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Risk factors associated with stillbirths among women delivered at Muhimbili National Hospital, Tanzania: Unmatched case-control study

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Abstract

Background: Tanzania ranks among the top ten countries globally for the highest number of stillbirths. Risk factors associated with stillbirth are often vague and differ across settings. Little is known about whether these factors drive the high stillbirth rate in Tanzania. The study aimed to identify the risk factors associated with stillbirths at a major healthcare facility in the country.

Methods: An unmatched case-control study was conducted in 2017 involving 146 cases and 292 controls of women who delivered stillbirths and live babies, respectively. Structured questionnaires and clinical checklists collected socio-demographic, maternal health, and obstetric data. Bivariate analysis using chi-square tests identified associations between variables and stillbirth occurrence. Logistic regression analysis determined independent risk factors for stillbirth.

Results: During the study period, 2537 newborns were delivered. Stillbirths were 153, giving a stillbirth rate of 60 per 1000 total live births. Factors that were independently associated with stillbirth after controlling for potential confounders were gestational hypertension (AOR=2.3; 95%CI: 1.1- 4.6), preeclampsia (AOR=3.0; 95%CI: 1.5- 5.8), previous history of stillbirth (AOR=3.5; 95%CI: 1.7- 6.9), intrauterine growth restriction (AOR=3.2; 95%CI: 1.4-7.1), antepartum hemorrhage (AOR=20.5; 95%CI: 7.5-56.0) and fetal distress (AOR=3.3; 95%CI: 1.5-7.6).

Conclusion: Hypertensive disorders in pregnancy and antepartum hemorrhage are critical risk factors associated with stillbirth at Muhimbili National Hospital that require timely management. Improved intrapartum monitoring using tools like a partograph could help prevent stillbirths. Local research is important to identify setting-specific factors associated with stillbirth to reduce the substantial stillbirth burden in developing countries like Tanzania.

Keywords: Stillbirth, risk factors, women delivery, unmatched case-control study, Tanzania

Introduction

About 2.6 million stillbirths occur globally each year (Ashish et al., 2015). Of these deaths, developing countries carry 98% of the burden (Elizabeth M McClure, Saleem et al., 2015). Three-

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quarters of stillbirths occur in South Asia and Sub-Saharan Africa, and 60% of these deaths occur in rural families (Hannah Blencowe et al., 2015; Joy E Lawn, Blencowe et al., 2016). Most developing countries have rates ten times higher than those of developed countries (Elizabeth M McClure, Saleem et al., 2015). Every Newborn Action Plan (ENAP) targets national stillbirth rates of 12 or fewer per 1000 births by 2030 (Joy E Lawn, Blencowe et al., 2016).

Stillbirths are classified according to time of occurrence, such as death occurring before the initiation of labor (Antepartum stillbirth) or during labor and delivery (Intrapartum stillbirth) (JE Hirst, Villar et al., 2016). Almost 50% of stillbirths happen during the intrapartum period due to poor quality of care during childbirth, such as infrequent fetal monitoring and infrequent use of Partograph as a tool for monitoring labor. About 49.8% of stillbirths occur during the antepartum period (Elizabeth M. McClure, Wright et al., 2012; Hussein L Kidanto et al., 2009; JE Hirst, Villar et al., 2016). The causes of stillbirths are categorized into two groups: explained and unexplained causes. Explained causes are determined after postmortem investigation (autopsy), physical examination of the body after death, placental examination, genetic testing and detailed medical history. Unexplained causes account for 50-70% of which remain unknown regardless of investigation, complete examinations and detailed history.

In 2015, Tanzania had 47,000 stillbirths and the National stillbirth rate was 30.2 per 1000births (Hannah Blencowe et al., 2015; Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), 2015). At Muhimbili National Hospital, the rate was 49 per 1000 births, and in some other hospitals in the country, the rate was alarming (Georgina Msemo, Massawe et al., 2013; Marandu, 2007). In Zanzibar, the overall stillbirth rate was 59 per 1000 births. Poor quality of intrapartum care during labor was the main factor for the occurrence of the majority of stillbirths (Nanna Maaloe, Housseine et al., 2016). Tanzania is among the top ten countries with the highest number of stillbirths worldwide. Muhimbili National Hospital receives many referrals from pregnant women with hypertensive disorders during pregnancy, antepartum hemorrhages and obstructed labor requiring immediate delivery. However, whether these contribute to the high number of stillbirths at Muhimbili National Hospital is unclear. This study provides insight into the risk factors associated with stillbirths. It also highlights intrapartum management and patient care deficits while reminding healthcare providers to adhere to protocols and guidelines to prevent stillbirths.

