Maternal outcome of selective feticide due to fetal anomaly in late trimester: A retrospective 10 years' experience in Taiwan

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Abstract

Background: Feticide was suggested to avoid delivering children with abnormalities. Recently, twin pregnancies have increased. Selective feticide was proposed to achieve a good outcome of pregnancy. This study aimed to evaluate the performance of feticide in twin pregnancy with fetal anomaly.

Methods: This was a retrospective study enrolled from 2009 to 2018. A total of 68 pregnancies with fetal anomalies received feticide. Potassium chloride was injected into the left ventricle to induce fetal asystole. Maternal and fetal characteristics of 16 dichorionic twins were documented to compare before and after 24th gestational week.

Results: All pregnant women received feticide without any maternal or fetal complication. The reasons for choosing feticide were divided into four groups, including morphologic defect (61.8%), genetic-chromosomal abnormality (30.9%), obstetrical complication (5.9%), and maternal request (1.5%). Mean gestational age at delivery was significantly higher in dichorionic twins who underwent selective feticide before than after 24th gestational week (36.7 vs 33.4, $p = 0.04$).

Conclusion: Intracardiac injection of potassium chloride was effective for feticide and safe for mothers and fetuses. Selective feticide served as an alternative approach for twin pregnancy with fetal anomaly after sufficient discussion.

Keywords: Dichorionic twin; Feticide; Fetal anomaly; Late trimester; Potassium chloride

1. INTRODUCTION

The gradual evolution of high-resolution ultrasound sonography (US) and prenatal diagnostic technique has assisted in the early diagnosis of fetal abnormality. However, certain diseases are lately identified in the second or third trimester. Induced feticide is necessary for avoiding the termination of pregnancy with a viable fetus.[1] Feticide refers to causing the death of a fetus, which is generally conducted prior to mid-to late-second trimester of pregnancy. Parents could opt for feticide before termination of pregnancy to relieve themselves of the unwarranted legal, financial or emotional burden.

In recent years, the number of twin pregnancies has increased gradually, and more complications have been observed in mothers and fetuses.[2] Twin pregnancy achieved a higher rate of chromosomal or structural abnormality than a singleton pregnancy.[3] Therefore, selective feticide is considered a way to avoid giving birth to a viable fetus with severe disease.[4] In this article, we assessed several cases of late termination of pregnancy in a tertiary medical center in Taiwan. Maternal and fetal outcomes of surgery were documented to evaluate the performance of feticide in pregnancies with fetal anomaly.

2. METHODS

This retrospective study collected data from patients who underwent feticide in Linkou and Taipei Chang Gung Memorial Hospital in Taiwan between January 2009 and December 2018. All cases admitted for feticide were previously reviewed by primary healthcare facilities and transferred to Linkou, or Taipei Chang Gung Memorial Hospital. Patients diagnosed with congenital abnormality were frequently referred. Written informed consents were obtained from all pregnant women for participation. The study was approved by Chang Gung Medical Foundation Institutional Review Board (CGMF Ref. No. 201801716B0C601). All procedures were performed in line with the principle of the Declaration of Helsinki.

2.1. Participants

The flow chart of study design was showed in Fig. 1. A total of 115 women were admitted for feticide between January 2009 and December 2018. With exclusion of pregnancies with multiple gestations receiving elective feticide, 68 cases with fetal anomalies remained in the study. All cases were divided into four groups according to their reasons for choosing feticide, including morphologic defect, genetic-chromosomal abnormality,

