

Fetal Survival in Second-Trimester Termination of Pregnancy Without Feticide

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OBJECTIVE: To evaluate the rate of live birth and the duration of survival after termination of pregnancy without feticide.

METHODS: We conducted a retrospective analysis of 241 terminations of pregnancy without feticide for fetal anomalies or genetic abnormalities between 20 0/7 and 24 0/7 weeks of gestation at a single tertiary care referral center in Europe between February 2003 and May 2017. A multivariate binary regression model was used to evaluate factors associated with live birth.

RESULTS: Pregnancies were terminated at a mean gestational age of 22.1 ± 1.1 completed weeks of gestation. Median birth weight was 440 g (range 141–1,890 g). Live birth occurred in 122 cases (50.6%, 95% CI 44.4–56.8); median survival time was 32 minutes (range 1–267 minutes). Factors associated with live birth were gestational age at labor induction (odds ratio 1.41, 95% CI 1.01–2.01; $P=.049$) and fetal anomalies ($P=.046$).

CONCLUSION: After termination of pregnancy without feticide between 20 0/7 and 24 0/7 weeks of gestation, the live birth rate was 50.6% (95% CI 44.4–56.8). A lower gestational age at labor induction and the presence of skeletal, cerebral, renal, or multiple fetal anomalies increased the chance of stillbirth.

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Of the 42 million terminations of pregnancy that occur worldwide annually, 1.4% are performed after 20 0/7 weeks of gestation according to the Centers for Disease Control and Prevention.¹ According to the recommendations of the Society of Family Planning and the guidelines of the Royal College of Obstetricians and Gynaecologists, in cases of late termination of pregnancy, feticide should be offered beyond 22 weeks of gestation to ensure stillbirth.^{2–4} Although existing studies have included a large number of patients, ranging from 31–12,141 patients of all gestational weeks, data on live birth rates and survival times after termination of pregnancy between 20 0/7 and 24 0/7 weeks of gestation are scarce and contradictory, with rates ranging from 3.5–51.6%.^{2,5,6} Life signs were found for up to 276 minutes, with 90% of fetuses dying within the first 3 hours after termination of pregnancy.^{5,6}

We aimed to review our experience with termination of pregnancy procedures between 20 0/7 and 24 0/7 weeks of gestation that were not preceded by feticide. The main objective was to evaluate the live birth rate and, in cases of live birth, the duration of neonatal survival.

MATERIALS AND METHODS

This is a retrospective study of patients treated from February 2003 to May 2017 at the Medical University of Vienna, a tertiary care referral center where terminations of pregnancy for fetal or genetic anomalies were performed. All patients with initiation of induction between 20 0/7 and 24 0/7 weeks of gestation and without feticide have been included. Until 23 6/7 weeks of gestation, feticide is not mandatory in Austria. The study was approved by the Ethics Committee of the Medical University of Vienna (institutional review board number 542/2010, last approved January 27, 2014, after several extensions of validity).



Relevant data were acquired retrospectively using Viewpoint software. This is the basic perinatology database used at the department. Data were entered in Viewpoint by the supervising obstetricians. The primary outcome parameter was live birth after termination of pregnancy. According to the World Health Organization, a live birth was defined as “the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached.”⁷ The secondary outcome parameter was the duration of survival of neonates with signs of life. Notably, all women had undergone detailed anomaly ultrasound scan by which fetal malformations, if any, had been diagnosed. In addition, fetal magnetic resonance imaging had been performed in 129 cases (53.5%, 95% CI 47.3–60.1).

Psychological support was offered to all patients. Every termination of pregnancy for fetal anomalies was discussed in an internal clinical committee. To prevent live births, the possibility of feticide was offered to all patients. The decision to undergo feticide was made by the parents. Before making their choice, the parents had to attend counseling by specialists in prenatal diagnosis, a psychologist, and, if necessary, pediatricians. Feticide was performed with intracardiac injection of either lidocaine or potassium chloride.^{8–11}

Labor was induced with mifepristone and misoprostol or with gemeprost.^{12,13} During labor induction, fetal well-being was not assessed. A skilled resident or a specialist in obstetrics and gynecology attested to postpartum death. After fetal death, post-mortem examination was routinely performed. Psychological debriefing was offered to all parents postpartum.

Numeric data are presented as either mean \pm SD in cases of normal distribution or median and range in the absence of a normal distribution, which was tested using the Kolmogorov-Smirnov test. Categorical data are presented as numbers and frequencies. Differences between groups were tested using χ^2 test for categorical parameters and Kruskal-Wallis test for numeric parameters. Correlation analyses were performed by the Spearman test, including testing for significance. To predict live birth after termination of pregnancy, a multivariate binary logistic regression model was used to test the statistical significance of all coefficients. Odds ratios with their 95% CIs and *P*

values of likelihood ratio tests are provided for these analyses. *P* values $<.05$ were considered statistically significant. Ninety-five percent CIs for frequencies were calculated using the bootstrapping tool with a standardized initial value of 1 for the Mersenne twister where feasible. Statistical analysis was performed using SPSS Statistics for Windows 24.0.

