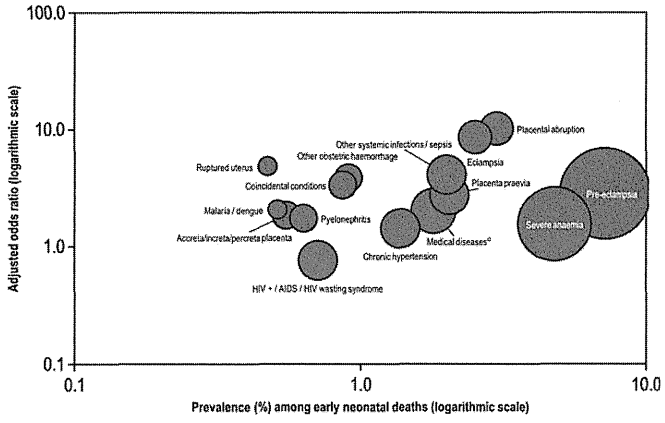

Figure 6. Prevalence and adjusted odds ratios of early neonatal deaths in maternal complications. The area of each bubble is proportional to the prevalence of these complications among all women; 95% confidence intervals are not displayed. Medical diseases: any one or more of embolic disease (thromboembolism,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

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

Interpretation

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

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

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

Conclusion

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

Disclosure of interests

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

Contribution to authorship

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

Details of ethics approval

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

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Supporting Information

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

Appendix S1. Key definitions.

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

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

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

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

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Original article

Development of criteria for identifying neonatal near-miss cases: analysis of two WHO multicountry cross-sectional studies

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Objective To develop and test markers of neonatal severe morbidity for the identification of neonatal near-miss cases.

Design This is a database analysis of two World Health Organization cross-sectional studies: the Global Survey on Maternal and Perinatal Health (WHOGS) and the Multicountry Survey on Maternal and Newborn Health (WHOMCS).

Setting The WHOGS was performed in 373 health facilities in 24 countries (2004–2008). The WHOMCS was conducted in 359 health facilities in 29 countries (2010–2011).

Population Data were collected from hospital records of all women admitted for delivery and their respective neonates.

Methods Pragmatic markers (birthweight <1750 g, Apgar score at 5 minutes <7, and gestational age <33 weeks) were developed with WHOGS data and validated with WHOMCS data. The diagnostic accuracy of neonatal characteristics and management markers of severity was determined in the WHOMCS.

Results This analysis included 290 610 liveborn neonates from WHOGS and 310 436 liveborn neonates from WHOMCS. The diagnostic accuracy of pragmatic and management markers of severity for identifying early neonatal deaths was very high: sensitivity, 92.8% (95% CI 91.8–93.7%); specificity, 92.7% (95% CI 92.6–92.8%); positive likelihood ratio, 12.7 (95% CI 12.5–12.9); negative likelihood ratio, 0.08 (95% CI 0.07–0.09); diagnostic odds ratio, 163.4 (95% CI 141.6–188.4). A positive association was found between the frequency of neonatal near-miss cases and Human Development Index.

Conclusion Newborn infants presenting selected markers of severity and surviving the first neonatal week could be considered as neonatal near-miss cases. This definition and criteria may be seen as a basis for future applications of the near-miss concept in neonatal health. These tools can be used to inform policy makers on how best to apply scarce resources for improving the quality of care and reducing neonatal mortality.

Keywords Early neonatal death, neonatal morbidity assessment, neonatal near-miss criteria, perinatal care assessment, quality of care.

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Introduction

The near-miss concept is being increasingly used as a tool to evaluate and improve the quality of care, especially for maternal health, where it has been used in clinical audits and epidemiological surveillance, similar to maternal deaths.[1] It has been hypothesised that this concept could also be useful in the neonatal context, to accelerate progress towards achieving Millennium Development Goals four and five by facilitating the assessment of quality of perinatal care.[2] Nevertheless, until now, there is no standard definition or internationally agreed identification criteria for neonatal near-miss cases. The term neonatal near miss has been used inconsistently, and also to describe survivors of rare conditions.[3–6] Similarly to the maternal near-miss concept, a neonatal near-miss case would refer to 'an infant who nearly died but survived a severe complication that occurred during pregnancy, birth or within 7 days of extra-uterine life'.[7]

This is a new concept being proposed for addressing issues on quality of perinatal care, and should be differentiated from other already established entities such as apparent life-threatening events and survivors of sudden infant death syndrome.[6,8,9] The absence of standard identification criteria for near-miss cases makes it very difficult to establish the relationship between near-miss cases and neonatal deaths. This is a necessary step for quality of care assessments based on the near-miss concept.