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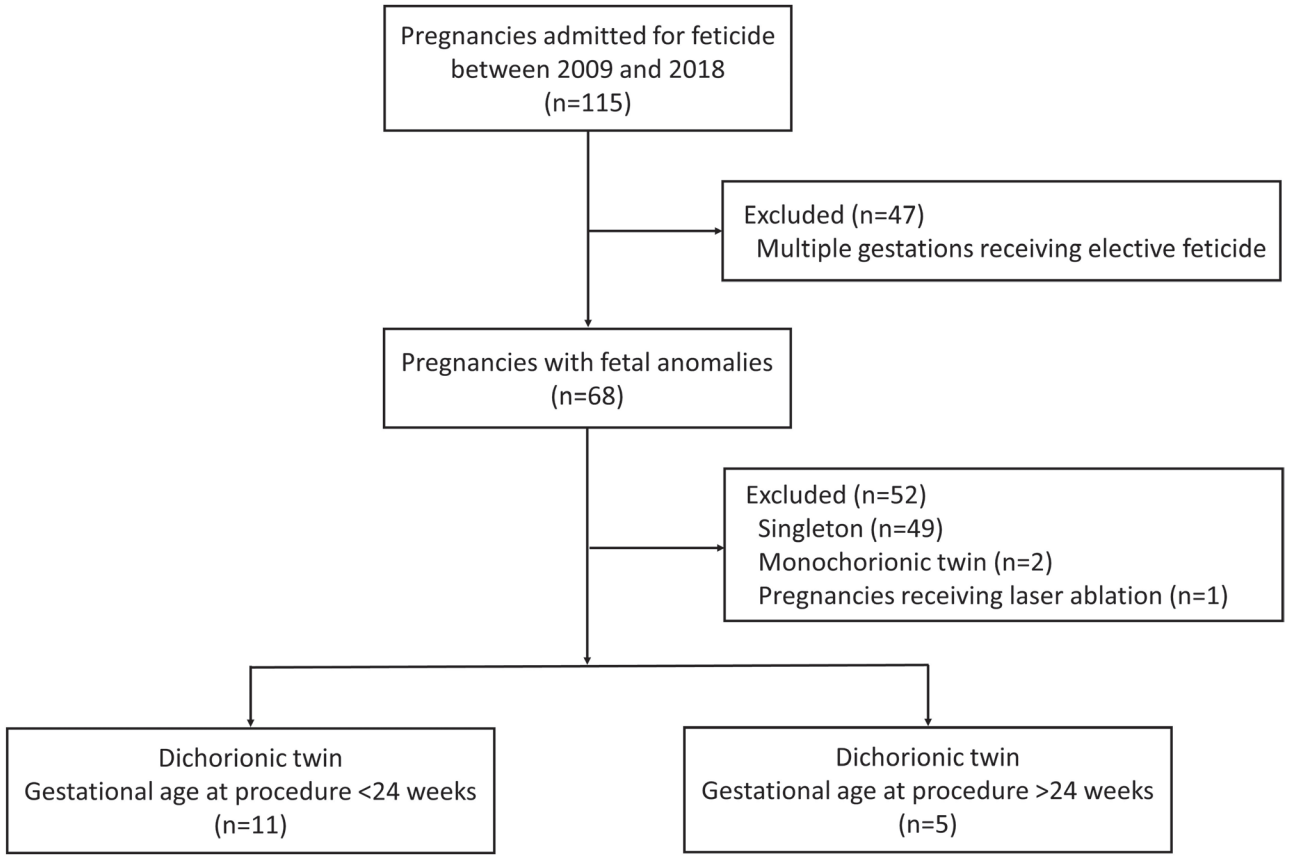

Fig. 1 Flow chart of study design.

obstetrical complication, and maternal request. In the beginning, the patient was taken over by a consultation team. The professional consultant would obtain prenatal information, confirm the diagnosis and inform potential neonatal outcomes. Then, feticide was suggested in the discussion about termination of pregnancy diagnosed with the fetal anomaly in the second or third trimester. If the agreement of feticide was reached, the patient should sign a written consent form. A committee would examine the feasibility of the procedure based on national legal requirements whose limited gestational age of termination is 24th gestational week. The early and late second trimester was divided by 24th gestational week.