Data were entered in SPSS by study doctors. There were no missing data. For validation of accuracy, we looked at the distribution and ranges of our data. Extreme values were double-checked. In addition, we conducted random checks by two independent investigators to ensure the accuracy of our data.

RESULTS

From February 2003 to May 2017, 302 terminations of pregnancy were performed. Women were excluded for the following reasons: three women (1.0%) delivered at another hospital and were therefore lost to follow-up; 12 fetuses (4.0%) had intrauterine fetal death before initiation of induction of labor; and 46 (15.2%) had undergone feticide before termination of pregnancy. Thus, the final study cohort comprised 241 cases of termination of pregnancy (Table 1). In the whole study population, a live birth rate of 50.6% (122/241, 95% CI 44.4–56.8) was observed. Fetuses with signs of life survived for a median of 32 minutes (range 1–267 minutes). Survival time was 1–10, 11–30, 31–60, and greater than 60 minutes in 32 (25.8%, 95% CI 17.8–33.9), 28 (22.6%, 95% CI 15.4–29.8), 27 (21.8%, 95% CI 14.5–28.9), and 37 (29.8%, 95% CI 21.8–38.7) cases, respectively.

A detailed list of congenital anomalies and fetal genetic aberrations is provided in Appendix 1 and Appendix 2, respectively, available online at <http://links.lww.com/AOG/B69>. These tables also include live birth rates and median survival times based on the congenital or genetic abnormalities.

In weeks 22 1/7+1–23+0/7, the highest live birth rate was found (60.8%, 95% CI 48.5–72.1; Table 2). In contrast to survival times (*P*=.496), live birth rates differed between gestational age groups in a statistically significant manner (*P*=.013; Table 2). A Spearman correlation of gestational age at delivery with survival times revealed a correlation coefficient of *r*=0.115 (*P*=.075).

By multivariate analysis, two parameters of significant influence remained: a higher gestational age at labor induction was associated with a higher chance for live birth (*P*=.049). Skeletal, cerebral, renal, and



Table 1. Characteristics of the Study Cohort

Characteristics	Value
Total no. of patients	241
Maternal age (y)	30.9±5.9
BMI (kg/m ²)	23.3±4.2
Invasive prenatal genetic testing	159 (66.0, 59.5–80.0)
Gestational age at labor induction (completed weeks)	21.8±1.1
Gestational age at delivery (completed weeks)	22.1±1.1
Duration of induction (h)	38.5 (4.6–152.8)
Live birth rate (%)	50.6 (122, 44.4–56.8)
Fetal sex (%)	
Male	53.1 (128, 47.7–68.7)
Female	46.9 (113, 31.3–52.3)
Birth weight (g)	440 (141–1,890)
Birth length (cm)	27 (17–45)
Survival time (min)	32 (1–267)
Congenital anomaly, normal or absent fetal karyotype (%)	69.7 (168, 63.1–75.1)
Fetal chromosomal aberrations (%)	30.7 (74, 25.3–37.3)

BMI, body mass index.

Data are n, mean±SD, n (%), 95% CI, or median (range).

multiple anomalies were associated with an increased chance of a stillbirth (Table 3).

DISCUSSION

In this retrospective cohort study, a live birth rate of 50.6% (95% CI 44.4–56.8) was found in fetuses with genetic aberrations or fetal anomalies after termination of pregnancy without feticide at 20 0/7–24 0/7 weeks of gestation. Compared with the results of Wyldes and Tonks,² our incidence was much higher. In their population-based study from 1995 to 2004, the authors reported a 5.5% rate of life signs in the period of 20–23 weeks of gestation. Because the use of feticide was not described in that study, it can be surmised that feticide might have contributed to that lower rate. In contrast, Vadeyar et al⁵ described a live birth rate of 51.6% in pregnancies after termination of pregnancy between 18 0/7 and 24 6/7 weeks of gestation, which is similar to our results (study period: 1996–2001).

A median survival time of 32 minutes, with a wide range of up to 267 minutes, was observed. Vadeyar et al⁵ reported similar survival times of 5–276 minutes after termination of pregnancy but no median survival duration. The smaller sample size of that study (N=31) was obviously attributable to the fact that feticide was routinely applied in the United Kingdom. In comparison, Wyldes et al,² who focused on the survival duration of fetuses at 17–31 weeks of gestation, found a median survival duration of 80 minutes. Moreover, Auger et al⁶ evaluated the median survival duration of all fetuses after termination of pregnancy (study period: 1986–2012), which was 60 minutes. More than 90% of all fetuses died within the first 3 hours of life. As a result of the differences in gestational age at delivery, a direct comparison of these studies with ours is not possible.