Materials and methods

Study area and design

This unmatched hospital-based case-control study was conducted at Muhimbili National Hospital in Tanzania. Muhimbili National Hospital, being the largest tertiary referral and teaching hospital, provides an ideal setting to investigate risk factors behind the country's high stillbirth rate. The study included 146 cases defined as women who delivered stillbirths (fetal death ≥28 weeks of gestation age or ≥ 1000 grams when gestational age was unknown) and 292 controls defined as women who delivered live babies. Participants were recruited from the labor ward and operating theater, encompassing all eligible births at this facility, to compile a representative sample suited to determine significant correlates of stillbirth in the local context. The case-control design allowed comparison of exposure histories in order to infer critical determinants of this vital public health issue.

Study population

Cases were all women who delivered stillbirths, and controls were women who delivered live babies with an Apgar score above seven in the 5th minute. Women who delivered stillbirths with gross anomalies were excluded from the study due to their incompatibility with life. Cases were recruited as they happened. Controls were selected by picking the next two women who delivered live babies after the selected case in a ratio of case: control 1:2. In a situation where two cases happened at once and recorded consecutively. The next four women who delivered live babies were selected.

Data collection

Data was collected using a validated structured Swahili-translated questionnaire from similar studies and modified to suit our situation (Goldenberg, Griffin, Kamath-Rayne, et al., 2018; KC et al., 2015). The questionnaire had three parts. The first part was the socio-demographic factors of the participants, which included age, level of education, occupation, marital status, and antenatal particulars. The second part was maternal risk factors, which included hypertensive disorders in pregnancy, smoking, alcohol use, and a previous history of stillbirth. The last part was the obstetrics risk factor, which included the history of antepartum hemorrhage. Data collection was conducted in 24 hours, day and night, in order to interview all participants who delivered stillbirths before discharge.

Antenatal cards were used to extrapolate gestational age. The patient's clinical notes were used for confirmation of the diagnosis of hypertensive disorders in pregnancy using recorded blood pressure, protein in the urine, symptoms, and biochemistry results during management in the ward. During data collection, we took blood pressure after delivery and protein in urine for those who came into labor. All women who had elevated blood pressure above 140/90mmhg but below 160/110mmhg without protein in urine or trace protein in urine and symptoms of preeclampsia were considered to have gestational hypertension. Similarly, women who had elevated blood pressure ≥ 140/90mmHg with proteinuria or hypertension with end-organ dysfunction with or without proteinuria were considered to have preeclampsia. Those who had preeclampsia with a history of convulsion were considered to have eclampsia.

We had two checklists containing protocol criteria for diagnosing obstructed labor and fetal distress using information from the partograph. Appendix V assessed the presence of obstructed labor and fetal distress during labor. Fetal birth weight was compared with WHO's estimated fetal weight of the 10th percentile. The comparison was done retrospectively after the baby was delivered. Those whose birth weight was below the WHO's estimated 10^{th} percentile were considered babies with intrauterine growth restrictions.

Data Analysis

Data was entered into a template in IBM SPSS Statistics version 23 following the development of the coding scheme. Prior to analysis, frequency tables were run to evaluate data consistency. After data cleaning, descriptive frequencies of all variables were computed separately for cases and controls. Bivariate analysis served to identify candidate risk factors for stillbirth by assessing differences between groups. Statistical tests included chi-square and, where appropriate due to small cell counts, Fisher's exact tests produced odds ratios with 95% confidence intervals. Significance was defined as $p<0.05$. These Bivariate comparisons determined which socio-demographic, maternal, and obstetric variables demonstrated a significant association with stillbirth occurrence. After controlling for confounders, Such factors were entered into a multivariate logistic regression model to determine independently significant risk markers. Adjusted Odds Ratios (AORs) were reported

from this model alongside 95% confidence limits. This sequential analytic approach allowed inference of both univariate and multivariate-adjusted risk profiles from this case-control study's comprehensive variable set.

