Table 1. Maternal characteristics and associations with antibiotic prophylaxis.

	Number of caesarean deliveries (*n*)	Coverage of antibiotic prophylaxis for caesarean section (%)		
		In all caesarean deliveries (*n* = 89 121)	In institutes with ≥90% prophylaxis coverage (*n* = 66 271)	In institutes with <90% prophylaxis coverage (*n* = 22 850)
Total	89121	87	97	60
Age (years)				
<20	7145	87	97	60
20–34	68249	85	96	66
≥35	13572	88	97	60
Marital status				
Single	8395	86	96	67
Married/cohabiting	80182	87	97	60
Education (years)				
0	6801	82	96	61
1–6	9986	84	97	57
7–9	16275	86	97	60
10–12	28575	89	97	66
>12	21161	89	97	55
Parity				
0	42347	88	97	63
1–2	37757	88	97	59
≥3	8874	81	96	57
Any previous caesarean section	30835	88	97	59
Congenital malformation	1077	89	97	63
Multiplicity				
Singleton	86759	87	97	60
Twin	2284	85	97	51
Triplet or more	76	85	97	47
Anaemia (haemoglobin < 7mg/dl)	2218	88	97	79
Obstetric haemorrhagic disorders*	3458	87	97	62
Hypertensive disorders				
Chronic hypertension	776	87	98	55
Pre-eclampsia/ eclampsia	4684	89	97	60
Infection				
HIV+/AIDS	491	92	98	74
Malaria/dengue	173	49	98	32
Onset of labour				
Spontaneous labour	42782	85	97	57
Induction	8274	88	95	69
No labour	37865	90	97	63
Preterm delivery	8638	88	96	62
Stillbirth	1273	82	94	82
Other maternal medical conditions**	1169	90	97	55

*Placenta praevia, accreta/increta/percreta placenta, abruptio placenta, ruptured uterus, postpartum haemorrhage and any other obstetric haemorrhage.
**Any chronic or acute injury or disorder affecting the kidneys, heart, lungs or liver.

Statistical analysis

First, we examined the variation within facilities with regard to the coverage of antibiotic prophylaxis, as well as whether this variation was associated with institutional characteristics.

Next, we compared coverage of antibiotic prophylaxis by maternal characteristics, as well as within strata of facilities based on whether they provided above or below 90% coverage of prophylaxis. All subgroups were tested for significant difference between coverage by chi-squared tests.

To determine the effect of maternal characteristics on antibiotic coverage, we constructed multilevel, multivariate logistic regression models, using the maternal characteristics as shown in Table 1, and with three levels [country (level 1), facility (level 2) and individual (level 3)], allowing random effects at higher levels. We took into account differences between countries and institutions by adjusting for country development (HDI categories) and facility capacity (by facility capacity index category), as well as using a multilevel model which allowed evaluation of the differences in the baseline coverage and infection rate between institutions within each country. We repeated this analysis in subgroups of facilities based on whether they provided above or below 90% coverage of antibiotic prophylaxis.

To determine the relationship between maternal characteristics and bacterial infection, we constructed multilevel, multivariate logistic regression models, using the maternal characteristics as shown in Table 1 and with the three levels. We repeated this analysis in subgroups of women based on whether they did or did not receive prophylaxis.

Statistical analysis was conducted using Stata/MP version 12.0 (Stata Corp LP, College Station, TX, USA), and $P < 0.05$ was considered to be statistically significant.

Results

Of the 359 facilities in 29 countries, three facilities in Uganda replied that they could not administer parenteral antibiotics and 27 facilities, including these three, did not perform any caesarean section. Of the remaining 332 facilities that performed caesarean delivery, coverage of antibiotic prophylaxis varied greatly from 0% to 100% (Figure 1A). From this distribution, coverage was categorised into three categories: 220 facilities as 'good' (≥90% coverage), 77 facilities as 'poor' (50–89% coverage) and 37 facilities as 'very poor' (<50% coverage), 13 of which had 0% coverage. Institutional variability was large within each country, with 13 countries having institutions with coverage both below 50% and above 90% (Figure 1B).

In Table 2, we describe the characteristics of the facilities, stratified into three categories by coverage. Facilities with higher coverage reported more WHO and local

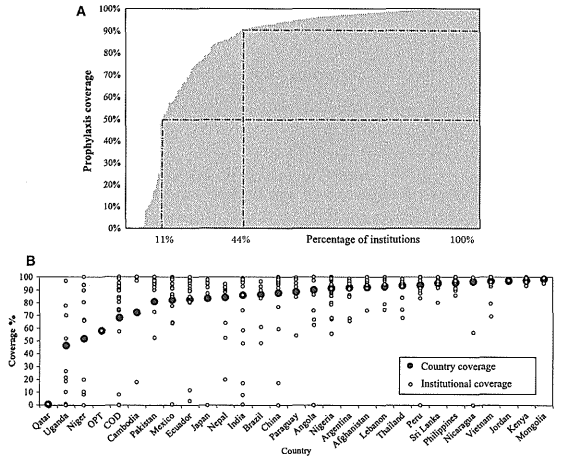

Figure 1. (A) Distribution of prophylaxis coverage for caesarean section. Analysis of 332 facilities in 29 countries. Facilities are in Japan, Qatar, Argentina, Mexico, Lebanon, Peru, Brazil, Ecuador, Sri Lanka, Jordan, China, Thailand, Mongolia, Occupied Palestinian Territory, Paraguay, Philippines, Vietnam, Nicaragua, India, Cambodia, Kenya, Pakistan, Angola, Nigeria, Nepal, Uganda, Afghanistan, Democratic Republic of Congo and Niger. (B) Distribution of prophylaxis coverage for caesarean section. Analysis of 332 facilities in 29 countries. COD, Democratic Republic of Congo; OPT, Occupied Palestinian Territory.

guideline use, with 66% of facilities with 'good' coverage using either WHO or local guidelines, compared with 32% of facilities with 'very poor' coverage reporting that they used neither.

Similarly, the percentages of facilities reporting that they had clinical audits in practice ($P = 0.009$), or had an obstetric specialist available on site or on call at all hours ($P < 0.001$), were significantly smaller in facilities with lower coverage. Clinical audits were in practice for 88% of facilities with 'good' coverage, compared with 68% in the 'very poor' group, and obstetric specialist availability was 85% compared with 57%.

In addition, facilities with 'very poor' coverage were more likely to be categorised with a lower facility index ($P = 0.002$), and had a smaller proportion of caesarean births before labour ($P = 0.001$), compared with institutes with higher coverage.

The HDI of the country, number of maternal beds, location, proportion of women receiving care free of charge and whether the hospital was a maternity exclusive hospital did not show a significant association with coverage.

Infection rate among caesarean births was 7.8% overall. The rate of infection in mothers who had caesarean births did not decline with coverage. Institutions with an extremely high rate of infection (20–80%) mostly had 'poor' coverage of prophylaxis, and 23 (66%) facilities with 'very poor' coverage had a low bacterial infection rate of below 1%.

In Table 2, we describe the coverage in various populations. Of the 89 121 caesarean births, 87% were covered with antibiotics. This was 97% in facilities with 'good' coverage and 60% in facilities with 'poor' or 'very poor' coverage.

In facilities with 'good' coverage overall, coverage varied only slightly in the range 94–98% when stratified by individual maternal characteristics. This variability was larger (32–82%) in facilities with 'poor' or 'very poor' coverage, with mothers of triplets or more (coverage 47%), and those with malaria or dengue (32%), having the lowest proportion receiving prophylaxis. Alternatively, mothers with anaemia (79%), HIV or AIDs (74%) and those delivering stillborns (82%) had a larger proportion receiving prophylaxis.

In Tables 3 and 4, we show the adjusted odds ratios (aORs) for the estimated effect of maternal and infant characteristics on the lack of prophylaxis, as well as on bacterial infection, adjusted by country and facility, in addition to other maternal characteristics.

Maternal age, marital status and education did not show a significant relationship with the non-use of prophylaxis,

Table 2. Characteristics of facilities by coverage of prophylactic antibiotics for caesarean section. Analysis of 332 facilities in 29 countries

	Total	Institutional coverage of prophylaxis			*P*
		0–49% (%)	50–89% (%)	90–100% (%)	
Number of facilities	332	35 (11)	77 (23)	220 (66)	
Location					
Urban	226	20 (65)	54 (77)	152 (74)	0.60
Peri-urban	44	6 (19)	7 (10)	31 (15)	
Rural	43	5 (16)	9 (13)	22 (11)	
Average number of maternity beds in use					
<46	154	18 (58)	36 (51)	100 (51)	0.42
47–100	75	7 (23)	22 (31)	46 (23)	
101–190	43	5 (16)	6 (8.6)	32 (16)	
>191	30	1 (3.2)	6 (8.6)	23 (12)	
Maternity exclusive hospital	58	9 (29)	13 (19)	36 (18)	0.34
Proportion of delivering women receiving care free of charge					
<25%	141	13 (42)	23 (33)	105 (52)	0.05
25–50%	33	1 (3.2)	11 (16)	21 (11)	
50–99%	38	4 (13)	10 (15)	24 (12)	
100%	87	13 (42)	25 (36)	49 (25)	
Guideline use in facility					
Both WHO and local	187	10 (32)	42 (61)	135 (66)	0.001
Only WHO or local	79	11 (36)	16 (23)	52 (23)	
None	38	10 (32)	11 (16)	17 (8)	
Clinical audits in practice	255	21 (68)	55 (81)	179 (88)	0.009
Obstetric specialist available on call	268	20 (57)	60 (78)	188 (85)	<0.001
Proportion of caesarean sections before labour					
<20%	118	22 (63)	30 (39)	66(30)	0.001
20–60%	129	8 (23)	34 (44)	87 (40)	
60%	85	5 (14)	13 (17)	67 (30)	
Rate of bacterial infections among caesarean section deliveries					
<1%	177	23 (66)	30 (39)	124 (57)	0.001
1–10%	131	10 (29)	34 (45)	87 (40)	
>10%	22	2 (5.7)	12 (16)	8 (3.6)	
Facility capacity*					
Good	68	4 (10)	9 (17)	55 (29)	0.02
Poor	115	15 (37)	22 (42)	78 (41)	
Very poor	98	21 (53)	21 (18)	56 (30)	
Human Development Index (HDI) of country**					
Low	124	19 (54)	35 (44)	70 (32)	0.13
Medium	87	6 (6.9)	16 (21)	65 (30)	
High	96	8 (23)	21 (27)	67(30)	
Very high	25	2 (8.0)	5 (6.5)	18 (8.2)	

WHO, World Health Organization.
*Proxy for the medical level of each health facility comprising six categories reflecting the standard of building/basic services, medical services, emergency obstetric services, laboratory tests, hospital practices and human resources.
**As of 2012. Very high HDI countries included Japan, Qatar and Argentina. High HDI countries included Mexico, Lebanon, Peru, Brazil, Ecuador and Sri Lanka. Medium HDI countries included Jordan, China, Thailand, Mongolia, Occupied Palestinian Territory, Paraguay, Philippines, Vietnam, Nicaragua, India and Cambodia. Low HDI countries included Kenya, Pakistan, Angola, Nigeria, Nepal, Uganda, Afghanistan, Democratic Republic of Congo and Niger.

except for mothers with 10–12 years of education in facilities with low coverage, but single marital status was a significant individual risk factor for infection despite prophylactic status, and a lower age and lower education were also significant risk factors for infection in deliveries receiving prophylaxis.

