries. However, this difference was not significant when adjusted for gestational age. Serious maternal complications were few. The birth weight and placental weight were lower in the stillbirth group. Also, major congenital anomalies were more common in stillborns.

Primiparity is a known risk-factor for stillbirth [13]. However, in our study, women with stillbirth were more often multiparous than the controls. They also more often had history of stillbirth. Our previous study of the same stillbirth cohort showed, however, that in general, the probability of a favorable outcome in a subsequent pregnancy after stillbirth is high [14].

Labor induction was performed in more than 80% of the stillborn deliveries. This is not surprising since waiting for spontaneous delivery would be psychologically unacceptable and might predispose to severe life-threatening complications [15–18].

ACOG recommends the use of normal obstetrical protocols in the management of labor induction in stillbirth [7]. Prostaglandin was the method of choice at our institution during most of the study period. The balloon catheter was introduced at our institution during year 2011. In stillbirth, where there is no demand of fetal follow-up, prostaglandin has remained the method of choice. Studies comparing cervical ripening agents and mechanical dilatators in stillbirth delivery inductions are insufficient [7, 19, 20]. The balloon catheter induction has been associated with fewer uterine ruptures [7, 17]. Oxytocin use or amniotomy for induction and augmentation of delivery was more common among live births in our study. This was, however, explained by the different gestational-age distribution. These results might reflect the benign course and shorter duration of delivery among women with stillbirth. The reason for differences in pain relief might be the same, partly explained by the fact that many stillbirth deliveries are preterm.

Not surprisingly, cesarean section was performed rarely in cases of stillbirth and always by an obstetric indication. The reasons for planned cesarean sections were fetal macrosomia or malpresentation preventing vaginal birth, uterine scars, placenta previa and accreta, and maternal coronary heart disease. Urgent and crash cesarean sections were performed due to labor dystocia or heavy bleeding, in association with placental abruption or uterine rupture. Most of the women with antepartum stillbirth with a prior cesarean section underwent labor induction. The trial-of-labor rate of over 80%, the VBAC-delivery success rate of over 80%, and uterine rupture rate of below 3% were similar to results reported elsewhere [6]. The results of the Stillbirth Collaborative Research Network from 59 United States hospitals from 2006 to 2008 show that 15.2% of stillborns were born by cesarean section; no clear obstetric indication became evident for 38.3% of the primary and 78.3% of the repeat cesarean deliveries [9]. A Romanian study concerning mode of delivery in stillbirth during 2005–2015 reported a remarkable decrease in cesarean sections: in 2008 almost a half of stillborns were born by cesarean section, whereas in 2015 90% were delivered vaginally. This decline was due to adoption of guidelines based on evidence-based medicine [11]. On the other hand, the rates of cesarean section in stillbirths in the United States during a ten-year period increased by 15% [8].

In a recent study, breech presentation was seen more frequently in term births of women with prior stillbirth. Developmental anomalies and younger gestational age also predisposed to this malpresentation [21] which might explain the overrepresentation of breech presentation in the stillbirth group in our study. In the Romanian study, the corresponding rate was 16.1%, which is in line with our data [11].

Only few life-threatening complications requiring resuscitation emerged in the stillbirth group. Altogether our rates of serious maternal complications were low and comparable to another report [10]. In our study the risk of placental abruption was higher in case women compared to controls (15 vs. 0.9%). In another study, placental abruption explained 7% of all perinatal deaths. Of these 77% were stillborns [22]. It is possible that placental abruption may be one of the explanations why women with stillbirth needed blood transfusion more often, although the median amount of blood loss was clinically similar in both groups.

Interventions for massive bleeding were needed more often among the case women. Retained placenta has been linked to stillbirth as well as preterm birth also in other studies [23–25]. Hence, it is expectable that manual removal of placenta and curettage are more often required, especially in cases of preterm stillbirth.

The lower median weight of the newborn and the placenta reflect not only the younger gestational age at delivery but also the higher proportion of growth restricted newborns among stillborns. Many stillbirths are caused by placental insufficiency leading to growth restriction [26, 27]. However, the proportion of growth restricted stillborns is often overestimated because dead fetuses lose weight during retention *in utero* [28]. Major congenital anomalies were more common among stillborns, perhaps because of detection bias due to autopsy. In the Romanian

study, 60% of the stillborns had major congenital anomalies [11].

The strength of our study was the possibility to link the hospital database and the Medical Birth Register which includes systematically collected data. One weakness was that although there were more than 60,000 deliveries during the study period the sample size of the study group was still relatively small. This small sample size may be explained by Finland's low and constant stillbirth rate of approximately 3/1,000 births at or after 22 gestational weeks and 2/1,000 births at or after 28 gestational weeks [29, 30].

Conclusions

In conclusion, compared to live births, the delivery course was shorter among women with stillbirth, and the vast majority of them delivered vaginally. On the other hand, the risk for postpartum interventions and bleeding complications was increased. The results of this study, alongside the data from our previous publications, will improve the counseling of women with stillbirth in a local setting.

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