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Aetiology and trends of rates of stillbirth in a tertiary care hospital in the north of India over 10 years: a retrospective study

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Objective To analyse the aetiology of stillbirth and its changing trends in a single tertiary care referral institute of northern India over a 10-year period (2007–2016).

Design Retrospective study.

Setting Tertiary care hospital in the north of India.

Sample Medical records of all mothers who delivered a stillborn at the institute.

Methods Data was collected from monthly and annual perinatal audits and causes of stillbirths were classified using Simplified CODAC classification. Annual reduction rate was calculated by linear regression analysis and Cusick test for the changing trends over 9 years.

Main outcome measures Of 54 160 births, 3678 babies were stillborn. Over 9 years, the annual stillbirth rate has reduced

significantly from 73.6 to 62.0 per 1000 total births with an average annual reduction rate of 1%. The most common causes of stillbirths were hypertensive disorders of pregnancy (27.6%), antepartum haemorrhage (19.5%), and congenital anomalies (9.3%).

Conclusion The annual reduction rate (1%) of stillbirth remains low. The aetiology of stillbirths remains unchanged over a 10-year period and hypertensive disorder of pregnancy remains the single most preventable cause of stillbirth.

Keywords Cause of death associated condition (CODAC) classification, hypertensive disease of pregnancy, low-/middle-income countries, stillbirth, stillbirth rate.

Tweetable abstract Analysis of stillbirths over a 10-year period in an Indian institute showed a high but declining trend with annual reduction rate of 1%.

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Introduction

Stillbirth or intrauterine fetal death is defined as a baby born with no sign of life at, or after, 28 weeks of gestation.¹ The definition varies widely in different countries. In India, a fetus of \geq 20 weeks of gestation or weight of \geq 500 g with no sign of life is considered stillborn.^{2,3} It is the most common unfavourable pregnancy outcome; 2.6 million stillbirths occur globally each year.⁴ The highest burden of stillbirths continues to be in the sub-Saharan Africa and southern Asian regions⁴ Many are intrapartum stillbirths and 60% are from rural areas with limited healthcare services.^{5,6}

The stillbirth rate (SBR) is defined as the number of stillbirths per 1000 total births (live birth + stillbirth). India

is among top 10 countries with the highest stillbirth numbers, with stillbirth rate of 23.3 per 1000 births in 2015.⁶ There is wide variation of SBR in different states ranging between 20 to 66/1000 births.⁷ The stillbirth rate of low middle-income countries (LMIC) is tenfold higher than the high middle-income countries.⁸

To plan preventive strategies, it is crucial to understand the aetiology, risk factors, and associated factors leading to stillbirth. The cause of death should be attributed to stillbirth clinically or pathologically. However, there are welldocumented risk factors associated with stillbirth without a clear causal pathway, e.g. advanced age, maternal obesity, and smoking.^{9,10} There are many classification systems available in the literature based on fetal, associated maternal conditions or placental pathology.^{11–13} Further, in many maternal conditions the exact patho-physiology leading to intrauterine death remains unclear.¹⁴

The SBR has declined worldwide but the annual rate of reduction of stillbirths is 2%, which is much slower than the reduction of maternal mortality (3.0%) and mortality of children of younger than 5 years (4.5%).⁴ With this rate it seems impossible to achieve the target of national stillbirth rates of 12/1000 births by 2030 set by Every Newborn Action Plan in 2014.¹⁵ Bernis et al.¹⁶ proposed various strategies for stillbirth prevention which included acknowledging the actual burden, providing high-quality antenatal care and intrapartum care, using stillbirth rate as the indicator of quality of healthcare and mother–baby dyad approach.

The objective of this study was to explore the trends of stillbirth rate and aetiology of all babies born stillborn from a single tertiary care referral institute in the north of India over a period of 10 years.

Methods

This was a retrospective study analysing all babies born as stillborn in a tertiary care referral institute over 10-year period (2007–2016). Data was collected from monthly and annual perinatal audits of the departments of obstetrics and gynaecology, and neonatology and causes of stillbirths along with details of each case were systematically reviewed by doctors.

