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Original Research Paper

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INCIDENCE AND RISK FACTORS OF STILLBIRTH

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ABSTRACT **Objectives:** To study the incidence and risk factors of stillbirth in Udon Thani Hospital. **Materials and Methods:** A case-control study was performed by retrospective review of medical records of pregnant patients who delivered in Udon Thani Hospital between 2015-2019. The incidence of stillbirths each year were calculated by the number of stillbirths per 1,000 total births. The possible risk factors were compared between the stillbirth group and the control group which was selected from the patients who delivered before and after stillbirth cases (1 case: 2 control). **Results:** There were 22,254 total births between 2015-2019 with 172 stillbirths (7.7 per 1,000 total births). The incidence of stillbirths per year were: 6.7(2015), 6.3(2016), 8.9(2017), 9.3(2018), and 7.7(2019) per 1,000 total births. The causes of stillbirth were: fetal anomalies 19.2%, hydrops fetalis 5.8%, other causes (placental and umbilical cord complications etc.) 20.9%, birth asphyxia 5.2% and unknown cause 48.8%. Maternal diseases were found in 15.7% of cases: hypertension 11.1% and diabetes mellitus 4.1%. The following stillbirth risk factors with their adjusted odd ratio and 95% confidence interval were: the late first antenatal visit (ANC) (after 12 weeks of gestation) 1.79(1.04-3.07), hepatitis B infection 7.17(1.23-41.73), multiple pregnancy 7.03(1.65-29.78), non-vertex fetal presentation 5.14(2.42-10.87), meconium strained amniotic fluid (AF) 3.37(1.63-6.95), and fetal growth restriction (FGR) 7.37(2.76-19.66). **Conclusion:** Stillbirth in Udon Thani Hospital is still problematic. The incidence of stillbirth was 7.7 per 1,000 total births in 2015-2019. The antenatal and intrapartum associated risk factors from this study were history of no ANC or first ANC after 12 weeks, hepatitis B, multiple pregnancy, non-vertex fetal presentation, meconium strained AF and FGR. The associated risk factors can be used to increase awareness and monitoring in risk cases.

KEYWORDS : stillbirth, perinatal mortality, risk factor

INTRODUCTION

Globally, there are nearly 2 million stillbirths every year. A loss that could be avoided with improved quality and respectful care during childbirth including routine monitoring and timely access to emergency obstetric care when required. There are psychological costs to women, and their families, such as maternal depression, financial consequences and economic percussions.[1]

World Health Organization defines stillbirth as a baby born with no signs of life at or after 28 weeks gestation[2]. *American College of Obstetricians and Gynecologists* defines fetal death at 20 weeks or greater of gestation, or a weight greater than or equal to 350 grams if the gestational age is not known [3]. The Department of Health, Ministry of Public Health of Thailand defines stillbirth fetal deaths at 22 weeks or greater of gestation [4]. Stillbirth is an important global maternal and child health problem, the incidence in 2015 was 2.6 million worldwide with three-fourths occurred in developing countries [2]. In Thailand, incidence of stillbirth was 5.7 per 1,000 total births in 2019 [5]. The Eighth Regional Health Center of Thailand reported the stillbirth rate was 5.3 per 1,000 total births in 2019[6] in upper Northeast area of Thailand.

Several studies reported the incidence and associated risk factors of stillbirth [7-11]. Previous study in England during 2009-2011 by Gardosi J et al.[7] reported the stillbirth rate was 4.2 per 1,000 total births. The significant risk of stillbirth was parity (para 0 and para ≥3), ethnicity (African, African-Caribbean, Indian, and Pakistani), maternal obesity (body mass index ≥30), smoking, pre-existing diabetes, and history of mental health problems, antepartum hemorrhage, and fetal growth restriction (birth weight below 10th customized birthweight centile). Prasunnakarn S et al. [12] reported the stillbirth rate was 11.3 per 1,000 total births in Udon Thani province in 1996. The causes of death were macerated stillbirth 29.7%, prematurity 28.4%, asphyxia 18.5%, congenital malformation 13.6% and some specific conditions 9.8%.