2.2. Procedures

The procedure is performed by an experienced and skillful obstetrician. After eligible patients are admitted, serum hemogram and prothrombin time should be tested. Patients receive surgical draping in order to establish aseptic areas. Under US guidance, the obstetrician utilizes a 22G × 150 mm needle (TOP Corporation, Japan) to puncture the left ventricle of the fetus and administer potassium chloride (KCl) to induce asystole. The first dose of KCl is 2–3 mL, and an additional dose (1–2 mL) could be given if bradycardia is not observed. Fetal asystole is identified with US 30 minutes after the procedure. The total amount of KCl is recorded until fetal death is confirmed. A total of 49 singleton pregnancies with fetal anomalies were terminated after feticide. Termination of pregnancy is conducted with misoprostol in the oral, sublingual, or vaginal route. The viability of 19 survivors of twin pregnancies should be checked one day after selective feticide. Patients are recommended weekly follow-up at the outpatient clinic until delivery. With the exclusion of two monochorionic twins and one dichorionic twin with previous laser ablation for twin-twin transfusion syndrome, the detail of delivery time, maternal outcome, and complication of the procedure from 16 dichorionic twins are all recorded.

2.3. Statistical analysis

Maternal and fetal outcomes between gestational age of receiving feticide before and after 24th gestational week were analyzed by two-sample t-test. Considering statistical software, Prism version 8.0.1 (GraphPad Software Inc., San Diego, CA) was used for data analysis.

3. RESULTS

3.1. Characteristics of pregnancy with fetal anomaly and maternal outcome

Maternal characteristics of pregnancy with fetal anomaly were listed in Table 1. The mean maternal age of patients was 32.3 (maximum: 42; minimum: 18) years. The mean gestational age of fetus receiving feticide was 21.1 (maximum: 35; minimum: 15) weeks. Primigravida and multigravida account for 45.6% and 54.4%. Nulliparous and multiparous account for 66.2% and 33.8%. All reasons for choosing feticide were listed in Table 2, which included morphologic defect (61.8%), genetic-chromosomal abnormality (30.9%), obstetrical complication (5.9%), and maternal request (1.5%). In the morphologic defect group, brain anomaly is the most common (27.9%), followed by limbs (10.3%), and multiple anomalies (10.3%). In the genetic-chromosomal abnormality group, trisomy 21 is the most common (10.3%), followed by other causes (8.8%) and trisomy 18 (5.9%). In obstetric disorder

Table 1

Maternal characteristics of pregnancies with fetal anomalies

	All pregnancies (n = 68)
Maternal age, y	32.29 ± 5.15
Gestational age, w	21.11 ± 7.99
Gravidity	
Primigravida, % (n)	45.6% (31)
Multigravida, % (n)	54.4% (37)
Parity	
Nulliparous, % (n)	66.1% (45)
Multiparous, % (n)	33.8% (23)

groups, three patients received feticide for severe oligohydramnios and one for twin-twin transfusion syndrome. In the maternal request group, one patient with thyroid malignancy received feticide. All the pregnant women received feticide smoothly without any maternal complications. The procedures, including singleton or twins, were completed within 20 minutes.

3.2.Selective feticide in twin pregnancy

All singleton pregnancies underwent feticide with KCl and were terminated with misoprostol. the meantime of feticide was 19.3 (maximum: 36; minimum: 1) minutes. The mean volume of injected KCl was 3.6 (maximum: 10; minimum: 2) mL. No immediate maternal complications were noted after the termination of pregnancy. Other twin pregnancies received selective feticide. Maternal and fetal characteristics of selective feticide in dichorionic pregnancies were described in Table 3. All patients were divided into two groups according to the gestational age of receiving feticide before or after 24th gestational week (groups 1 and 2). No immediate maternal complications were noted after selective feticide. Mean gestational age at delivery was significantly higher in group 1 than group 2 (36.7 vs 33.4, $p = 0.04$) weeks (Fig. 2). Mean maternal age was lower in group 1 than group 2 (33.3 vs 34.6) years with no significant difference. The ratio of conception by assisted reproductive technology was lower in group 1 than group 2 (36.3% vs 60.0%) with no significant difference. Mean gestational age of procedure was significantly lower in group 1 than group 2 (20.2 vs 27.6, $p < 0.001$) weeks. Mean procedure time was higher in group 1 than group 2 (16.8 vs 13.0) minutes with no significant difference. Average hospitalization time was lower in group 1 than group 2 (2.7 vs 8.4) days with no significant difference.