In this study, stillbirth is defined as the birth of a baby with no sign of life after 20 weeks or . a birthweight of \geq 500 g.³ A booked case was defined as a woman who attended for four or more antenatal visits and who received two doses of tetanus toxoid. The remainder were classified as unbooked. As per institutional protocol, all stillbirths were evaluated by detailed history, examination, and

investigations including ultrasound to confirm intrauterine fetal death. Expectant management was offered to women who did not require immediate delivery, e.g. due to abruption or chorioamniotis. Women who opted for expectant management were followed by weekly coagulation profile for 4 weeks. After delivery of a stillborn baby, an autopsy was offered and performed if parenteral consent was given. The stillbirth data was recorded by the resident doctor who conducted the birth, verified by the faculty, and then the cause of stillbirth was verified and assigned by multidisciplinary team of experts involving obstetricians, neonatologists, and pathologists in monthly perinatal audits. The most probable cause of stillbirth was assigned based on available history, clinical findings, and available investigations.

All these stillbirths were classified according to simplified cause of death associated conditions (CODAC) classification retrospectively, although associated condition could not be retrieved for each one. The stillbirth rate and aetiology were entered on an EXCEL spreadsheet and Cusick test was used to analyse the changing trends over years. Linear regression was conducted to find out the trend equation between SBR and time in years. Linear regression model was obtained as SBR = 72.72 + (-1.01) Year (P = 0.002) with $R^2 = 0.73$. Chi-square test was applied to find any association between categorical variables and a two-tailed *P*-value ≤ 0.05 was considered statistically significant.

Results

During the study period, 51 552 women delivered in the study setting, giving birth to 54 160 babies, of which 3678 were stillborn. The delivery rates along with stillbirth rate and proportion of women who had poor

Year	Total births	Stillbirth (<i>n</i>)	Still birth rate (per 1000 total births)	Stillbirth in women who received no or inadequate antenatal care	Autopsy rate (%)
2007	4645	342	73.6	81.9	50.8
2008	4701	321	68.3	79.2	42.6
2009	5220	367	70.3	76.5	39.2
2010	5161	367	71.1	75.7	35.1
2011	5178	368	71.1	86.1	29.1
2012	5280	368	69.6	88.3	29.1
2013	5755	373	64.8	91.4	34.3
2014	5889	382	64.8	90.1	28.5
2015	6271	412	65.7	83.0	31.7
2016	6060	378	62.4	86.3	42.3
Total	54 160	3678	67.9 per 1000 total births	83.85% of total stillbirths	36%

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antenatal care are detailed in Table 1. The SBR ranges from 62.4 to 73.6/1000 total births with average SBR of 67.9/1000 birth over a decade (from 2007 to 2016). However, there was a significant downward trend in SBR (P = 0.016) from 2007 to 2016 (Figure 1A) with an annual reduction rate of 1%.

Based on the appearance of the baby at the time of birth, stillbirths were classified as 'macerated' or 'fresh'; 40% were macerated (antepartum) and the remainder were fresh (intrapartum). The clinical and demographic characteristics are detailed in Table 2. The highest rates of stillbirth occurred in women aged 24-27 years. Fifty per cent of stillborn babies weighed >1500 g. The average stillborn autopsy rate during the study period was 36% (1326 of 3678) (Table 1). Of these 1326 autopsies, 325 babies (24.5%) were found to have congenital abnormalities. Defects of the central nervous system were the most common (52.5%), followed by renal defects (21.6%), congenital heart defects (8.7%), and musculoskeletal defects (19.5%). Of 51 552 births in the study site, 29 149 women (56%) were booked, and the rest were unbooked or inadequately booked with fewer than four antenatal visits. Most of these mothers were referrals and unbooked cases (83.9%), admitted with absent fetal heart on admission, i.e. had a stillbirth before reaching our hospital. Of the unbooked cases, 13.8% (3088/22 403) women delivered babies that were stillborn, whereas the rate in booked cases was only 2% (590/29 149) (Table 2).