There were many causes and risk factors that were different by region. The knowledge of incidence and risk factors of stillbirth in the Thai population will help obstetricians and Health policy maker for accurate planning and care of risk cases. The objective of this study was to find the incidence and risk factors of stillbirth for better understanding and management for preventing this problem.

MATERIAL AND METHOD

A case-control study was conducted with pregnant women who delivered in Udon Thani Hospital between 2015-2019. The retrospective medical records were reviewed. The inclusion criteria were pregnant women who delivered at 22 weeks or greater of gestation in Udon Thani Hospital between 2015-2019. The study protocol was approved by Udon Thani Research Ethics Committee (number 65/2019).

Data were collected which consisted of baseline characteristics, gravidity, parity, maternal disease such as hypertension, diabetes mellitus, thyroid disease, asthma, HIV infection, thalassemia, maternal education, antenatal visit history,

history of previous surgery, previous stillbirth, alcohol, smoking, illicit drug use, delivery and complication, intrapartum fetal distress, PROM, serology, maternal vital signs, and causes of stillbirth. The causes of stillbirth were fetal anomalies, hydrops fetalis, birth asphyxia (a lack of blood flow or gas exchange to the fetus in the process during labor [13], diagnosis criteria is APGAR score at 1 minute less than 7 [14]), other causes include placental complication (placental abruption, placenta previa, placenta accreta, retained placenta or piece of placenta), umbilical cord complication (tight nuchal cord, cord prolapse or avulsion), uterine rupture, rupture vasa previa, multifetal pregnancy complication (*Twin* to *Twin Transfusion Syndrome, One fetal demise*), chorioamnionitis.

The sample size was calculated according to primary outcome by the formula for a estimated proportion using the estimated incidence of stillbirth at 1% [12], a 5% chance of making a type 1 error and acceptable error of 0.15%. The result was 16,903 women were needed for the study. According to the number of deliveries in Udon Thani Hospital was about 4,000 per years, the estimated period of study was 5 years. The incidence of stillbirths each year were calculated by the number of stillbirths per 1,000 total births. For secondary outcome to identify the risk factors of stillbirth, the possible risk factors were compared between the stillbirth group and the control group which was the patients who delivered before and after stillbirth cases. (1 case: 2 control).

Statistical analysis was performed using StataCorp Release 13 statistical software. The sample size was calculated by the statistical program using the proportion estimation formula with 0.80 power and 0.05 alpha error. The descriptive variables were presented by mean ± standard deviation or number with percentage depended on character of variable. The possible associated factors of stillbirth were evaluated by bivariate and multivariable logistic regression. Comparison of the two groups was shown by crude and adjusted odd ratio and 95% confidence interval for magnitude of effect. The adjusted odd ratio was calculated by multivariable logistic regression analysis if p-value from bivariate analysis < 0.1 and p-value <0.05 was considered statistically significant.

RESULTS

There were 22,254 total births with 172 stillbirths (7.7 per 1,000 total births) between 2015-2019 in Udon Thani Hospital. The incidence of stillbirths each year were 6.7, 6.3, 8.9, 9.3, 7.7 per 1,000 total births during 2015-2019, respectively. A total of 516 patients were in this study which was 172 case group and 344 control group. Stillbirth rates by year and causes are shown in Table 1. The causes of stillbirth were: fetal anomalies 19.2%, hydrops fetalis 5.8%, Others causes 20.9% (Placental and umbilical cord complication, uterine rupture, rupture vasa previa, preterm, multifetal pregnancy complication (*Twin* to *Twin Transfusion Syndrome, One fetal demise*) and chorioamnionitis), birth asphyxia 5.2% and unknown cause 48.8%.

Most patients delivered at term gestation. The route of delivery was mostly vaginal route in either stillbirth or control group. The mean birthweight was 2649.4±875.7 grams. The stillbirth group had more preterm births (GA<37weeks), more low birthweight (mean birthweight 1878.9±915.0 grams), fetal anomalies (N=46; 26.7%). The delivery detail is presented in Table 2.