Nulliparous mothers were significantly more likely to be given prophylaxis than multiparous mothers in facilities

Table 3. Risk factors for the non-use of prophylactic antibiotics for caesarean section stratified by the institutional use of prophylaxis. Analysis of 82 320 caesarean sections in 29 countries

	All caesarean deliveries (*n* = 82 320)		Deliveries in institutions with above 90% coverage (*n* = 61 476)		Deliveries in institutions with below 90% coverage (*n* = 20 844)	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Age (years)						
<20	1.92	(0.96; 1.18)	1.05	(0.88; 1.26)	1.07	(0.94; 1.21)
20–34	1	REF	1	REF	1	REF
≥35	1.00	(0.92;1.09)	0.95	(0.83,1.09)	1.04	(0.93; 1.16)
Marital status						
Single	0.97	(0.88; 1.08)	1.06	(0.89, 1.25)	0.92	(0.81; 1.06)
Married/cohabiting	1	REF	1		1	REF
Education (years)						
0	1.10	(0.96; 1.26)	1.19	(0.93; 1.51)	1.02	(0.87; 1.21)
1–6	1.05	(0.94;1.18)	0.95	(0.78; 1.15)	1.07	(0.93, 1.22)
7–9	0.96	(0.87; 1.06)	1.03	(0.88; 1.21)	0.90	(0.79; 1.02)
10–12	0.90	(0.82; 0.98)*	0.99	(0.86; 1.13)	0.83	(0.74; 0.93)***
>12	1	REF	1	REF	1	REF
Parity						
0	0.87	(0.80; 0.94)**	0.78	(0.69; 0.88)***	0.93	(0.84; 1.03)
1–2	1	REF	1	REF	1	REF
≥3	1.01	(0.92; 1.12)	1.11	(0.93; 1.33)	0.96	(0.85; 1.09)
Any previous caesarean section	0.77	(0.71; 0.84)***	0.62	(0.54; 0.71)***	0.88	(0.80; 0.97)*
Congenital malformation	0.83	(0.62; 1.11)	1.01	(0.70; 1.55)	0.67	(0.44; 1.01)
Multiplicity						
Singleton	1	REF	1	REF	1	REF
Twin	0.76	(0.63; 0.93)**	0.78	(0.53; 1.02)	0.77	(0.61; 0.98)*
Triplet or more	1.48	(0.67; 3.23)	1.11	(0.21; 3.65)	1.91	(0.63; 5.77)
Anaemia (haemoglobin <7mg/dl)	0.59	(0.49; 0.71)***	1.05	(0.74; 1.48)	0.51	(0.42; 0.63)***
Obstetric haemorrhagic disorders**	0.98	(0.84; 1.15)	0.87	(0.66; 1.13)	1.02	(0.83; 1.24)
Hypertensive disorders						
Chronic hypertension	0.92	(0.68; 1.25)	0.63	(0.33; 1.19)	1.04	(0.72; 1.50)
Pre-eclampsia/eclampsia	0.80	(0.69; 0.92)**	0.75	(0.59; 0.96)*	0.79	(0.66; 0.94)*
Infection						
HIV+/AIDS	0.63	(0.40; 0.99)*	0.90	(0.45; 1.77)	0.53	(0.30; 0.94)*
Malaria/dengue	0.93	(0.53; 1.64)	1.10	(0.15; 8.21)	0.92	(0.51; 1.65)
Onset of labour						
Spontaneous labour	1	REF	1	REF	1	REF
Induction	0.83	(0.75; 0.93)***	1.07	(0.91; 1.27)	0.72	(0.63; 0.82)***
No labour	0.69	(0.64; 0.74)***	0.61	(0.54; 0.68)***	0.74	(0.68; 0.81)***
Preterm delivery	1.08	(0.98; 1.20)	1.22	(1.04; 1.42)*	0.98	(0.85; 1.12)
Stillbirth	1.25	(1.01; 1.55)*	1.85	(1.33; 2.58)***	1.01	(0.78; 1.32)
Other maternal medical conditions***	0.93	(0.64; 1.36)	1.39	(0.88; 2.18)	0.53	(0.30; 0.94)*

aOR, adjusted odds ratio; CI, confidence interval.
Multilevel, multivariate logistic regression models were used to obtain aORs: outcome was 'absence of prophylactic antibiotics'; multilevel analysis was structured as three levels (individual, health facility, country) with random intercepts.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.
****Placenta praevia, accreta/increta/percreta placenta, abruptio placenta, ruptured uterus, postpartum haemorrhage and any other obstetric haemorrhage.
*****Any chronic or acute injury or disorder affecting the kidneys, heart, lungs or liver.

Table 4. Risk factors for bacterial infection stratified by use of antibiotic prophylaxis for caesarean section. Analysis of 82 320 caesarean sections in 29 countries

	All caesarean sections		Caesarean sections with prophylaxis		Caesarean sections without prophylaxis	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Age (years)						
<20	1.16	(1.03; 1.28)*	1.22	(1.09; 1.36)**	0.70	(0.48; 1.03)
20–34	1	REF	1	REF	1	REF
≥35	1.07	(0.98; 1.16)	1.06	(0.97; 1.16)	1.07	(0.80; 1.43)
Marital status						
Single	1.17	(1.06; 1.30)**	1.15	(1.03; 1.28)*	1.47	(1.03; 2.10)*
Married/cohabiting	1	REF	1	REF	1	REF
Education (years)						
0	1.22	(1.05; 1.36)**	1.21	(1.03; 1.42)*	1.32	(0.88; 2.00)
1–6	1.12	(0.99; 1.26)	1.11	(0.98; 1.26)	1.22	(0.83; 1.78)
7–9	1.21	(1.09; 1.34)***	1.18	(1.06; 1.32)**	1.29	(0.92; 1.82)
10–12	1.05	(0.96; 1.14)	1.04	(0.95; 1.14)	1.14	(0.85; 1.55)
>12	1	REF	1	REF	1	REF
Parity						
0	1.05	(0.97; 1.13)	1.03	(0.95; 1.12)	1.01	(0.78; 1.30)
1–2	1	REF	1	REF	1	REF
≥3	1.19	(1.07; 1.32)***	1.25	(1.12; 1.39)***	0.92	(0.67; 1.26)
Any previous caesarean section	0.67	(0.61; 0.73)***	0.66	(0.60; 0.72)***	0.69	(0.52; 0.90)**
Congenital malformation	6.74	(5.72; 7.94)***	7.16	(6.02; 8.53)***	3.11	(1.76; 5.47)***
Multiplicitiy						
Singleton	1	REF	1	REF	1	REF
Twin	1.00	(0.86; 1.16)	0.91	(0.77; 1.06)	1.54	(0.98; 2.44)
Triplet or more	1.58	(0.88; 2.85)	1.68	(0.90; 3.16)	1.25	(0.21; 7.53)
Anaemia (haemoglobin <7 mg/dl)	1.87	(1.63; 2.15)***	2.00	(1.72; 2.31)***	1.22	(0.21; 2.10)
Obstetric haemorrhagic disorders**	1.33	(1.18; 1.50)***	1.47	(1.29; 1.67)***	1.92	(1.28; 2.88)**
Hypertensive disorders						
Chronic hypertension	1.17	(0.93; 1.47)	1.16	(0.91; 1.47)***	0.70	(0.27; 1.82)
Pre-eclampsia/eclampsia	1.68	(1.52; 1.85)***	1.71	(1.55; 1.90)***	1.44	(0.99; 2.11)
Infection						
HIV+/AIDs	1.28	(0.92; 1.78)	1.26	(0.90; 1.78)	1.12	(0.27; 4.55)
Malaria/dengue	1.93	(1.09; 3.41)**	2.92	(1.56; 5.48)**	0.23	(0.03; 1.86)
Onset of labour						
Spontaneous	1	REF	1	REF	1	REF
Induction	1.08	(0.98; 1.20)	1.10	(0.98; 1.23)	1.30	(0.92; 1.84)
No labour	0.85	(0.79; 0.91)***	0.83	(0.77; 0.90)***	0.92	(0.72; 1.16)
Preterm birth	7.43	(6.91; 7.98)***	8.18	(7.57; 8.84)***	6.59	(5.23; 8.30)***
Stillbirth	7.76	(5.60; 10.75)***	9.34	(6.46; 13.51)***	3.79	(1.82; 7.86)***
Other maternal conditions***	1.88	(1.53; 2.31)***	1.87	(1.51; 2.31)***	2.29	(0.93; 5.61)

aOR, adjusted odds ratio; CI, confidence interval.
Multilevel, multivariate logistic regression models were used to obtain aORs: outcome was any bacterial infection; multilevel analysis was structured as three levels (individual, health facility, country) with random intercepts.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.
****Placenta praevia, accreta/increta/percreta placenta, abruptio placenta, ruptured uterus, postpartum haemorrhage and any other obstetric haemorrhage.
*****Any chronic or acute injury or disorder affecting the kidneys, heart, lungs or liver.

with high coverage, but mothers with three or more previous births were significantly more likely to have infection among those who received prophylaxis.

Mothers who had undergone previous caesarean birth were significantly more likely to receive prophylaxis [aOR = 1.30; 95% confidence interval (CI), 1.19–1.41; $P < 0.001$] in facilities with both high and low coverage, but were significantly less likely to have infection (aOR = 0.67; 95% CI, 0.61–0.73; $P < 0.001$) despite antibiotic cover. Similarly, caesarean births prior to labour were significantly more likely to receive prophylaxis (aOR = 1.49; 95% CI, 1.35–1.56; $P < 0.001$), but were significantly less likely to have infection (aOR = 0.85; 95% CI, 0.79–0.91; $P < 0.001$). Twins were more likely to receive prophylaxis in facilities with low coverage, but we did not find a significant association with multiple pregnancies and infection.

Most maternal complications, i.e. anaemia, obstetric haemorrhagic disorders, chronic hypertension, pre-eclampsia/eclampsia, malaria/dengue and 'other maternal conditions', were significantly associated with a higher risk of infection. We did not find an association with HIV. Among these complications, anaemia, HIV and pre-eclampsia/eclampsia were associated with a significantly higher risk of receiving prophylaxis.

Preterm delivery and stillbirth were both highly associated with maternal infection regardless of prophylactic status, but only in facilities with 'good' prophylaxis coverage were preterm births and stillbirths given more prophylaxis than term and live births.

Discussion

Main findings

In our study, we found that institutional coverage of antibiotic prophylaxis for caesarean birth varied largely within most countries, with coverage being related more to guideline use and the practice of clinical audits than to size, location or development index of the country.

We also found that, although mothers with certain medical risk factors were more likely to receive antibiotics, those with several characteristics known to be associated with a lower risk of infection were also more likely to receive antibiotic prophylaxis. In our study, mothers with infection, such as HIV, anaemia or pre-eclampsia, were more likely to receive prophylaxis. At the same time, women with multiple pregnancies or previous caesarean births were also more likely to receive prophylaxis.

Interpretation

Multiple pregnancies and previous caesarean birth are themselves indications for 'scheduled' caesarean birth. The fact that these factors and scheduled birth itself (caesarean birth before labour or following labour induction) were associated with greater use of prophylaxis raises concern about whether there is a tendency to administer prophylaxis when the caesarean birth is planned, and therefore prophylaxis is part of the routine clinical protocol. Mothers who had spontaneous onset of labour, singleton birth and those who had not previously undergone caesarean section were less likely to receive prophylaxis. This may be related to possible gaps in practice, such as forgetting or skipping the administration of antibiotic prophylaxis, due to time constraints.

This might be more prevalent in facilities in which there is a lack of use of guidelines, compounded by a lack of institutional quality improvement measures when there are no clinical audits to retrospectively examine practices and their consequences. Previous reports have stated that continuous data collection and timely dissemination of the results are important factors catalysing improvements in practice.[22]

Interestingly, we did not find any related study examining maternal and/or institutional characteristics associated with use of antibiotic prophylaxis for caesarean birth. Studies from the USA have reported the increased risk of bacterial infections in socially disadvantaged populations,[23] and a report from Norway studied the variation in institutional guidelines towards the use of prophylaxis,[13] but we could not find any study examining what drives the variations in coverage.

Strengths and limitations

This analysis has several strengths. The WHO Multicountry Survey 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 obtained data on institutional and individual characteristics of deliveries in 332 facilities that performed caesarean section, which allowed us to investigate not only maternal but also institutional characteristics.

However, there are some limitations. First, as the primary data source was routine medical records, erroneous or absent documentation of prophylaxis and maternal complications in the records could have affected data quality. However, we believe that this bias was minimised as much as possible by training provisions prior to study commencement (building on our experiences in the WHO Global Survey) and data collectors consulting with clinical staff to complement information obtained from the records, where necessary. Missing prophylactic data were minimal.

Second, we could not verify whether infections other than puerperal endometritis occurred before or after birth.

However, as the risk of bacterial infections increases substantially after an operation,[6] we based our results on the assumption that bacterial infections were probably postpartum. If antepartum infections constituted a substantial proportion of all captured infections, we would have overestimated the effect of prophylaxis on preventing postpartum infection. However, as data collection was only conducted for the duration of the admission, we acknowledge that the risk of infection post-discharge is not small,[13] and was not captured by this survey or evaluated in our study, which could have led to an underestimation.

Third, we obtained a limited number of variables in the institutional data. Therefore, although we were able to identify several important characteristics related to antibiotic coverage, we may have failed to identify the fundamental common factor.

We also lacked several known factors related to bacterial infection, such as the length of the operation and the qualifications and experience of the surgeon, which could have affected our estimates of the effect of maternal characteristics on bacterial infection. However, surgeon experience is associated with the measured institutional characteristics (larger size, more maternal beds, more frequent caesarean delivery), and a longer operation would be associated with the measured underlying medical factors as well as the skill of the surgeon; therefore, the unmeasured confounding may be small.

Finally, although we produced estimates in Table 3 under the assumption that the effect of each maternal characteristic on the presence of prophylaxis was the same in every facility, this is unlikely. Therefore, our results on factors leading to lower coverage should be considered as an overview of the 332 countries participating in this survey, and it should be taken into account that our findings may not be applicable to each individual facility.

