Risk Factor of Stillbirth among Pregnant Women at Dr. Hasan Sadikin General Hospital Bandung from 2017–2020

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Abstract

Background: Stillbirth is one of the most devastating pregnancy outcomes that affects approximately 2.6 million pregnancies worldwide. Several factors have been identified to be associated with stillbirth, and grouped based on the pathophysiological aspects, such as maternal, placental, fetal, and unknown or unexplained factors. This study aimed to describe the prevalence, along with the baseline and risk factor characteristics of stillbirth among singleton pregnancies at Dr. Hasan Sadikin General Hospital Bandung.

Methods: A descriptive, cross-sectional study design was conducted, including all stillbirth medical records from 2017 to 2020 obtained from the Department of Obstetrics and Gynecology, Dr. Hasan Sadikin General Hospital Bandung. Medical records with complete baseline data, 2nd–3rd trimester pregnancies, and singleton pregnancies were collected.

Results: The prevalence of stillbirth cases in this study was 2.2%. Most of the cases occurred in the age range of 20–35 years old (64.4%) with the gestational age of >28 weeks (65.8%). Of all risk factors observed, hypertensive disorders were the most common medical conditions found (45.6%), followed by unknown factors (17.8%), and congenital abnormalities (14.2%).

Conclusions: The majority of stillbirth patients are at their optimal reproductive age, nulliparity, and have hypertensive disorders during pregnancy, specifically the superimposed preeclampsia subtype. Although the prevalence is considerably low, early management of the risk factors, particularly hypertensive disorder, is important to prevent its occurrence.

Keywords: Characteristics, prevalence, risk factor, stillbirth

Introduction

Stillbirth is a pregnancy condition when the fetus dies at 20 weeks' gestation or after.[1] The World Health Organization (WHO) has different criteria in defining stillbirth, primarily from the gestational age and fetal weight aspects. For international comparison and reporting, WHO set 28 weeks of gestation as the cut-off and 1,000 grams as the weight. Classification of stillbirth is based on the gestational age (in weeks) when the diagnosis is established, for stillbirth that occurrs from 20 to 28 weeks of gestation is called early stillbirth, and after 28 weeks as late stillbirth. Another classification relies on its occurrence between any time during labor/delivery period, with antepartum stillbirth that occurred before labor onset and intrapartum stillbirth that occurred during the labor process.[2]

On average, 2.6 million stillbirth cases were reported worldwide in 2015 (varies from 2.4–3.0 million), with 98% of cases reported being from low and middle-income countries and 66% from developing countries. One of them is Indonesia which took the eighth position as a country with the highest number of stillbirth cases, along with other nations such as India, China, and Pakistan.[3] In Indonesia, there were 3,097 cases reported in West Java province from a total of 935,003 births and 129 cases in Bandung city from a total of 39,571 births, with the number of cases mentioned were accumulated from both male and female fetuses.[4]

Several factors associated with stillbirth are classified based on the pathological origin, such as maternal, fetal, placental,

external/obstetric, and unknown origin. Other classification systems are also available: Relevant Condition at Death (ReCoDe), Causes of Death and Associated Conditions (CODAC), Tulip, Perinatal Society of Australia and New Zealand-Perinatal Death Classification (PSANZ-PDC), and International Classification of Diseases 10th Revision-Perinatal Mortality (ICD-PM).[2,6,7]

Stillbirth affects the mother and the family psychologically, and researches have shown that higher depression and anxiety level were found in women with prior history of stillbirth compared to women with no prior history.[5] This study aimed to describe the prevalence, baseline, and risk factor characteristics of stillbirth among singleton pregnancies at a tertiary hospital from 2017–2020.

Methods

This study was a descriptive cross-sectional study; samples were collected from the Department of Obstetrics and Gynecology, Dr. Hasan Sadikin General Hospital Bandung by total sampling. Inclusion criteria were stillbirth medical records with complete baseline characteristics data, 2nd–3rd trimester pregnancies, and singleton pregnancies. Medical records with incomplete baseline data and multiple gestations (twin pregnancies) were excluded from this study.

