Global Network for Women's and Children's Health Research: Probable causes of stillbirth in low- and middle-income countries using a prospectively defined classification system

28 authors, including:

Ana Garcés
Institute of Nutrition of Central America And Panama
110 PUBLICATIONS   **2,529** CITATIONS

SEE PROFILE

Sarah Saleem
Aga Khan University, Pakistan
144 PUBLICATIONS   **2,762** CITATIONS

SEE PROFILE

Fabian Esamai
Moi University
152 PUBLICATIONS   **3,652** CITATIONS

SEE PROFILE

Shivaprasad S Goudar
Jawaharlal Nehru Medical College
223 PUBLICATIONS   **3,961** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Project Maternal and Newborn Health Registry View project

Project Community Level Interventions for Pre-eclampsia (CLIP) - A community based cluster randomized trial View project

Global Network for Women's and Children's Health Research: probable causes of stillbirth in low- and middle-income countries using a prospectively defined classification system

EM McClure,[a] A Garces,[b] S Saleem,[c] JL Moore,[a] CL Bose,[d] F Esamai,[e] SS Goudar,[f] E Chomba,[g] M Mwenechanya,[g] O Pasha,[c] A Tshefu,[h] A Patel,[i] SM Dhaded,[j] C Tenge,[e] I Marete,[e] M Bauserman,[d] S Sunder,[c] BS Kodkany,[j] WA Carlo,[k] RJ Derman,[l] PL Hibberd,[m] EA Liechty,[n] KM Hambidge,[o] NF Krebs,[o] M Koso-Thomas,[p] M Miodovnik,[p] DD Wallace,[a] RL Goldenberg[q]

[a] RTI International, Durham, NC, USA [b] Materno Infantil Unidad de Planificación, INCAP, Guatemala City, Guatemala [c] Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan [d] Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA [e] Department of Paediatrics, Moi University College of Health and Sciences, Eldoret, Kenya [f] KLE University's JN Medical College, Belagavi, India [g] Department of Paediatrics, University of Zambia, Lusaka, Zambia [h] Kinshasa School of Public Health, Kinshasa, DRC [i] Lata Medical Research Foundation, Nagpur, India [j] KLE University's JN Medical College, Belagavi, India [k] Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, USA [l] Department of Obstetrics, Thomas Jefferson University, Philadelphia, PA, USA [m] Boston University, Boston, MA, USA [n] Department of Pediatrics, Indiana University, Indianapolis, IN, USA [o] Department of Pediatrics, University of Colorado, Denver, CO, USA [p] Perinatology and Pregnancy Branch, NICHD, Bethesda, MD, USA [q] Columbia University Medical Center, New York, NY, USA

Correspondence: EM McClure, PhD, Social, Statistical and Environmental Health Sciences, RTI International, Durham, NC 27709, USA. Email mcclure@rti.org

Accepted 5 November 2016. Published online 31 January 2017.

Objective We sought to classify causes of stillbirth for six low-middle-income countries using a prospectively defined algorithm.

Design Prospective, observational study.

Setting Communities in India, Pakistan, Guatemala, Democratic Republic of Congo, Zambia and Kenya.

Population Pregnant women residing in defined study regions.

Methods Basic data regarding conditions present during pregnancy and delivery were collected. Using these data, a computer-based hierarchal algorithm assigned cause of stillbirth. Causes included birth trauma, congenital anomaly, infection, asphyxia, and preterm birth, based on existing cause of death classifications and included contributing maternal conditions.

Main outcome measures Primary cause of stillbirth.

Results Of 109 911 women who were enrolled and delivered (99% of those screened in pregnancy), 2847 had a stillbirth (a rate of 27.2 per 1000 births). Asphyxia was the cause of 46.6% of the stillbirths, followed by infection (20.8%), congenital anomalies (8.4%) and prematurity (6.6%). Among those caused by asphyxia, 38% had prolonged or obstructed labour, 19% antepartum haemorrhage and 18% pre-eclampsia/eclampsia. About two-thirds (67.4%) of the stillbirths did not have signs of maceration.

Conclusions Our algorithm determined cause of stillbirth from basic data obtained from lay-health providers. The major cause of stillbirth was fetal asphyxia associated with prolonged or obstructed labour, pre-eclampsia and antepartum haemorrhage. In the African sites, infection also was an important contributor to stillbirth. Using this algorithm, we documented cause of stillbirth and its trends to inform public health programs, using consistency, transparency, and comparability across time or regions with minimal burden on the healthcare system.

