

Short Communication

# Analysis of intrauterine fetal demise—A hospital-based study in Taiwan over a decade

Li-Chun Liu<sup>a</sup>, Han-Bin Huang<sup>b</sup>, Mu-Hsien Yu<sup>a</sup>, Her-Young Su<sup>a,\*</sup>

<sup>a</sup>Department of Obstetrics and Gynecology, National Defense Medical Center, Tri-Service General Hospital, Taipei, Taiwan

<sup>b</sup>School of Public Health, National Defense Medical Center, Taipei, Taiwan

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## Abstract

**Objective:** To identify timing-specified risk factors for stillbirth, in order to help physicians to reduce preventable factors and stillbirths, and improve general outcomes of pregnancy.

**Materials and Methods:** A retrospective analysis was performed of births registered in our hospital, a medical center in Taiwan, between September 1, 1999 and December 31, 2011. We collected basic characteristics from the medical records, including maternal and fetal conditions. All stillbirths were divided into two groups according to gestational age: the second trimester group and the third trimester group. Comparisons were made between these groups.

**Results:** There were a total of 12,290 births and 121 stillbirths during our study period. The 121 stillbirths were divided into two groups: 67/121 (55.4%) were in the second trimester group and 54/121 (44.6%) were in the third trimester group. The overall incidence for intrauterine fetal demise was 0.98% (121/12,290). The increased risks in the third trimester stillbirths, as compared with the second trimester group, were significantly associated with males born, increased maternal body mass index (BMI) at delivery, habitual cigarette smoking, previous history of intrauterine fetal demise, and diabetic or hypertensive pregnancies. Unexplained causes (29.85%) were the most common causes of second trimester intrauterine fetal demise and the most common cause of third trimester intrauterine fetal demise was umbilical cord pathology (33.33%).

**Conclusion:** Management of any pregnant patient remains a challenge. Identifying upstream and cost-effective solutions will improve these pregnancy outcomes.

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**Keywords:** fetal death; pregnancy outcome; pregnancy trimesters; risk factors; stillbirth

## Introduction

Intrauterine fetal demise indicates no fetal heartbeat detected after 20 weeks' gestation, while missed abortion refers to the event occurring prior to 20 weeks' gestation. Intrauterine fetal demise is also called stillbirth, which means that after induction of labor, a fetus without spontaneous breath, heartbeat, or movement was delivered. The total estimated number of global stillbirths is 3.2 million annually. The

prevalence of intrauterine fetal demise varies from 5–32/1000 between nations; stillbirth rates in developing countries are higher than in developed countries [1]. These results may represent different levels of healthcare among distinct, geographically-defined communities between countries. By contrast, stillbirth rates may be one of the quality indicators of a country's medical system. Intrauterine fetal demise has multifactorial etiologies; little research has been conducted on other aspects of specific trimesters of pregnancy and stillbirth causes, and no such data is available in Taiwan. Our aims in this study were to analyze different risk factors for stillbirth in the second and third trimesters, and to set up a local database in Taiwan for global evaluation and comparison; early identification of timing-specified risk factors for stillbirth helps

\* Corresponding author. 5F, 325, Section 2, Cheng-Gong Road, Nei-Hu District, 114 Taipei, Taiwan.

E-mail address: [su108868@gmail.com](mailto:su108868@gmail.com) (H.-Y. Su).

physicians to reduce preventable factors and stillbirths, and improves general outcomes of pregnancy.

## Materials and methods

A retrospective analysis was performed of births registered in our hospital, a medical center in Taiwan, between September 1, 1999 and December 31, 2011. Terminations of pregnancies due to known chromosomal and congenital abnormalities were not included. We collected basic characteristics from medical records, including maternal age, maternal body mass index (BMI) at delivery, parity, habitual smoking, obstetric associated data of gestational age, cause of stillbirth, maternal condition, fetal gender and birth weight, and previous history of stillbirths. Gestational age was determined by the estimated date of delivery, while daily cigarette consumption during pregnancy was defined as the habit of smoking. The fetal birth weights and percentiles were calculated by the percentile sheet of fetal birth weight and corresponding gestational age, and fetal gender matched for the same residency and time period [2]. Stillbirths were classified according to the Executive Summary of a National Institute of Child Health and Human Development Workshop [3]. Some were classified as unexplained fetal losses, due to the absence of sufficient and evident obstetric history or findings at delivery. A single cause was assigned to each stillbirth. Stillbirths presented with primary causes and reasonable complications, such as hypertension and non-traumatic placental abruption, were assigned to the former etiology. All stillbirths were divided into two groups according to gestational age: the second trimester group included stillbirths occurring between 20 weeks and 0 days, and 27 weeks and 6 days of gestation, and stillbirths after 28 weeks and 0 days of gestation were assigned to the third trimester group. After obtaining oral informed consent via telephone and completing the data check, SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) was used for analysis. Comparisons of data between the groups were made by an independent sample *t* test for continuous data, and the Chi-square test and Fisher's exact test for

categorical data. A *p* value <0.05 in the two-tails hypothesis represented significance.