Baseline characteristics consisted of maternal age (years), gestational age (weeks), obstetrical status (parity and abortion), on-site body mass index, and a number of risk factors. The risk factors assessed were hypertensive disorders in pregnancy that comprised of preeclampsia, superimposed preeclampsia, eclampsia, and chronic hypertension,[8,9] intrauterine infection, diabetes mellitus, that further subdivided into type 1 and type 2, amniotic fluid abnormalities, anemia in pregnancy, premature rupture of membrane (PROM), intrauterine growth restriction (IUGR), antepartum hemorrhage (APH), placental abruption, umbilical cord prolapse. Congenital abnormalities, specifically major type, were based on the National Birth Defects Prevention Network (NBDPN) and defined as abnormalities that required surgery or medical treatment, had a serious impact on health, or had a significant impact on appearance.[10] Unknown/unexplained factor is defined as the absence of any clinical risk factors or causes of death based on the antenatal examination, placental, and fetal autopsy.[2,11]

Data from medical records were collected after obtaining ethical clearance from the Research Ethics Committee Universitas Padjadjaran (739/UN6.KEP/EC/2021) and Dr. Hasan Sadikin General Hospital Bandung (LB.02.01/X/2.2.1/19986/2021). Eligible data were processed by using Microsoft Excel 2019 and IBM® SPSS® 25.

Results

There were 385 stillbirth cases recorded from a total of 10,166 births counted from 2017 to 2020. Of 385 stillbirth cases, 92 data were not available, and 74 data did not meet the inclusion criteria, with the distribution as follows: three twin pregnancies, one data with unknown maternal age, five patients with a gestational age of <20 weeks (miscarriage), 11 patients with unknown gestational age, and 54 incorrect/inaccurate data. Hence, the rest 219 subjects were used, making the prevalence of stillbirth in this study 2.2%, with a case rate of 22 per 1,000 births.

Baseline characteristics (Table 1) showed the highest cases count among patients aged 20–35 years old (n=141, 64.4%) and >28 weeks' gestational age group (n=144, 65.8%). The mean and median for the maternal age were 30 and 31 years old, respectively. Meanwhile for the gestational age, both the mean and median were 30 years old. Obstetrical status showed high cases among zero parities and one parity. Most of the patients had never had an abortion. Data regarding the body mass index (BMI) of patients were obtained from the measurement done in the first 12 hours since the patients admitted to the hospital, not from the pre-pregnancy nor first trimester BMI due to the absence of data.

Based on the risk factor characteristics, most patients had hypertensive disorders during pregnancy (n=100, 45.6%), which further classified into preeclampsia (n=27, 12.3%), superimposed preeclampsia (n=55, 25.1%), eclampsia (n=16, 7.3%), and chronic hypertension (n=2, 0.9%); followed by unknown origin (n=39, 17.8%) the diagnosis was made from the absence of any pathological evidence from the antenatal history, physical and laboratory examinations (as indicated) and fetal autopsy; and major congenital abnormalities (n=31, 14.2%).

Some abnormalities in this study were classified based on the organs involved, such as (1) neural tube defects (NTDs) comprised of anencephaly, hydranencephaly, corpus callosum agenesis, and alobar holoprosencephaly, (2) congenital heart

Table 1 Baseline Characteristics of Mothers who Had a Stillbirth at the Department of Obstetrics & Gynecology, Dr. Hasan Sadikin General Hospital Bandung 2017–2020

Characteristics	Results (n= 219)		
	n	%	x̄ (min-max)
Age (years)			30 (14 – 44)
<20	14	6.4	
20–35	141	64.4	
>35	64	29.2	
Gestational age (weeks)			30 (20 – 42)
20–28	75	34.2	
>28	144	65.8	
Obstetrical status			
Parity			
0	67	30.6	
1	66	30.1	
2	56	25.6	
≥3	30	13.7	
Abortion			
0	181	82.7	
1	29	13.2	
2	9	4.1	
≥3	0	0	
Body mass index* (kg/m^2)	20–28 weeks n=75	>28 weeks n=144	26.9 (17.6 – 50.4)
<18.5	1	0	
18.5–22.9	33	27	
23–24.9	15	22	
≥25	26	95	

defects (CHD): Tetralogy of Fallot (ToF), ectopia cordis, and fetal pericardial effusion, and (3) congenital gastrointestinal disorders consisting gastroschisis, duodenal atresia and congenital diaphragmatic hernia. The results showed hydrops fetalis outnumbered the other abnormalities subtypes (n=12, 5.5%) (Table 2). Assessment of the distribution of risk factors showed the highest cases among patients with single risk factors (Table 3).