Keywords Cause of death classification system, low-income countries, stillbirth.

Tweetable abstract Major causes of stillbirth are asphyxia, pre-eclampsia and haemorrhage. Infections are important in Africa.

Introduction

Globally, stillbirth rates remain high in resource-limited settings with few global estimates of cause of stillbirth published.[1–3] Knowing the medical causes of stillbirth is important for development of strategies to reduce stillbirths.[4–6] To date, over 50 stillbirth classification systems have been developed,[7–22] most requiring extensive diagnostics and most relevant in high-income countries (HIC). Additionally, systems vary in definitions of primary and secondary causes, associated causes, contributing causes, underlying cause and preventable causes. Few systems have been developed for low/middle-income countries (LMIC) where diagnostic tools such as autopsy or placental histology are usually unavailable. Examples of systems include Frøen et al.'s Cause of Death and Associated Conditions (CODAC) system, which focuses on perinatal death and includes 10 categories[19,20] and Neonatal and Intrauterine deaths Classification according to Etiology (NICE), including 13 causes for perinatal death.[22] However, to date, these systems have only been used in small studies in LMIC and generally do not distinguish between stillbirth and neonatal deaths to characterise aetiology.[20–24]

Determining cause of stillbirth has historically been challenging, as the fetus is not directly observed when death occurs and the pathway to death is often unclear.[5] Thus, cause has often been defined by maternal or obstetric conditions that may be associated directly or indirectly with the fetal death.[25–27] In LMIC, common clinical conditions associated with stillbirth include prolonged and obstructed labour, pre-eclampsia/eclampsia, multiple births, and abnormal presentations. Most stillbirths associated with these conditions are caused by diminished placental or fetal blood flow and fetal asphyxia is the final common pathway leading to death[25,28] Stillbirths are also classified as macerated or non-macerated stillbirths, with the former generally occurring more than 24 hours before delivery.[29] Non-maceration suggests that the death likely occurred during labour. Recognising these limitations, the World Health Organization (WHO) has established an international classification of diseases (ICD) perinatal mortality system, which examines the timing of the perinatal death, associated maternal conditions, and cause of perinatal death.[30,31] However, the factors used to determine cause of death vary.

To improve upon existing systems to determine cause of stillbirth in LMIC, we developed a hierarchal classification system, the Global Network Classification System,[32] which relies exclusively on readily available clinical data. Our objective for this analysis was to determine cause of stillbirth across sites in six LMICs and to compare these results with current evidence.

Methods

The study was conducted in seven sites in six LMICs: India (two sites: Nagpur, Belagavi), Pakistan, Guatemala, Democratic Republic of Congo (DRC), Kenya and Zambia. Data were collected as part of the Global Network's Maternal and Newborn Health Registry (MNHR), a population-based registry of all pregnant women residing in designated regions. The MNHR includes pregnancy-related data as well as outcomes from consenting women through to 6 weeks postpartum.[33,34] Registry Administrators (RAs), who are trained staff (generally nurses or health workers), identified and obtained consent and basic demographic data from pregnant women, and gathered the perinatal and maternal outcomes at delivery, with additional follow-up visits conducted at 6 weeks postpartum. For any woman who experienced a stillbirth, a cause of stillbirth form was completed by a trained RA to document systematically additional potential risk factors. Methods for the registry and cause of death study are described in detail elsewhere.[33] This analysis used cause of stillbirth data collected from 2014 (start dates varied by study site) through 31 December 2015.

The stillbirth classification algorithm

Stillbirths were defined as deaths in utero occurring at 20 weeks' gestation or greater.[1] The definitions for each cause were defined (Table S1).[32] The algorithm (Figure S1) first determines whether the stillbirth was associated with maternal or fetal trauma (i.e. assault, suicide, accident, fetal trauma); if so, the cause of death is classified as trauma. If no trauma was identified, and there is a major (visible) congenital anomaly, this is defined as the cause of the stillbirth. If neither of these conditions is identified and signs of maternal or fetal infection such as malaria, syphilis or fetal or vaginal odor are present, the stillbirth is classified as due to infection. If none of these is present and any maternal or fetal condition associated with intrauterine asphyxia is present, asphyxia is determined as the cause. Finally, because very preterm fetuses may die due to trauma or asphyxia associated with labour, preterm birth is listed as the cause of death if none of the prior conditions was present and the stillbirth was <32 weeks and non-macerated.[35] If none of these conditions was identified, the stillbirth was classified as unknown cause.

