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A comprehension of the etiologies of stillbirths through clinical, radiographic and autopsy findings: A study at Srinagarind Hospital, Khon Kaen, Thailand

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Abstract

Women experiencing stillbirths are at risks for postpartum depression and subsequent stillbirths. Determining the causes aids maternal coping and may prevent a similar outcome in subsequent pregnancies. The aim of the study is thus to determine the causes of stillbirth by clinical information, radiography, fetal autopsy, and placental examination. Medical records and autopsy studies of stillbirths between 2014 and 2018 at Srinagarind Hospital, Khon Kaen University were reviewed. Stillbirths with the parental consent, delivered at gestational age greater than or equal to 20 weeks or weight more than or equal to 500 grams, were grouped into 8 categories based on causes. Out of 102 stillbirths, the most common cause of stillbirths was placental abnormalities (38.2%). The most common cause of placental abnormalities was placental insufficiency (82.0%). The most common causes of stillbirth in gestational age 20-27^{+6} weeks were fetal malformations (29.0%) and placental abnormalities (29.0%). The most common cause of stillbirth in gestational age 28-33^{+6} weeks and gestational age >34 weeks was placental abnormalities (54.1% and 43.4%, respectively). Undetermined cause of stillbirth in all gestational ages was 8.8% and found mostly in gestational age 20-27^{+6} weeks (12.7%). We thus propose that the most prevalent cause of stillbirth was placental abnormality in every gestational age. The undetermined causes are low because of complete clinical information, radiography, fetal autopsy, and placental examination.

Keywords: Stillbirths, Fetal autopsy, Placental abnormalities, Placental insufficiency, Fetal malformations, Undetermined cause

1. Introduction

Fetal death is a psychological trauma for the woman and her family. Moreover, the woman experiencing stillbirth is at increased risk for postpartum depression and should be closely monitored [1].

The definition of stillbirth is a fetal death prior to complete extraction from the mother at gestational age (GA) ≥ 20 weeks or body weight (BW) ≥ 500 gm which is not performed termination of pregnancy [1]. 98% of stillborn fetuses occurring each year are from low- and middle-income countries [1,2,3]. The highest rates are in South Asia and sub-Saharan Africa [3,4]. Despite of improving medical technology, the rate of stillbirth is still high [1].

In general, the causes of stillbirths are classified into eight categories: obstetrical complications, placental abnormalities, fetal malformations, infections, umbilical cord abnormalities, hypertensive disorders, medical complications, and undetermined [1]. Many factors are associated with an increased risk of stillbirth. But it is specifically fivefold higher in women with a prior stillbirth [1].

Determining the causes of stillbirth can improve parental understanding and may prevent a similar outcome in subsequent pregnancies [1,5].

To ascertain the stillbirth causes, standardized evaluations are performed such as placental examination, maternal or fetal blood/tissues testing, fetal chromosome and autopsy [1].

Aim of this study is to determine the causes of stillbirth, through clinical information, radiography, fetal autopsy, and placental examination.

2. Materials and methods

After approval from the Khon Kaen University Ethics Committee for Human Research, medical records and autopsy results of stillbirths between January 2014 and December 2018 at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand were reviewed. There were 139 stillbirths in total, after excluding the terminated cases, with no autopsy consent form and no placental examination, the remaining cases were 102.

The clinical information of the cases (e.g. gestational age, maternal age, maternal history and underlying disease) was collected, fetal autopsies and placental examinations were performed by expert perinatal pathologists and residents of pathology department within 7 days. Radiographies were managed before autopsies. Histological examinations conducted within 1 month after autopsies. Then the final anatomical diagnosis was completed before postpartum follow-up in 6 weeks.

The causes of stillbirths were classified into eight categories: obstetrical complications, placental abnormalities, fetal malformations, infections, umbilical cord abnormalities, hypertensive disorders, medical complications, and undetermined. If there were two or more causes of stillbirth, the case was classified into multiple causes.

Statistical analysis was carried out with SPSS software (IBM, Armonk, NY, USA). The data were summarized as mean ± SD and number (percentage). Univariate analyses using the Chi-square test (X^2) were carried out to identify variables potentially associated with stillbirths, including maternal age, gestational age, and associated obstetrical conditions. A p-valve that is smaller than 0.05 was considered statistically significant.

3. Results

During the study period, 102 stillbirth information obtained from fetal autopsy findings, the mean maternal age was 27.5 years (ranging from 14 to 43 years) and mean gestational age was 28 weeks (ranging from 20 to 39^{+5} weeks). Baseline characteristics of the study samples summarized in Table 1. One stillbirth had the mother with preeclampsia, idiopathic thrombocytopenic purpura and HELLP syndrome. Three cases of vascular disease in mothers were composed of valvular heart disease, mycotic aneurysm and stroke. Two cases of thalassemia consisted of unknown type and beta-thalassemia/ hemoglobin E.