Table 2

Categorization of fetal anomalies

	All pregnancies (n = 68)
Morphologic defect, % (n)	61.8% (42)
Brain, % (n)	27.9% (19)
Limbs, % (n)	10.3% (7)
Heart, % (n)	7.4% (5)
Face, % (n)	5.9% (4)
Multiple organs, % (n)	10.3% (7)
Genetic-chromosomal disorder, % (n)	30.9% (21)
Trisomy 21, % (n)	10.3% (7)
Trisomy 18, % (n)	5.9% (4)
22q 11.2 deletion, % (n)	2.9% (2)
Microdeletion, % (n)	2.9% (2)
Other, % (n)	8.8% (6)
Obstetrical complication, % (n)	5.9% (4)
Maternal request, % (n)	1.5% (1)

Table 3

Maternal and fetal characteristics of feticide in dichorionic twin pregnancy

	GA < 24 week (n = 11)	GA > 24 week (n = 5)	*p*
Age, y	33.3	34.6	0.743
Parity			
Nulliparity, n	7	4	
Multiparity, n	4	1	
Causes of fetal anomaly			
Morphological, n	5	2	
Chromosomal, n	6	3	
Conception by ART, n (%)	IUI: 0; IVF: 4 (36.3%)	IUI: 2; IVF: 1 (60.0%)	0.630
GA at procedure, w	20.2	27.6	<0.001*
Procedure time, min	16.8	13.0	0.913
Hospitalization period, d	2.7	8.4	0.900
Mode at delivery, n (%)	SD: 6; CS: 5 (45.5%)	SD: 4; CS: 1 (20.0%)	0.580
GA at delivery, w	36.7	33.4	0.04*
Preterm labor, n (%)	6 (54.4%)	4 (80%)	>0.99
Birth weight, g	2257	2020	0.503
NICU admission, n (%)	2 (22.2%)	3 (75%)	0.25

*$p < 0.05$ was regarded as statistical significance.

ART = Assisted reproductive technology; CS = Cesarean section; GA = Gestational age at procedure; IUI = Intrauterine insemination; IVF = In vitro fertilization; NICU = Neonatal intensive care unit; SD = Spontaneous delivery; SF = Selective feticide.

4. DISCUSSION

In spite of technological and technical advancements, some abnormalities occurred after 24th gestational week. According to the report from World Health Organization, administration of misoprostol alone or with Mifepristone is not directly feticidal.[1] With increasing gestational age of termination, transient fetal survival rate also elevates. Therefore, before termination with medical methods in the third trimester, inducing preprocedural fetal demise should be considered. World Health Organization recommends two regimens, including KCl and Digoxin. KCl was injected into the umbilical cord or cardiac chamber. This procedure is highly effective because fetal asystole could be identified with US immediately.[5] However, the advanced technique requires more expertise. Injection of Digoxin into the amniotic

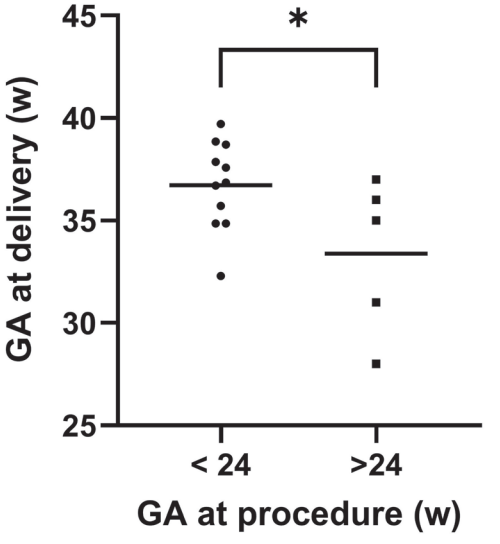

Fig. 2 Comparison of gestational age (GA) at delivery between pregnancies receiving feticide before and after 24th gestational week. GA = gestational age.

fluid is technically more accessible. However, the whole procedure takes almost one day for the fetus to absorb.[6,7] Intracardiac injections of KCl is our first choice to perform feticide. This technique consists of good quality of US and skillful obstetricians. Pasquini et al. conducted a retrospective study of 239 women who undertook feticide with the same method.[5] Successful fetal asystole was confirmed in all cases, and no patients needed a second injection. Our result was consistent with the above study. Intracardiac KCl serves as a safe and effective method for feticide.