Conclusions

Our study suggests that coverage of antibiotic prophylaxis for caesarean birth may be related to the perception of the importance of guidelines and clinical audits in the facility. Although obstetricians presumably acknowledge the increased risk of infections in many maternal complications when they administer antibiotic prophylaxis, there may also be a tendency to use prophylaxis when caesarean birth has been scheduled and prophylaxis is already included in the routine clinical protocol.

To our knowledge, no other study has assessed the maternal and institutional characteristics associated with coverage of antibiotic prophylaxis for caesarean birth. This study may act as a signal to re-evaluate individual practices in order to identify areas with the possibility of improvement.

Disclosure of interests

We declare that we have no competing interests or conflicts of interest.

Contribution to authorship

NM, RM and AMG initiated the concept. NM and TG designed the study and performed the data analysis. NM wrote the initial manuscript. EO, JPV and JPS provided advice and editing of the manuscript. All authors read and approved the final version of the manuscript.

Details of ethics approval

The UNDP/UNFPA/UNICEF/WHO/World Bank 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 WHO Ethical Review Committee and the relevant ethical clearance mechanisms in all countries.

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Original article

Mode and timing of twin delivery and perinatal outcomes in low- and middle-income countries: a secondary analysis of the WHO Multicountry Survey on Maternal and Newborn Health

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Objective To describe the mode and timing of delivery of twin pregnancies at ≥34 weeks of gestation and their association with perinatal outcomes.

Design Secondary analysis of a cross-sectional study.

Population Twin deliveries at ≥34 weeks of gestation from 21 low- and middle-income countries participating in the WHO Multicountry Survey on Maternal and Newborn Health.

Methods Descriptive analysis and effect estimates using multilevel logistic regression.

Main outcome measures Stillbirth, perinatal mortality, and neonatal near miss (use of selected life saving interventions at birth).

Results The average length of gestation at delivery was 37.6 weeks. Of all twin deliveries, 16.8 and 17.6% were delivered by caesarean section before and after the onset of labour, respectively. Prelabour caesarean delivery was associated with older maternal age, higher institutional capacity and wealth of the country. Compared with spontaneous vaginal delivery, lower risks of neonatal near miss (adjusted odds ratio, aOR, 0.63; 95% confidence interval, 95% CI, 0.44–0.94) were found among prelabour caesarean deliveries. A lower risk of early neonatal mortality (aOR 0.12; 95% CI 0.02–0.56) was also observed among prelabour caesarean deliveries with nonvertex presentation of the first twin. The week of gestation with the lowest rate of prospective fetal death varied by fetal presentation: 37 weeks for vertex–vertex; 39 weeks for vertex–nonvertex; and 38 weeks for a nonvertex first twin.

Conclusions The prelabour caesarean delivery rate among twins varied largely between countries, probably as a result of overuse of caesarean delivery in wealthier countries and limited access to caesarean delivery in low-income countries. Prelabour delivery may be beneficial when the first twin is nonvertex. International guidelines for optimal twin delivery methods are needed.

Keywords Neonatal morbidity, perinatal morbidity, perinatal mortality, planned caesarean section, stillbirth, timing of birth, twin pregnancy.

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Introduction

Twin gestations account for 0.5–2.0% of all pregnancies, with rates varying largely by race/ethnicity and country.[1] Twins are at a higher risk for preterm delivery,[2] and for infant morbidity and mortality,[3,4] and many epidemiological studies and a recent multicentred randomised controlled trial (RCT) show that the optimal duration of pregnancy may be shorter in multiple pregnancies compared with singletons.[2,5–8] Such outcomes are addressed in the current clinical guidelines of several countries.[9–12]

Recent studies state that there is no evidence of better perinatal outcomes for prelabour caesarean delivery versus planned vaginal delivery, as long as the first twin is in the vertex position in an otherwise uncomplicated pregnancy.[13–16] Despite the lack of evidence, there is a continuing increase in caesarean section rates for twins in many low-, middle- and high-income countries,[17–19] and as noted by Blickstein we are in danger of 'a vicious circle in favour of caesarean section',[13] through decreasing experience in vaginal delivery.[20]

On the other hand, sub-Saharan Africa seems to be excluded from this trend of increased rates of caesarean section,[21,22] and in many low- and middle-income countries, inequalities in access to caesarean delivery still reflect socio-economic inequities for skilled delivery.

In this secondary analysis of the WHO Multicountry Survey on Maternal and Newborn Health—a large multicentre cross-sectional survey of deliveries in 29 countries in Africa, Latin America, Asia and the Middle East—we sought to describe the mode and timing of twin deliveries in institutions capable of caesarean delivery, and to address their association with perinatal outcomes.

Methods

Study design and data collection

This is a secondary data analysis of the WHO Multicountry Survey on Maternal and Newborn Health (WHOMCS) carried out in 359 health facilities from 29 countries in Africa, Asia, Latin America, and the Middle East. Full methodological details are available in our previous article.[23,24] In brief, a multistage cluster sampling method was applied to acquire samples of health facilities in 29 countries. Trained health professionals at these facilities retrieved information from medical records, including individual data on demographics and reproductive characteristics, medical conditions during pregnancy, birth outcomes, complications, and received interventions for all women who were admitted for delivery or had severe maternal outcomes. In addition, health facility data were obtained, regarding capacity on laboratory tests, blood transfusions, availability of intensive care for mothers and babies, surgical procedures, human resources and training, and the capabilities of obstetrics and neonatal healthcare services. Data were collected in each facility over a period of 2–4 months from May 2010 to December 2011.

Study population

For our analysis we used a subpopulation of the available data set that included all twin pregnancies delivered at or later than 34 weeks of gestation in low- or middle-income countries, with no medical contraindication for vaginal delivery. As approximately 50% of twins are delivered preterm, with 30% delivered in the late preterm period (34–36 weeks of gestation),[9] a cut-off of 34 weeks of gestation was chosen in accordance with previous studies.[16,25]

Of the 317,107 deliveries observed in this subpopulation, 4112 were twin deliveries. We excluded 468 twin deliveries in seven countries where data on all second twins were missing (Paraguay, Peru, Philippines, Qatar, Thailand, Vietnam, and Uganda). Thirty-eight deliveries in high-income countries (Japan) were included only in a descriptive analysis on variability between countries. We further excluded deliveries with congenital malformations or macerated fetal deaths of either twin (n = 82), maternal complications (n = 557), women with previous caesarean section (n = 389), as well as deliveries with missing data on gestational age, onset of labour, fetal presentation, birthweight, infant status at birth or at seventh day of life of either infant (n = 108), and retrieved 2134 twin deliveries at or later than 34 weeks of gestation that had no medical indication for urgent delivery.

As only 121 (5.6%) were deliveries after induction of labour, we also excluded these and focused on the remaining 2013 deliveries from 21 countries that were either prelabour caesarean delivery (n = 384) or delivery following spontaneous onset of labour (n = 1629) (Figure 1).

Exposure and potential confounding variables

Our main comparison of interest was to compare prelabour caesarean delivery with 'expectant management': the decision to not perform a prelabour caesarean delivery at a specific gestational age (in which case the comparison groups would be all deliveries after that gestational age).[26,27] We also defined intrapartum caesarean section as caesarean section after the spontaneous onset of labour.

The WHOMCS individual data set includes demographic characteristics, obstetric and medical history, mode of delivery, and maternal and perinatal outcomes until discharge from hospital, or up to the seventh postpartum day or death, whichever occurred first. Morbidity and mortality occurring post-discharge or during a subsequent readmission were not captured.

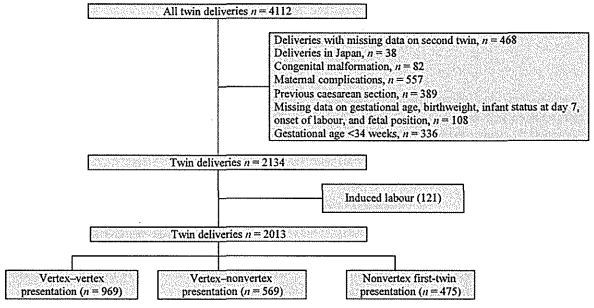

Figure 1. Population flow chart.

Medical conditions or complications, such as intubation, were recorded as binary variables (yes/no), and severity, time of onset, and management were not captured. All continuous variables, such as maternal age, were converted into categorical variables. Gestational age was recorded in completed weeks based on the best available obstetric estimate; the method of estimation was not recorded. Chorionicity and amnionicity were not available in the WHOMCS database, and thus were not accounted for in the analysis.

The maternal-level confounding factors included were: maternal age (<20, 20–35, >35 years), maternal education (0, 1–4, 5–9, ≥10 years), and parity (0, 1–2, ≥3). Perinatal-level confounding factors were fetal presentation (vertex–vertex, vertex–nonvertex, nonvertex first twin), infant concordance (concordant, discordant, both of severe small gestational age, SGA), and prematurity (preterm, term). Discordancy was defined as an inter-twin birthweight difference of over 20% of the smaller twin,[28–31] and severe SGA as a birth weight below the third percentile of the singleton reference, using a population-based standard developed by Mikoliaczyk and collegues,[32] which was applied to our data set.

Additionally, the analyses were adjusted for the Human Development Index (HDI), based on the 2012 rankings,[33] as well as for the facility capacity index category, a proxy for the capacity of the institution to provide essential obstetric care and additional services, which was calculated as the total score of services, and categorised into low, medium, and high.

Main outcomes and definitions

Neonatal adverse outcomes were the main outcome of interest: stillbirth, early neonatal mortality, and neonatal near miss. Neonatal near miss was defined as any of the following: any intubation (at birth or at any time within the first week of life); nasal continuous positive airway pressure (CPAP); surfactant administration; cardiopulmonary resuscitation (cardiac massage); any surgery; or the use of any vasoactive drug, anticonvulsants, phototherapy in the first 24 hours, steroids to treat refractory hypoglycaemia, or therapeutic intravenous antibiotics. This set of life-saving interventions has previously been used to study the applicability of the near-miss concept in newborn infants, developed by Avenant,[34] and explored as 'management markers of severity' by Pileggi-Castro et al.[35]

Analysis and statistical methods

First we described country-specific prelabour caesarean rates, intrapartum caesarean section rates, and the mean age of delivery for twin pregnancies, stratified by fetal presentation and HDI ranking. For this analysis we included deliveries in Japan and in countries where all second-infant data were missing.

Next we reported the frequencies for maternal and neonatal characteristics in prelabour caesarean deliveries and spontaneous deliveries. We also used multilevel multivariate logistic regression to calculate the association of each characteristic and the odds ratios of prelabour caesarean delivery. This method enabled us to take into account the clustering effect within mothers, facilities, and within HDI subgroups, as well as adjusting for maternal characteristics.

To calculate the effect of gestational age for delivery on neonatal adverse outcomes, we adopted the prospective risk approach originally proposed by Feldman,[36] and calculated the 'prospective perinatal mortality' according to Kramer.[37] Prospective fetal death was calculated as the probability of stillbirth in deliveries at or after a certain gestational age, and prospective perinatal mortality was calculated as the probability of either early neonatal death or stillbirth in deliveries at or after a certain gestational age. This

approach allows us to compare the risk of adverse outcomes between different gestational lengths, as well as between the termination and the continuation of the pregnancy, and between prelabour caesarean section and expectant management, both at a given gestational age. Our small sample size limited us from adjusting for potential confounding factors in this analysis.

As perinatal mortality and the neonatal near-miss rate were lower in women undergoing prelabour caesarean delivery, compared with those receiving expectant care for most gestational ages between 34 and 40 weeks of gestation, we also compared prelabour caesarean section at any age above 34 weeks of gestation with women undergoing expectant management. We accounted for any clustering effects within mother, facility, and HDI subgroups, as well as adjusting for maternal characteristics other than gestational age; however, we did not adjust for gestational week in this analysis. Adjustment for gestational age would have created a comparison between prelabour delivery and spontaneous labour both at the same gestational age, when actually the correct comparison for prelabour delivery at a given gestational age is to directly compare prelabour delivery with women undergoing expectant management.[27,38,39] We repeated this with stratification by fetal presentation.

To make a direct comparison of prelabour delivery and expectant management, we compared prelabour delivery at 34–36 weeks of gestation with expectant management (i.e. delivery after 37 weeks of gestation), as well as prelabour delivery at 37–38 weeks of gestation with expectant management (delivery after 39 weeks of gestation). In this analysis we also used multilevel analyses to account for clustering within the mother, institutions, and HDI subgroups, and adjusted for maternal characteristics. We further investigated effect modification by HDI subgroups.

For all analyses, estimates were adjusted for survey design and $P < 0.05$ was considered significant. We have reported all odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs). Missing values were excluded from all logistic regression models. Statistical analysis was conducted using STATA/MP 13.0 (StataCorp LP, College Station, TX, USA).