Ethics approval

The institutional review boards and ethics committee at the participating study sites and their affiliated U.S. partner institutions and the data coordinating centre (RTI International) approved the study. All women provided informed consent to be part of the study.

Results

In all, 112 768 pregnant women were screened in 2014–2015, and of those 111 883 (99.7%) consented and enrolled in the registry. Of these women, 103 409 delivered at ≥20 weeks' gestation and were eligible for the stillbirth cause of death study. Deliveries ranged from 19 685 in Pakistan to 10 366 in Zambia (Table 1). Hospital deliveries occurred for 42.8% of births (ranging from 74.7% in Nagpur to 9.7% in DRC), 34.5% occurred at health centres (ranging from 63.3% in DRC to 1.0% in Guatemala) and 22.7% of the deliveries occurred in home settings (ranging from 35.4% in Pakistan to 0.6% in Nagpur). For women delivering a stillbirth, delivery at a hospital was slightly more common at each of the sites compared with all births.

From 2014 to 2015, the study included 2847 stillbirths. The stillbirth rate was 27.2 per 1000 births, ranging from 43.5 per 1000 in the Pakistan site to 13.6 per 1000 in the Zambia site. During that period, the overall stillbirth rates declined about 10%, from 28.7 to 26.2 per 1000 births, in 2014 and 2015, respectively. Overall, 6.6% of stillbirths were multiple gestations, ranging from more than 11% in the DRC site to approximately 4% in the Kenya, Zambia and Pakistan sites.

Across all sites, 46.6% of stillbirths were attributed to asphyxia, 21.3% to infection, 8.4% to congenital anomalies and 6.6% to prematurity (Figure 1). No cause was assigned in 17.1% of stillbirths. No stillbirths were attributed to maternal trauma or accident. The cause of stillbirth varied by site, although for the most part, the proportion of stillbirths attributed to each cause was relatively similar, with a few notable exceptions (Table 1). Asphyxia was identified as the cause of stillbirth for 56.7% of stillbirths in Zambia compared with 28.2% in DRC. Infection had the greatest variation in the proportion of stillbirths and was estimated as a cause of stillbirth from 55.7% of stillbirths in DRC to 2.6% in Nagpur, India. Congenital anomalies were identified as the primary cause for 19.6% of stillbirths in Belagavi, India, compared with 5% or less in the African sites. Finally, prematurity was considered the cause of stillbirth for about 10% in both India sites but 4% or less in the Zambian and Kenyan sites.

We next examined the presence of several maternal conditions by cause of stillbirth (Table 2). Of the 2883 women with a stillbirth, 1400 (48.8%) had one or more of the maternal antepartum conditions including pre-eclampsia/eclampsia (10.1%), antepartum haemorrhage (11.6%), prolonged or obstructed labour (21.9%), abnormal lie (10.2%), and maternal infection (9.4%). When pre-eclampsia/eclampsia, antepartum haemorrhage or prolonged or obstructed labour was present, about 80% of the stillbirths were classified as having asphyxia as the cause of death. Of the stillbirths with breech or abnormal lie, 62.8% were classified as having asphyxia as the cause of death. Of those stillbirths where there was evidence of maternal infection, 83.6% were classified as the death due to infection. Among those stillbirths classified as asphyxia-related deaths, 38.0% had obstructed or prolonged labour, 19.2% had antepartum haemorrhage and 18.4% had pre-eclampsia/eclampsia (Figure S2). Among those with asphyxia-attributed stillbirth, 23% had no maternal condition identified but did have a fetal condition such as fetal distress or cord prolapse.

Finally, we examined the cause of stillbirth versus the presence or absence of signs of maceration (Table 3). Among all stillbirths, 67.8% did not have signs of maceration, with the death likely to have occurred <12–24 hours prior to delivery. There were important differences in the cause of death between macerated and non-macerated stillbirths. If the fetus was macerated, the cause of stillbirth was nearly equally divided among infection, asphyxia and unknown, with a smaller proportion due to a congenital anomaly (10.8%). If the fetus was not macerated, the majority of deaths were caused by asphyxia (55.4%), with smaller percentages due to infection (16.1%), unknown (11.8%), prematurity (9.7%) and congenital anomalies (7.2%). Thus, macerated stillbirths were more likely due to infection or having an unknown cause, whereas among those not macerated, asphyxia was the most common cause. Among those classified as asphyxia-related stillbirths, 80.5% were non-macerated, whereas among those with infection, 31.3% were macerated.