The development of a standard benchmark for evaluating the quality of perinatal care would allow comparisons between different settings, regardless of the local development level and across time.[10] In this context, the development of tools able to contribute to the improvement of quality of perinatal care and the reduction of adverse neonatal outcomes is a priority for global health research.[11] The main purpose of this study is to explore traditional predictors of early neonatal mortality as criteria to identify neonatal near-miss cases among high-risk babies.

Therefore, we: (1) assessed the accuracy of the selected combination of criteria to predict early neonatal deaths; (2) developed and validated a set of pragmatic neonatal near-miss criteria; and (3) explored the relationship of these indicators with the Human Development Index (HDI).[2]

Methods

Study design and data collection

This article reports on the analysis of two large WHO data sets, the Global Survey on Maternal and Perinatal Health (WHOGS, a cross-sectional study carried out in 373 health facilities from 24 countries in Africa, Asia, and Latin America) and the Multicountry Survey on Maternal and Newborn Health (WHOMCS, a cross-sectional study carried out in 359 health facilities from 29 countries in Africa, Asia, Latin America, and the Middle East). The methodological details of both studies have been published elsewhere.[12–15] Briefly, in both surveys trained health professional staff retrieved data from the hospital records of women and newborns, including individual data on demographics and reproductive characteristics, medical conditions during pregnancy, birth outcomes, complications, and the health interventions deployed during the hospital stay, until 7 days after birth or hospital discharge. Using a different approach from WHOGS, the WHOMCS collected specific data on the management of severe neonatal morbidity. In addition, data on the capacity of the health facilities were obtained in both surveys, including laboratory tests, infrastructure, and the capacity of obstetrics and neonatal healthcare services. The data collection for WHOGS took place between 2004 and 2008, for 2–3 months per facility, and data were collected from May 2010 to December 2011 for WHOMCS, for 2–4 months in each facility. A multistage cluster sampling method was used to select countries, provinces, and health facilities to participate in the WHOGS; this network of health facilities was adjusted with a similar strategy, and for convenience, in the WHOMCS. Both studies were ethically approved by the WHO and by the relevant authorities and institutional review boards in all of the participating countries. Box S1 shows the operational definitions used in this analysis. Table S1 shows the tabulation of participating countries per HDI and number of liveborn neonates per participant country. Table S2 presents the number of neonatal near-miss cases, early neonatal deaths, severe neonatal outcomes, and case-fatality ratios, stratified by country.

Methodological considerations about the 'near-miss' concept

A fundamental aspect of the near-miss concept is the similarity between deaths and near-miss cases. Thus, near-miss cases should be as similar as possible to deaths. The ideal near-miss case would mirror a death, the only difference being that the infant is alive at the point of assessment of the vital status. The development of criteria to identify near-miss cases is challenged by the absence of a gold standard for near-miss cases. In addition, survival must be established first in order to attribute the near-miss status, which makes the identification of near-miss cases always retrospective. Taking a step back in the continuum of severity, and considering case identification criteria as a diagnostic test, a specific set of criteria able to identify only very severe cases would have true-positive cases as those resulting in death. Consequently, in a specific set of criteria (able to identify only very severe cases), false-positive cases could be considered as near-miss cases (i.e. those that narrowly survived). True-positive cases (deaths) would be similar to false-positive cases (near-miss cases), except for the vital status. This approach has been used in the development and validation of identification criteria for maternal near-miss cases.[10]

Study population and analysis

For this analysis, we used data of liveborn infants with known vital status at birth and at 7 days of life/hospital

discharge. This analysis was carried out in two steps: first, pragmatic markers of severe neonatal morbidity were developed using the WHOGS data set; second, a full set of criteria combining the previously developed pragmatic markers with management markers of severe neonatal morbidity was developed.