In this study, the stillbirths from elderly mothers (≥ 35-year-old) were mostly in and significantly associated with the first gestational age group (20-27^{+6} weeks) (p= 0.002).

Table 1 Baseline characteristics of the study samples.

Characteristics	All cases	Gestational age (weeks)		
	n = 102 (100%)	20-27^{+6}	28-33^{+6}	≥ 34
Gestational age (weeks)	27.8 ± 5.8	55 (53.9)	24 (23.5)	23 (22.5)
Maternal age (years)	27.5 ± 6.5	55 (53.9)	24 (23.5)	23 (22.5)
Fetal sex				
Male	46 (44.1)	25 (24.5)	8 (7.8)	13 (12.7)
Female	56 (54.9)	30 (29.4)	16 (15.6)	10 (9.8)
Maternal age (years)				
< 20	13 (12.7)	5 (4.9)	4 (3.9)	4 (3.9)
20- <35	75 (73.5)	37 (36.2)	20 (19.6)	18 (17.6)
≥ 35	14 (13.7)	13 (12.7)	0 (0)	1 (0.9)
Maternal U/D				
None	90 (88.2)	49 (48.0)	20 (19.6)	21 (20.5)
Hypertension	3 (2.9)	2 (1.9)	1 (0.9)	0 (0)
Other vascular disease	3 (2.9)	3 (2.9)	0 (0)	0 (0)
Infection	4 (3.9)	0 (0)	3 (2.9)	1 (0.9)
Thalassemia	2 (1.9)	1 (0.9)	0 (0)	1 (0.9)

Data are present as number (percentage) or mean ± standard deviation (SD).

Overall, the most common cause of stillbirths was placental abnormalities (38.2%, confidence interval [CI] 28.79% to 48.39%). The most common causes in gestational age 20-27^{+6} weeks were fetal malformations and placental abnormalities. The most common cause in gestational age 28-33^{+6} weeks was placental abnormalities. The most common cause in gestational age ≥34 weeks was placental abnormalities. Undetermined causes of stillbirths were 8.8%, which discovered mostly in gestational age 20-27^{+6} weeks (12.7%) (Table 2).

Table 2 Causes of stillbirth.

Cause of Stillbirths	All cases n = 102 (100%)	Gestational age (weeks) 20-27^{+6} n = 55 (53.9%)	28-33^{+6} n = 24 (23.5%)	≥ 34 n = 23 (22.5%)
Placental abnormalities	39 (38.2%)	16 (29.0%)	13 (54.1%)	10 (43.4%)
Fetal malformations	26 (25.4%)	16 (29.0%)	6 (25.0%)	4 (17.3%)
Obstetrical complications	18 (17.6%)	11 (20.0%)	2 (8.3%)	5 (21.7%)
Undetermined	9 (8.8%)	7 (12.7%)	0 (0%)	2 (8.6%)
Umbilical cord abnormalities	3 (2.9%)	1 (1.8%)	1 (4.1%)	1 (4.3%)
Infections	3 (2.9%)	1 (1.8%)	2 (8.3%)	0 (0%)
Multiple causes	2 (1.9%)	1 (1.8%)	0 (0%)	1 (4.3%)
Hypertensive disorders	1 (0.9%)	1 (1.8%)	0 (0%)	0 (0%)
Medical complications	1 (0.9%)	1 (1.8%)	0 (0%)	0 (0%)

There were two cases with multiple causes of stillbirth (1.9%). The first case causes were obstetrical complication (conjoined twins) with fetal malformation (thoraco-omphalophagus) and placental insufficiency. The second case causes were infection (acute funisitis and acute chorioamnionitis) with fetal malformation (hypoplastic lungs, ventricular septal defect, hypoplastic left side of heart and right ventricular hypertrophy) and placental insufficiency.

In the cases of placental abnormalities, the most common cause was placental insufficiency (82.0%). In the cases of fetal malformation, the most common cause was hydrops fetalis with anemia (19.2%). In the case of obstetrical complications, the most common cause was twins with twin-twin transfusion syndrome (38.8%) (Figure 1 A-C). Two cases of placental abruptions had history of maternal accident.