Ethical consideration

Ethical clearance was obtained from the Senate Research and Publications Committee of the Muhimbili University of Health and Allied Sciences (MUHAS), and permission to conduct the study was obtained from the Executive Director of Muhimbili National Hospital (MNH) and the head of the Department of Obstetrics and Gynecology. Written informed consent was obtained from the participant after being informed of the purposes of the study, benefits, and risks. The participant had the right to withdraw from the study whenever she wished, and it would not affect her subsequent postpartum care. We assured the participants of confidentiality and privacy; thus, the information given was used only for study purposes. Counseling on the grief aspect was conducted for women who delivered stillbirths.

Results

During the study period, 2537 newborns were delivered at Muhimbili National Hospital, as shown in Figure 1. The stillbirth rate was 60 per 1000 total live births. The analysis included 146 women who delivered stillbirth and 292 women who delivered live babies with an Apgar score above seven in the 5th minute.

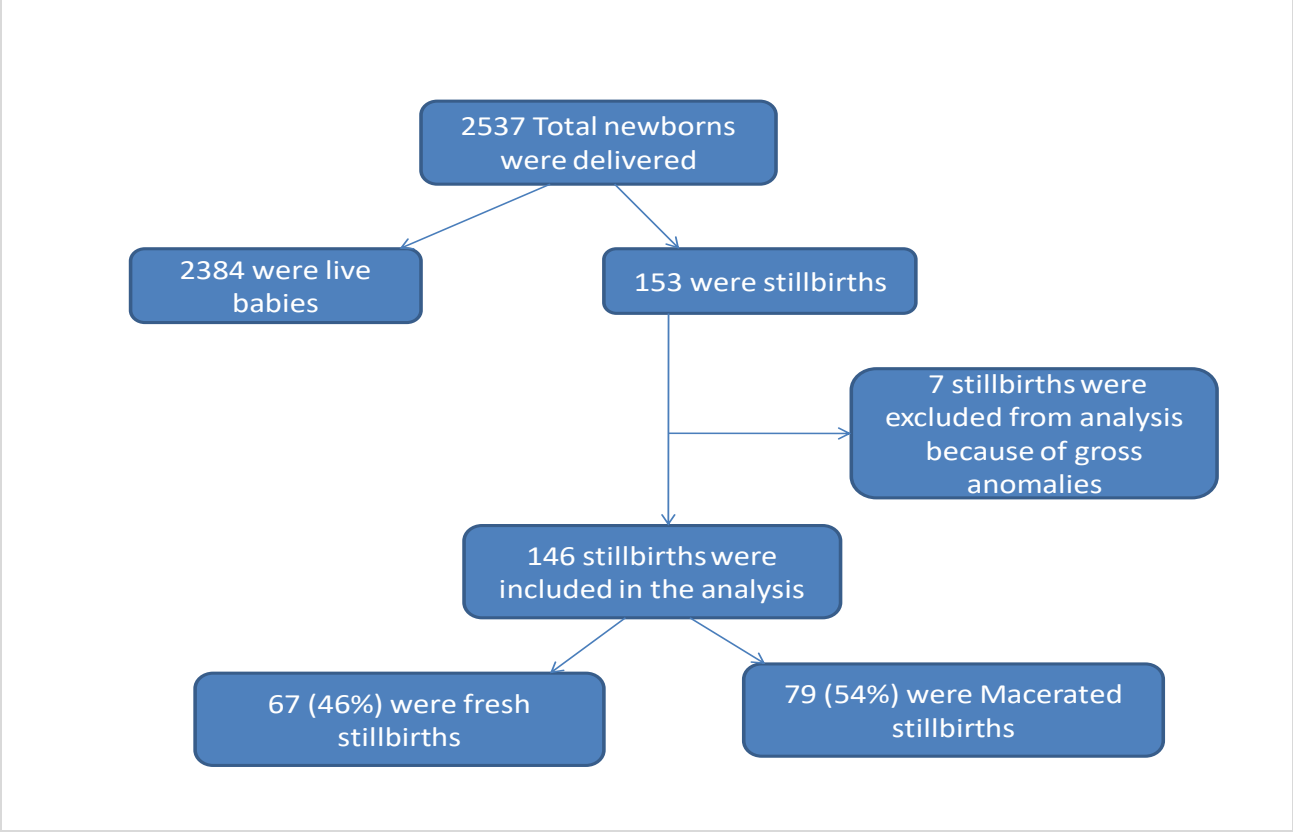

Figure 1: Flowchart of newborns delivered during the study period.