Aetiology of stillbirth in 10-year cohort (2007–2016)

The causes of stillbirths were categorised according to the simplified CODAC system of classification. Maternal conditions and placental causes ranked highest in the causes of stillbirths (Table 3). Twenty per cent of stillbirths were unexplained or unclassifiable. Over the years, common causes of stillbirths remained hypertensive disease in pregnancy, antepartum haemorrhage, congenital abnormalities, and labour complications. Obstructed labour was the only cause that has significantly reduced over the years (3.8% to 1.3%, P = 0.024) (Figure 1B).

Hypertensive disorder of pregnancy

Hypertensive disorders of pregnancy contributed to onethird of the stillbirths (1069/3678, 29%). Hypertensive disorders of pregnancy include chronic (pre-existing) hypertension, gestational hypertension, pre-eclampsia, and eclampsia. Among women with hypertensive disorders of pregnancy, 223 had eclampsia and 126 had chronic (preexisting) hypertension. There is no change in trends of hypertensive disorders of pregnancy-related stillbirths over the last decade.





Figure 1B: Trends of various causes of stillbirths over 10 years (2007-2016)



Figure 1. (A) Trends of stillbirth rate over a period of 10 years (2007–2016). (B) Trends of various causes of stillbirths over 10 years (2007–2016).

 Table 2. Demographic and clinical details of mothers and their stillborns

Variables	Number (<i>n</i>)	Proportion (%)
Types of still birth		
Fresh (Intrapartum)	2204	59.9%
Macerated (antepartum)	1474	40.1%
Gestational age		
<28 weeks (Early stillbirths)	754	13.9 (Early stillbirth rate per 1000 total births)
≥28 weeks (Late stillbirths)	2924	53.9 (Late stillbirth rate per 1000 total births)
Sex distribution		
Male	1989	54.1
Female	1674	45.5
Ambiguous/sex not identified	15	0.40
Birth weight		
<1000 g	992	26.9
1000–1499 g	861	23.4
1500–2499 g	1049	28.5
2500–3499 g	687	18.6
≥3500 g	89	2.41
Stillbirths with	334	92 per 1000 stillbirths
birth defects		
Maternal age		
<20	87	2.36
20–23	890	24.1
24–27	1364	37.0
28–31	753	20.5
32–35	389	10.5
36–39	116	3.15
≥40	79	2.14
Antenatal care		
Total deliveries	51552	
Booked	29149	56.54
Stillbirth in booked	590	2 per 100 Booked mothers
Unbooked	22 403	13.7 per 100 Unbooked mothers
Stillbirth in unbooked	3088	

Antepartum hemorrhage

There were 719 (19.5%) stillbirths secondary to antepartum hemorrhage: 85 (11.8%) were in cases of placenta praevia, in which there was a delay in caesarean section due to delayed referral or other logistic issues which led to suboptimal care and ultimately stillbirth. However, the majority cases of antepartum haemorrhage were because of placental abruption (88.2%) and most of them had absent fetal heart at the time of admission. Less than 10% of these abruption cases were of <28 weeks' gestation, with very low birthweight in case where a caesarean was not done for the extremely preterm baby due to refusal of the family. There seems to be no change in trends in abruption cases over the study period but cases of placenta **Table 3.** Causes of stillbirth-classifying total stillbirths (2007–2016)according to simplified CODAC

Cause of death	Total number of cases	Proportion
Infection	100	2.7
Hepatitis	58	
Syphilis	6	
Malaria	0	
Group B streptococcus	0	
Others (Chorioamnionitis)	36	
Intrapartum causes	159	4.3
Malpresentation	20	
Prolonged/obstructed labour	27	
Rupture uterus	77	
Fetal distress	35	
Congenital anomaly	334	9.08
Other fetal causes	145	3.94
Allo immunisation	22	
Hydrops of unknown origin	25	
Extreme prematurity	98	
Cord accidents	51	1.38
Loops	4	
Cord prolapse	47	
Placental causes	719	19.54
Abruption	634	
Placenta praevia	85	
Maternal conditions	1439	39.12
Hypertensive disorder	1069	
Pre-eclampsia	720 (19.5%)	
Eclampsia	223 (6.06%)	
Chronic hypertension	126 (3.42%)	
Diabetes	52	
Cholestasis	15	
Others	303	
Unknown	731	19.87
Unknown		
Unexplained		
Unclassified		
Total	3678	100
Associated perinatal		
Small for gestation age	156	
Multiple pregnancy	64	
Associated maternal		
Anaemia	612	
Others	406	

praevia have reduced from 3.8% (13/342) to 1.3% (5/378) (P = 0.05).