## Results

There were a total of 12,290 births and 121 stillbirths for intrauterine fetal demise after pregnancy at 20 weeks in our hospital during the period from September 1, 1999 to December 31, 2011. The 121 stillbirths were divided into two groups: 67/121 (55.4%) were in the second trimester group and 54/121 (44.6%) were in the third trimester group. In addition, there were 18/121 (14.9%) stillbirths that occurred at term pregnancy (after 37 weeks of gestation).

We observed no significant difference in the average age at delivery and parity between the second trimester group and the third trimester group. The average fetal birth weight for all stillbirths was 1129.2 g, compatible with the 11.9th percentile by the gestational age adjusted with gender ratio. The increased risks of third trimester stillbirths were significantly associated with males born, increased maternal BMI at delivery, habitual cigarette smoking, previous history of intrauterine fetal demise, and diabetic or hypertensive pregnancies, as compared with the second trimester group (Table 1).

The overall incidence for intrauterine fetal demise was 0.98% (121/12,290). The most common cause of second trimester intrauterine fetal demise was unexplained causes (29.85%), while the most common cause of third trimester intrauterine fetal demise was umbilical cord pathology (33.33%). Among the maternal medical conditions that resulted in stillbirths in the second trimester, two cases of out-of-hospital cardiac arrest due to traffic accidents were assigned to "others". Hypertensive disorders, all of which were pre-eclampsia in our study, accounted for the most common maternal medical conditions that resulted in stillbirth in the third trimester, and showed a significant increase over those in the second trimester (0% vs. 11.11%, *p* < 0.001). There were six diabetic pregnancies (6/121, 4.96%) in all stillbirths. Three of these were overt diabetes mellitus, including two cases of type I diabetes mellitus, and three were gestational diabetes

Table 1  
Patients' characteristics.

Characteristics	Average ( <i>n</i> = 121)	Second trimester <sup>a</sup> ( <i>n</i> = 67)	Third trimester <sup>a</sup> ( <i>n</i> = 54)	<i>p</i> <sup>a</sup>
Age (y)	31.02 ± 5.35	31.06 ± 5.33	30.96 ± 5.42	0.922
Gestational age (wk)	28.25 ± 6.42	23.20 ± 2.28	34.51 ± 3.83	<0.001
Parity	0.57 ± 0.73	0.58 ± 0.74	0.54 ± 0.72	0.736
BMI (kg/m <sup>2</sup> )	22.61 ± 1.72	22.32 ± 1.80	22.97 ± 1.56	0.037
Fetal gender (Male/female) (ratio)	63/58 (1.09)	34/33 (1.03)	29/25 (1.16)	<0.001
Birth weight (g)/percentile	1129.2 ± 989/11.9	475.9 ± 249.1/5.45	1939.8 ± 963.7/4.92	<0.001 <sup>b</sup> 0.249 <sup>c</sup>
Smoking (Y/N) (%)	8/113 (6.61%)	3/64 (4.48%)	5/49 (9.26%)	<0.001
Previous IUFD (Y/N) (%)	6/115 (4.96%)	3/64 (4.48%)	3/51 (5.56%)	<0.001
DM (Y/N) (%)	6/115 (4.96%)	1/66 (1.49%)	5/49 (9.26%)	<0.001
HTN (Y/N) (%)	6/115 (4.96%)	0/67 (0%)	6/48 (11.11%)	<0.001

Data are presented as *n* (%) or mean ± standard deviation.

BMI = body mass index; DM = diabetes mellitus; HTN = hypertension; IUFD = intrauterine fetal demise.

<sup>a</sup> Comparisons were made between the second and third trimester's results; <sup>b</sup> The comparison was made between the birth weights; <sup>c</sup> The comparison was made between the birth weight percentiles.

mellitus. In our cases of uterine complications that resulted in stillbirth, 9/13 (69.2%) were preterm premature rupture of membranes (PPROM) (8 in the second trimester and 1 in the third trimester), and 5/13 (38.5%) developed subsequent chorioamnionitis. The remaining stillbirth causes were three from cervical incompetence in the second trimester and one due to uterine fibroids in the third trimester (Table 2).