In our data set, the observed positive correlation between gestational age at delivery and survival times was weak ($r=0.115$) and not statistically significant ($P=.075$). Notably, the longest median survival time

Table 2. Live Birth Rate and Survival Time Depending on Gestational Age at Delivery

Week of Gestation	No. of Fetuses Delivered	No. of Live Births	Survival Time (min)
20 0/7–21 0/7	46 (19.1, 14.5–24.5)	14 (30.4, 18.8–46.6)	18 (1–230)
21 1/7–22 0/7	72 (29.9, 24.1–35.7)	38 (52.8, 39.4–63.6)	43 (1–179)
22 1/7–23 0/7	74 (30.7, 24.9–36.5)	45 (60.8, 48.5–72.1)	28 (1–155)
23 1/7–24 0/7	49 (20.3, 15.8–24.9)	25 (51.0, 37.1–65.5)	27 (1–267)

Data are n (%), 95% CI or median (range).

For median survival time, stillborn fetuses (survival time=0 minutes) were excluded.

Differences in live birth rates were significant using χ^2 test ($P=.013$) in contrast to differences in survival time using Kruskal-Wallis test ($P=.230$).



Table 3. Factors Associated With Live Birth After Termination of Pregnancy Without Feticide

Parameter	Live Birth (n=122)	No Live Birth (n=119)	OR (95% CI)	P*
Gestational age labor induction (completed weeks)	22.0±0.9	21.7±1.2	1.41 (1.01–2.01)	.049
Gestational age at delivery (completed weeks)	22.2±0.9	22.0±1.2	1.04 (0.90–1.20)	.613
Female fetal sex	57 (46.7)	56 (47.1)	1.00 (0.56–1.78)	.993
Birth weight (g)	449 (202–1,019)	430 (141–1,890)	1.00 (0.99–1.01)	.459
Duration of induction (h)	37.8 (32.4–50.7)	40 (32.5–54.3)	0.99 (0.97–1.00)	.077
Chromosomal abnormality—none	83 (68.0)	84 (70.6)	Reference	.318
Trisomy 21	21 (17.2)	5 (4.2)	4.12 (1.23–13.84)	
Trisomy 13	4 (3.3)	5 (4.2)	0.96 (0.23–3.99)	
Trisomy 18	5 (4.1)	9 (7.6)	0.49 (0.14–1.71)	
Turner syndrome	0	4 (3.4)	1.24×e ⁻⁹ (0–∞)	
Triploidy	0	2 (1.7)	4.22×e ⁻¹⁰ (0–∞)	
Monogenic diseases and microdeletions	3 (2.5)	6 (5.0)	0.60 (0.12–2.95)	
Other abnormalities	6 (4.9)	4 (3.4)	1.34 (0.32–5.53)	
Anatomic anomaly—none	5 (4.1)	3 (2.5)	Reference	.046
Skeletal anomalies	2 (1.6)	5 (4.2)	0.39 (0.03–5.49)	
Cerebral anomalies and neural tube defects	41 (33.6)	36 (30.3)	0.98 (0.12–8.12)	
Cardiac defects	27 (22.1)	10 (8.4)	1.92 (0.22–16.9)	
Multiple anomalies	39 (32.0)	47 (39.5)	0.62 (0.08–4.86)	
Renal or urinary tract anomalies	4 (3.3)	15 (12.6)	0.23 (0.02–2.45)	
Respiratory tract anomalies	0	2 (1.7)	5.31×e ⁻¹⁰ (0–∞)	
Gastrointestinal anomalies and abdominal wall defects	4 (3.3)	1 (0.8)	3.35 (0.17–65.07)	

OR, odds ratio.

Data are mean±SD, n (%), or median (range) unless otherwise specified.

Results of a multivariate binary logistic regression model.

Bold indicates statistical significance.

* Likelihood ratio test.

was found between 21 1/7 and 22 0/7 weeks of gestation. The decline thereafter might have been caused by selection bias. In anticipation of a higher live birth rate and longer survival times in these higher weeks of gestation, parents might have opted for feticide more often when a good overall condition of the fetus was expected. However, Vadeyar et al⁵ neither found a correlation between gestational age and duration of survival using regression analysis and Spearman correlation ($r=2.14$, $P=.5$).

In the multivariate predictive model for the occurrence of live birth, a higher gestational age at labor induction was associated with a higher chance of live birth (Table 2). The second factor in live birth prediction was the presence and type of fetal anomalies: skeletal, cerebral, renal, and multiple anomalies were associated with a substantially increased chance of stillbirth (Table 3).

We consider the comparatively large sample size a study strength; the main limitations are the retrospective design and the potential selection bias. Women with severe fetal anomalies and those with a lower gestational age more likely declined feticide because survival expectation was lower. Moreover,

our data cannot be extrapolated to normal fetuses or those with minor anomalies. In addition, one might argue that some of the fetuses might have died during labor induction or labor. However, in the predictive model for live birth, the duration of labor induction was not of significant influence (Table 3).

In conclusion, the present study demonstrated a significant number of fetuses with signs of life after termination of pregnancy without feticide between 20 0/7 and 24 0/7 weeks of gestation. Gestational age at labor induction plays a major role in fetal survival as does the presence and type of fetal anomalies.

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