Uterine rupture

Of 3678 stillbirths, 2.1% were due to uterine rupture because of prolonged labour. Over the years, the proportion of referrals of uterine rupture cases was almost same but the underlying aetiology changed. Previously, uterine rupture occurred in multigravida women with unscarred

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uterus following prolonged or obstructed labour; more recently, however, most of the cases are the result of previous caesarean sections.

Congenital abnormalities

Congenital abnormalities contributed to 92/1000 stillbirths, of which neural tube defects are the most frequent. There was no change in trends of congenital abnormalities in stillbirths over the study period (P = 0.106).

Maternal disease

Maternal disease was assigned as a cause of stillbirth in all those cases where there was clinical evidence of maternal medico-surgical illness and no other direct cause of fetal demise was available. These included chronic hypertension in 3.4% (n = 126), diabetes or gestational diabetes mellitus in 1.4% (n = 52), and other maternal conditions in 9.9% (n = 303), which comprised critically ill mothers with hepatitis in hepatic encephalopathy, acute fatty liver of pregnancy, sepsis, disseminated intravascular coagulation, and infections such as swine flu or dengue. While approximately 75% of these mothers were admitted with fetal demise only, in the remaining 25%, the fetus was alive at the time of admission, but mothers were very sick and delivered stillborn during the course of management.

Infections

Of the 3678 babies who were stillborn, infection, for example, clinically suspected chorioamnionitis, was assigned as the cause in 36 cases, 25 of which were confirmed with laboratory cultures.

Discussion

Main findings

This study shows a significant declining trend of the stillbirth rate over a decade. However, the total stillbirth rate remains unacceptably high. The estimated annual rate of reduction (ARR) of SBR is 1%, half of the global ARR (2%).⁶ There was 15.4% decline in the SBR over 10 years (2007–2016), from 74/1000 births in 2007 to 63/1000 births in 2016. This decline is an indicator of improvement in healthcare services over years as reported by the National Family Health Surveys of 2005–2006 and 2015–2016.¹⁷ Globally, there has been a 25.5% decline in SBR over 15 years from 2000 to 2015 (SBR 24.7/1000 births in 2000 and 18.4/1000 births in 2015).⁶ But in our set-up with an ARR of 1%, achieving the national target of SBR of 12/ 1000 total births by 2030 seems to be impossible.¹⁵

Strengths and limitations

This study gives us an insight into trends of SBR and various causes of stillbirth from a tertiary referral institution in an LMIC. The study results are limited by its retrospective design. The time of stillbirth was classified according to the maceration of the skin of the baby rather than fetal heart documentation. The cause of death was assigned on the basis of clinical history with limited investigation. Associated and modifiable factors, which have significant contribution in an LMIC such as India, need further evaluation to make recommendations for corrective measures to reduce the number of stillbirths, both at the facility and the national level.

Interpretation

In this study, hypertensive disease of pregnancy is the most common assigned cause of stillbirth. However, it has not been separately classified as due to placental cause (abruption, thrombosis), fetal (intrauterine uterine growth restriction and abnormal Doppler studies), complication of labour or acute hypoxia, due to unstable maternal condition secondary to eclampsia or intracranial bleed. In this study, we have followed the simplified CODAC classification in which hypertension is assigned as the cause of a fetal demise.¹⁸ In our centre, most of these women were referred from the healthcare facility and received poorquality antenatal care. Additionally, complete postmortem investigation was not available in all cases and the cause of stillbirth was assigned on the available clinical findings and investigations when no other obvious direct cause was available. In this study, 29% of stillbirths were attributed to hypertensive disease of pregnancy, 3.4% of which were associated with chronic hypertension, whereas pre-eclampsia and eclampsia made up the majority. This is in contrast to the global stillbirth statistics that reflect chronic hypertension (16% of an estimated 2.6 million stillbirths) rather than pre-eclampsia or eclampsia (5%) to be the leading cause of stillbirth.⁴ This discrepancy of data may be a result of the high number of unbooked women in this study, which may have led to misclassification of chronic hypertension as gestational hypertension.