Discussion

Main findings

The overall stillbirth rate of 27.2 per 1000 is similar to those reported for LIC and somewhat higher than the estimated world average of about 20 per 1000 births.[1] The Pakistan site recorded the highest rate (43.5 per 1000) followed by the DRC site (38.6 per 1000) and Kenya (22.8 per 1000), also similar to the regional stillbirth patterns reported.[1]

Classifying stillbirths by maceration status and by cause of death provides some interesting observations and potential validation for the system. The fact that most deaths classified as asphyxia-related were non-macerated, suggests that they occurred during labour, consistent with many observations about intrapartum deaths.[22] Our system classified macerated stillbirths more commonly as infection-related or of unknown aetiology, which also appears consistent with previous reports.[3,29] In this analysis, all stillbirths classified as preterm in origin were non-macerated,

Table 1. MNH Registry characteristics and cause of stillbirth by site, 2014–2015*

	Total	Africa			Latin America	Asia		
		DRC	Zambia	Kenya	Guatemala	Pakistan	Belagavi	Nagpur
Deliveries, n	103 409	12 112	10 366	11 311	16 111	19 687	19 089	14 733
Delivery location, n (%)								
Hospital	44 239 (42.8)	1172 (9.7)	2455 (23.7)	2511 (22.2)	8800 (54.6)	7292 (37.0)	11 006 (57.7)	11 003 (74.7)
Clinic	35 668 (34.5)	7671 (63.3)	6035 (58.2)	5522 (48.8)	169 (1.0)	5426 (27.6)	7199 (37.7)	3646 (24.7)
Home/Other	23 499 (22.7)	3269 (27.0)	1876 (18.1)	3278 (29.0)	7141 (44.3)	6967 (35.4)	884 (4.6)	84 (0.6)
Delivery location for stillbirths, n (%)								
Hospital	1439 (50.5)	118 (24.8)	51 (35.9)	101 (38.7)	187 (57.2)	375 (43.3)	372 (80.2)	235 (75.8)
Clinic	717 (25.2)	212 (44.5)	49 (34.5)	87 (33.3)	2 (0.6)	262 (30.2)	54 (11.6)	51 (16.5)
Home/Other	691 (24.3)	146 (30.7)	42 (29.6)	73 (28.0)	138 (42.2)	230 (26.5)	38 (8.2)	24 (7.7)
Stillbirths, n (rate/1000)	2847 (27.2)	476 (38.6)	142 (13.6)	261 (22.8)	327 (20.1)	867 (43.5)	464 (24.1)	310 (20.9)
Stillbirths from multiple birth, n (%)	180 (6.3)	54 (11.4)	6 (4.2)	15 (4.6)	24 (5.2)	37 (4.3)	24 (7.7)	20 (7.7)
Cause of Stillbirth*, % (95% CI)								
Congenital anomaly	8.4 (7.3, 9.4)	3.2 (1.6, 4.7)	5.2 (1.5, 9.0)	2.7 (0.7, 4.7)	12.8 (9.2, 16.5)	5.2 (3.7, 6.7)	19.6 (15.9, 23.2)	10.0 (6.7, 13.3)
Infection	21.3 (19.8, 22.8)	55.7 (51.2, 60.1)	17.9 (11.4, 24.4)	34.7 (28.9, 40.5)	7.6 (4.8, 10.5)	17.1 (14.6, 19.6)	9.3 (6.7, 12.0)	2.6 (0.8, 4.3)
Asphyxia	46.6 (44.8, 48.5)	28.2 (24.1, 32.2)	56.7 (48.3, 65.1)	47.1 (41.0, 53.2)	45.3 (39.9, 50.7)	52.7 (49.4, 56.0)	46.5 (42.0, 51.1)	54.8 (49.3, 60.4)
Prematurity	6.6 (5.7, 7.5)	6.1 (3.9, 8.2)	3.7 (0.5, 6.9)	4.2 (1.8, 6.7)	6.4 (3.8, 9.1)	4.8 (3.4, 6.3)	9.8 (7.1, 12.5)	11.0 (7.5, 14.4)
Unknown	17.1 (15.7, 18.5)	6.9 (4.7, 9.2)	16.4 (10.1, 22.7)	11.2 (7.4, 15.0)	27.8 (23.0, 32.7)	20.2 (17.5, 22.9)	14.8 (11.5, 18.0)	21.6 (17.0, 26.2)