Results

In Figure 2(A,B) we show the timing and mode of delivery in twin pregnancies for each country. Mean gestational age for delivery decreased and the proportion of prelabour caesarean deliveries increased with higher HDI: the coefficients of determination were $R^2 = 0.26$ and 0.51, respectively.

Figure 2(A) shows the average gestational length of delivery by the HDI ranking of the country. Of the 21 countries participating in our study, the average length of gestation for all twins delivered after 34 weeks of gestation was 37.6 weeks of gestation. In seven low- and middle-HDI countries (Afghanistan, Angola, Cambodia, Congo, Nicaragua, Niger, and Uganda), twin pregnancies have an average length of gestation above 38 weeks of gestation.

Figure 2(B) shows the prelabour caesarean section rate by the HDI ranking of the country, in which 16.8% of all twins were delivered by prelabour caesarean section, and another 17.6% were delivered through intrapartum caesarean delivery following the spontaneous onset of labour. The prelabour caesarean rate differed by HDI, with 11% in low-, 27% in medium-, 35% in high-, and 56% in very high-HDI countries, with rates in Japan, China, and Brazil of over 60%, and rates in Cambodia, Angola, Uganda, and Afghanistan of below 5%.

A more complete overview is shown in Table S1, where average gestational length and caesarean section rate (prelabour and emergency) are shown by fetal presentation for each country. The overall rate of prelabour delivery (19.1% overall) differed largely by presentation: 14% of deliveries were for vertex–vertex presentation; 17% were vertex–nonvertex presentation; and 32% occurred for nonvertex first-twin presentation. Rates of prelabour caesarean section for nonvertex first-twin presentation were significantly higher compared with vertex–vertex presentation in Ecuador, Jordan, Afghanistan, India, Pakistan, Kenya, and Nigeria, however.

Table 1 illustrates maternal, obstetric, and institutional characteristics, as well as their association with the estimated risks of receiving prelabour caesarean delivery. Of the pregnancies experiencing a spontaneous onset of labour, 25% were delivered through intrapartum caesarean section.

For maternal characteristics, lower age and multiparity were associated with fewer prelabour caesarean deliveries. Mothers aged under 20 years and parous mothers were nearly three times more likely to experience the spontaneous onset of labour, compared with women aged over 20 years and nulliparous women.

Marital status was not significantly associated with the onset of labour, but those who had completed over 12 years of education were 1.9 times more likely to have a prelabour caesarean section.

Fetal presentation was highly associated with the onset of labour: a nonvertex first-twin presentation increased the odds of prelabour delivery by four times, compared with vertex–vertex presentation. The risk of intrapartum caesarean section after an attempted vaginal delivery was five times higher in a nonvertex first-twin presentation, compared with vertex–vertex twins.

Concordance was not significantly associated with the onset of labour, but women with small-for-gestational-age (SGA) twins were more likely to experience spontaneous labour.

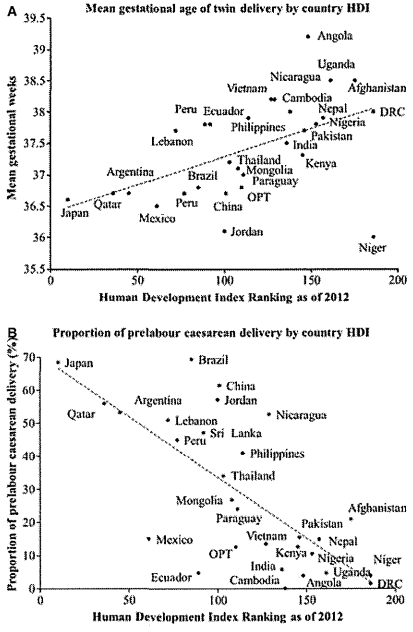

Figure 2. (A) Mean gestational age of twin delivery by country HDI. (B) Proportion of prelabour caesarean delivery by country HDI.

The capacity of the healthcare facility and the level of development of the country were both associated with the onset of labour. Deliveries in low-capacity facilities and low-income countries were 2.5–5.0 times more likely to experience spontaneous labour.

Next we investigated the distribution of timing of twin deliveries, rates of prelabour caesarean section, as well as their perinatal outcomes for each gestational week by fetal presentation. The largest number of deliveries was at 37–38 weeks of gestation, which was the same when limited to only prelabour caesarean delivery. Most prelabour caesarean deliveries were performed at 38 weeks of gestation for vertex–vertex presentation, and at 37 weeks of gestation for vertex–nonvertex and nonvertex first-twin presentations. The lowest rate of prospective fetal death was observed at 36–37 weeks of gestation, and varied slightly by fetal presentation: 37 weeks of gestation for vertex–vertex; 39 weeks of gestation for vertex–nonvertex; and 38 weeks of gestation for nonvertex first twin. The prospective fetal death rate was higher in vertex–nonvertex and nonvertex first-twin presentations, compared with vertex–vertex twins, at every gestational age, except for 41 weeks of gestation. Detailed results are shown in Table 2.

As shown in Table S2, we also compared perinatal adverse outcomes between prelabour delivery and expectant management for each week of gestation from 34 to 41 weeks of gestation. Perinatal mortality was lower at each gestational week in prelabour caesarean deliveries compared with spontaneous labour deliveries. Our small sample size made comparison difficult after stratification by fetal presentation.

Following these analyses, we further compared perinatal adverse outcomes between prelabour caesarean delivery and spontaneous labour, adjusting for institutional, maternal, and neonatal characteristics, and stratifying by fetal presentation. Table 3 shows that the early neonatal near-miss rate and early neonatal mortality were 0.39 (95% CI 0.19–0.80) and 0.63 (95% CI 0.44–0.94) times lower, respectively, in

Table 1. Maternal, obstetric, and institutional characteristics and their associations with prelabour caesarean delivery. Analysis of 2013 twin deliveries at ≥34 weeks of gestation

	All deliveries *n* (%)	Prelabour caesarean section *n* (%)	Spontaneous labour *n* (%)	OR	aOR (95% CI)
Number of deliveries	2013	384	1629		
Age					
<20 years	112 (5.6)	15 (3.9)	97 (6.0)	Ref.	Ref.
20–34 years	1587 (78.8)	303 (78.9)	1284 (78.8)	1.52	2.58 (1.22–5.46)*
≥35 years	314 (15.6)	66 (17.1)	248 (25.2)	1.72	3.62 (1.38–9.47)**
Marital status					
Single	127 (6.4)	23 (6.1)	104 (6.4)	Ref.	Ref.
Married	1872 (93.6)	357 (93.9)	1515 (93.6)	1.07	1.40 (0.46–2.95)
Education					
0 years	504 (25.0)	58 (15.1)	446 (27.4)	Ref.	Ref.
1–6 years	257 (12.8)	32 (8.3)	225 (13.8)	1.09	0.786 (0.42–1.42)
7–9 years	390 (19.4)	65 (16.9)	325 (20.0)	1.54	0.79 (0.45–1.38)
10–12 years	452 (22.4)	87 (22.7)	365 (22.4)	1.84	1.07 (0.58–2.00)
>12 years	410 (20.4)	142 (37.0)	268 (16.4)	4.01***	1.89 (1.07–3.34)*
Parity					
0	624 (31.0)	217 (56.5)	407 (25.0)	Ref.	Ref.
1–2	895 (44.5)	111 (28.9)	784 (48.2)	0.26***	0.30 (0.20–0.45)
≥3	493 (24.5)	56 (14.6)	437 (26.8)	0.24***	0.25 (0.14–0.44)
Mode of delivery					
Vaginal	1223 (60.7)	–	1223 (75.1)	–	–
Intrapartum caesarean	406 (20.2)	–	406 (24.9)	–	–
Prelabour caesarean	384 (19.1)	384 (100)	–	–	–
Fetal presentation					
Vertex–vertex presentation	969 (48.1)	136 (35.4)	833 (51.1)	Ref.	Ref.
Vertex–nonvertex presentation	569 (28.3)	96 (25.0)	473 (29.1)	1.24	1.24 (0.96–1.71)
Nonvertex first-twin presentation	475 (23.6)	152 (39.6)	323 (19.8)	2.89***	3.85 (2.30–6.44)***
Birthweight concordance					
Concordant twin	835 (41.5)	179 (46.6)	656 (40.3)	Ref.	Ref.
Discordant twin	883 (43.8)	169 (44.0)	714 (43.8)	0.87	0.90 (0.68–1.18)
Both severe SGA twins	295 (14.7)	36 (9.4)	259 (15.9)	0.51*	0.52 (0.34–1. 13)
Prematurity					
Preterm delivery (<37 weeks)	1484 (73.7)	411 (77.7)	1218 (82.1)	1.13	0.85 (0.60–1.21)
Term delivery (≥37 weeks)	529 (26.3)	118 (22.3)	266 (17.9)	Ref.	Ref.
Facility capacity					
High	458 (26.4)	139 (38.5)	319 (23.2)	Ref.	Ref.
Medium	708 (40.8)	193 (53.5)	515 (37.4)	0.89	1.44 (0.72–2.88)
Low	570 (32.8)	29 (8.0)	541 (39.4)	0.12***	0.37 (0.15–0.97)*
HDI country groups					
Very high and high	492 (24.4)	202 (52.6)	290 (17.8)	Ref.	Ref.
Medium	440 (21.9)	52 (13.5)	388 (23.8)	0.19***	0.17 (0.06–0.49)**
Low	1081 (53.7)	130 (34.0)	951 (58.4)	0.20***	0.23 (0.10–0.87)***

Adjusted odds ratio (aAOR), adjusted for maternal age, marital status, education, parity, fetal presentation, birthweight concordance, prematurity, facility capacity, and country HDI (as of 2012). Severe SGA: birthweight below third percentile of singleton reference.
Level of significance: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

twins delivered by prelabour caesarean delivery, compared with deliveries following the spontaneous onset of labour. As shown in Table 3, after stratification by fetal presentation this protective effect for reducing neonatal mortality was not present in vertex–vertex twins (1.07; 95% CI 0.44–2.57), and was stronger in nonvertex first-twin deliveries (0.12; 95% CI 0.02–0.56). All effects for neonatal near miss were insignificant after stratification, but produced similar estimates: 0.64 for vertex–vertex; 0.66 for vertex–nonvertex; and 0.59 for nonvertex first-twin presentation.

Table 2. Distribution of fetal and neonatal adverse outcomes* by gestational age. Analysis of 2013 twin deliveries at ≥34 weeks of gestation

	Gestational age at birth by completed weeks [*n* (%)]							
	34	**35**	**36**	**37**	**38**	**39**	**40**	**41**
All deliveries, *n* = 2013								
Deliveries (*n*)	128	155	246	433	444	240	318	49
Prelabour caesarean section [*n* (%)]	26 (20)	36 (23)	56 (23)	85 (20)	90 (20)	40 (17)	45 (14)	6 (12)
Live births (*n*)	247	294	472	833	852	459	608	92
Prospective fetal death**	41.7	42.2	41.3	41.4	42.8	46.1	47.6	51.0
Early neonatal death***	32.4	27.2	31.8	40.8	43.4	41.4	39.5	54.3
Neonatal near miss***	161.9	176.9	178.0	196.9	186.6	176.5	190.8	250.0
Vertex–vertex presentation, *n* = 969								
Deliveries (*n*)	58	74	112	199	235	115	152	24
Prelabour caesarean section [*n* (%)]	11 (19)	13 (18)	26 (23)	20 (10)	39 (17)	13 (11)	12 (8)	2 (8)
Live births (*n*)	111	138	215	387	452	217	293	43
Prospective fetal death**	40.8	40.6	38.2	37.9	41.8	48.1	42.6	83.3
Early neonatal death***	34.5	27	40.2	42.7	51.1	47.8	49.5	62.5
Neonatal near miss***	206.9	243.2	218.8	226.1	238.3	221.7	184.8	333.3
Vertex–nonvertex presentation, *n* = 569								
Deliveries (*n*)	39	46	68	126	115	68	91	16
Prelabour caesarean section [*n* (%)]	5 (13)	9 (20)	14 (21)	24 (19)	20 (17)	12 (18)	9 (10)	3 (18)
Live births (*n*)	76	89	131	239	217	133	174	31
Prospective fetal death**	87.9	90.6	93.0	96.2	93.1	80.0	102.8	62.5
Early neonatal death***	39.5	22.5	15.3	41.8	32.3	37.6	40.2	32.3
Neonatal near miss***	184.2	168.5	167.9	205.0	170.5	157.9	224.1	193.5
Nonvertex first-twin presentation, *n* = 475								
Deliveries (*n*)	31	35	66	108	94	57	75	9
Prelabour caesarean section [*n* (%)]	10 (32)	14 (40)	16 (24)	41 (38)	31 (33)	15 (26)	24 (32)	10 (11)
Live births (*n*)	60	67	126	207	183	109	141	18
Prospective fetal death**	82.1	83.3	83.1	81.6	80.9	99.3	107.1	0.0
Early neonatal death***	16.7	29.9	31.7	38.6	38.3	27.5	21.3	55.6
Neonatal near miss***	150.0	164.2	238.1	227.1	191.3	183.5	205.7	277.8

A neonatal near miss is considered as any of the following: any intubation (at birth or at any time within the first week); nasal CPAP; surfactant administration; cardiopulmonary resuscitation (cardiac massage); use of any vasoactive drug; use of therapeutic intravenous antibiotics; use of blood products; use of steroids to treat refractory hypoglycaemia; or any surgery.
*Defined as events in one or both twins.
**Calculated as (all fetal deaths occurring at or after given gestational age/all fetuses delivered at or after given gestational age) × 1000.
***Calculated as (number of events at a given gestational age/total live births at a given gestational age) × 1000.