Discussion

The prevalence of stillbirth in this study is 2.2%, resulting in the SBR of 22 cases per 1,000 births. This result is almost two times higher than the goal set by Sustainable Development Goals (SDGs); with an SBR target of fewer than 12 cases per 1,000 births. The mean age of the patients included in this study is 30 years old. Approximately 64.4% of cases occurred in the age range of 20–35 years, corresponding with the previous study done on the nearby region, Tasikmalaya district, West Java Province in 2017, where the highest occurrence of stillbirth belong to the population between 20–

35 years old with the percentage of 68.4%.[12] Other studies done in Nepal from 2017–2019 and Ethiopia in 2018 showed similar results, where most of the cases have occurred at the age range of 21–30 years old (67.1%) and 20–34 years old (77.7%), respectively.[13,14]

Stillbirth at 28 weeks gestation or after was more frequently seen in this study with a median of 30 weeks. Similar results were also reported in the United States of America from March 2020–September 2021, 55.8% with a median of 29 weeks.[15] Obstetrical status based on the previous study from Tasikmalaya district in 2017 and Global Network Sites from 2010–2019 both showed the highest cases count among primiparity and multiparity rather than nulliparity, meanwhile, nulliparity accounted for the highest cases count (30.6%) in this study.[12,16] BMI was measured in the first 12 hours since the patient was admitted to the hospital. Pre-pregnancy and first-trimester anthropometry data were unavailable since most of the patients got antenatal care outside the study location, and the rest of them got no antenatal care.

Almost half of the patients in this study had

Table 2 Risk Factor of Stillbirth at the Department of Obstetrics and Gynecology Dr. Hasan Sadikin General Hospital Bandung 2017–2020

Risk Factors	Subtypes	Results	
		n	**%**
Unknown/unexplained		39	17.8
Maternal	Hypertensive disorders in pregnancy		
	Preeclampsia	27	12.3
	Superimposed preeclampsia	55	25.1
	Eclampsia	16	7.3
	Chronic hypertension	2	0.9
	Intrauterine infection		
	Unspecified	2	0.9
	Diabetes mellitus		
	Type I	0	0
	Type II	1	0.5
	Amniotic fluid abnormalities		
	Oligohydramnios	2	0.9
	Polyhydramnios	1	0.5
	Anemia		
	Unspecified	6	2.7
	Iron deficiency	3	1.4
	PROM	28	12.8
	IUGR	16	7.3
	Unspecified APH	1	0.5
Placental	Placental abruption with APH	10	4.6
	Placenta previa with APH	6	2.7
	Placental abruption without APH	8	3.7
Cord	Cord prolapse	2	0.9
Fetal	Congenital abnormalities		
	Hydrops fetalis	12	5.5
	Dandy Walker syndrome	1	0.5
	Neural tube defects		
	Anencephaly	3	1.4
	Hydranencephaly	1	0.5
	Corpus callosum agenesis	1	0.5
	Alobar holoprosencephaly	2	0.9
	Congenital heart disorders		
	Tetralogy of Fallot	1	0.5
	Ectopia cordis	2	0.9
	Fetal pericardial effusion	1	0.5
	Congenital gastrointestinal disorders		
	Gastroschisis	2	0.9
	Duodenal atresia	1	0.5
	Congenital diaphragmatic hernia	1	0.5
	Macrosomia	2	0.9
	Megavesica	1	0.5
Others	Previous cesarean section	6	2.7
	Obstetric complication (asphyxia)	2	0.9
	Maternal sepsis	1	0.5

Note: PROM= Premature rupture of membrane, IUGR= Intrauterine fetal growth restriction, APH= Antepartum hemorrhage, unspecified= no information regarding the etiology or underlying cause.