Possible associated factors by bivariate analysis were maternal age <20 years, no ANC or first antenatal visit after 12 weeks, maternal syphilis and hepatitis B infection, smoking, multiple gestation, history of decreased fetal movement, antepartum hemorrhage, weight gain during pregnancy, decrease amount of amniotic fluid, meconium strained amniotic fluid, and fetal growth restriction. Maternal diseases were found in 15.7% of cases; hypertension in 11.1% and diabetes mellitus in 4.1%. Possible associated factors are shown in Table 3.

The associated factors of stillbirth after adjusted by multivariable logistic regression analysis were: no history of antenatal care or late antenatal care visit (after 12 weeks of gestation), hepatitis B infection, multiple pregnancy, non-vertex fetal presentation, meconium strained amniotic fluid, and fetal growth restriction. Associated factors are shown in Table 4.

Table 1 Stillbirth rate by year and cause.

Cause	2015	2016	2017	2018	2019	Total(N)
Total birth (N)	4,948	4,621	4,460	4,208	4,017	22,254
Stillbirth, N (rate/ 1,000 total births)	33 (6.7)	29 (6.3)	40 (8.9)	39 (9.3)	31 (7.7)	172 (7.7)
Hydrops fetalis	2	1	2	4	1	10
Fetal anomalies	6	7	9	5	6	33
Birth asphyxia	1	1	3	1	3	9
Others*	7	5	6	11	7	36
Unknown	17	15	20	18	14	84

*Others includes placental and umbilical cord complication, uterine rupture, rupture vasa previa, multifetal pregnancy complication (*Twin* to *Twin Transfusion Syndrome, One fetal demise*), chorioamnionitis

Table 2 Detail of delivery

	Total (N=516)	Stillbirth (N=172)	Control (N=344)	P value*
GA (weeks), mean ± SD	36.4±3.7	33.3±4.2	37.9±2.2	<0.001**
<37	181(35.1%)	126(73.3%)	55(15.9%)	<0.001**
≥37	335(64.9%)	46(26.7%)	289(84.0%)	
Route of delivery				
Vagina	308(59.7%)	128(74.4%)	180(52.3%)	<0.001**
Cesarean	208(40.3%)	44(25.6%)	164(47.7%)	
Birthweight(grams), mean ± SD	2,649.4±875.7	1,878.9±915.0	3,024.5±551.3	<0.001**
Fetal sex				
Male	264(52.1%)	97(58.4%)	167(48.9%)	0.045**
Fetal anomalies	50(9.7%)	46(26.7%)	4(1.2%)	<0.001**
Placental complication***	47(9.1%)	34(19.8%)	13(3.8%)	<0.001**

* P-value was calculated from unpaired t test for continuous data and Pearson's chi-square for discrete data

** Statistical significance

*** placental complications include placental abruption, placenta previa, placenta accreta, retained placenta or piece of placenta

Abbreviation; GA: gestational age, SD: standard deviation

Table 3 Possible associated factors and Odd ratio with 95% confidence interval

Factors	Total (N=516)	Stillbirth (N= 172)	Control (N = 344)	Odd ratio (95% CI)	p-value*
Age(years), mean ± SD	26.7±7.3	26.4±7.9	26.8±6.9	0.9(0.9-1.0)	0.623
<20	**94(18.2%)**	**40(23.3%)**	**54(15.7%)**	**1.6(1.0-2.6)**	**0.037**
20-34	337(65.3%)	103(59.9%)	234(68.0%)	Ref	Ref
≥35	85(16.5%)	29(16.9%)	56(16.3%)	1.0(0.6-1.7)	0.867
Gravida, mean ± SD	1.9±1.1	1.9±1.0	2.0±1.1	0.9(0.8-1.1)	0.344

