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Original article

Maternal complications and perinatal mortality: findings of the World Health Organization Multicountry Survey on Maternal and Newborn Health

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Objective We aimed to determine the prevalence and risks of late fetal deaths (LFDs) and early neonatal deaths (ENDs) in women with medical and obstetric complications.

Design Secondary analysis of the WHO Multicountry Survey on Maternal and Newborn Health (WHOMCS).

Setting A total of 359 participating facilities in 29 countries.

Population A total of 308 392 singleton deliveries.

Methods We reported on perinatal indicators and determined risks of perinatal death in the presence of severe maternal complications (haemorrhagic, infectious, and hypertensive disorders, and other medical conditions).

Main outcome measures Fresh and macerated LFDs (defined as stillbirths ≥ 1000 g and/or ≥28 weeks of gestation) and ENDs.

Results The LFD rate was 17.7 per 1000 births; 64.8% were fresh stillbirths. The END rate was 8.4 per 1000 liveborns; 67.1% occurred by day 3 of life. Maternal complications were present in 85.6, 86.5, and 88.6% of macerated LFDs, fresh LFDs, and ENDs, respectively. The risks of all three perinatal mortality outcomes were significantly increased with placental abruption, ruptured uterus, systemic infections/sepsis, pre-eclampsia, eclampsia, and severe anaemia.

Conclusions Preventing intrapartum-related perinatal deaths requires a comprehensive approach to quality intrapartum care, beyond the provision of caesarean section. Early identification and management of women with complications could improve maternal and perinatal outcomes.

Keywords Early neonatal death, fetal death, maternal complications, perinatal mortality.

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Introduction

Despite enormous global progress in child survival since the 2000 Millennium Declaration, only 23 of the 75 'Countdown to 2015' priority countries are on track to meet Millennium Development Goal 4 (MDG4) targets.[1] The last decade has seen a 2.5% annual reduction in child mortality, but only a 2.1% reduction in neonatal mortality. Newborn deaths now

account for over 40% of all deaths in children under the age of 5 years.[1,2] An estimated 2.6 million stillbirths occur worldwide every year, of which over 40% are intrapartum related.[3–5] Stillbirths are likely to be underestimated, because of the lack of vital registration in many countries, the lack of consistent definitions and classification systems, as well as poor reporting as a result of cultural taboos and social stigma.[5–7]

Perinatal survival is intimately linked to effective maternal and newborn care throughout the continuum of pregnancy, labour, and the postpartum period.[8,9] Stillbirth risk factors include short interpregnancy interval, low socio-economic status, lower education, no antenatal care, history of stillbirth, smoking, alcohol use, multiple pregnancy, obesity, hypertension, diabetes, HIV, fetal growth restriction and post-term pregnancy.[10–12] In many low- and middle-income countries (LMICs) with high stillbirth rates and inadequate access to diagnostic tools and quality maternal care, these risk factors can go untreated. Preventing antepartum stillbirths requires improved maternal health and antenatal care,[13] whereas intrapartum interventions (such as caesarean section) can reduce the number of intrapartum stillbirths.[13–15] Approximately 85% of neonatal deaths can be attributed to preterm birth complications, infections, and intrapartum-related causes.[1] The majority of these can be prevented without high-cost interventions like intensive care.[16,17] A South African study by Pattinson et al. identified suboptimal obstetric care and critical staff shortages as being associated with early neonatal mortality,[8] whereas Lawn et al.[9] identified prevention via antenatal care, skilled birth attendance, and emergency obstetric care as the most effective interventions to reduce intrapartum-related newborn deaths.

The risk of perinatal mortality associated with maternal complications has been well described in high-income countries with the capacity to diagnose and manage obstetric complications.[18,19] These findings cannot necessarily be extrapolated to lower-resource settings, with significant restrictions in human resources, diagnostic capacity, and availability of obstetric interventions, however. The existing studies of perinatal mortality in LMICs have generally been limited in size (single or few institutions) and power (unable to consider stillbirth and early neonatal death as separate outcomes),[20–23] despite accounting for 98% of the global burden. Previous large epidemiological surveys of perinatal deaths in LMICs have not captured data on maternal complications.[2,24] Such studies are necessary to understand the epidemiological patterns of these conditions and their effect on perinatal mortality, and to prioritise interventions in low-resource settings. We described the prevalence and risks of macerated and fresh stillbirth and early neonatal death in women with severe medical and obstetric complications in 29 countries, using the WHO Multicountry Survey on Maternal and Newborn Health (WHOMCS) data set.

Methods

Survey methodology

The WHOMCS is a cross-sectional survey of deliveries at 359 participating institutions in 29 countries, conducted from May 2010 to December 2011, and included 314,692 women. This survey collected data on maternal deaths and 'near-miss' cases (women who experience severe complications of pregnancy or delivery, and who nearly die but survive), irrespective of gestational age and site of pregnancy. The methodological details of the WHOMCS have been described previously,[25,26] building on the existing network from the WHO Global Survey.[27] In brief, a stratified, multistage cluster sampling approach was used to obtain a global sample of countries from Africa, Asia, Latin America, and the Middle East. Two randomly selected provinces and the capital city were sampled from within each country. From these, seven institutions with over 1000 deliveries per year and caesarean section capacity were randomly selected. Data were collected for 2 months in institutions with ≥6000 annual deliveries, and for 3 months in institutions with <6000 annual deliveries. In countries where less than 3000 annual deliveries were anticipated, the data collection period was extended to 4 months.

All women giving birth and all women with a severe maternal outcome (death or near miss) associated with pregnancy or childbirth in participating institutions during the data collection period were the study population (including women that had a severe maternal outcome as a result of an abortion or ectopic pregnancy). Data were captured on all eligible participants from presentation to the institution until discharge or day 7 postpartum, whichever came first. Consequently, adverse outcomes occurring before admission, after discharge/day 7, or during a postpartum referral were not captured. Trained data collectors reviewed medical records during the study period and used this to complete the data form at hospital discharge, transfer, or death. There was no contact between data collectors and the admitted women; however, data clarification was occasionally sought from institutional staff. Data were then entered onto a web-based data management system. In addition, an institutional data form was completed by the data collector in consultation with the head of the obstetrics department on facility characteristics, including infrastructure, obstetric and intensive care services, as well as their capacity to identify a range of laboratory, clinical, and management severity indicators for mothers and newborns.

Variables and definitions

We used three perinatal mortality outcomes: (1) macerated late fetal deaths; (2) fresh late fetal deaths; and (3) early neonatal deaths (definitions summarised in Appendix S1).