Table 3 Risk Factor(s) Distribution of Stillbirth

Number of Risk Factor(s)	Results (n = 219	
	n	%
0	39	17.8
1	141	64.4
2	32	14.6
3	7	3.2

hypertensive disorders during pregnancy that werer further subdivided into preeclampsia, superimposed preeclampsia (preeclampsia preceded by chronic hypertension), eclampsia, and chronic hypertension. This finding is in accordance with another study conducted in the United States of America which showed that most of the stillbirth patients had hypertensive disorders (20.9%) and were subdivided into chronic hypertension and pregnancy–related hypertension, which consisted of gestational hypertension, superimposed preeclampsia, preeclampsia, HELLP syndrome, and eclampsia.[15] Similar result was reported from a cross sectional research conducted among Middle-East population in 2015 with a percentage of 22.5%.[17] However, different results were reported by studies from Tasikmalaya district, West Java Province, and a systematic review involving 85 reports across 50 countries worldwide in 2017, that most of the stillbirth patients had unknown/unexplained stillbirths, with a percentage of 56.7% and ranging from 32.1% to 43.7%, respectively.[6,12]

In this study, 17.8% of patients had no known etiology or possible cause for the occurrence of stillbirth. This finding is different from the studies previously mentioned which unknown origin was the leading factor.[6,12] Different results were also reported by a study in Nepal from 2017–2019, where one-third of stillbirth patients had unknown causes or possible causes of stillbirth.[13]

Congenital abnormalities affect 31 (14.2%) stillbirth patients in this study. This finding is higher from the previous systematic review involving several countries worldwide, with an overall percentage of 11%, but lower than what was reported from a study in Qatar with the percentage of 21.6%.[6,17]

Superimposed preeclampsia is a condition where preeclampsia is preceded by chronic hypertension (hypertension beginning before 20 weeks gestation and or persisting after 12 weeks postpartum).[8] The 'conversion' from chronic hypertension (uncomplicated

state) to preeclampsia remains unclear. However, several factors were suspected to be involved in its pathological process, such as the imbalance between the pro-angiogenic factors: vascular endothelial growth factor (VEGF) & placental growth factor (PlGF); and anti-angiogenic factors: soluble Fms like tyrosine kinase-1 (sFlt-1) & soluble endoglin (sEng), it is also mentioned that the preexisting endothelial dysfunction due to the vascular shear stress and endothelial injury in women with longstanding (chronic) hypertension may contribute to the imbalance of the previously mentioned angiogenic factors and thus exacerbate the occurrence of preeclampsia.[18,19]

Preeclampsia could lead to stillbirth by several mechanisms: abnormality or pathology of placentation in preeclampsia characterized by the defect in spiral artery remodeling, abnormal trophoblastic invasion, along with the increased vascular resistance could lead to placental ischemia and fetal hypoperfusion; hence, several adverse effects could ensue such as IUGR, fetal distress, and stillbirth.[20]

This study has several limitations. Previous data regarding the maternal and risk factor characteristics of stillbirth in Indonesia were not available. Hence, the similarity and comparison between the result in this study and data before 2017 could not be concluded. This study was also single–centered, which the results might not represent the actual condition in West Java Province and Indonesia. Pre-pregnancy BMI could not be obtained since the subjects had prenatal/antenatal care (PNC/ANC) outside the study location.

In conclusion, the prevalence of stillbirth in this study is considerably low. Of all recorded factors available, most patients have hypertensive disorders, specifically superimposed preeclampsia subtype, followed by an unknown factor and congenital abnormalities. Among the abnormalities, hydrops fetalis accounts for the highest proportion. Multi-centered study with a prolonged period is recommended to increase the study population. Thus more

precise results can be obtained. Analysis of the correlation between the risk factor and stillbirth occurrence is also recommended to establish further and differentiate significant and possible risk factor(s) of stillbirth.