Table 4 shows a direct comparison between prelabour caesarean section and expectant management, stratified by the HDI of the country. The perinatal mortality and neonatal near-miss rates were lower at 37–38 weeks of gestation for prelabour caesarean delivery, and higher for expectant management, when compared with 34–36 weeks of gestation. Although all estimates were nonsignificant, perinatal mortality and the neonatal near-miss rate were estimated to be 1.2–1.9 times higher at 37–38 weeks of gestation in the expectant management group, compared with prelabour caesarean delivery, for all HDI subgroups. When comparing perinatal mortality and the neonatal near-miss rate between prelabour caesarean delivery and expectant management at 34–36 weeks of gestation, estimates ranged from 0.8 for medium-HDI countries to 1.1 for very high- and high-HDI countries.

Discussion

Main findings

We observed a higher proportion of prelabour caesarean delivery in twin pregnancies of older women, women with a higher level of education, women who delivered at higher capacity facilities, and women from wealthier countries. Overall, the neonatal near-miss rate was lower among prelabour caesarean deliveries compared with expectant management. After adjusting for institutional, maternal, and neonatal characteristics, prelabour caesarean delivery was

Table 3. (a) Risks of perinatal adverse outcomes associated with prelabour caesarean delivery, (b) by fetal presentation. Analysis of 2013 twin deliveries at ≥34 weeks of gestation

(a)		Prelabour caesarean delivery [*n* (%)]		Spontaneous labour [*n* (%)]	OR	aOR (95% CI)
	Total [*n* (%)]					
Fetal death	168 (8.4)	30 (7.8)		138 (8.5)	0.92	0.92 (0.56–1.50)
Early neonatal death	150 (7.5)	15 (3.9)		135 (8.3)	0.73	0.39 (0.19–0.80)**
Neonatal near miss	647 (32.1)	103 (26.8)		544 (33.4)	0.45**	0.63 (0.44–0.94)**

(b)	Fetal death			Early neonatal death			Neonatal near miss		
	Total [*n* (%)]	**Prelabour caesarean section [*n* (%)]**	**aOR (95% CI)**	**Total [*n* (%)]**	**Prelabour caesarean section [*n* (%)]**	**aOR (95% CI)**	**Total [*n* (%)]**	**Prelabour caesarean section [*n* (%)]**	**aOR (95% CI)**
All deliveries	168 (100)	30 (100)	0.92 (0.56–1.50)	150 (100)	15 (32.1)	0.39 (0.19–0.80)*	647 (100)	103 (100)	0.63 (0.44–0.94)**
Vertex–vertex presentation, *n* = 969	79 (47.0)	8 (26.7)	0.61 (0.23–1.62)	86 (57.3)	10 (66.7)	1.07 (0.44–2.57)	300 (46.4)	37 (35.9)	0.64 (0.37–1.10)
Vertex–nonvertex presentation, *n* = 569	50 (29.8)	8 (26.7)	0.73 (0.26–2.05)	36 (24.0)	2 (13.3)	0.12 (0.01–1.06)	183 (28.3)	28 (27.2)	0.66 (0.34–1.26)
Nonvertex first-twin presentation, *n* = 475	39 (23.2)	14 (46.8)	1.09 (0.48–2.45)	28 (18.7)	3 (20.0)	0.12 (0.02–0.56)**	164 (25.3)	38 (36.9)	0.59 (0.30–1.15)

Adverse outcomes defined as events in one or both twins. Neonatal near miss is considered as any of the following: any intubation (at birth or at any time within the first week); nasal CPAP; surfactant administration; cardiopulmonary resuscitation (cardiac massage); use of any vasoactive drug; use of therapeutic intravenous antibiotics; use of blood products; use of steroids to treat refractory hypoglycaemia; or any surgery. Adjusted odds ratio (aOR), adjusted for: maternal age, marital status; education; parity; birthweight concordance; prematurity; facility capacity; and country HDI.
Levels of significance: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Table 4. Risk of perinatal mortality and neonatal near miss in expectant management, compared with prelabour caesarean delivery at given periods (34–36 versus 37–38 weeks of gestation). Analysis of 2013 twin deliveries at ≥34 weeks of gestation

	34–36 weeks	37–38 weeks
Prelabour caesarean delivery		
Number of deliveries (*n*)	118	175
Perinatal mortality and neonatal near miss [*n* (%)]	49 (41.5%)	58 (33.1%)
Expectant management*		
Number of deliveries (*n*)	1484	607
Perinatal mortality and neonatal near miss [*n* (%)]	589 (39.7%)	247 (40.7%)
Odds ratio comparing expectant management with prelabour caesarean delivery, for each period. Stratified by Human Development Index (HDI), as of 2012 (95% CI)*		
All countries	0.92 (0.63–1.36)	1.38 (0.97–1.97)
Very high- and high-HDI countries	1.12 (0.62–2.02)	1.23 (0.63–2.41)
Medium-HDI countries	0.79 (0.39–1.61)	1.89 (1.00–3.59)
Low-HDI countries	0.99 (0.45–2.19)	1.64 (0.89–3.01)

*Denominator is all fetuses delivered after given gestational age, or were delivered at given gestational age following spontaneous onset of labour.
Level of significance: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

associated with lower neonatal mortality, perinatal mortality, and neonatal near-miss rate for nonvertex first-twin presentation. We also found the wealth of a country to be associated with higher rates of prelabour caesarean section and a lower mean gestational age for delivery in twins.

Strengths and limitations

To the best of our knowledge, this is the first multicountry study to describe the timing and mode of delivery for twin pregnancies in low- and middle-income settings. To take account of heterogeneity in different settings, we stratified countries by HDI and adjusted for health institutional capacity. To correctly calculate the risk of adverse outcomes at different gestational lengths, as well as to compare between termination and continuation of the pregnancy, we followed the prospective risk approach originally proposed by Feldman,[36] which has been recommended in other work.[7,37]

Our study has two main limitations, however. First, as our study was conducted in relatively large health institutions capable of performing caesarean section, our findings may not be generalisable to deliveries in smaller facilities, especially in those with limited capacity of performing surgery or other more complex interventions, and our calculated proportions and averages may differ from those at the national level. As multiple pregnancies are considered to be high risk, however, and are often referred to higher institutions, we believe our study is likely to reflect existing practice and the risk of adverse perinatal outcomes. Second, as a result of a relatively small number of deliveries and events, our study lacks the scope to detect significant differences, and our estimations are unstable when stratified by each gestational week.

Third, we were not able to incorporate data on chorionicity or amnionicity, as these data were not collected. Although these are inevitably important factors when managing twin pregnancies, in many developing countries this information is not available before delivery because of the low consultation and ultrasound rate during the first trimester.

Interpretation

We found that countries with a lower HDI had lower rates of prelabour caesarean section and higher mean gestational age at delivery. Seven of the 21 low- and middle-income countries in our study had a mean length of gestation above 38 weeks of gestation. Although we had restricted our population to deliveries later than 34 weeks of gestation, this is longer than previously reported in high-income countries,[2,5,7,40,41] and is also higher in lower HDI settings.

Although longer gestational length may provide time for maturation of twin fetuses, the risk of perinatal death may outweigh this benefit beyond 37–38 weeks of gestation. Our study showed that expectant management after 37–38 weeks of gestation could increase perinatal morbidity and mortality. Perinatal outcomes may be improved in such cases if twins are closely monitored and if delivery is performed by 37–38 weeks of gestation. This is supported by studies in developed countries that balanced the risk of intrauterine stillbirth and neonatal morbidity,[2,5–8] as well as a recent multicentred RCT that found planned twin deliveries at 37 weeks of gestation did not increase adverse outcomes,[8,42,43] and is reinforced by current guidelines that recommend twin delivery at 34–38 weeks of gestation.[9–11]

In most current guidelines on the management of twin pregnancies, fetal presentation is the determining factor for

mode of delivery, with maternal characteristics such as maternal age, multiparity, and natural conception modifying the beneficial effect of prelabour caesarean delivery.[44] Several countries have specific recommendations for vertex–vertex or nonvertex first-twin presentations.[3,11,12] An attempted trial of vaginal delivery is recommended for vertex–vertex presentation, whereas a prelabour caesarean section is recommended for nonvertex first-twin presentation.[10,12,13,45] In the case of vertex–nonvertex presentation, there is little available evidence upon which to base recommendations for delivery methods.[20,46] A recent large trial of over 1400 women with twins showed that planned vaginal delivery was equally as feasible as planned caesarean section when delivering at 38 weeks of gestation;[47] however, the recommended method of delivery is still under debate. Observational studies using existing data sets covering births of routine clinical practice should be further explored for supportive evidence.

Our findings, as supported by other studies,[17,20–22] show that experience and preference, as well as disparities in access to care, may be significant determinants as to who delivers by prelabour caesarean delivery. Only seven (25%) countries had significantly higher rates of prelabour caesarean section for nonvertex first-twin presentation, compared with vertex–vertex presentation. On the other hand, the proportion of prelabour caesarean deliveries was higher in older women, with a higher level of education, and in those admitted to higher capacity facilities and in higher HDI countries.

The difference by HDI was prominent. In five countries, prelabour caesarean section was performed in over 50% of vertex–vertex presentations, whereas in 11 countries the procedure was performed in less than 10% of such cases.

Surprisingly, differences were also observed in deliveries that featured a nonvertex first-twin presentation, a state where prelabour caesarean delivery is recommended in multiple guidelines,[12–14] because of the possibility of the fatal complication of interlocking twins and the high rate of intrapartum caesarean section after attempted vaginal delivery. In low-HDI countries 75% of women with a nonvertex first-twin presentation experienced the spontaneous onset of labour, 40% of whom required an intrapartum caesarean section.

A recent study in France on mothers undergoing a trial of vaginal delivery also reported that nearly half of such mothers required intrapartum caesarean section,[45] and made recommendations to avoid attempting vaginal delivery for nonvertex first-twin presentation. Our analysis also showed that prelabour caesarean section was associated with reduced neonatal morbidity and mortality in non-vertex twins. Although experience and high multiparity may contribute to the high success rate of vaginal delivery in 60% of low- and middle-income countries (in high-HDI countries, the success rate of vaginal delivery was 5%), an increase in prelabour caesarean section for nonvertex twin pregnancies would most likely lead to improved perinatal outcomes.

Many reports state that the human resources required for caesarean deliveries are still lacking in many low- and middle-income countries,[21,48] which is one of the likely reasons why vaginal deliveries are attempted for cases where such delivery is not normally recommended: for example, in the case of nonvertex first-twin presentation. Our previous study shows that twin pregnancy is a significant risk factor for maternal and perinatal morbidity in low- and middle-income countries.[49] In light of this high risk and the 3–5% prevalence of multiple births, as well as the protective effect of prelabour caesarean delivery on the fetus, it is critical to develop measures that advance timely access to facilities capable of performing safe caesarean delivery in order to greatly improve twin pregnancy outcomes.

Conclusion

We found that the prelabour caesarean delivery rate was lower in countries with a low-HDI ranking, and that prelabour caesarean delivery may be beneficial for twins with nonvertex first-twin presentation.

Further studies, as well as the development of international guidelines on the optimal delivery method of twins, such as those implemented in developed countries, combined with training for the antepartum diagnosis of fetal presentation, could play an important role in enhancing maternal and neonatal outcomes in the management of twin pregnancy.

Disclosure of interests

None.

Contribution to authorship

NM and TG initiated the idea and designed the analysis plan, to which JB, JGC, JPV, KJ, and EO provided substantial advice. TG and NM performed the data analysis. NM and TG interpreted the results, wrote the article, and made revisions. Additionally, CC, JEOP, SM, JPS, and RM contributed to revisions, and approved the final version of the article.

Details of ethics approval

The HRP Specialist Panel on Epidemiological Research reviewed and approved the study protocol for technical content. This study was approved by the WHO 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:

Table S1. Number of twin deliveries, timing of birth, and proportion of prelabour caesarean delivery by country.