The tenth edition of the International Classification of Diseases (ICD-10) describes stillbirth as death prior to complete expulsion or extraction from the mother, indicated by the absence of any evidence of life.[28] The WHO recommends reporting on late fetal deaths, defined as stillbirths of birthweight ≥ 1000 g, or if birthweight is unknown stillbirths at ≥28 weeks of gestation, for international comparison.[29] When the timing of birth is not known, the absence of skin maceration ('fresh') in a fetus that died <12 hours before delivery is generally used as a proxy for intrapartum death.[2] This is an imprecise measure (delays in delivering an intrapartum stillbirth can cause maceration), and can underestimate the true number of intrapartum-related stillbirths[30]; however, it is of practical use in resource-limited settings where fetal status at the onset of labour is often not known. The reference group for both was liveborn neonates with the same birthweight/gestational age restrictions. Early neonatal death was defined as a death occurring by day 7 postpartum or prior to discharge in a liveborn neonate (the reference group was liveborn neonates who were alive at discharge/day 7). This definition slightly underestimates the true early neonatal mortality, as deaths occurring after discharge or during a subsequent readmission were not captured. Gestational age was based on the best obstetric estimate: the method used was not recorded, but varied between institutions. We elected to use these three outcomes separately, as they have different (yet often overlapping) patterns of prevalence, risk factors, and causal pathways. Despite this, few multicountry studies of perinatal mortality in LMICs have considered these outcomes individually, potentially confounding the results. The exposure variables considered were 16 maternal antepartum and intrapartum complications (categorised as haemorrhage disorders, infections, hypertensive disorders, and other complications or diseases) available in the WHOMCS data set as part of the WHO maternal near-miss criteria (described in Appendix S2). Dystocia/prolonged labour was not captured in the WHOMCS and postpartum haemorrhage was not included for this analysis, as it is not temporally related to perinatal deaths.

Statistical analysis

We included all women (including those experiencing a severe maternal outcome) with singleton deliveries of ≥500 g or, if the birthweight was missing, at ≥22 weeks of gestation. Multiple pregnancies were excluded, as their underlying mortality risk is higher and they may be more susceptible to the effect of maternal complications, potentially distorting risk estimates. Amongst 308,392 singleton deliveries, there were 5462 late fetal deaths and 2528 early neonatal deaths (Figure 1). We reported on the proportions of maternal, newborn, and delivery characteristics and conditions in perinatal mortality groups, and tested significance using chi-square tests. Rates of perinatal morbidity

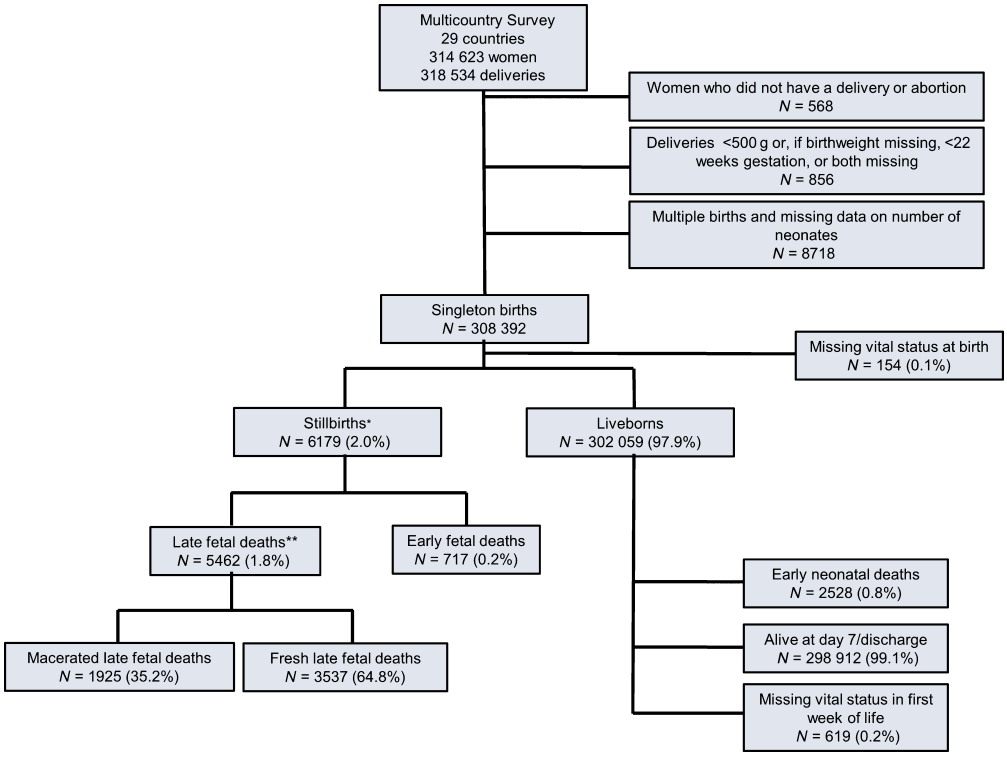

Figure 1. Study flow chart.

Table 1. Maternal, neonatal, delivery, and institutional characteristics in all births and perinatal mortality groups