*Study start date in 2014 varied by site.
**Fourteen stillbirths did not have a cause of death recorded.
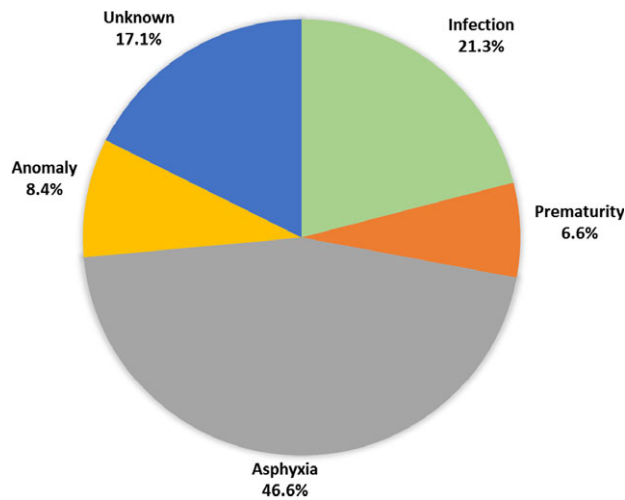
Figure 1. Cause of stillbirth as determined by algorithm among all Global Network sites, 2014–2015.

suggesting that they mostly occurred in labour and were due to the fetus not being able to tolerate the preterm labour.[35]

Using this system, we found the major cause of stillbirth to be asphyxia (46.6%), with infections contributing to 21%. Congenital anomalies represented 8.4% of all causes, with Belagavi, India having a substantially higher proportion (nearly 20%) due to congenital anomalies. A prior study conducted at this site in India found 24% of pregnant women were in consanguineous partnerships, which is a high risk for birth defects.[36] Finally, in this study, prematurity was responsible for nearly 7% of all stillbirths.

However, we also observed important regional differences. Infection was the leading cause of stillbirths in the DRC site (55.7%), one-third of the stillbirths in western Kenya and 17.9% in Zambia. Thus, the top three sites with the largest percent of infection-related stillbirths were all in

sub-Saharan Africa. Congenital anomalies represented a higher proportion of the stillbirths in the Indian sites and Guatemala relative to the sites in Africa.

Asphyxia appeared to cause a substantial proportion of stillbirths across all sites. Among those with asphyxia as a cause of stillbirth, obstructed or prolonged labour was present among 38%, antepartum haemorrhage was present for 19% and pre-eclampsia or eclampsia was present among 18% of those with stillbirth. About one-fourth of the stillbirths attributed to asphyxia had no specific maternal condition identified but did have a fetal condition such as cord prolapse or fetal distress identified. Seventeen percent of stillbirths had no attributable cause identified using the algorithm.

Strengths and limitations

There are a number of weaknesses and strengths associated with the Global Network Stillbirth Classification System and its use in this study. Most important, the cause of stillbirth attributed in this system has not been validated with fetal autopsy, culture or other, more sophisticated techniques, as the gold standard.[15,37] To address this gap, future analyses are

Table 3. Cause of stillbirth by signs of maceration

	Signs of maceration		
	Macerated	Non-macerated	Unknown
Stillbirths, n (%)	891	1920	22
Cause of stillbirth by algorithm, n (%)			
Congenital anomaly	96 (10.8)	138 (7.2)	3 (1.2)
Infection	288 (32.3)	310 (16.1)	5 (22.7)
Asphyxia	250 (28.1)	1063 (55.4)	8 (0.6)
Prematurity	0 (0.0)	187 (9.7)	0 (0.0)
Unknown	266 (30.1)	227 (11.8)	6 (1.2)