Table S2. Adverse perinatal outcomes in expectant management compared with prelabour caesarean delivery at each given gestational week. ■

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Original article

Risk factors for spontaneous and provider-initiated preterm delivery in high and low Human Development Index countries: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health

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Objective To evaluate how the effect of maternal complications on preterm birth varies between spontaneous and provider-initiated births, as well as among different countries.

Design Secondary analysis of a cross-sectional study.

Setting Twenty-nine countries participating in the World Health Organization Multicountry Survey on Maternal and Newborn Health.

Population 299 878 singleton deliveries of live neonates or fresh stillbirths.

Methods Countries were categorised into very high, high, medium and low developed countries using the Human Development Index (HDI) of 2012 by the World Bank. We described the prevalence and risk of maternal complications, their effect on outcomes and their variability by country development.

Main outcome measures Preterm birth, fresh stillbirth and early neonatal death.

Results The proportion of provider-initiated births among preterm deliveries increased with development: 19% in low to 40% in very high HDI countries. Among preterm deliveries, the socially disadvantaged were less likely, and the medically high risk were more likely, to have a provider-initiated delivery. The effects of anaemia [adjusted odds ratio (AOR), 2.03; 95% confidence interval (CI), 1.84; 2.25], chronic hypertension (AOR, 2.28; 95% CI, 1.94; 2.68) and pre-eclampsia/eclampsia (AOR, 5.03; 95% CI, 4.72; 5.37) on preterm birth were similar among all four HDI subgroups.

Conclusions The provision of adequate obstetric care, including optimal timing for delivery in high-risk pregnancies, especially to the socially disadvantaged, could improve pregnancy outcomes. Avoiding preterm delivery in women when maternal complications, such as anaemia or hypertensive disorders, are present is important for countries at various stages of development, but may be more challenging to achieve.

Keywords Preterm birth, scheduled delivery, spontaneous labour.

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Introduction

As a primary cause of neonatal death, preterm birth presents a major public health problem, with an estimated 15 million births, or 11% of all births worldwide, occurring preterm.[1] Approximately 90% of these preterm births are concentrated in developing countries, with 11 million (85%) in Africa and Asia, and 0.9 million in Latin America and the Caribbean.[2] Although multiple pregnancies and improved management of high-risk pregnancies leading to improved neonatal outcomes may account for the rise in preterm delivery in developed countries,[3–5] the highest preterm birth rates occur in low-income settings,[6] where the majority of preterm deliveries are caused by spontaneous labour, and it is estimated that avoidance of preterm delivery could save over 1 million neonatal deaths each year.[7]

Maternal complications, such as infectious diseases and hypertension, are the most common direct causes of preterm delivery.[8] Malaria is the most widespread infectious disease that is known to contribute to spontaneous preterm labour and preterm birth[9]; bacterial infections leading to chorioamnionitis are also associated with a large proportion of very preterm births,[10] and HIV has been reported as a risk factor for preterm delivery.[11,12] However, hypertension is the leading cause of provider-initiated preterm delivery,[8] with the definitive management of eclampsia and gestational hypertension being termination of pregnancy.

Although maternal complications and social settings play a substantial role in the underlying risk of preterm delivery,[13] it is less clear how the risk of maternal complications of preterm birth varies between spontaneous and provider-initiated delivery, and whether better interventions and treatment of these complications would improve pregnancy outcomes.

Therefore, by utilising an international dataset of developed and developing countries, we sought to understand the risk factors and outcomes of spontaneous and provider-initiated preterm birth, and their variety, by demographic and socio-economic features.

Methods

Study population

We conducted a secondary data analysis of the WHO Multicountry Survey on Maternal and Newborn Health. The survey was carried out in 359 health facilities from 29 countries in Africa, Asia, Latin America and the Middle East. A multistage cluster sampling method was applied to acquire samples of health facilities in two randomly selected provinces as well as the capital city of the 29 countries. We have included full methodological details of this survey in previous papers.[14,15] The survey recruited all women who were admitted for delivery, as well as all women with severe maternal outcomes, irrespective of gestational age. Trained medical staff sourced individual data on demographics and reproductive characteristics, medical conditions during pregnancy, birth outcomes, and complications and received interventions from the women's medical records. Health facility capacity data were obtained, including laboratory tests, human resources and training, and the capabilities of obstetrics and neonatal healthcare services. Data were collected over a period of 2 months from May 2010 to December 2011 in institutions with ≥6000 annual deliveries and 3 months in institutions with <6000 annual deliveries. In countries in which <3000 deliveries were anticipated, it was extended to 4 months in all institutions. The average number of deliveries in an institution over the study period was 463 (range, 17–6002).

There were 318 534 deliveries observed in our study. We restricted our analysis to 302 376 deliveries of singletons of over 22 completed weeks of gestation who weighed over 500 g and were alive before labour and delivery, excluding all macerated fetal deaths. We further excluded deliveries with congenital malformations (2115) or with missing data on labour (381), with a total of 299 878 deliveries retained in the analysis.

Variables and definitions

We collected data on the best clinical estimate of gestational age in weeks, and categorised delivery at gestational age 22–36 weeks as preterm, 37–41 weeks as term and 42 weeks and over as post-term. We defined provider-initiated delivery as delivery in which induction of labour or caesarean section was performed without any preceding spontaneous labour. Our main outcome of interest was delivery timing, categorised as 'spontaneous preterm birth', 'provider-initiated preterm birth', 'spontaneous term birth', 'provider-initiated term birth' and 'post-term birth'.

For risk factors of spontaneous preterm birth and provider-initiated preterm birth, we considered the following variables as exposures at the individual level: maternal age at delivery; marital status; educational attainment, parity; previous caesarean section; infant sex; severe anaemia, defined as haemoglobin <7 mg/dl; bacterial infections, defined as pyelonephritis, sepsis or other systemic infection; HIV or AIDS; malaria or dengue; chronic hypertension; pre-eclampsia or eclampsia; and other maternal conditions, defined as the presence of diseases or injuries affecting the heart, lungs, liver or kidneys. Infant sex and best clinical estimate of gestational age were considered as confounders associated with stillbirth and early neonatal death.

In addition, in our analysis, we adjusted for the 'facility capacity index' category – a proxy for the institution's capacity to provide obstetric care – comprising six areas reflecting the standard of facility and basic services, medical services, emergency obstetric services, laboratory tests, hospital practices and human resources, calculated into a

continuous index and categorised as 'good', 'poor' or 'very poor'. Countries were categorised into very high, high, medium and low developed countries using the Human Development Index (HDI) of 2012 by the World Bank.[16]

In this study, we considered stillbirths and intra-hospital early neonatal deaths as perinatal outcomes. We defined early neonatal deaths as intra-hospital deaths that occurred on or before the seventh day after delivery.

Statistical analysis

First, we examined the distribution of the duration of pregnancy and the risk of spontaneous delivery in preterm birth stratified by the duration of pregnancy within each HDI group. Next, we compared the timing of delivery with maternal characteristics by performing adjusted chi-squared tests, taking into account the survey design.

To determine the effect of maternal complications on spontaneous and provider-initiated preterm delivery, we constructed multilevel, multinomial, multivariate logistic regression models comparing the five delivery outcomes, as well as multivariate logistic regression models comparing spontaneous with provider-initiated delivery in preterm and term deliveries separately. We also adjusted for individual maternal characteristics (see Table 1) and for random effects at each level: country (level 1), facility (level 2) and individual (level 3). We repeated this analysis in HDI subgroups across country (level 1) and individual (level 2) levels, and adjusted for facility capacity, which was quantified using a scale of available utilities and interventions in each facility.

For outcomes of preterm birth, we examined the risk of intrapartum-related stillbirth, defined as fresh stillbirth (delivery of a dead fetus that does not show any sign of maceration), and early neonatal mortality, defined as death before discharge or within 7 days of hospitalisation, in both spontaneous preterm and provider-initiated preterm deliveries by HDI group. As deliveries before 28 completed weeks of gestation are considered as stillbirths in some countries, we restricted this analysis to 19 333 singletons born above 28 weeks of gestation. Using multilevel, multivariate logistic regression models adjusted for maternal characteristics, as shown in Table 1, as well as the method of delivery and fetal presentation, we calculated the risk of stillbirth and early neonatal death in spontaneous preterm delivery compared with provider-initiated preterm delivery. We further stratified this analysis by HDI subgroup. Statistical analysis was conducted using Stata/MP version 12.0 (Stata Corp LP, College Station, TX, USA), and $P < 0.05$ was considered to be statistically significant.

Table 1. Maternal characteristics stratified by timing and initiation of delivery: analysis of 299 878 singleton deliveries in 29 countries

Maternal characteristics	All deliveries, *n*	Preterm delivery		Term delivery		Post-term delivery, *n* (%)	Adjusted χ^2 *P*
		Provider-initiated delivery, *n* (%)	Spontaneous labour, *n* (%)	Provider-initiated delivery, *n* (%)	Spontaneous labour, *n* (%)		
N	299878	5315	14916	60968	213881	4798	
Age (years)							
<20	30923	479 (2)	2014 (8)	4620 (15)	23261 (75)	550 (2)	<0.001
20–34	232462	3786 (2)	1599 (6)	47310 (20)	166349 (72)	3761 (2)	
≥35	36493	1031 (3)	11259 (6)	8922 (25)	23635 (66)	470 (1)	
Marital status							
Single	30597	581 (2)	1780 (6)	5292(17)	22240 (73)	687 (2)	0.001
Married/cohabiting	267427	4683 (2)	13032 (5)	55084 (21)	190180 (71)	4093 (2)	
Education (years)							
0	45040	508 (1)	2487 (6)	4501 (10)	36796 (82)	679 (2)	<0.001
1–6	39216	649 (2)	2182 (6)	6639 (17)	28917 (74)	741 (2)	
7–9	57112	881 (2)	3246 (6)	10506 (18)	41284 (72)	1133 (2)	
10–12	87175	1672 (2)	4204 (5)	19192 (22)	60444 (69)	1557 (2)	
>12	48876	1092 (2)	1616 (3)	14504 (30)	31084 (64)	554 (1)	
Parity							
0	127880	2298 (2)	6653 (5)	28847 (23)	87895 (69)	2049 (2)	<0.001
1–2	124446	2216 (2)	6010 (5)	26289 (21)	87858 (71)	1917 (2)	
≥3	47544	792 (2)	2240 (5)	5733 (12)	37873 (80)	828 (2)	
Previous caesarean section	36645	1302 (4)	1562 (4)	16366 (45)	16909 (46)	394 (1)	<0.001
Anaemia (haemoglobin <7 mg/dl)	4077	323 (8)	498 (12)	941 (23)	2268 (46)	37 (1)	<0.001
Infection							
Puerperal endometritis	254	17 (7)	25 (10)	59 (23)	150 (59)	3 (1)	<0.001
Systemic bacterial infection	1393	97 (7)	228 (16)	325 (23)	720 (56)	21 (2)	<0.001
HIV/AIDs	1109	34 (3)	88 (8)	236 (21)	729 (52)	22 (2)	<0.001
Malaria/dengue	312	38 (12)	49 (16)	70 (22)	150 (66)	5 (2)	<0.001
Hypertensive disorders							
Chronic hypertension	1148	173 (15)	125 (11)	415 (36)	425 (48)	10 (1)	<0.001
Pre-eclampsia/eclampsia	6299	87 (1)	766 (5)	2258 (20)	2693 (72)	69 (2)	<0.001
Other maternal conditions*	1957	240 (12)	204 (10)	658 (34)	843 (43)	8 (0)	<0.001

*Any chronic or acute injury or disorder affecting the kidneys, heart, lungs or liver.

Results

Of the 29 9878 singleton deliveries, 6.7% were preterm. The proportion of preterm births among all deliveries was not necessarily higher in lower HDI countries, and varied largely in the range 1–10% by country (shown in Table S1). Alternatively, the proportion of preterm births that were provider initiated increased as HDI increased, with the percentage being 20% in low HDI countries and 40% in high HDI countries. This difference persisted through subgroups of length of gestation (Table 2), with HDI ranking and proportion of provider-initiated deliveries showing a mild significant correlation ($R = 0.25$, $P = 0.007$) (Figure 1).

Table 1 illustrates the distribution of the timing of delivery by maternal characteristics. Mothers who were unmarried, had a low number of previous births, had a previous caesarean section, anaemia, or any infection or chronic hypertension showed a higher prevalence of spontaneous and provider-initiated preterm delivery. Mothers who received less education and who were younger had a higher proportion of spontaneous preterm delivery, but not provider-initiated preterm delivery. However, older mothers had a higher prevalence of provider-initiated preterm delivery, but not spontaneous preterm delivery.