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Table 1: Socio-demographic characteristics of sampled women

Variables	Cases N (%) n=146	Control N (%) n=292	*P*-value
Maternal age (yrs)			
< 20	8(5.5)	22(7.5)	0.171
20-34	106(72.6)	226(77.4)	
≥ 35	32(21.9)	44(15.1)	
Marital status			
Single	14(9.6)	24(8.2)	0.685
Married	130(89.0)	266(91.1)	
Divorced	2(1.4)	2(0.7)	
Education level			
Primary	79(54.1)	120(41.1)	< 0.001
Secondary	54(37.0)	95(32.5)	
College and higher	13(8.9)	77(26.4)	
Occupation			
Unemployed	78(53.4)	112(38.4)	< 0.001
Self-employed	57(39.0)	118(40.4)	
Employed	11(7.5)	62(21.2)	
Parity			
Primepara	24(16.4)	93(31.8)	0.004
2	40(27.4)	79(27.1)	
3-5	71(48.6)	106(36.3)	
≥6	11(7.5)	14(4.8)	
Admission status			
Referral	130(89.0)	220(75.3)	0.001
Originate MNH	16(11.0)	72(24.7)	

Table 1 shows that the two populations differ in characteristics where the *P*-value was statistically significant. Low levels of education, unemployment, and high parity predominated the case group.

Table 2: Bivariate analysis of maternal risk factors

Variables	Cases N (%) n=146	Control N (%) n=292	COR (95%CI)	*P*-value
Gestational hypertension				
Yes	40(27.4)	36(12.3)	2.7 (1.6- 4.4)	< 0.001
No	106(72.6)	256(87.7)	1	
Preeclampsia				
Yes	76(52.1)	70(24.0)	3.4(2.3- 5.2)	< 0.001
No	70(47.9)	222(76.0)	1	
Eclampsia				
Yes	29(19.9)	19(6.5)	3.6(2.0- 6.6)	< 0.001
No	117(80.1)	273(93.5)	1	
Previous history of stillbirth*				
Yes				
No	63(51.2)	48(23.6)	3.4(2.1- 5.5)	< 0.001
	60(48.8)	155(76.4)	1	
History of taking alcohol				
Yes	24(16.4)	28(9.6)	1.9(1.1- 3.3)	0.042
No	122(83.6)	264(90.4)	1	
ANC booking				
<16wks	21(14.4)	42(14.4)	1	
16-28wks	111(76.0)	232(79.5)	0.9(0.5- 1.7)	0.426
>28wks	14(9.6)	18(6.1)	1.6(0.7- 3.7)	
ANC visits				
1	9(6.2)	15(5.1)	3.3(2.1- 5.0)	
2-3	72(49.3)	70(24.0)	1.9(0.8- 4.6)	< 0.001
≥4	65(44.5)	207(70.9)	1	
PMTCT status				
1	8(5.5)	13(4.5)	1.2(0.5- 3.1)	0.640
2	138(94.5)	279(95.5)	1	

*Variable excluded Primipara

Table 2 shows that gestational hypertension, preeclampsia, eclampsia, previous history of stillbirth and antenatal care visits were significantly associated with stillbirths.

Table 3: Bivariate analysis of obstetrics and fetal risk factors

Variables	Cases N (%) n=146	Controls N (%) n = 292	COR (95%CI)	*P*- value
Antepartum hemorrhage				
Yes	36(24.7)	9(3.1)	10.3(4.8- 22.1)	< 0.001
No	110(75.3)	283(96.9)	1	
Intrauterine growth restriction				
Yes				
No	51(34.9)	21(7.2)	7.0 (4.0- 12.1)	< 0.001
	95(65.1)	271(92.8)	1	
Fetal distress**				
Yes	41(29.9)	44(15.8)	2.1(1.3- 3.4)	0.003