Table 2. Cause of stillbirth by maternal conditions

	Maternal condition present					None of the specified conditions
	Pre-eclampsia/ eclampsia	Antepartum haemorrhage	Obstructed or prolonged labour	Breech or transverse lie	Maternal infection	
Stillbirths, n	293	337	630	296	268	1433
Cause of Stillbirth by Algorithm, n (%)						
Congenital anomaly	12 (4.1)	8 (2.4)	17 (2.7)	15 (5.1)	10 (3.7)	187 (13.0)
Infection	36 (12.3)	73 (21.7)	109 (17.3)	49 (16.6)	224 (83.6)	261 (18.2)
Asphyxia	243 (82.9)	254 (75.4)	502 (79.7)	186 (62.8)	34 (12.7)	364 (25.4)
Prematurity	0 (0.0)	0 (0.0)	1 (0.2)	9 (3.0)	0 (0.0)	177 (12.4)
Unknown	2 (0.7)	2 (0.6)	1 (0.2)	37 (12.5)	0 (0.0)	444 (31.0)

planned to validate the Global Network system with other sources, especially where autopsy and other sophisticated testing are available to confirm cause of stillbirths.[15] Also, because fetal monitoring is generally not performed in these settings, we do not attempt to quantify the number of stillbirths associated with fetal distress, which is a common consideration in many stillbirths. We also recognise that this system is necessarily a simplification and, as a result, subtle or rare causes of stillbirth may be missed.

For a few of the categories, among the sites, there are also fairly large differences in the percent of stillbirths attributed to various causes which may be a result of site ascertainment differences due to a number of factors. For example, infection as a cause of death may be especially variable among sites with different access to tests and laboratory capabilities varying by study site. Thus, the extent to which the differences in reported infection reflect local health facility access and capability is also unknown. This system also omits categorising social or other factors that may contribute to stillbirth in low-resource settings. However, within these limitations, the major causes of stillbirth related to pregnancy appeared to be generally consistent with other external sources of cause of death data.

The strengths of our methodology are consistency, transparency, and comparability across time or regions. The methodology places little additional burden on the healthcare system. This system uses minimal, basic data from the mother, family or lay-health providers without reliance on laboratory tests, placental examinations or autopsies to determine cause of stillbirth using well-established categories. Because we use these data to assign cause of stillbirth by an algorithm, potential sources of inconsistency and bias from clinician or lay coders are reduced. In addition, using this system, we identified the maternal conditions that also were present among women having a stillbirth. Finally, the Global Network system uses principles that are consistent with the WHO's development of the perinatal mortality classification system.[30]

Interpretation

To date, only a relatively small number of stillbirth cause of death studies using a variety of classification systems have been completed in LMIC. For example, a study in India using CODAC to classify 87 stillbirths found that prolonged labour, hypertension in pregnancy and congenital anomalies were the main causes of stillbirth. In that study, nearly half of all stillbirths were intrapartum.[20] In Tanzania, a 10-year study of nearly 2000 perinatal deaths (including 1219 stillbirths) used the NICE classification and also found that obstructed/prolonged labour and hypertension were the leading maternal conditions associated with perinatal death.[22] About one-fifth of the deaths occurred among women referred to the health facility for an obstetric or medical complication.

Allanson et al.[24] have completed a recent study of cause of perinatal mortality ($n = 687$) in South Africa. They noted, similar to our study, a high rate of intrapartum deaths (non-macerated stillbirths) and, similar to other studies, found that haemorrhage and hypertension were the main maternal conditions identified among stillbirths. However, as we found, a substantial proportion of *all* stillbirths—nearly half—occurred among women with no apparent obstetric complication.

The concept of 'preventable stillbirths' has been highlighted in the recent *Lancet* stillbirth series.[2] Similar to our study, the group estimated that only 7.4% of stillbirths are associated with congenital anomalies and that the majority of stillbirths, especially in LMICs, are preventable with appropriate care. Our study confirms this opinion, as we found that most stillbirths were not macerated and were associated with obstetric conditions that if treated appropriately would prevent the stillbirth.

Conclusion

In summary, when using this system to classify causes of stillbirth, we found asphyxia as the most common cause. These stillbirths were associated with a number of major obstetric conditions, including obstructed and prolonged labour and pre-eclampsia/eclampsia. However, nearly half of all stillbirths were not associated with an identifiable maternal condition. In addition, the majority of stillbirths lacked signs of maceration and likely occurred during labour, and thus many of the stillbirths should be preventable with appropriate obstetric labour and delivery care. Our study reinforces the importance of a system to classify cause of stillbirth that is reliable across low-resource settings to inform effective interventions in order to ultimately reduce preventable stillbirths.

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting Information.

Contributions to authorship

EMM, ALG, CLB, WAC, and RLG designed the algorithm; SS, FE, SSG, EC, MM, OP, AT, AP, SMD, CT, IM, SS(2) oversaw study implementation and with MB, BSK, WAC, RJF, PLH, EAL, KMH, NFK, MKT, MM(2) and RLG monitored quality of data collection. JLM, DDW performed analyses with EMM. EMM and RLG wrote the first draft of the paper and all authors reviewed subsequent drafts and approved the final version of the paper.