To estimate the effect of the maternal characteristics shown in Table 1 on preterm delivery, we used a multivariate, multilevel, multinomial logistic regression model. In Table 3, we show the difference in prevalence and effect of maternal complications, stratified by HDI groups. The prevalence of HIV/

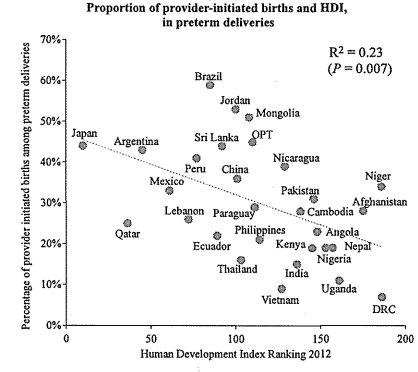

Figure 1. Proportion of provider-initiated births and Human Development Index (HDI) in preterm deliveries. DRC, Democratic Republic of Congo; OPT, Occupied Palestinian Territory.

Table 2. Proportion of provider-initiated delivery among preterm deliveries, stratified by the duration of pregnancy and Human Development Index (HDI)

	HDI group			
	Very high	High	Medium	Low
	Provider-initiated births (*n*)/All births (*N*) [proportion of provider-initiated births (%)]			
All preterm deliveries (%)	369/921 (40)	1856/4945 (38)	1720/7675 (22)	1370/6690 (20)
Extremely premature deliveries (22–27 weeks)	19/41 (46)	61/228 (27)	66/271 (24)	81/358 (23)
Severely premature deliveries (28–31 weeks)	37/75 (49)	195/508 (38)	260/994 (26)	234/995 (24)
Moderately preterm deliveries (32–33 weeks)	37/85 (44)	260/680 (38)	276/1139 (24)	207/783 (26)
Late preterm deliveries (34–36 weeks)	276/720 (38)	1340/3529 (38)	1118/5271 (21)	848/4554 (19)

Very high HDI countries included Japan, Qatar and Argentina; high HDI countries included Mexico, Lebanon, Peru, Brazil, Ecuador and Sri Lanka; medium HDI countries included Jordan, China, Thailand, Mongolia, Occupied Palestinian Territory, Paraguay, Philippines, Vietnam, Nicaragua, India and Cambodia; low HDI countries included Kenya, Pakistan, Angola, Nigeria, Nepal, Uganda, Afghanistan, Democratic Republic of Congo and Niger.

AIDS and malaria/dengue was higher, and that of chronic hypertension, pre-eclampsia, eclampsia, systemic infection and puerperal endometritis was lower, in low HDI countries. The effects of anaemia and hypertension were significant in all HDI groups, and the risk of preterm delivery caused by these complications did not decrease despite higher levels of country development. The effects of all bacterial infections (pyelonephritis, puerperal endometritis, systemic infection) were strongest in the high HDI country group, and the effect of HIV/AIDs was larger in the higher HDI groups.

Detailed data on associations between all maternal characteristics and spontaneous and provider-initiated preterm delivery are shown in Table S2. Individual risk factors for both spontaneous and provider-initiated preterm delivery included lower (<20 years) and higher (>35 years) maternal age, unmarried status, poorer education, severe anaemia, systemic bacterial infection, malaria and/or dengue, hypertensive disorders (chronic hypertension, pre-eclampsia or eclampsia) and other maternal conditions. No significant differences were observed by difference in parity or presence of HIV/AIDS.

To further estimate the effect of maternal characteristics on spontaneous labour compared with provider-initiated delivery in preterm, as well as term, deliveries, we used a multilevel, multivariate logistic regression model comparing these two outcomes. In Table 4, we show the results. Mothers of lower age, poorer education or with pyelonephritis were more likely to have spontaneous labour, and

Table 3. Variation in prevalence (A) and adjusted odds ratios (B) of selected maternal medical conditions of preterm birth by country with the Human Development Index (HDI): analysis of 299 878 singleton deliveries in 29 countries

Maternal condition	All countries (%)***	Very high HDI (%)****	High HDI (%)****	Medium HDI (%)****	Low HDI (%)****
(A) Prevalence of selected maternal medical conditions					
Anaemia	4077 (1.4)	181 (1.0)	164 (1.7)	208 (1.4)	151 (1.2)
Infection					
Pyelonephritis	453 (0.2)	18 (0.1)	96 (0.1)	235 (0.2)	104 (0.1)
Puerperal endometritis	270 (0.1)	93 (0.6)	67 (0.1)	58 (0.1)	52 (0.0)
Systemic infection	966 (0.3)	137 (0.8)	249 (0.4)	355 (0.4)	225 (0.2)
HIV/AIDS	1109 (0.4)	27 (0.2)	86 (0.1)	113 (0.1)	883 (0.8)
Malaria/dengue	312 (0.1)	2 (0.0)	13 (0.0)	52 (0.1)	245 (0.2)
Hypertensive disorders					
Chronic hypertension	1148 (0.4)	83 (0.5)	346 (0.5)	446 (0.4)	273 (0.2)
Pre-eclampsia/eclampsia	7066 (2.4)	445 (2.7)	1908 (2.9)	2811 (2.9)	1902 (6)
(B) Adjusted odds ratios and 95% confidence intervals for estimates of effect of maternal medical conditions on preterm delivery					
Anaemia	2.0 (1.8; 2.2)**	2.0 (1.3; 3.0)*	1.8 (1.3; 2.5)*	2.0 (1.7; 2.3)**	2.3 (2.0;2.7)**
Infection					
Pyelonephritis	1.5 (1.1; 2.0)*	0.6 (0.1; 5.4)	6.4 (3.5; 12)**	1.3 (0.8; 2.1)	1.1 (0.7; 1.9)
Puerperal endometritis	1.8 (1.2; 2.7)	0.4 (0.1; 1.3)	3.7 (1.9; 7.1)**	1.5 (0.6; 3.8)	2.7 (1.3;5.8)*
Systemic infection	2.8 (2.3; 3.4)**	1.6 (0.8; 3.1)	5.8 (3.9; 8.6)**	2.4 (1.8; 3.2)**	2.7 (1.9;4.0)**
HIV/AIDS	1.2 (1.0; 1.5)	5.5 (2.0; 15)*	1.4 (0.6; 3.5)	1.0 (0.5; 1.9)	1.2 (0.9; 1.6)
Malaria/dengue	4.4 (3.2; 6.13)**	NE*****	3.2 (0.5; 19)	2.5 (1.3; 4.8)**	5.4 (3.6; 8.0)**
Hypertensive disorders					
Chronic hypertension	2.3 (1.9; 2.7)**	3.0 (1.5; 6.0)*	3.3 (2.5; 4.3)**	2.3 (1.8; 2.9)**	1.1 (0.8; 1.7)
Pre-eclampsia/eclampsia	5.0 (4.7; 5.4)**	5.0 (3.8; 6.6)**	6.1 (5.4; 6.9)**	3.7 (3.3; 4.1)**	6.7 (5.9; 7.5)**

Very high HDI countries included Japan, Qatar and Argentina; high HDI countries included Mexico, Lebanon, Peru, Brazil, Ecuador and Sri Lanka; medium HDI countries included Jordan, China, Thailand, Mongolia, Occupied Palestinian Territory, Paraguay, Philippines, Vietnam, Nicaragua, India and Cambodia; low HDI countries included Kenya, Pakistan, Angola, Nigeria, Nepal, Uganda, Afghanistan, Democratic Republic of Congo and Niger.
*$P < 0.01$.
**$P < 0.001$.
***Multinomial, multilevel, multivariate logistic regression models were used to obtain adjusted odds ratios (AORs): the outcome was of five categories (spontaneous preterm birth, spontaneous term birth, provider-initiated preterm birth, provider-initiated term birth, post-term birth; reference is spontaneous term birth); multilevel analysis was structured on three levels (individual, health facility, country) with random intercepts, and adjusted for maternal age, marital status, education, parity and previous caesarean section.
****Multinomial, multilevel, multivariate logistic regression models were used to obtain odds ratios (ORs): the outcome was of five categories (spontaneous preterm birth, spontaneous term birth, provider-initiated preterm birth, provider-initiated term birth, post-term birth; reference is spontaneous term birth); multilevel analysis was structured on two levels (individual, country) with random intercepts, and adjusted for maternal age, marital status, education, parity and previous caesarean section, maternal medical conditions, and facility capacity and services.
*****Not estimated due to small numbers.

nulliparous mothers, mothers with previous caesarean section or mothers with anaemia, malaria/dengue, chronic hypertension or pre-eclampsia were more likely to have provider-initiated delivery, in both term and preterm deliveries. Multiparity (more than two previous births) was associated with spontaneous delivery only in term births, and pyelonephritis was associated with spontaneous delivery in preterm delivery, but with provider-initiated delivery in term delivery.

Table 5 illustrates the risk of stillbirth and early neonatal death among preterm deliveries for both spontaneous labour and provider-initiated delivery by HDI subgroup. Risks of stillbirth and early neonatal death were both lower in spontaneous preterm deliveries compared with provider-initiated deliveries within all HDI subgroups. Stillbirth and early neonatal death within both spontaneous preterm delivery and provider-initiated preterm delivery decreased as HDI increased. After adjustment for maternal characteristics, the odds ratio of stillbirth in spontaneous delivery compared with provider-initiated delivery was lower in all HDI subgroups, and this effect was larger as HDI increased.

Table 4. Adjusted odds ratios of risk factors for spontaneous compared with provider-initiated delivery, in term and preterm delivery: analysis of 299 878 singleton preterm deliveries in 29 countries

Maternal characteristics	Spontaneous versus provider-initiated delivery [adjusted odds ratio (95% confidence interval)]	
	Preterm delivery	Term delivery
Age (years)		
<20	1.24 (1.08; 1.39)**	1.44 (1.38; 1.51)***
20–34	REF	REF
≥35	0.67 (0.60; 0.76)***	0.66 (0.64; 0.69)***
Marital status		
Single	1.25 (1.08; 1.45)**	1.10 (1.05; 1.15)***
Married	REF	REF
Education		
None	2.28 (1.89; 2.75)***	1.94 (1.83; 2.06)***
1–6 years	1.77 (1.51; 2.07)***	1.40 (1.33; 1.46)***
7–9 years	1.75 (1.51; 2.02)***	1.30 (1.25; 1.36)***
10–12 years	1.35 (1.19; 1.53)***	1.25 (1.21; 1.30)***
>12 years	REF	REF
Parity		
0	0.79 (0.72; 0.87)***	0.51 (0.49; 0.52)***
1–2	REF	REF
≥3	1.02 (0.89; 1.15)	1.46 (1.40; 1.52)***
Previous caesarean section	0.37 (0.33; 0.41)***	0.15 (0.15; 0.16)***
Infant sex (female)	0.97 (0.90; 1.05)	1.04 (1.03; 1.07)***
Severe anaemia (haemoglobin <7 mg/dl)	0.54 (0.44; 0.65)***	0.83 (0.76; 0.91)***
Infection		
Pyelonephritis	2.21 (1.17; 4.15)*	0.76 (0.58; 0.99)*
Puerperal endometritis	1.10 (0.54; 2.26)	0.90 (0.64; 1.27)
Systemic bacterial infection	0.81 (0.57; 1.15)	0.80 (0.66; 0.97)*
HIV/AIDs	1.00 (0.61; 1.66)	0.49 (0.41; 0.59)***
Malaria/dengue	0.27 (0.16;0.47)***	0.48 (0.33; 0.68)***
Hypertension		
Chronic hypertension	0.60 (0.45; 0.81)**	0.34 (0.29; 0.41)***
Pre-eclampsia/ eclampsia	0.20 (0.18; 0.22)***	0.32 (0.30; 0.34)***

Multilevel, multivariate logistic regression models were used to obtain adjusted odds ratios: the outcome was preterm delivery; multilevel analysis was structured on three-levels (individual, health facility, country) with random intercepts, and adjusted for maternal age, marital status, education, parity and previous caesarean section.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.

Discussion

Main findings

In our study, we found an increase in the percentage of provider-initiated preterm delivery, as well as a decrease in stillbirth and early neonatal mortality, in higher HDI groups. Younger mothers and those who received less education were also less likely to have a provider-initiated delivery for a preterm birth.

However, we did not observe a decrease in preterm birth associated with improved human development of the country, and the effects of maternal complications, such as anaemia or hypertensive disorders, on preterm delivery were similar across countries.

Once obstetric complications are present, the avoidance of preterm delivery may be difficult, even with the care standards of more developed countries. On top of an increased effort to prevent pregnancy complications, developing countries and those socially disadvantaged may benefit from management care, including interventions to optimise the timing of delivery.