	All births	Perinatal mortality					
	n (%)	Late fetal deaths*	Liveborn neonates*	Adjusted χ^2, *P***	Early neonatal death***	Infants alive at discharge/ day 7***	Adjusted χ^2, *P****
		n (%)	*n* (%)		*n* (%)	*n* (%)	
Total deliveries	308,392 (100.0)	5462 (1.8)	301,473 (97.8)		2528 (0.8)	298,912 (99.2)	
Maternal							
Maternal age							
<20 years	31,896 (10.3)	517 (9.5)	31,170 (10.3)	<0.001	320 (12.7)	30,839 (10.3)	0.010
20–34 years	238,679 (77.4)	3952 (72.4)	233,713 (77.5)		1895 (75.0)	231,788 (77.5)	
≥35 years	36,907 (12.0)	974 (17.8)	35,707 (11.8)		305 (12.1)	35,415 (11.8)	
Missing	910 (0.3)	19 (0.3)	883 (0.3)		8 (0.3)	870 (0.3)	
Marital status							
Without partner	31,214 (10.1)	536 (9.8)	30,487 (10.1)	0.793	344 (13.6)	30,176 (10.1)	0.002
With partner	273,572 (88.7)	4853 (88.9)	267,473 (88.7)		2162 (85.5)	265,259 (88.7)	
Missing	3606 (1.2)	73 (1.3)	3513 (1.2)		22 (0.9)	3477 (1.2)	
Education							
0 years	46,580 (15.1)	1855 (34.0)	44,464 (14.7)	<0.001	421 (16.7)	43,899 (14.7)	0.002
1–6 years	39,964 (13.0)	876 (16.0)	38,867 (12.9)		368 (14.6)	38,505 (12.9)	
7–9 years	58,190 (18.9)	912 (16.7)	57,008 (18.9)		555 (22.0)	56,501 (18.9)	
10–12 years	88,799 (28.8)	1002 (18.3)	87,427 (29.0)		741 (29.3)	86,744 (29.0)	
>12 years	49,616 (16.1)	340 (6.2)	49,092 (16.3)		247 (9.8)	48,884 (16.4)	
Missing	25,243 (8.2)	477 (8.7)	24,615 (8.2)		196 (7.8)	24,379 (8.2)	
Previous births							
0	130,675 (42.4)	1874 (34.3)	128,203 (42.5)	<0.001	1066 (42.2)	127,142 (42.5)	0.105
1 or 2	127,637 (41.4)	1929 (35.3)	125,123 (41.5)		1007 (39.8)	124,157 (41.5)	
>2	49,465 (16.0)	1648 (30.2)	47,550 (15.8)		451 (17.8)	47,023 (15.7)	
Missing	615 (0.2)	11 (0.2)	597 (0.2)		4 (0.2)	590 (0.2)	
Any previous caesarean section							
0	266,845 (86.5)	4783 (87.6)	260,816 (86.5)	0.058	2150 (85.0)	258,585 (86.5)	<0.001
1	28,768 (9.3)	444 (8.1)	28,197 (9.4)		243 (9.6)	27,987 (9.4)	
>1	8606 (2.8)	145 (2.7)	8407 (2.8)		110 (4.4)	8309 (2.8)	
Missing	4173 (1.4)	90 (1.6)	4053 (1.3)		25 (1.0)	4031 (1.3)	
Neonatal							
Sex of neonate							
Male	157,891 (51.2)	2940 (53.8)	154,256 (51.2)	<0.001	1418 (56.1)	152,867 (51.1)	<0.001
Female	150,077 (48.7)	2463 (45.1)	146,921 (48.7)		1102 (43.6)	145,798 (48.8)	
Missing	424 (0.1)	59 (1.1)	296 (0.1)		8 (0.3)	247 (0.1)	
Delivery							
Presentation							
Cephalic	294,479 (95.5)	4609 (84.4)	288,795 (95.8)	<0.001	2138 (84.6)	286,534 (95.9)	<0.001
Breech	10,359 (3.4)	611 (11.2)	9497 (3.2)		307 (12.1)	9265 (3.1)	
Other	2960 (1.0)	209 (3.8)	2676 (0.9)		74 (2.9)	2629 (0.9)	
Missing	594 (0.2)	33 (0.6)	505 (0.2)		9 (0.4)	484 (0.2)	
Labour							
Spontaneous	238,558 (77.4)	3971 (72.7)	233,606 (77.5)	<0.001	1846 (73.0)	231,660 (77.5)	<0.001
Induced	32,513 (10.5)	1021 (18.7)	31,221 (10.4)		262 (10.4)	30,953 (10.4)	
No labour	36,883 (12.0)	451 (8.3)	36,242 (12.0)		415 (16.4)	35,907 (12.0)	
Missing	438 (0.1)	19 (0.3)	404 (0.1)		5 (0.2)	392 (0.1)	
Mode of delivery							
Vaginal delivery	220,836 (71.6)	4139 (75.8)	215,616 (71.5)	0.001	1525 (60.3)	213,963 (71.6)	<0.001
caesarean Section	87,137 (28.3)	1253 (22.9)	85,531 (28.4)		992 (39.2)	84,635 (28.3)	
Missing	419 (0.1)	70 (1.3)	326 (0.1)		11 (0.4)	314 (0.1)	

Table 1. (Continued)

	All births	Perinatal mortality					
	n (%)	Late fetal deaths*	Liveborn neonates*	Adjusted χ^2, *P***	Early neonatal death***	Infants alive at discharge/ day 7***	Adjusted χ^2, *P****
		n (%)	*n* (%)		*n* (%)	*n* (%)	
Institutional							
Location of facility							
Urban	242,545 (78.6)	4059 (74.3)	237,272 (78.7)	0.382	2073 (82.0)	235,304 (78.7)	0.246
Peri-urban	29,436 (9.5)	588 (10.8)	28,743 (9.5)		175 (6.9)	28,463 (9.5)	
Rural	14,635 (4.7)	308 (5.6)	14,274 (4.7)		108 (4.3)	14,154 (4.7)	
Missing	21,776 (7.1)	507 (9.3)	21,184 (7.0)		172 (6.8)	20,991 (7.0)	
Level of facility							
Primary	16,846 (5.5)	205 (3.8)	16,578 (5.5)	0.128	112 (4.4)	16,461 (5.5)	0.001
Secondary	96,905 (31.4)	1948 (35.7)	94,633 (31.4)		634 (25.1)	93,838 (31.4)	
Tertiary	133,262 (43.2)	2106 (38.6)	130,365 (43.2)		1394 (55.1)	129,183 (43.2)	
Other referral level	37,017 (12.0)	667 (12.2)	36,164 (12.0)		196 (7.8)	35,912 (12.0)	
Missing	24,362 (7.9)	536 (9.8)	23,733 (7.9)		192 (7.6)	23,518 (7.9)	

*Late fetal deaths, defined as fetal death of birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation. Reference group is liveborn neonates with same birthweight/gestational age restrictions.
**Adjusted chi-square *P* value for comparison of late fetal deaths with liveborn neonates only.
***Early neonatal deaths, defined as death of a liveborn neonate by discharge/day 7 of life (deaths occurring after discharge were not captured). Reference group is liveborn neonates alive at discharge/day 7. Denominator is liveborn neonates only.
****Adjusted chi-square *P* value for comparison of early neonatal deaths with liveborn neonates only. Denominator is liveborn neonates only.

and mortality indicators were reported by country. As health facilities were the primary sampling unit of the WHOMCS, individual-level analyses may be affected by clustering. All estimates of association (chi-square tests) were corrected for the cluster effects (health facilities as sampling units, countries as strata) and $P < 0.05$ was regarded as significant.

To determine the relationship between maternal complications and perinatal mortality, we reported prevalences for the three outcome groups and calculated odds ratios. The complications as described in Appendix S2 were considered predictors in separate multilevel, multivariate logistic regression models of macerated and fresh late fetal death and early neonatal death. Using the GENLINMIXED procedure in SPSS 20, the model accounted for the clustering of mothers within facilities and facilities within countries, as well as adjusting for confounding factors at the maternal (maternal age, marital status, maternal education, number of previous births, and number of previous caesarean sections), perinatal (fetal presentation, congenital malformation, gestational age, and infant sex), and facility level (facility capacity index). The onset of labour and mode of delivery were not considered as confounding factors, as they lie in the causal pathway for several maternal conditions. Missing data were excluded from all modelling. We developed and applied a facility complexity index (FCI) to adjust for the level of services available in each facility, based on a similar index used in the WHO Global Survey.[31] The development and application of the FCI is described in Appendix S3. FCI scores were available for 295 facilities, and ranged from 12 to 57 points (only facilities with no missing data were included in the index).