## Discussion

To the best of our knowledge, this is the first article focusing on stillbirth causes in Taiwan with matched trimesters of pregnancy. Stillbirth remains an event that has an important impact on global health issues. The incidences differ between countries and represented influences, such as development status, ethnicity, and even dietary habits. In our study, fetal demises more commonly occurred in the second trimester, and the overall stillbirth rate was 0.98%, which was similar to the reported rate of 0.9% from a nationwide survey in the same residency during 2001–2004 [4]. Although stillbirth events have declined by nearly half in Taiwan over the past decade, when compared with the international stillbirth rates in 2000, our national stillbirth rate was lower than that of East Asia (2.3%), but still higher than that of developed countries (0.5%) [1]. Despite the fact that national health support is provided to every pregnant woman, more progress on physician attendance and education in self-awareness among pregnant women is required to make further reductions in Taiwan's stillbirth rate.

With regards to maternal characteristics in our study, there was no significant difference in the average maternal age and parity between the two stages of pregnancy, but increased BMI was positively associated with stillbirths in the later stages of pregnancy. The trend of increased maternal age at delivery increases the risk of adverse perinatal outcomes [4]. Through routine antenatal care, advice regarding acceptable body weight increase should be followed.

The association between smoking, whether being a smoker during pregnancy or through passive exposure to environmental smoke, and increased risk of stillbirth is well documented [5]. Our study showed a more significant influence from smoking on stillbirths in the third trimester than the second trimester. This may result from longer cigarette exposure having a greater impact on the fetoplacental circulation. Smoking is a modifiable lifestyle, and through education and improvement of health literacy, opportunities are presented to reduce the potential and preventable stillbirths.

Our data showed that most stillbirths were small for gestational age, which is defined as birth weight below the 10th percentile for gestational age, especially in the third trimester. The lower average percentile of stillbirths in the third trimester than in the second trimester was probably because of the faster fetal growth in late pregnancy compared with the same time interval in early pregnancy, resulting in more prominent intrauterine growth restriction or delayed detection. Other studies revealed a similar finding, that nearly half of the stillbirths were small for gestational age [6]. The fetal weight is generally smaller in Asia than in America [7]. Using a regional growth chart makes identification of the growth-restricted fetus more readily available, and reduces false positives in the diagnosis of the physiological small fetus.

In our study, the average sex ratio (male/female) at birth of 1.09 was similar to the national data, from 1.088 to 1.096 [2]. Our data supported the finding of others, that there is no association between stillbirth rate and fetal sex [6]. However, we observed significantly male dominant stillbirths in the third trimester compared with the second trimester stillbirths. This may be due to the small sample size, and further study is needed on this association.

In the present study, umbilical cord pathology, including stricture, true knots, strangulation of fetus, and prolapse, was the third most common cause of stillbirth in the second trimester (16.42%), but became the leading cause in the third

Table 2  
Causes of intrauterine fetal demise (IUFD).

Causes	Second trimester IUFD n (%)	Third trimester IUFD n (%)	Total IUFD n (%)	Overall stillbirths rate (per 1000 births)
Umbilical cord pathology	11 (16.42%)	18 (33.33%)	29 (23.97%)	2.360
Unexplained causes	20 (29.85%)	8 (14.81%)	28 (23.14%)	2.278
Maternal medical conditions	4 (5.97%)	13 (24.07%)	17 (14.05%)	1.383
Hypertensive disorders	0 (0%)	6 (11.11%)	6 (4.96%)	0.488
Diabetes mellitus	1 (1.49%)	5 (9.26%)	6 (4.96%)	0.488
Thyroid disease	0 (0%)	1 (1.85%)	1 (0.83%)	0.081
SLE	1 (1.49%)	1 (1.85%)	2 (1.65%)	0.163
Others <sup>a</sup>	2 (2.99%)	0 (0%)	2 (1.65%)	0.163
Congenital anomaly and malformations	13 (19.40%)	3 (5.56%)	16 (13.22%)	1.302
Uterine complications	11 (16.42%)	2 (3.70%)	13 (10.74%)	1.058
Multifetal gestation complications	3 (4.48%)	4 (7.41%)	7 (5.79%)	0.570
Chromosomal abnormalities	4 (5.97%)	1 (1.85%)	5 (4.13%)	0.407
Placental abruption	0 (0%)	5 (9.26%)	5 (4.13%)	0.407
Antiphospholipid syndrome	1 (1.49%)	0 (0%)	1 (0.83%)	0.081
Total	67 (100%)	54 (100%)	121 (100%)	9.845

SLE = systemic lupus erythematosus.