Primigravida	210(40.7%)	72(41.9%)	138(40.1%)	1.1(0.7-1.6)	0.704
No ANC	**27(5.2%)**	**15(8.7%)**	**12(3.5%)**	**2.6(1.2-5.8)**	**0.015**
First ANC after 12 weeks	**102(23.3%)**	**42(33.1%)**	**60(19.3%)**	**2.1(1.3-3.3)**	**0.002**
HIV	4(0.8%)	3(1.7%)	1(0.3%)	6.1(0.6-58.6)	0.120
Maternal syphilis	**11(2.1%)**	**7(4.1%)**	**4(1.2%)**	**3.6(1.0-12.4)**	**0.044**
Hepatitis B	**9(1.8%)**	**6(3.5%)**	**3(0.9%)**	**4.1(1.0-16.5)**	**0.049**
Maternal anemia (Hct<33%)	117(23.3%)	45(27.3%)	72(21.3%)	1.4(0.9-2.1)	0.138
Education					
Primary school or less (≤6 years)	**101(19.6%)**	**41(23.8%)**	**60(17.4%)**	**1.5(0.9-2.3)**	**0.085**
Secondary school or more (>6 years)	415(80.4%)	131(76.2%)	284(82.6%)	Ref	
Smoking (primary and secondary)	**131(24.8%)**	**34(19.8%)**	**97(28.2%)**	**0.6(0.4-0.9)**	**0.039**
Alcohol	6(1.2%)	2(1.2%)	4(1.2%)	1.0(0.2-5.5)	1.00
Previous stillbirth	35(6.8%)	9(5.2%)	26(7.6%)	0.7(0.3-1.5)	0.325
Maternal disease	65(12.6%)	27(15.7%)	38(11.1%)	1.5(0.9-2.5)	0.135
Hypertension	**39(7.6%)**	**19(11.1%)**	**20(5.8%)**	**2.0(1.0-3.9)**	**0.037**
Diabetes Mellitus	20(3.9%)	7(4.1%)	13(3.8%)	1.1(0.4-2.8)	0.872
Multiple pregnancy	**17(3.3%)**	**14(8.1%)**	**3(0.9%)**	**10.1(2.9-35.5)**	**<0.001**
PROM	53(10.3%)	17(9.9%)	36(10.5%)	0.9(0.5-1.7)	0.838
Antepartum hemorrhage	**14(2.7%)**	**11(6.4%)**	**3(0.9%)**	**7.8(2.1-28.2)**	**0.002**
Intrapartum Fetal distress	77(14.9%)	30(17.4%)	47(13.7%)	1.3(0.8-2.2)	0.257
Maternal weight gain, mean ± SD	12.9±6.0	10.3±5.5	14.3±5.9	0.9(0.8-0.9)	<0.001
BMI, mean ± SD	**27.3±4.9**	**26.3±4.9**	**27.7±4.8**	**0.9(0.9-0.9)**	**0.003**
<18.5	7(1.4%)	3(1.8%)	4(1.2%)	1.5(0.3-6.9)	0.582
≥30	135(26.3%)	38(22.4%)	97(28.2%)	0.7(0.5-1.1)	0.157
Non vertex fetal presentation	**55(10.7%)**	**41(23.8%)**	**14(4.1%)**	**7.4(3.9-13.9)**	**<0.001**
Oligohydramnios (AFI<5)	**36(6.9%)**	**21(12.2%)**	**15(4.4%)**	**3.1(1.5-6.1)**	**0.002**
Meconium strained AF	**54(10.5%)**	**31(18.0%)**	**23(6.7%)**	**3.1(1.7-5.5)**	**<0.001**
Nuchal cord	68(13.2%)	22(12.8%)	46(13.4%)	0.9(0.6-1.6)	0.854
FGR	**39(7.6%)**	**29(16.9%)**	**10(2.9%)**	**6.8(3.2-14.3)**	**<0.001**

* P-value was calculated from bivariate logistic regression analysis

Abbreviation; ANC: antenatal care, HIV: *human immunodeficiency virus*, Hct: hematocrit, PROM: premature rupture of membranes, BMI: body Mass Index, AFI: amniotic fluid index, AF: amniotic fluid, FGR: fetal growth restriction

Table 4 Possible associated factors and adjusted odd ratio with 95% confidence interval