Interpretation

Recent reports have shown an increase in provider-initiated preterm delivery and improved neonatal outcomes in developed countries.[17,18] In the USA, provider-initiated delivery increased from 30% to 42% of all preterm deliveries during 1995–2005,[3] with stillbirths and neonatal mortality also decreasing. In our study, we observed an increase in provider-initiated preterm delivery associated with country HDI, as well as a decrease in the risk of stillbirth in spontaneous preterm deliveries compared with provider-initiated preterm deliveries in higher HDI countries, even after controlling for maternal and infant characteristics.

Table 5. Neonatal outcomes of spontaneous labour and provider-initiated preterm delivery: analysis of 19 333 singleton preterm deliveries above 28 weeks of gestation in 29 countries

	Human Development Index (HDI) group				
	All countries (19 333)	**Very high (921)**	**High (4945)**	**Medium (7675)**	**Low (6690)**
	Stillbirths/preterm deliveries (%)				
(A) Fresh stillbirths					
Spontaneous preterm deliveries	781/14245 (5.4)	4/530 (0.8)	62/2922 (2.1)	284/5750 (4.9)	431/5043 (8.5)
Provider-initiated preterm deliveries	374/5088 (7.4)	17/350 (4.9)	77/1795 (4.3)	105/1654 (6.4)	175/1289 (13.6)
Adjusted odds ratio****	0.69 (0.58; 0.81)***	0.18 (0.04; 0.78)*	0.42 (0.28; 0.65)***	0.71 (0.53; 0.96)*	0.85 (0.67; 1.09)
	HDI group				
	All countries (18178)	**Very high (859)**	**High (4578)**	**Medium (7015)**	**Low (5726)**
	Early neonatal deaths/live preterm births (%)				
(B) Early neonatal deaths					
Spontaneous preterm deliveries	623/13464 (4.6)	6/526 (1.1)	68/2860 (2.4)	259/5466 (4.7)	290/4612 (6.3)
Provider-initiated preterm deliveries	249/4714 (5.3)	5/333 (1.5)	38/1718 (2.2)	97/1549 (6.3)	109/1114 (9.8)
Adjusted odds ratio****	0.73 (0.59; 0.90)**	0.39 (0.10; 1.45)	0.73 (0.45; 1.18)	0.80 (0.58; 1.09)	0.78 (0.56; 1.06)

Very high HDI countries included Japan, Qatar and Argentina; high HDI countries included Mexico, Lebanon, Peru, Brazil, Ecuador and Sri Lanka; medium HDI countries included Jordan, China, Thailand, Mongolia, Occupied Palestinian Territory, Paraguay, Philippines, Vietnam, Nicaragua, India and Cambodia; low HDI countries included Kenya, Pakistan, Angola, Nigeria, Nepal, Uganda, Afghanistan, Democratic Republic of Congo and Niger.

*$P < 0.05$.

**$P < 0.01$.

***$P < 0.001$.

****Multilevel, multivariate logistic regression models were used to obtain adjusted odds ratio of spontaneous preterm delivery compared with provider-initiated delivery. Multilevel analysis was structured on two levels (individual, country) with random intercepts, and adjusted for facility capacity index, maternal characteristics (maternal age, marital status, education, parity, previous caesarean section and maternal medical conditions) and infant characteristics (sex, gestational age).

Our results also support previous findings which show that lower socio-economic status is a strong factor for increased risk of preterm birth[8] and preterm labour,[19] and for increased risk of not receiving pregnancy terminations when needed.[20] We found that younger mothers and those with a poorer education were at a lower risk of receiving a provider-initiated preterm delivery compared with spontaneous labour, even though most complications were risk factors for both spontaneous and provider-initiated preterm birth, and high-risk pregnancies with hypertensive disorders, malaria or dengue were more likely to receive a provider-initiated delivery. It is important to expand the provision of skilled birth attendance and emergency obstetric care and increase accessibility for the disadvantaged.[21]

However, we found that the risk of preterm delivery remained high in most developed countries, which underscores the fact that preterm delivery is a global health problem for countries at all stages of development. In addition, though anaemia and hypertensive disorders were associated with both spontaneous and indicated preterm birth in all HDI groups, the risk of preterm delivery caused by these complications did not decrease with higher HDI.

Our findings may be supportive of previous studies which observed that few medical interventions aimed at reducing maternal complications can successfully prevent preterm birth. Peña-Rosas et al.[22] reported that, although antenatal iron supplementation decreased maternal anaemia and increased birthweight, it did not significantly reduce

preterm birth. Thangaratinam et al.[23] reported that, currently, there is no test sufficiently accurate for the early recognition of women at risk of pre-eclampsia and, although supplemental calcium significantly reduced the risk of pre-eclampsia, it did not decrease the risk of preterm birth.

Interestingly, AIDS did not have a significant effect overall on preterm birth (adjusted odds ratio [AOR], 1.21; 95% confidence interval [CI], 0.97; 1.51), which contradicted previous studies.[11,12] Yet, the effect of AIDS on preterm deliveries was higher in countries with high HDI, and was a significant risk factor for preterm delivery in very high HDI countries. A similar effect has been observed in the USA,[12] and may be explained by behavioural, socio-economic characteristics associated with having HIV in a setting in which prevalence is low.

Strengths and limitations

Our study has several limitations. First, we did not collect data on fetal indications for the termination of pregnancy, including fetal distress and intrauterine growth restriction, or prolonged rupture of membranes (PROM). These are important factors leading to spontaneous and provider-initiated preterm delivery, and the absence of this information prevented us from focusing on the direct causes of provider-initiated delivery, as well as from calculating the coverage of provider-initiated delivery in pregnancies with indications. Therefore, we focused on effects of maternal age, education and complications and their effect on preterm delivery.

Second, we also lacked data on maternal characteristics associated with preterm delivery, such as smoking, malnutrition, and familial and maternal history of recent preterm delivery. As previous studies have found that these characteristics are mostly associated with lower socio-economic status, as well as preterm delivery,[13,24,25] the lack of adjustment for these confounders may have led to an overestimation of the risk of preterm delivery in mothers of a younger age, a lower level of education or from less developed countries. The additional risk observed in mothers with a lower socio-economic status in our study can be interpreted by considering adverse behaviour, such as smoking, which has been reported to be associated with lower societal status and preterm birth, but not measured in our survey.[25–27]

Third, as routine hospital records served as the primary data source, the prevalence of maternal complications in our data could have been affected by a lack of documented diagnosis because of the inability to diagnose the condition, failure to recognise the condition or failure to document the diagnosis, and the skill of the personnel involved in data collection. However, to minimise this bias, we trained the data collectors, double-checked the data collection forms before data entry and asked medical staff to complete the information in the record in the case of unclear or missing information, in order to reduce methodological heterogeneity and increase data quality as much as possible.

Finally, as this study was facility based, with facilities being mainly secondary and tertiary facilities, we were likely to have an over-representation of maternal complications and perinatal deaths, and a higher coverage of interventions, compared with smaller facilities in the community, with the magnitude of bias varying between countries. Therefore, our data are not representative of the population, and can only be extrapolated to similar settings.

Conclusions

Our study shows that preterm delivery is less likely to be provider initiated in less well developed countries, even when limited to facilities in which caesarean section and induction of labour can be performed. When maternal complications, such as anaemia or hypertensive disorders, are present, the impact on preterm delivery is difficult to reduce even with the care standards of more highly developed countries.

To improve pregnancy outcomes, it is important to provide adequate obstetric care, including optimal timing for delivery in high-risk pregnancies, especially to the socially disadvantaged. There is a need for further interventions that aim to prevent maternal complications and improve the capacity to manage provider-initiated delivery in low-income countries.

Disclosure of interests

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

Contribution to authorship

RM, NM, EO and GT initiated the concept. NM, GT and EO contributed to the design of the study. NM performed the data analysis and wrote the initial manuscript. JPV, JPS, CJRH and KJ provided advice to the study design and edited the manuscript. All authors read and approved the final version of the manuscript.

Details of ethics approval

The UNDP/UNFPA/UNICEF/WHO/World Bank 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 WHO 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:

Table S1. Prevalence of preterm delivery by country. Analysis of 299 878 singleton deliveries in 29 countries.

Table S2. Adjusted odds ratios for risk factors for spontaneous labour and provider-initiated preterm delivery. Analysis of 16 474 singleton preterm deliveries in 29 countries. ■

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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

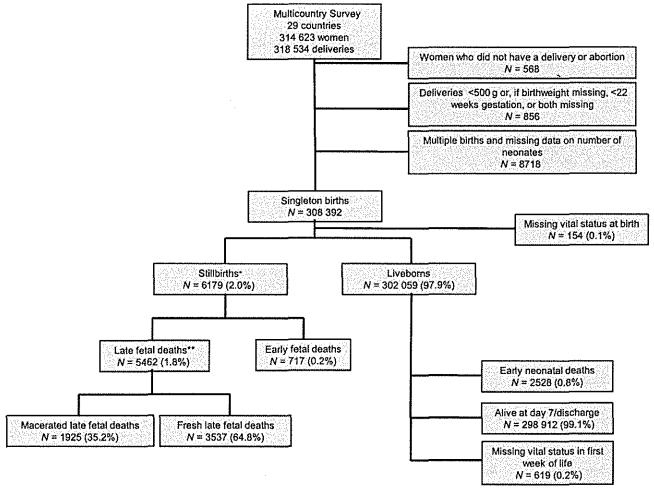

Figure 1. Study flow chart.

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.

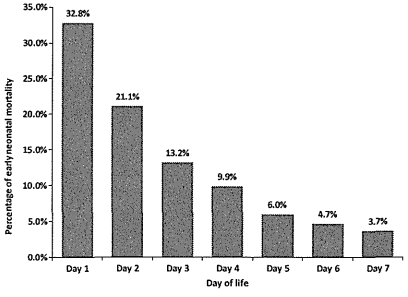

Figure 2. Distribution of early neonatal mortality by day of life.
*Missing information on the date of birth/death for the remaining 8.6% of early neonatal deaths.

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.

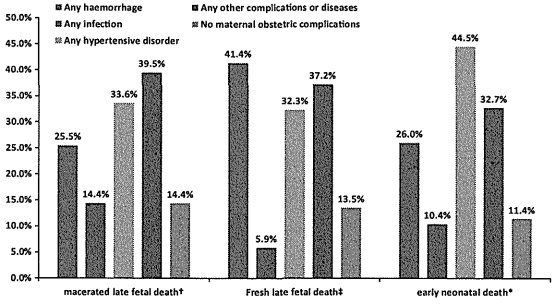

Figure 3. Prevalence of maternal complications in macerated and fresh late fetal deaths and early neonatal deaths. †Macerated late fetal deaths, defined as late fetal death (birthweight ≥ 1000 g or, if birthweight unknown, at ≥28 weeks of gestation) with signs of maceration. ‡Fresh late fetal deaths, 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

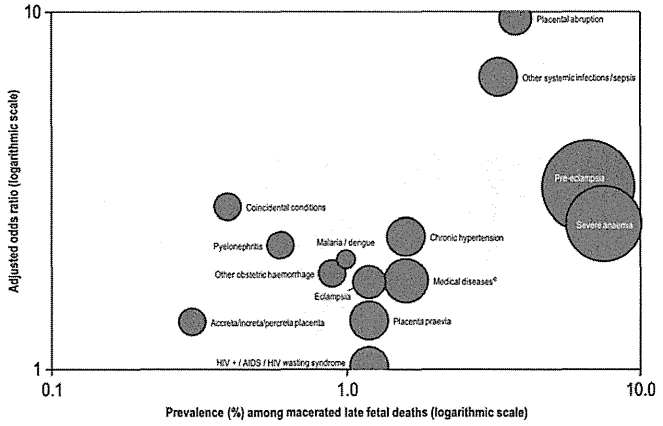

Figure 4. Prevalence and adjusted odds ratios of macerated late fetal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism,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

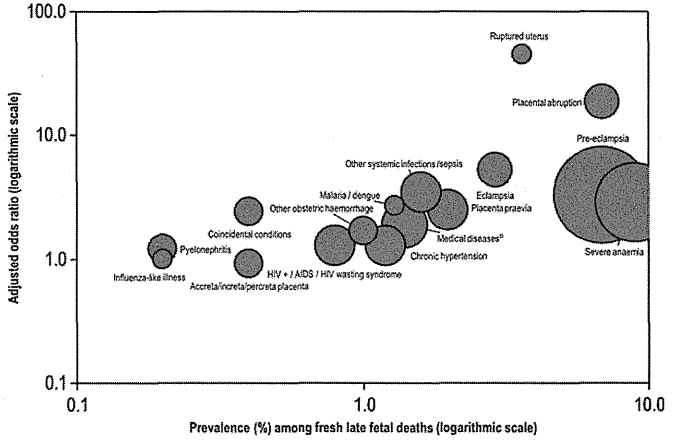

Figure 5. Prevalence and adjusted odds ratios of fresh late fetal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism,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