<sup>a</sup> Two cases of out-of-hospital cardiac arrest were assigned to the 'others' category of maternal medical conditions.

trimester (33.33%) and total intrauterine fetal demise (23.97%). The significantly increased risk of stillbirths from cord pathology in the third trimester may be due to more fetal movement and growth in late pregnancy, where a sufficiently long umbilical cord may tighten over the fetal body and compress the cord in the relatively small intrauterine space, resulting in vessel compression and the ceasing of blood flow and fetal perfusion in the higher risks. Most cord accidents are sudden and unpredictable, and the prognosis for future pregnancies is believed to be favorable.

In our study, unexplained reasons accounted for the most stillbirths in the second trimester (29.85%), and were found to be the third highest cause (14.81%) in the third trimester and second most common for total stillbirths (23.14%). The proportion of uncertain reasons for intrauterine fetal demise ranged from 25% to 60%, despite extensive evaluation [8]. To identify the exact etiologies of stillbirth, experience and developed equipment are required.

Maternal medical conditions represented the fifth most common cause of stillbirth in the second trimester (5.97%), becoming the second most common in the third trimester (24.07%) and the third most common cause of total stillbirths (14.05%), with an incidence of 1.383/1000 births in our study. In general, when pregnancies occur along with maternal disease, the estimated stillbirth rate would be 6–7/1000 births, and hypertension and diabetes mellitus are the most common problems [9]. Our findings, in general, concurred with this. The trend of maternal medical conditions having a greater responsibility for stillbirths in late pregnancy may be because of the prominent disease's impact on the overall change of pregnancy as it progresses.

Fetuses born with abnormal anatomy may result from infection, genetic abnormalities, or maternal diseases such as diabetes mellitus [10]. Our data revealed that most congenital anomalies that caused fetal demise were located in the vital organs, such as the brain, and found in the second trimester, as the stillbirths resulting from chromosomal abnormalities. It is probable that the fetuses failed to thrive due to the lack of function of the vital organs. Many of these are syndromes and uniformly lethal *in utero* in the early stage of pregnancy. Subsequent genetic evaluations were insufficient. Fortunately, most of the genetic etiologies of stillbirth are from mutation, and most patients can be reassured in future pregnancies [11].

In our data, the most common uterine complication that resulted in stillbirth was PPRM that occurred in the second trimester. The causes of PPRM are multifactorial and the results differ with the gestational age. In PPRM in the second trimester, the stillbirth rate can be as high as 43% [12]. When subsequent chorioamnionitis developed, either primary or secondary, the stillbirth rate increased to 90.8% [13].

Multifetal gestation has a higher rate of complication, including fetal abnormalities, growth restriction, or twin-twin transfusion syndrome. Twin pregnancies complicated by growth restriction or growth discordance were associated with a high risk of intrauterine fetal demise. The overall incidence of intrauterine fetal demise for twin pregnancies was 55–57/1000 [14]. In our study, the demise of one twin was mostly

found in the third trimester, probably because the gestational week was counted when the surviving newborn was delivered. When one fetal demise in twin pregnancy occurs, the adverse effect on the surviving co-twin can be favorable [15]. More careful and intensive monitoring for multifetal gestation is necessary to reduce preventable complications.

Placental abruption is a condition where the placenta is separated from the uterine wall before labor, with the most immediate effect on the fetus being a cessation of blood flow causing acute asphyxia of the fetus. Stillbirths in placenta abruption are strongly associated with later gestation [16], and our data supported this conclusion.

Women who have experienced a stillbirth event require, not only a complete evaluation for this fetal loss, but also detailed information about the risk of recurrence to prepare for future pregnancy. When the current pregnancies are complicated with preterm delivery, growth restriction, placental abruption, or preeclampsia, the women are at increased risk of fetal demise in their subsequent pregnancies [16]. Our data showed that most stillbirths were due to umbilical cord complications, and recurrent fetal demise was only seen in six cases. The significant recurrence in late pregnancy may have resulted from our small sample size. The rarity of fetal demise means a promising outcome for the next pregnancy.

## Conclusion

In conclusion, it is an unfortunate fact that not all pregnancies end with healthy babies and healthy mothers. Management of any pregnant patient remains a challenge. Adequate antepartum testing is necessary to identify any potential underlying risk of stillbirth. More resources must be directed toward accelerating our understanding of these complex processes, and identifying upstream and cost-effective solutions that will improve these pregnancy outcomes.

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