Factors	Odd ratio (95% CI)	Adjusted Odd ratio* (95% CI)	p-value
Teenage pregnancy	1.63(1.02-2.57)	1.17(0.62-2.21)	0.635
No ANC or ANC after 12 weeks	2.06(1.30-3.29)	1.79(1.04-3.07)	0.035
Maternal syphilis	3.59(1.04-12.42)	2.79(0.46-16.96)	0.266
Hepatitis B	4.08(1.00-16.53)	7.17(1.23-41.73)	0.028
Education ≤6 years	1.49(0.95-2.31)	1.65(0.89-3.05)	0.111
Smoking (primary and secondary)	0.63(0.40-0.98)	0.61(0.34-1.10)	0.098
Maternal disease (Hypertension)	2.01(1.04-3.87)	1.75(0.64-4.81)	0.276
Multiple pregnancy	10.07(2.85-35.54)	7.03(1.65-29.78)	0.008
Antepartum hemorrhage	7.77(2.13-28.22)	5.00(0.88-28.48)	0.070
BMI, mean ± SD	0.94(0.90-0.98)	0.96(0.91-1.01)	0.182
Non vertex fetal presentation	7.38(3.89-13.99)	5.14(2.42-10.87)	<0.001
Oligohydramnios (AFI <5)	3.05(1.52-6.08)	1.68(0.65-4.27)	0.281
Meconium strained AF	3.07(1.72-5.45)	3.37(1.63-6.95)	0.001
FGR	6.77(3.22-14.27)	7.37(2.76-19.66)	<0.001

*Adjusted odd ratio was calculated by multivariable logistic regression analysis if p-value from bivariate analysis < 0.1

DISCUSSION

Stillbirth remains a problem in maternal healthcare worldwide. From this study, incidence of stillbirth in Udon Thani Hospital was 7.7 per 1,000 total births. This rate is similar to a 2019 report from Khonkean Hospital, Khonkean which reported 7.1 stillbirths per 1,000 total births but is less than a report from Buddhachinaraj Hospital, Phitsanulok [15] which was 12.5 stillbirths per 1,000 total births. In developing countries, stillbirth rate remains high. Saleem S et al. [16] reported stillbirth rates were 21.3 per 1,000 total births for Africa, 25.3 per 1,000 total births for India, 56.9 per 1,000 total births for Pakistan and 19.9 per 1,000 total births for Guatemala. These data collected from 2010-2016.

The results of this study showed that the causes of stillbirth were: unknown 48.8 %, other causes (placental and umbilical cord complication, uterine rupture, rupture vasa previa, multifetal pregnancy complication, chorioamnionitis) 20.9%, fetal anomalies 19.2%, hydrops fetalis 5.8%, and birth asphyxia 5.2%. This was similar to previous studies from Canada by Smith SN et al. [8] and from the United States by Hoyert DL et al. [11] which reported causes of fetal death were unspecified causes and others causes such as complications of placenta, umbilical cord and membranes, respectively. The autopsy was not done in most cases of stillbirth due to lack of facility, therefore the cause which are unknown might be due to this limitation.

The associated risk factors of stillbirth from this study were history of no antenatal care or late antenatal care (ANC after 12 weeks of gestation), Maternal hepatitis B, Multiple pregnancy, non-vertex fetal presentation, meconium strained amniotic fluid and fetal growth restriction. A significant risk of stillbirth from a previous study by Gardosi J et al. [7] which is similar to this study is fetal growth restriction.

Most of the risk factors can be detected during the antenatal care period. For instance, maternal hepatitis B, multiple pregnancy, non-vertex fetal presentation, fetal growth restriction, and fetal anomalies. The preventable causes of stillbirth were encourage early antenatal care. These associated risk factors can be used to increase awareness and monitoring in risk cases. The clinical application is the

findings indicate the importance of improving current strategies and protocols for improved fetal surveillance throughout the antenatal period. Confounding variables could not be determined and missing data because we collected by retrospective medical record review. An autopsy was not done in all cases of stillbirth due to lack of facility, therefore the cause which is unknown might be due to this limitation.

CONCLUSION

Stillbirth in Udon Thani Hospital is still problematic. The incidence of stillbirth was 7.7 per 1,000 total births in 2015-2019. The antenatal and intrapartum associated risk factors from this study were history of no ANC or first ANC after 12 weeks, Hepatitis B, Multiple pregnancy, Non vertex fetal presentation, Meconium strained AF and FGR. The associated risk factors can be used to increase awareness and monitoring in risk cases.

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Potential conflicts of interest

The authors declare no conflict of interest.

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