Dichorionic twin pregnancies with one abnormal fetus could choose selective feticide and continue the pregnancy. A previous study showed that selective feticide increased gestational age at delivery and birth weight.[8] Hence, selective feticide is regarded as a choice for twin pregnancy with a fetal anomaly. It is crucial to identify chorionicity in twin pregnancy.[9] The placenta in dichorionic twin is separated that made it possible to perform intracardiac injection of KCl for inducing asystole. However, rich anastomosis in the placenta allows KCl to affect the other fetus. To avoid the effect of cardiotoxic agents toward healthy fetus, selective feticide in monochorionic twin is suggested to be completed with radiofrequency ablation in the umbilical cord.

The timing to perform selective feticide in twin pregnancy is also under debate. A retrospective study concluded that selective feticide performing in the third trimester seemed to be a safe approach to reduce total fetal loss and early preterm birth rate.[10] In our study, patients were categorized according to the gestational age of receiving feticide. Higher gestational week at delivery was observed in selective feticide before than after 24th gestational week. That is, selective feticide in later gestation might cause preterm delivery. However, no fetal loss occurred in twin pregnancy demonstrated a highly successful rate of selective feticide.

Our study demonstrated a similar proportion of reasons for choosing feticide with previous literatures.[5,11] Brain abnormality and aneuploidy accounted for major causes of feticide. Reasons for late diagnosis might be derived from misdiagnosis in early gestation and variation of the disease. When an abnormality is discovered, an obstetrician will initiate a series of surveys to determine a definite diagnosis. Amniocentesis is offered to patients older than 34 years with reduction of fee by the government in Taiwan. Level II ultrasound scan is self-paid for detailed examination of fetal anatomy. Finally, referral to tertiary medical center which takes few days is often required for further evaluation and management.

Legal regulation in Taiwan is illustrated in the Genetic Health code. According to the Enforcement Rules of Genetic Health Act, medical abortion is indicated when pregnancy or childbirth might affect the physical or mental health or when potential abnormalities are identified during the development of the fetus. Law in Taiwan puts an emphasis on induced abortion before 24th gestational weeks. Certain conditions, including identification of anomaly and exposure to teratogenic agents or radiation, are beyond the above regulation. All termination after 24th gestational weeks would be examined and reviewed by a joint committee and agreed upon by two obstetricians. In the United Kingdom, RCOG stated that feticide should only be recommended after 22th gestational week because the live birth rate increased significantly then.[12] Patients might deliver fetus with an abnormality or short lifespan without feticide in an adequate period. Between 2002 and 2008, 120–130 out of 1900 terminations occurred after 20th gestational week every year in the United Kingdom. If patients decide to receive feticide due to a diagnosis with abnormality in the second or third trimester, the procedure could be performed before medical termination. The comfort and dignity of the fetus count throughout the period of terminal care.

This is the first study to evaluate maternal and fetal characteristics in pregnancies with fetal anomalies after selective feticide in Taiwan. Reasons for receiving feticide were collected and classified. GA at procedure was divided by 24th gestational week, and the pregnancy outcomes were compared. Selective feticide served as an alternative for pregnancies with fetal anomalies. However, there were still some limitations in our study. First, our participants represented a small population. A large-scale study should be conducted for further investigation. Second, this was a retrospective study. To acquire a more powerful conclusion, matching of the data was needed for analysis. Third, the information of long-term follow-up was not available. Selective feticide might affect neonatal outcomes after birth.

In conclusion, intracardiac injection of KCl was effective for feticide and safe for mothers and surviving fetuses. Selective feticide showed therapeutic potential in the late second trimester of dichorionic twin pregnancy. With sufficient discussion about all related benefits and risks with the patient and family, selective feticide could be suggested for twin pregnancy with a fetal anomaly.

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