Statistical analyses were conducted using SPSS 20.0.0.[32] The article was prepared in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[33] The WHOMCS was approved by the World Health Organization Ethical Review Committee and relevant ethical clearance bodies in participating countries. This study was supported by the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), World Health Organization (WHO), United States Agency for International Development (USAID), the Ministry of Health, Labour and Welfare of Japan, and Gynuity Health Projects.

Results

In these 308 392 singleton deliveries, the prevalence of late fetal death was 1.8% (64.8% were fresh) and early neonatal

mortality was 0.8% (Figure 1). There was a higher prevalence of maternal age >35 years, education of 0 or 1–5 years, more than previous births, male gender, non-cephalic presentation, induced labour, and vaginal delivery in pregnancies resulting in late fetal death (Table 1). Comparatively, the early neonatal mortality group had a higher prevalence of mothers who were <20 years of age, without partners, with education of ≤9 years, with a history of more than one caesarean section, male gender, non-cephalic presentation, no labour, and delivery by caesarean section. Both late fetal and early neonatal deaths had a higher prevalence of low birthweight and preterm birth, and 72.9% of liveborn neonates that died were admitted to a neonatal intensive care unit (NICU; Table 2). Of early neonatal deaths, 67.1% had occurred by day 3 of life, and nearly 33% occurred on the first day (Figure 2). At the country level (Table S1), the median late fetal death rate was 6.6 per 1000 deliveries (interquartile range 4.2–26.8 per 1000 deliveries), and the median early neonatal death rate was 7.5 per 1000 live births (interquartile range 4.5–10.7 per 1000 live births). The overall rates of maternal morbidities by country are described in Table S2. Hypertensive disorders were the most common (2.7%), followed by other complications/diseases (2.5%), haemorrhagic disorders (1.1%), and infective disorders (0.6%).

The prevalence of all maternal complications was significantly higher in macerated and fresh late fetal deaths and early neonatal deaths, except for placenta accreta/increta/percreta ($P = 0.071$), influenza-like illness ($P = 0.819$), and coincidental conditions ($P = 0.457$) in macerated late fetal deaths, pyelonephritis ($P = 0.581$) and coincidental conditions ($P = 0.149$) in fresh late fetal deaths, and influenza-like illness ($P = 0.801$) in early neonatal deaths (Tables 3 and 4). Figure 3 shows the prevalence of categories of maternal complications in perinatal mortality groups: only 14.4% of macerated late fetal deaths; 13.5% of fresh late fetal deaths; and 11.4% of early neonatal deaths did not have a maternal complication present. The risks of macer-

Table 2. Prevalence of neonatal conditions in all births and perinatal mortality groups

	All births	Perinatal mortality					
		Late fetal death			Liveborn neonates		
	n (%)	Late fetal death*	Liveborn neonates*	Adjusted χ^2, *P***	Early neonatal death***	Neonates alive at discharge/ day 7***	Adjusted χ^2, *P****
		n (%)	*n* (%)		*n* (%)	*n* (%)	
Total deliveries	308,392 (100.0)	5462 (1.8)	301,473 (97.8)		2528 (0.8)	298,912 (99.2)	
Birthweight							
Low birthweight, <2500 g	32,547 (10.6)	2390 (43.8)	28,896 (9.6)	<0.001	1530 (60.5)	27,873 (9.3)	<0.001
2500–3999 g	261,843 (84.9)	2531 (46.3)	259,234 (86.0)		944 (37.3)	258,121 (86.4)	
≥4000 g	13,177 (4.3)	194 (3.6)	12,976 (4.3)		54 (2.1)	12,918 (4.3)	
Missing birthweight	825 (0.3)	347 (6.4)	367 (0.1)		0 (0.0)	0 (0.0)	
Gestational age							
All preterm births (<37 weeks)	22,222 (7.2)	2117 (38.8)	18,849 (6.3)	<0.001	1320 (52.2)	17,950 (6.0)	<0.001
Term birth (37–42 weeks)	278,290 (90.2)	3196 (58.5)	274,934 (91.2)		1135 (44.9)	273,350 (91.4)	
Post-term birth (≥42 weeks)	4860 (1.6)	85 (1.6)	4768 (1.6)		46 (1.8)	4714 (1.6)	
Missing gestational age	3020 (1.0)	64 (1.2)	2922 (1.0)		27 (1.1)	2898 (1.0)	
Apgar score***							
Apgar score <7 at 5 minutes	7798 (2.5)				1457 (57.6)	6255 (2.1)	<0.001
Apgar score ≥7 at 5 minutes	293,023 (95.0)				1010 (40.0)	291,636 (97.6)	
Neonatal ICU***							
Admitted to NICU	19,519 (6.3)				1842 (72.9)	17,578 (5.9)	<0.001
Not admitted to NICU	282,390 (91.6)				684 (27.1)	281,291 (94.1)	

*Late fetal deaths, defined as fetal death of birthweight ≥ 1000 g or, if birthweight unknown, ≥28 weeks of gestation. Comparator group is liveborn neonates with same birthweight/gestational age restrictions.
**Adjusted chi-square *P* value for comparison of late fetal deaths with liveborn neonates only.
***Early neonatal deaths, defined as death of a liveborn neonate by discharge/day 7 of life (deaths occurring after discharge were not captured). Reference group is liveborn neonates alive at discharge/day 7.
****Adjusted chi-square *P* value for comparison of early neonatal deaths with liveborn neonates only.
*****Denominator is liveborn neonates only.