Details of ethics approval

The ethics review committee of all participating institutions reviewed and approved the study.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Global Network cause of stillbirth algorithm.

Figure S2. Maternal conditions present among stillbirths caused by asphyxia as determined by algorithm.

Table S1. Causes of stillbirth and their hierarchical position in the Global Network Classification System. ∎

References

1 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:e98–108.

2 Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. *Lancet* 2016;387:587–603.

3 McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in low-middle income countries 2010–2013: a population-based, multi-country study from the Global Network. *Reprod Health* 2015;12(Suppl 2):S7.

4 Frøen JF, Friberg IK, Lawn JE, Bhutta ZA, Pattinson RC, Allanson ER, et al. Stillbirths: progress and unfinished business. *Lancet* 2016;387:574–86.

5 Goldenberg RL, Saleem S, Pasha O, Harrison MS, Mcclure EM. Reducing stillbirths in low-income countries. *Acta Obstet Gynecol Scand* 2016;95:135–43.

6 Frøen JF, Gordijn SJ, Abdel-Aleem H, Bergsjø P, Betran A, Duke CW, et al. Making stillbirths count, making numbers talk—issues in data collection for stillbirths. *BMC Pregnancy Childbirth* 2009;9:58.

7 Flenady V, Frøen JF, Pinar H, Torabi R, Saastad E, Guyon G, et al. An evaluation of classification systems for stillbirth. *BMC Pregnancy Childbirth* 2009;9:24.

8 Edmond KM, Quigley MA, Zandoh C, Danso S, Hurt C, Owusu Agyei S, et al. Aetiology of stillbirths and neonatal deaths in rural Ghana: implications for health programming in developing countries. *Paediatr Perinat Epidemiol* 2008;22:430–7.

9 Agampodi S, Wickramage K, Agampodi T, Thennakoon U, Jayathilaka N, Karunarathna D, et al. Maternal mortality revisited: the application of the new ICD-MM classification system in reference to maternal deaths in Sri Lanka. *Reprod Health* 2014;11:17.

10 Ego A, Zeitlin J, Batailler P, Cornec S, Fondeur A, Baran-Marszak M, et al. Stillbirth classification in population-based data and role of fetal growth restriction: the example of RECODE. *BMC Pregnancy Childbirth* 2013;13:182.

11 Korteweg FJ, Gordijn SJ, Timmer A, Holm JP, Ravisé JM, Erwich JJ. A placental cause of intra-uterine fetal death depends on the perinatal mortality classification system used. *Placenta* 2008;29:71–80.

12 Measey M, Charles A, d'Espaignet E, Harrison C, Douglass C. Aetiology of stillbirth: unexplored is not unexplained. *Aust NZ J Public Health* 2007;31:5.

13 Gardosi J, Kady SM, McGeown P, Francis A, Tonks A. Classification of stillbirth by relevant condition at death (ReCoDe): population based cohort study. *BMJ* 2005;331:1113–7.

14 CESDI. Confidential Enquiry into Stillbirths and Deaths in Infancy: 8th Annual Report. London: Maternal and Child Health Research Consortium, 2001.

15 Dudley DJ, Goldenberg R, Conway D, Silver RM, Saade GR, Varner MW, et al. A new system for determining the causes of stillbirth. *Obstet Gynecol* 2010;116:(2 Pt 1)254–60.

16 Reddy UM, Goldenberg R, Silver R, Smith GC, Pauli RM, Wapner RJ, et al. Stillbirth classification—developing an international consensus for research: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol* 2009;114:901–14.

17 Chan A, King JF, Flenady V, Haslam RH, Tudehope DI. Classification of perinatal deaths: development of the Australian and New Zealand classifications. *J Paediatr Child Health* 2004;40:340–7.

18 Committee on Genetics. ACOG Committee Opinion No. 383: evaluation of stillbirths and neonatal deaths. *Obstet Gynecol* 2007;110:963–6.

19 Frøen JF, Pinar H, Flenady V, Bahrin S, Charles A, Chauke L, et al. Causes of death and associated conditions (Codac): a utilitarian approach to the classification of perinatal deaths. *BMC Pregnancy Childbirth* 2009;9:22.