No	96(70.1)	234(84.2)	1	
Obstructed labor**				
Yes	9(6.6)	35(12.6)	0.4(0.2- 0.9)	0.04
No	128(93.4)	243(87.4)	1	
GA at delivery				
28-33wks	74(50.7)	32(11.0)	10.8(6.3- 18.5)	
34-36wks	32(21.9)	73(25.0)	2.0(1.2- 3.5)	< 0.001
≥ 37wks	40(27.4)	187(64.0)	1	
Mode of delivery				
SVD	102(69.9)	111(38.0)	4.1(2.6- 6.2)	< 0.001
CS	44(30.1)	181(62.0)	1	
Birth weight				
1-2.4kg	112(76.7)	75(25.7)	9.5(6.0- 15.2)	< 0.001
≥ 2.5kg	34(23.3)	217(74.3)	1	
Sex of the baby				
Male	78(53.4)	142(48.6)	0.8(0.6- 1.2)	0.363
Female	68(46.6)	150(51.4)	1	

**Variables excluded women who had an elective caesarian section and those whose labor monitoring was not conducted by using a partograph

Table 3 shows that antepartum hemorrhage, intrauterine growth restriction, fetal distress, obstructed labor, premature delivery, and low birth weight were significantly associated with stillbirths.

Table 4: Multivariate logistic regression analysis of risk factors associated with stillbirths

Variables	COR (95% CI)	AOR (95% CI)
Occupation		
Unemployed	3.9 (1.3- 5.6)	2.2 (0.8- 6.0)
Self-employed	2.7 (1.3- 5.6)	3.2 (1.2- 8.7)
Employed	1	1
Mode of delivery		
SVD	4.1 (2.6- 6.2)	4.9 (2.5- 9.6)
C/S	1	1
Birth weight		
1-2.4kg	9.5 (6.0- 15.2)	3.4 (1.4- 8.8)
≥ 2.5kg	1	1
Gestational hypertension		
Yes	2.8 (1.7- 4.6)	2.3 (1.1- 4.6)
No	1	1
Preeclampsia		
Yes	3.4 (2.3- 5.2)	3.0 (1.5 – 5.8)
No	1	1
Previous history of stillbirth		
Yes	3.4 (2.1- 5.5)	3.5 (1.7- 6.9)
No	1	1
Intrauterine growth restriction		
Yes	7.0 (4.0- 12.1)	3.2 (1.4- 7.1)
No	1	1
Antepartum hemorrhage		

Yes	10.3 (4.8- 22.1)	20.5 (15.5- 36.0)
No	1	1
Fetal distress		
Yes	2.1 (1.3- 3.4)	3.3 (1.5- 7.6)
No	1	1

Table 4 shows that after controlling for all potential confounding factors, women who experienced antepartum hemorrhage were even twenty times more likely to have stillbirths as compared to women who did not have antepartum hemorrhage.

Discussion

In this study, the rate of stillbirths at Muhimbili National Hospital was 60 per 1000 births. This rate is two times higher than the national one, four times higher than North Africa's, and eighteen times higher than that of developed countries. Referrals of high-risk pregnant women and the decreased number of women with normal pregnancies delivering at Muhimbili National Hospital could be the reason for this burden.

Our study showed that the risk of stillbirth decreased with increased education. Women with high levels of education can afford personalized care and adhere to health education and counseling given during antenatal visits. The findings were consistent with previous studies in West Africa, Central Africa, Ghana, and Uganda (Badimsuguru et al., 2016; Cyril Engmann, Matendo et al., 2010; Martin Chalumeau, Bouvier-colle, 2012; Sanni Kujala, Waiswa et al., 2016). Unlike our study findings, a few studies demonstrated that women without formal education and those with low education were significantly associated with stillbirth even after controlling for potential factors (Ashish et al., 2015; Elizabeth M McClure, Saleem et al., 2015; Elizabeth M. McClure, Wright et al., 2012; Ghimire et al., 2017; Kc et al., 2016; Lakew et al., 2017).

Occupation was an important independent factor that was associated with stillbirths. The majority of women with unemployment are also characterized by poverty, lack of decision-making, and poor health-seeking behavior, which increases the likelihood of stillbirths. This finding was similar to other previous studies done elsewhere (Ibiebele et al., 2016; Tshibumbu & Blitz, 2016). However, UK and West Africa studies did not show an association between occupation and stillbirths (Chalumeau et al., 2002; Hirst et al., 2018).

There was no significant association between maternal age and stillbirths. The majority of study participants were below 34 years old, and this particular age group was less likely to have stillbirths as compared to advanced-age women who carried a higher risk of stillbirths (Gordon et al., 2013; Nahar et al., 2013b). This is a reflection of the composition of the majority of pregnant women admitted to our facility. As opposed to our study findings, studies done in Australia and Nepal found that maternal ages above 35 years were independently associated with stillbirths (Adrienne Gordon, Raynes-greenow et al., 2013; Ashish et al., 2015; Desire D. Tshibumbu & Blitz, 2016; Elizabeth M. McClure, Wright et al., 2012).