The second common cause of stillbirth was antepartum haemorrhage (19.5%), 12% of which (85/703) were due to placenta praevia. Although abruption is unpredictable, diagnosis and management of placenta praevia can be improved by the availability of ultrasound as part of routine antenatal care. Presence of risk factors for abruption such as smoking, hypertension, thrombophilia, advanced maternal age, premature rupture of membranes, trauma, and sudden decompression in polyhydramnios scan can also help to identify those women who may require more monitoring during pregnancy and childbirth; however, abruption is not always predictable. Most cases of abruption placenta in this study were admitted with fetal demise and half were associated with hypertensive disease of pregnancy. Data from similar studies from a high middle-income country also attribute 25% of stillbirths to abnormalities of placenta or umbilical cord, but none mentions fetal demise with placenta praevia.^{19,20} This is an indicator of the quality of healthcare services received by antenatal women. Further investigation into the root cause of the non-usage of healthcare facilities reveals the lack of awareness, logistical issues such as the non-availability of healthcare facilities equipped with blood bank and trained staff, lack of transportation, and poor financial conditions.

In this study, 1.3% of stillbirths were attributed to cord complication, i.e. cord prolapse. Previous studies from high middle-income countries also reported the significant contribution of umbilical cord accidents ranging from 2.5 to as high as 15%.^{20–23} Additionally, the high prevalence (9.08%) of congenital abnormalities among stillbirths is associated with late diagnosis of malformation, which restricts the option of the legal termination of pregnancy.

Infection-related stillbirths made up only 39 (0.9%), which is very low compared with findings from other LMIC, where more than 50% of stillbirth were infectionrelated, specifically, syphilis and chorioamnionits.²⁴⁻²⁷ This might be due to incomplete evaluation of stillbirths as culture report, and autopsy were not available of all cases in the present study. This is a facility-based data, although we had 35 (0.9%) cases of intrapartum stillbirths over a period of 10 years. The lack of adequate facilities for continuous electronic intrapartum fetal monitoring for women who meet the criteria and caesarean facilities in comparison with the high load of high-risk pregnancies also play an important role. Lawn et al.7 have compared stillbirth categories of high middle-income country and LMIC. In comparison, our data show a low proportion of cases of intrauterine growth restriction, which may be underreported or missed, as most stillbirths had occurred before admission and many of these women were unbooked. As compared with a high middle-income country, we also report a very high prevalence of hypertensive disease of pregnancy and antepartum haemorrhage which needs to be studied further.

Conclusion

The stillbirth rate has declined during the study period of 10 years (2007–2016) with an annual rate of reduction of 1%. The aetiology of stillbirths has changed little. However, there is a significant fall in cases of obstructed labour. Despite improvements in healthcare facilities, hypertensive disorders of pregnancy and related complications remain the single most major preventable cause of stillbirth and a significant proportion of women are not receiving adequate antenatal care. There is a need to highlight the detection,

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diagnosis, and management of hypertensive disorders of pregnancy by providing high-quality antenatal care to all pregnant women in order to achieve the national goal of a stillbirth rate of \leq 12/1000 total births by 2030.

Disclosure of interests

The authors declare that there are no financial or non-financial conflicts of interest. Completed disclosure of interests forms are available to view online as supporting information.

Contribution to authorship

BS, SS, and NA drafted the manuscript. GRVP, NA, SS, and NK provided the perinatal audit data. VS and NA reviewed the draft and approved the final manuscript.

Details of ethics approval

Ethical approval was obtained from Institutional ethics committee, Postgraduate Institute of Medical Education and Research, Chandigarh, date of approval 15.05.2018, reference number NK/4484/Study.

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