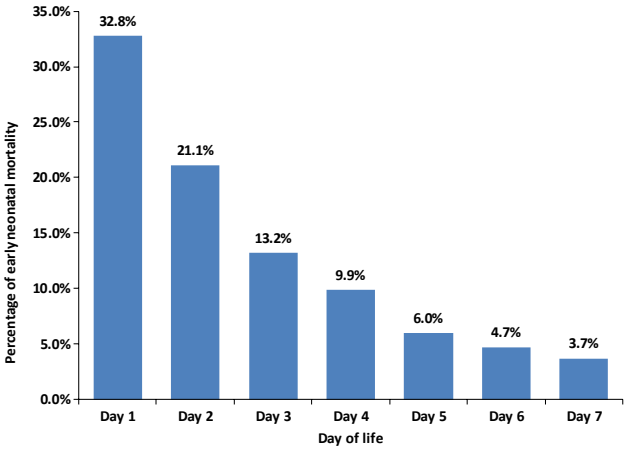

Figure 2. Distribution of early neonatal mortality by day of life. *Missing information on the date of birth/death for the remaining 8.6% of early neonatal deaths.

ated late fetal death, fresh late fetal death, and early neonatal death were consistently increased in mothers with placental abruption, ruptured uterus, systemic infections/sepsis, pre-eclampsia, eclampsia, and severe anaemia (Table 5). Figures 4–6 use logarithmic scales to graph the prevalence of maternal complications against the point estimates for adjusted odds ratios (95% confidence intervals not displayed). The complications plotted towards the upper right corner of these graphs are of higher prevalence and risk.

Discussion

Main findings

We conducted an analysis of the relationship between 16 maternal complications and perinatal mortality in 308 392 singleton deliveries at facilities in 29 countries, the largest such analysis conducted using consistent definitions of

Table 3. Prevalence of maternal complications in perinatal mortality groups

	All births	Late fetal deaths*				Liveborn neonates
		Macerated late fetal deaths**	Adjusted χ^2, *P***	Fresh late fetal deaths****	Adjusted χ^2, *P*****	
	n (%)	*n* (%)		*n* (%)		*n* (%)
All deliveries	308,392 (100.0)	1925		3537		301,473 (97.8)
Haemorrhage disorders						
Placenta praevia	1234 (0.4)	23 (1.2)	<0.001	69 (2.0)	<0.001	1112 (0.4)
Placenta accreta/increta/percreta	465 (0.2)	6 (0.3)	0.071	13 (0.4)	0.005	435 (0.1)
Placental abruption	1045 (0.3)	74 (3.8)	<0.001	245 (6.9)	<0.001	674 (0.2)
Ruptured uterus	297 (0.1)	17 (0.9)	<0.001	128 (3.6)	<0.001	145 (0.0)
Other obstetric haemorrhage	597 (0.2)	18 (0.9)	<0.001	35 (1.0)	<0.001	523 (0.2)
Infections						
Pyelonephritis	471 (0.2)	11 (0.6)	0.003	7 (0.2)	0.581	443 (0.1)
Influenza-like illness	225 (0.1)	0 (0.0)	0.819	6 (0.2)	0.022	216 (0.1)
Other systemic infections/sepsis	1081 (0.4)	63 (3.3)	<0.001	57 (1.6)	<0.001	923 (0.3)
Hypertensive disorders						
Chronic hypertension	1244 (0.4)	31 (1.6)	<0.001	41 (1.2)	<0.001	1122 (0.4)
Pre-eclampsia	6607 (2.1)	129 (6.7)	<0.001	244 (6.9)	<0.001	6063 (2.0)
Eclampsia	902 (0.3)	23 (1.2)	<0.001	101 (2.9)	<0.001	738 (0.2)
Other complications or diseases						
HIV+/AIDS/HIV wasting syndrome	1268 (0.4)	24 (1.2)	<0.001	30 (0.8)	<0.001	1206 (0.4)
Severe anaemia	4385 (1.4)	147 (7.6)	<0.001	320 (9.0)	<0.001	3840 (1.3)
Malaria/dengue	344 (0.1)	19 (1.0)	<0.001	46 (1.3)	<0.001	268 (0.1)
Medical diseases******	1590 (0.5)	31 (1.6)	<0.001	50 (1.4)	<0.001	1477 (0.5)
Coincidental conditions	645 (0.2)	7 (0.4)	0.457	14 (0.4)	0.149	605 (0.2)

*Late fetal deaths, defined as fetal death of birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation.
**Macerated late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation) with signs of maceration. Reference group is liveborn neonates with same birthweight/gestational age restrictions.
***Adjusted chi-square *P* value for comparison of macerated late fetal deaths to liveborn neonates only.
****Fresh late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, ≥28 weeks of gestation), with no signs of maceration. Reference group is liveborn neonates with same birthweight/gestational age restrictions.
*****Adjusted chi-square *P* value for comparison of fresh late deaths to liveborn neonates only.
******Medical disease, defined as any one or more of: embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.

Table 4. Prevalence of maternal complications in liveborn neonates

	All births	Liveborn neonates		Adjusted χ^2, *P***
	n (%)	Early neonatal death*	Neonates alive at discharge/day 7	
		n (%)	*n* (%)	
All deliveries	308,392 (100.0)	2528	298,912	
Haemorrhage				
Placenta praevia	1234 (0.4)	52 (2.1)	1074 (0.4)	<0.001
Placenta accreta/increta/percreta	465 (0.2)	14 (0.6)	427 (0.1)	<0.001
Placental abruption	1045 (0.3)	76 (3.0)	607 (0.2)	<0.001
Ruptured uterus	297 (0.1)	12 (0.5)	133 (0.0)	<0.001
Other obstetric haemorrhage	597 (0.2)	23 (0.9)	509 (0.2)	<0.001
Infection				
Pyelonephritis	471 (0.2)	16 (0.6)	431 (0.1)	<0.001
Influenza-like illness	225 (0.1)	0 (0.0)	216 (0.1)	0.801
Other systemic infections/sepsis	1081 (0.4)	51 (2.0)	883 (0.3)	<0.001
Hypertensive disorders				
Chronic hypertension	1244 (0.4)	35 (1.4)	1103 (0.4)	<0.001
Pre-eclampsia	6607 (2.1)	183 (7.2)	5957 (2.0)	<0.001
Eclampsia	902 (0.3)	64 (2.5)	674 (0.2)	<0.001
Other complications or diseases				
HIV+/AIDS/HIV wasting syndrome	1268 (0.4)	18 (0.7)	1190 (0.4)	0.022
Severe anaemia	4385 (1.4)	122 (4.8)	3730 (1.2)	<0.001
Malaria/dengue	344 (0.1)	13 (0.5)	253 (0.1)	<0.001
Medical diseases***	1590 (0.5)	46 (1.8)	1436 (0.5)	<0.001
Coincidental conditions	645 (0.2)	22 (0.9)	593 (0.2)	<0.001

*Early neonatal deaths, defined as death of a liveborn neonate by discharge/day 7 of life (deaths occurring after discharge were not captured). Reference group is liveborn neonates alive at discharge/day 7.
**Adjusted chi-square *P* value for comparison of early neonatal deaths with liveborn neonates only.
***Medical disease, defined as any one or more of: embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.