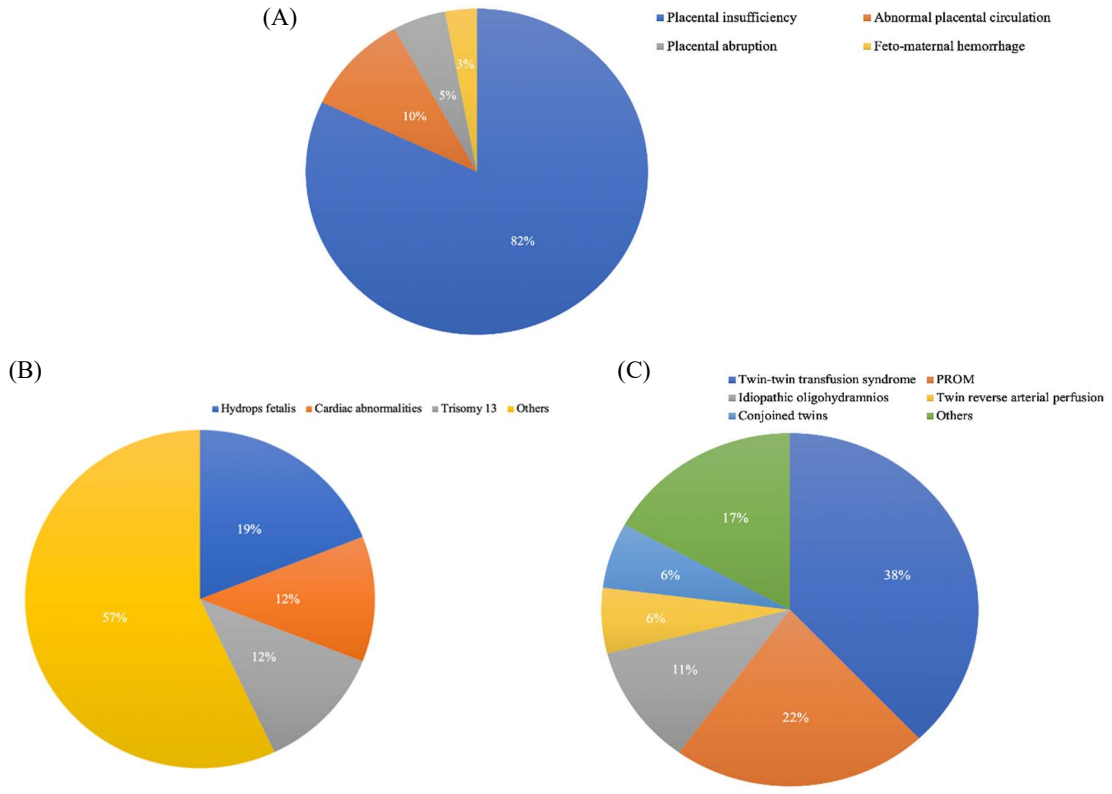

Figure 1 (A) Causes of placental abnormalities, (B) fetal malformation, and (C) obstetrical complications.

4. Discussion

In this study, most stillbirths are in early gestational age (gestational age 20-27+6 weeks), similar to the previous study [6]. The study shows an association between maternal age and gestational age statistical significance (p= 0.002), that early stillbirths occur more in elderly pregnancy (≥ 35-year-old) [7]. The most

common cause of stillbirths in all gestational age groups is placental abnormalities (38.2%), following by fetal malformations (25.4%) and obstetrical complications (17.6%). These three common causes are compatible with other previous studies [1,4,8].

The undetermined causes were 8.8% and found mostly in early gestational age. The percentage was lower than other studies [9,10,11] due to full clinical information, radiography, fetal autopsy, and placental examination.

Placental pathology is very important for identifying causes of fetal death, low birth weight and obstetrical complications. This study confirms the high frequency of placental abnormalities in stillbirths. In practice, obstetricians still neglect placenta in some cases. If they are aware the importance of placenta, then they could help perinatal pathologists to identify causes of stillbirth.

The elderly pregnancy increased the risk of stillbirth in early gestational age. The antenatal care of this special group is essential to perform and achieve improved good fetal outcomes.

The study had advantages because of no similar study ever conducted in Thailand, the excellent clinicopathological correlation in sending stillbirth cases for studies, having an expert perinatal pathologist and receiving placenta in almost all cases. In some cases of stillbirths did not undergo some standard testing, viral studies and karyotyping which was the limitation of this study.

In further study, mothers with stillbirths should be evaluated completely before and after delivery. The other interesting aspects such as psychosocial, postpartum counselling and future pregnancy needs further research study.

5. Conclusion

The most common cause of stillbirths in the present study is placental abnormalities in all gestational age groups and placental insufficiency is the most common cause of all placental abnormalities. The undetermined causes are low because of complete clinical information, radiography, fetal autopsy, and placental examination.

6. Ethical approval

The study was approved by the Khon Kaen University Ethics Committee for Human Research with # HE621364.

7. Acknowledgements

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