References

1. Stillbirth Collaborative Research Network Writing Group. Causes of death among stillbirths. JAMA. 2011;306(22):2459–68.
2. Tavares Da Silva F, Gonik B, McMillan M, Keech C, Dellicour S, Bhange S, et al. Stillbirth: case definition and guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2016;34(49):6057–68.
3. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health. 2016;4(2):e98–108.
4. Dinas Kesehatan Provinsi Jawa Barat. Profil kesehatan Provinsi Jawa Barat tahun 2012. Bandung: Dinas Kesehatan Provinsi Jawa Barat; 2012.
5. Gravensteen IK, Jacobsen EM, Sandset PM, Helgadottir LB, Rådestad I, Sandvik L, et al. Anxiety, depression and relationship satisfaction in the pregnancy following stillbirth and after the birth of a live-born baby: a prospective study. BMC Pregnancy Childbirth. 2018;18(1):41.
6. Reinebrant HE, Leisher SH, Coory M, Henry S, Wojcieszek AM, Gardener G, et al. Making stillbirths visible: a systematic review of globally reported causes of stillbirth. BJOG. 2018;125(2):212–24.
7. Wojcieszek AM, Shepherd E, Middleton P, Gardener G, Ellwood DA, McClure EM, et al. Interventions for investigating and identifying the causes of stillbirth. Cochrane Database Syst Rev. 2018;4(4):CD012504.
8. Khedagi AM, Bello NA. Hypertensive disorders of pregnancy. Cardiol Clin. 2021;39(1):77–90.
9. Wang W, Xie X, Yuan T, Wang Y, Zhao F, Zhou Z, et al. Epidemiological trends of maternal hypertensive disorders of pregnancy at the global, regional, and national levels: a population-based study. BMC Pregnancy Childbirth. 2021;21(1):364.
10. DeSilva M, Munoz FM, Mcmillan M, Kawai AT, Marshall H, Macartney KK, et al. Congenital anomalies: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2016;34(49):6015–26.
11. Man J, Hutchinson JC, Heazell AE, Ashworth M, Levine S, Sebire NJ. Stillbirth and intrauterine fetal death: factors affecting determination of cause of death at autopsy. Ultrasound Obstet Gynecol. 2016;48(5):566–73.
12. Mahardika A, Ningrum WM. Gambaran faktor risiko pada ibu dengan bayi lahir mati (Stillbirth) di Kabupaten Tasikmalaya tahun 2017. J Midwifery Public Health. 2019;1(2):3027.
13. Sharma B, Bhattarai S, Shrestha S, Joshi R, Tamrakar R, Singh P, et al. Maternal and fetal characteristics and causes of stillbirth in a tertiary care hospital of Nepal: secondary analysis of registry-based surveillance data. BMJ Open. 2021;11(8):e045012.
14. Berhe T, Gebreyesus H, Teklay H. Prevalence and determinants of stillbirth among women attended deliveries in Aksum General Hospital: a facility based cross-sectional study. BMC Res Notes. 2019;12(1):368.
15. Desisto CL, Wallace B, Simeone RM, Polen K, Ko JY, Meaney-Delman D, et al. Risk for stillbirth among women with and without COVID-19 at delivery hospitalization-United States, March 2020–September 2021. Morb Mortal Wkly Rep. 2021;70(47):1640–5.
16. McClure EM, Saleem S, Goudar SS, Garces A, Whitworth R, Esamai F, et al. Stillbirth 2010–2018: a prospective, population-based, multi-country study from the Global Network. Reprod Health. 2020;17(Suppl 2):146.
17. Maducolil MK, Abid H, Lobo RM, Chughtai AQ, Afzal AM, Saleh HAH, et al. Risk factors and classification of stillbirth in a Middle Eastern population: a retrospective study. J Perinat Med. 2018;46(9):1022–7.
18. Kametas NA, Nzelu D, Nicolaides KH. Chronic hypertension and superimposed preeclampsia: screening and diagnosis. Am J Obstet Gynecol. 2022 Feb;226(2S):S1182–95.
19. Phipps E, Prasanna D, Brima W, Jim B. Preeclampsia: updates in pathogenesis, definitions, and guidelines. Clin J Am Soc Nephrol. 2016;11(6):1102–13.
20. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: risk factors, diagnosis, management, and the cardiovascular impact on the offspring. J Clin Med. 2019;8(10):1625.