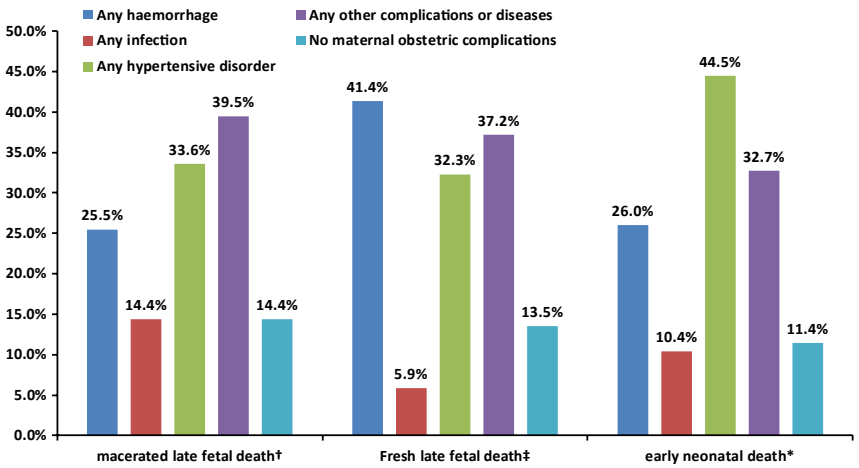

Figure 3. Prevalence of maternal complications in macerated and fresh late fetal deaths and early neonatal deaths. †Macerated late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation) with signs of maceration. ‡Fresh late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, ≥28 weeks of gestation) with no signs of maceration. *Early neonatal deaths, defined as the death of a liveborn neonate by discharge/day 7 of life (deaths occurring after discharge were not captured). The reference group is liveborn neonates alive at discharge/day 7.

Table 5. Crude and adjusted odds of perinatal mortality groups with maternal complications

	Macerated late fetal deaths*			Fresh late fetal deaths**			Early neonatal mortality***		
	Crude OR	Adjusted OR****	95% CI	Crude OR	Adjusted OR****	95% CI	Crude OR	Adjusted OR****	95% CI
Haemorrhage									
Placenta praevia	3.27	1.39	0.74–2.64	5.37	1.19	0.78–1.81	5.82	1.17	0.84–1.63
Placenta accreta/increta/ percreta	2.16	0.90	0.25–3.16	2.55	0.54	0.05–5.51	3.89	1.08	0.53–2.23
Placental abruption	17.84	**9.44**	**6.22–14.34**	33.21	12.38	**8.17–18.75**	15.23	**4.00**	**2.74–5.86**
Ruptured uterus	18.52	**7.48**	**4.02–13.91**	78.03	45.25	**23.22–88.17**	10.71	**4.18**	**1.85–9.45**
Other obstetric haemorrhage	5.43	**1.72**	**1.02–2.88**	5.75	1.47	0.88–2.48	5.38	**3.16**	**1.84–9.45**
Infection									
Pyelonephritis	3.91	**2.24**	**1.04–4.82**	1.35	1.20	0.16–9.13	4.41	1.65	0.91–3.01
Influenza-like illness	No cases	No cases	No cases	2.37	0.99	0.42–2.31	No cases	No cases	No cases
Other systemic infections/ sepsis	11.02	**6.64**	**3.57–12.34**	5.33	**2.72**	**1.85–3.99**	6.95	**2.29**	**1.31–4.01**
Hypertensive disorders									
Chronic hypertension	4.38	**2.37**	**1.60–3.50**	3.14	1.30	0.97–1.74	3.79	0.86	0.47–1.56
Pre-eclampsia	3.50	**3.27**	**2.10–5.07**	3.61	**2.25**	**1.80–2.81**	3.84	**1.72**	**1.36–2.19**
Eclampsia	4.93	**1.74**	**1.36–2.23**	11.98	**3.27**	**2.30–4.63**	11.49	**4.84**	**3.24–6.21**
Other complications or diseases									
HIV+/AIDS/HIV wasting syndrome	3.14	1.01	0.79–1.30	2.13	1.17	0.84–1.62	1.79	**0.70**	**0.51–0.95**
Severe anaemia	6.41	**2.46**	**1.80–3.36**	7.71	**2.64**	**2.23–3.11**	4.01	**1.37**	**1.07–1.77**
Malaria/dengue	11.20	**2.08**	**1.57–2.76**	14.81	**1.97**	**1.48–2.62**	6.10	1.68	0.45–6.32
Medical diseases*****	3.32	**1.78**	**1.00–3.17**	2.91	1.41	0.87–2.27	3.84	**1.55**	**1.08–2.22**
Coincidental conditions	1.82	2.84	0.82–9.84	1.98	**2.08**	**1.06–4.09**	4.42	2.24	0.65–7.65

*Macerated late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation) with signs of maceration. Reference group is liveborn neonates with same birthweight/gestational age restrictions.
**Fresh late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation) with no signs of maceration. Reference group is liveborn neonates with same birthweight/gestational age restrictions.
***Early neonatal deaths, defined as the death of a liveborn neonate by discharge/day 7 of life (deaths occurring after discharge were not captured). Reference group is liveborn neonates alive at discharge/day 7.
****Logistic regression adjusted for: maternal age; marital status; maternal education; number of previous births; number of previous caesarean sections; fetal presentation; congenital malformation; infant sex; gestational age category and facility capacity index. Also adjusted for facility and country as random effects.
*****Medical disease, defined as any one or more of: embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.
Bold values indicate adjusted ORs where the 95% CI does not excede 1 and are therefore significantly different.

maternal morbidities and able to distinguish types of perinatal mortality. The vast majority of perinatal deaths in participating facilities occurred in the presence of a maternal complication, and two-thirds were fresh (i.e. were likely to be intrapartum-related). These relationships are critical in settings where maternal morbidities are often common, under-diagnosed, and/or under-treated, and where perinatal mortality is high. The late fetal death rate (17.7 per 1000 births) was significantly higher than that of higher-income countries – Cousens et al.[3] estimated 3.9 per 1000 births (with a relative uncertainty range of – 1.6 to 6.3%) for high-income regions – but was comparable with the rate of 22 per 1000 births reported by McClure et al. in a study of 200 000 community deliveries in low-income countries.[2] Although recent global estimates suggested only 45% of stillbirths are intrapartum,[13] our facility data (64.8% fresh late fetal deaths) and McClure et al.'s community data (only 17.2% were macerated) strongly suggest that intrapartum stillbirths account for a greater proportion than has been previously thought.