Hypertensive disorders in pregnancy remain to be another important independent factor associated with stillbirths. Preeclampsia has many adverse outcomes, including eclampsia, abruption of the placenta, and intrauterine growth restriction, which increase the likelihood of stillbirths. Severe preeclampsia leads to premature delivery and low birth weight, which may be significant risks for stillbirths. The study findings were similar to other studies in the United Kingdom, England, Australia and North Carolina (ACOG, 2009; Ananth & Basso, 2010; Gardosi et al., 2013; Hirst et al., 2018; Ibiebele et al., 2016; McClure et al., 2015). Similarly, recent studies done in

Canada, Zanzibar and Nepal showed that preeclampsia had a fivefold increased risk of stillbirths (Nanna Maaloe, Housseine et al., 2016; Victoria M Allen, Joseph et al., 2010; WHO, 2016).

Women who delivered infants with intrauterine growth restrictions had increased odds of stillbirths even after controlling for potential confounders, including severe preeclampsia and cigarette smoking. Similar findings were reported in several other studies done in Australia, the UK, Sub-Saharan countries and Nepal (Goldenberg, Griffin, Kamath-Rayne, et al., 2018; Hirst et al., 2018; Ibiebele et al., 2016; KC et al., 2016). The risk increases more when there is a combination of cigarette smoking, alcohol use, obesity, and intrauterine growth restriction (Gardosi et al., 2013).

Antepartum hemorrhage is an independent risk factor strongly associated with stillbirth. Abruption of the placenta leads to fetal distress and hypoxia and, hence, fetal death. Placenta praevia and other causes of antepartum hemorrhage carry significant risks of stillbirths. Similar results findings were obtained from other studies done in the Netherlands, Nepal, the United Kingdom, the United States of America, and sub-Saharan countries (Ashish et al., 2015; Goldenberg, Griffin, Kamath-rayne, et al., 2018; Jason Gardosi et al., 2013; JE Hirst, Villar et al., 2016; Kayode et al., 2016; Kc et al., 2016; Millogo et al., 2016; Nahar et al., 2013a). We did not find an association between obstructed labor and intrapartum stillbirths. The reason could be the timely and proper management of women with obstructed labor and the effective use of partographs to monitor labor at Muhimbili National Hospital. Patients who were found with features of obstructed labor during labor were immediately taken to the theater for caesarian section delivery.

Moreover, fetal distress during labor was associated with a threefold increase in the odds of intrapartum stillbirths. Severe preeclampsia, eclampsia, undiagnosed early abruption of the placenta, prematurity, and low birth weight probably contributed to fetal distress. Despite the good use of a partograph and the availability of ultrasound and fetoscope to detect fetal distress during labor and delivery, fetal distress was one of the significant risk factors of stillbirths. Since this study was hospital-based, it may not be a reliable reflection of the general population. We used standardized hospital criteria protocols for the diagnosis of fetal distress during labor based on the paragraph documentation on the status of fetal heart rate and liquor. Healthcare bias on partograph documentation could be one of the limitations.

Conclusion

Stillbirth is among the adverse outcomes of pregnancy at Muhimbili National Hospital. Occupational, hypertensive disorders in pregnancy, intrauterine growth restrictions, antepartum hemorrhage, and fetal distress are independent risk factors associated with stillbirths. Timely and proper management of hypertensive disorders in pregnancy and antepartum hemorrhage is very crucial for the prevention of stillbirths. Proper labor monitoring using a partograph is an important intervention to prevent intrapartum stillbirths.

Healthcare providers should prioritize patients at risk of stillbirth when investigating and treating pregnancy-related conditions. They should vigilantly monitor all women in the labor ward using a partograph. During antenatal care, all pregnant women should be given adequate health education on the importance of focused antenatal care for early detection and immediate treatment of pregnancy-related disorders and complications.

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Author contributions

JDK and PW designed the study. JDK conducted and contributed to data analysis. JDK, CNM and PW interpreted the data. JDK and CNM prepared the original manuscript. All co-authors contributed to subsequent revisions. All authors read and approved the final manuscript.

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