20 Kaistha M, Kumar D, Bhardwaj A. Agreement between international classification of disease (ICD) and cause of death and associated conditions (CODAC) for the ascertainment of cause of stillbirth (SB) in the rural areas of north India. *Indian J Public Health* 2016;16:73–6.

21 Mmbaga BT, Lie RT, Olomi R, Mahande MJ, Olola O, Daltveit AK. Causes of perinatal death at a tertiary care hospital in Northern Tanzania 2000–2010: a registry based study. *BMC Pregnancy Childbirth* 2012;12:139.

22 Winbo IG, Serenius FH, Dahlquist GG, Källén BA. NICE, a new cause of death classification for stillbirths and neonatal deaths. Neonatal and Intrauterine Death Classification according to Etiology. *Int J Epidemiol* 1998;27:499–504.

23 Lori JR, Rominski S, Osher BF, Boyd CJ. A case series study of perinatal deaths at one referral center in rural post-conflict Liberia. *Matern Child Health J* 2014;18:45–51.

24 Allanson ER, Muller M, Pattinson RC. Causes of perinatal mortality and associated maternal complications in a South African province: challenges in predicting poor outcomes. *BMC Pregnancy Childbirth* 2015;15:37.

25 Goldenberg RL, Harrison M, McClure EM. Stillbirth: the hidden birth asphyxia—U.S. and global perspectives. *Clin Perinatol* 2016;43:439–53.

26 Aminu M, Unkels R, Mdegela M, Utz B, Adaji S, van den Broek N. Causes of and factors associated with stillbirth in low- and middle-income countries: a systematic literature review. *BJOG* 2014;121 (Suppl 4):141–53.

27 Nausheen S, Soofi SB, Sadiq K, Habib A, Turab A, Memon Z, et al. Validation of verbal autopsy tool for ascertaining the causes of stillbirth. *PLoS ONE* 2013;8:e76933.

28 Lawn JE, Lee AC, Kinney M, Sibley L, Carlo WA, Paul VK, et al. Two million intrapartum-related stillbirths and neonatal deaths: where, why, and what can be done? *Int J Gynaecol Obstet* 2009;107(Suppl 1):S5–18, S19.

29 Kc A, Nelin V, Wrammert J, Ewald U, Vitrakoti R, Baral GN, et al. Risk factors for antepartum stillbirth: a case-control study in Nepal. *BMC Pregnancy Childbirth* 2015;15:146.

30 Allanson ER, Tunçalp O, Gardosi J, Pattinson RC, Erwich JJ, Flenady VJ, et al. Classifying the causes of perinatal death. *Bull WHO* 2016;94:79–79A.

31 Allanson ER, Tunçalp Ö, Gardosi J, Pattinson RC, Francis A, Vogel JP, et al. The WHO application of ICD-10 to deaths during the perinatal period (ICD-PM): results from pilot database testing in South Africa and United Kingdom. *BJOG* 2016;123:2019–2028.

32 McClure EM, Bose CL, Garces A, Esamai F, Goudar SS, Patel A, et al. Global network for women's and children's health research: a system for low-resource areas to determine probable causes of stillbirth, neonatal, and maternal death. *Matern Health Neonatol Perinatol* 2015;1:11.

33 Bose CL, Bauserman M, Goldenberg RL, Goudar SS, McClure EM, Pasha O, et al. The Global Network Maternal Newborn Health Registry: a multi-national, community-based registry of pregnancy outcomes. *Reprod Health* 2015;12(Suppl 2):S1.

34 Goudar S, Carlo WA, McClure EM, Pasha O, Patel A, Esamai F, et al. Maternal newborn health registry of the global network for women's and children's health research. *Int J Gynaecol Obstet* 2012;118:190–3.

35 Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C, GAPPS Review Group. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. *BMC Pregnancy Childbirth* 2010;10(Suppl 1):S1.

36 Bellad MB, Goudar SS, Edlavitch SA, Mahantshetti NS, Naik V, Hemingway-Foday J, et al. Consanguinity, prematurity, birth weight and pregnancy loss: a prospective cohort study at four primary health center areas of Karnataka. *India. J Perinatol* 2011;32:431–7.

37 Korteweg FJ, Erwich JJ, Timmer A, van dMJ, Ravisé JM, Veeger NJ, et al. Evaluation of 1025 fetal deaths: proposed diagnostic workup. *Am J Obstet Gynecol* 2012;206:53.e1–53.e12.