Strengths and limitations

This analysis had several strengths. The WHOMCS was conducted in 29 countries, using trained data collectors and a standardised methodology that was refined from our experiences with the previous WHO global survey. We

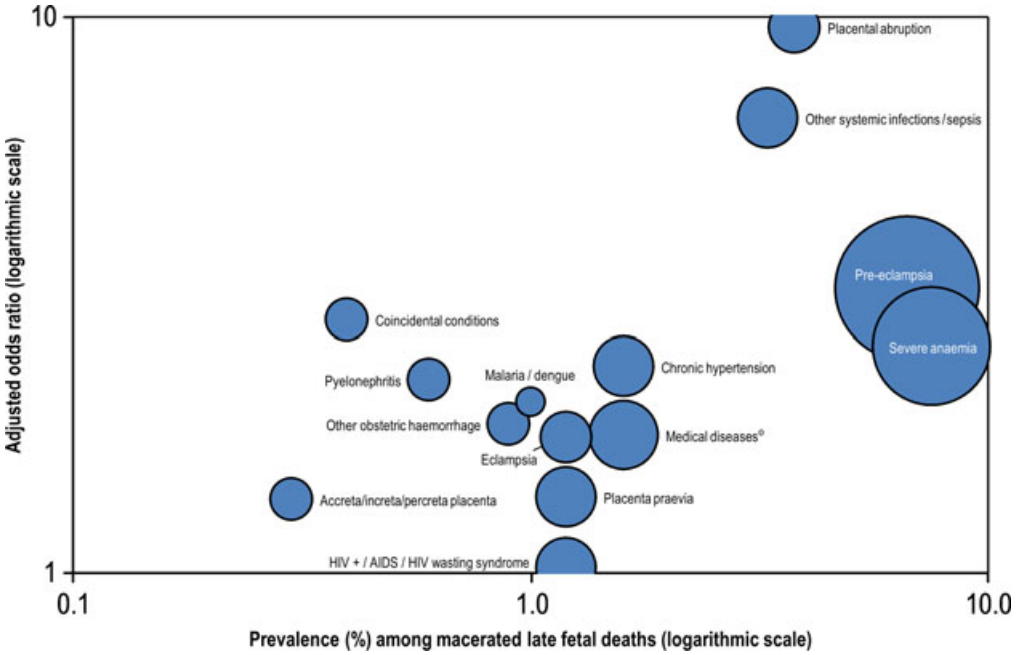

Figure 4. Prevalence and adjusted odds ratios of macerated late fetal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.

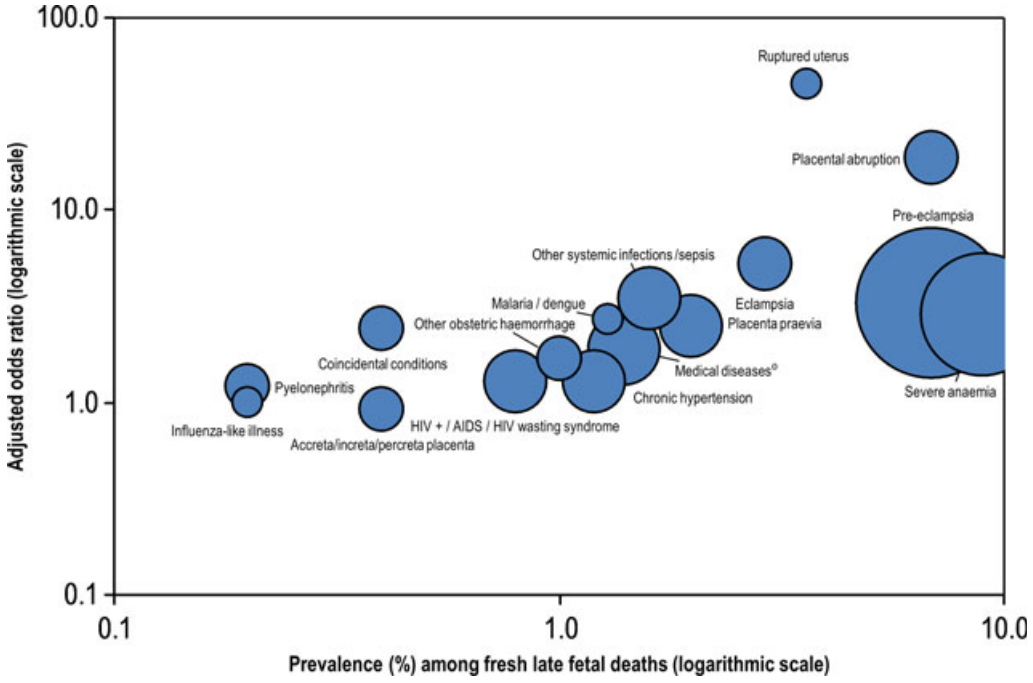

Figure 5. Prevalence and adjusted odds ratios of fresh late fetal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.

used a validated tool developed through an international collaborative process to assess maternal complications consistently.[34] To the best of our knowledge, it is the biggest international data set linking maternal complications with late fetal and early neonatal deaths. Some limitations must be acknowledged, however. We lacked information on sev-

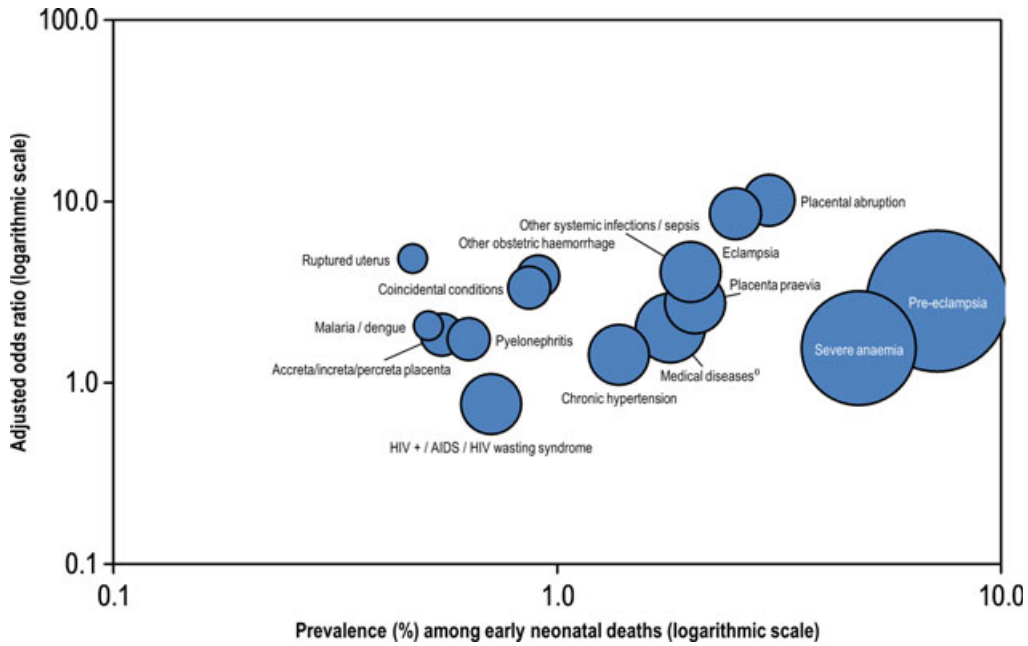

Figure 6. Prevalence and adjusted odds ratios of early neonatal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism, amniotic fluid embolism, or air embolism); cancer; heart disease; lung disease; renal disease; or hepatic disease.

eral variables known to contribute to fetal and neonatal mortality, such as diabetes, obesity, malnutrition, syphilis, smoking, length and difficulty of labour, and birth spacing. We were therefore unable to include obstructed labour as a maternal complication, despite its contribution to intrapartum-related stillbirths and early neonatal deaths. The temporality and severity of maternal complications was also not known. As the primary data source was routine medical records, erroneous or absent documentation of complications in the records could have affected data quality, diluting risk estimates; however, we believe this bias was minimised as much as possible by training provisions prior to the commencement of the study (building on our experiences in the WHO global survey) and by data collectors consulting with clinical staff to complement the information obtained from the records, where necessary. The facility-based sampling frame may have led to an over-representation of maternal complications and perinatal deaths, as more complicated cases are referred to these facilities. Similarly, the focus of the survey was on women experiencing severe maternal morbidity and mortality, who are more likely to experience adverse perinatal outcomes. Whereas we have reported on perinatal indicators at the country level to benefit national efforts, our data are not representative of the population and can only be extrapolated to similar settings. As data collection was only conducted for the duration of the admission, we acknowledge that perinatal deaths occurring in the community or post-discharge were not captured by this survey.

Interpretation

Aside from a few lower-income countries with a lower proportion of fresh late fetal deaths (such as Sri Lanka, 39.0%, and Kenya, 49.6%), we were surprised that the proportion of intrapartum-related stillbirths was so high when all participating facilities had the capacity to perform caesarean section: many (if not most) of these fresh stillbirths should have been preventable. Several factors may explain this pattern. Our research group previously reported that coverage of essential maternal interventions (such as uterotonics for the prevention and management of postpartum haemorrhage, magnesium sulfate for eclampsia, and intravenous antibiotics for maternal infections) in the WHOMCS data set was generally high, yet care performance and rates of adverse maternal outcomes were variable between countries.[26] We hypothesised that aspects of obstetric care other than coverage of essential interventions alone, such as delays or obstacles in implementation, or a lack of comprehensive supportive care (such as shock management in postpartum haemorrhage), are equally important to maternal survival. Similarly, although the availability of caesarean section is critical to prevent intrapartum-related stillbirths and early neonatal deaths, so is the early identification of at-risk pregnancies, close supervision during labour, timely access to safe caesarean section, and appropriate postpartum care for mother and baby. The very low late fetal death rates in Vietnam, China, and Paraguay are likely to represent outliers, but the misclassification or under-documentation of

stillbirths in some settings may be a factor. Similarly, Vietnam, Thailand, and Afghanistan had very low rates of early neonatal death – this could be related to early neonatal deaths occurring at home post-discharge, which may be increased if women are discharged very soon after delivery. The high rate of low Apgar scores (57.6%) amongst early neonatal deaths is suggestive of the contribution of prolonged labour; however, we lacked data on difficulties during labour and were therefore unable to estimate its impact.

Whereas only 7% of women in the WHOMCS had a potentially life-threatening complication,[26] 85.6% of macerated late fetal deaths, 86.5% of fresh late fetal deaths, and 88.6% of early neonatal deaths occurred in the presence of at least one of these complications. Although our sampling frame was based on larger facilities (and therefore was likely to have an over-representation of complicated pregnancies), this is significantly higher than the 50, 75, and 80% reported by Lawn et al. in a South African perinatal audit data set.[13] This implies that the continuum between maternal complications and perinatal mortality in facility deliveries is more important than previously thought. The early identification of these complications could permit prevention of a greater proportion of perinatal deaths. Although the risk of all types of perinatal mortality in women with complications was consistently high (for placental abruption, ruptured uterus, other systemic infections/sepsis, pre-eclampsia, eclampsia, and severe anaemia), combining information on prevalence and risks (Figures 4–6) implicates pre-eclampsia and severe anaemia as important targets for action. These conditions can be identified in the antenatal period, highlighting the need for improving the continuum of care between community-based antenatal identification of maternal complications and managing these at-risk deliveries and neonates in facilities to prevent perinatal deaths.

Conclusion

The majority of late fetal deaths in deliveries at the participating facilities with access to caesarean section were fresh (i.e. likely to occur in the intrapartum period). Preventing intrapartum-related perinatal deaths goes beyond the provision of caesarean section, requiring a comprehensive approach including the early identification of at-risk pregnancies and universal access to safe, timely caesarean section. The vast majority of perinatal deaths occur in women with a medical or obstetric complication: the early identification and management of these women could yield benefits for improving maternal outcomes, but could also reduce perinatal mortality rates. Maternal complications that can be detected and managed during the antenatal period (such as pre-eclampsia and severe anaemia) are of moderate prevalence and also moderately increase the risks of all types of perinatal mortality. Improving the continuum of care between community-based antenatal identification of maternal complications and managing these at-risk deliveries and neonates in facilities is essential in preventing perinatal deaths.

Disclosure of interests

The authors declare that they have no competing interests or conflicts of interest.

Contribution to authorship

JPV and JPS conceptualised the article and analysis plan. JPV performed the analysis. JPV wrote the draft article, and JPS, RM, NM, PL, ML, JEOP, BH, RPC, MR, SM, JGC, OT, and AMG contributed to the interpretation of the results, development of the article, and approved the final version of the article. This article gives the views of the named authors only.

Details of ethics approval

The Special Programme of Research, Development and Research Training in Human Reproduction (HRP) Specialist Panel on Epidemiological Research reviewed and approved the study protocol for technical content. This study was approved by the World Health Organization Ethical Review Committee and the relevant ethical clearance mechanisms in all countries (protocol ID, A65661; date of approval, 27 October 2009).

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Supporting Information

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

Appendix S1. Key definitions.

Appendix S2. Definitions of maternal complications of pregnancy and delivery.

Appendix S3. Development of the Facility Capacity Index (FCI) for the WHO Multicountry Survey.

Table S1. Prevalence of perinatal mortality and morbidity indicators, by country.

Table S2. Prevalence of categories of maternal complications, by country. ■

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