Pragmatic markers of severe neonatal morbidity

Prematurity and birth asphyxia are complications that are well known as major causes of neonatal deaths.[16] Using the WHOGS data set, we studied three conditions associated with prematurity and birth asphyxia: low Apgar score at 5 minutes of life (<7); low birthweight (<1750 g); and low gestational age (<33 weeks). The cut-offs for each condition were selected based on the diagnostic accuracy (DA) profile and on heterogeneity in the prediction of early neonatal death. These three variables were considered candidate predictors of intrahospital early neonatal mortality: neonatal death occurring within the first week of life. In each hospital, information from the best available method for estimating gestational age was used. Records with missing data on vital status at birth or on any of the exposure or outcome variables were excluded. Extreme outliers in terms of birthweight or gestational age were also excluded. These outliers are considered to most likely result from misreporting, and have been identified considering weight by gestational age curves. As the intention was to exclude only the extreme outliers, we used the intrauterine growth curve developed by Hadlock, Harrist, and Martinez-Poyer as the reference for determining the upper limit (percentile 99.99) and the WHOGS customised intrauterine growth curve for India for determining the lower limit (percentile 0.01).[17,18] The first curve was used to set the upper limit because it presents high weights by gestational age, even higher in comparison with those observed among the WHOGS country-customised curves. The WHOGS Indian customised curve was selected because it provides the lowest weights by gestational age among the WHOGS country-customised curves. We determined the relationship between early neonatal mortality and Apgar score. Similarly, the relationship between early neonatal mortality and birthweight and gestational age has been determined. Next, considering the mortality risk for each category of Apgar score, birthweight, and gestational age, we identified those categories with similar mortality risks (i.e. a certain Apgar score, gestational age, or birthweight). Then, these categories were grouped together and formed 'sets of conditions'. The stratum with the lowest mortality rate was used as the reference group. In order to promote some homogeneity in terms of death risk among the possible identification criteria, we searched for sets of cut-off points in each variable that could produce similar death risks. These sets of possible identification criteria were used to assess the predictive value as diagnostic tests in the identification of early neonatal deaths. In addition, a set of criteria used in a previous analysis of WHOGS was tested for comparison.[7] We evaluated the DA of each set of conditions in identifying neonatal near-miss cases by calculating sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and prevalence of near-miss cases identified by the proposed set of criteria. We used the I^2 test to assess the heterogeneity between the relative risks within the selected sets of criteria. In addition, we calculated the prevalence of the identified neonatal near-miss cases added to early neonatal deaths. We also determined the mortality rate among liveborn infants. Finally, an ideal set of criteria to identify neonatal near-miss cases should be simple and pragmatic, being as similar as possible to neonatal deaths, and homogeneous in terms of the severity of individual criteria. Considering all of this, we selected a set of criteria from the WHOGS that would be more appropriate to contribute to the development of a definition of neonatal near miss. The selected set of criteria was then tested in the WHOMCS data set.

Pragmatic and management markers of neonatal severity

Information about management markers of severity, based on life-saving interventions used in South African studies, were explored to assess the applicability of the near-miss concept in neonatal health in the WHOMCS.[4,19,20] The neonatal life-saving interventions surveyed were: use of therapeutic intravenous antibiotics; nasal continuous positive airway pressure (nasal CPAP); any intubation (anytime within the first week); use of phototherapy within the first 24 hours; need of cardiopulmonary resuscitation; use of any vasoactive drug; use of anticonvulsants; surfactant administration; use of any blood products; use of steroids to treat refractory hypoglycaemia; and any surgery during early neonatal life. We used the WHOMCS data set to test the previously developed pragmatic markers of neonatal severity, and to test the use of the set of management markers of severity adapted from South African studies.[4,19,20] We classed the frequency of pragmatic and management markers of neonatal morbidity in three groups: overall; among survivors (neonatal near-miss cases); and among infants that died in the first week after childbirth. We also determined the mortality associated with each severity marker. The accuracy of pragmatic markers of severity, management markers of severity, and of combined pragmatic and management markers of severity was estimated through sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, and diagnostic odds ratios.

Indicators

Based on the maternal near-miss indicators developed by WHO, we modified and adapted them to the neonatal context.[21] We determined the number of early neonatal deaths per 1000 live births, the number of neonatal near-miss cases per 1000 live births, and the number of infants with severe neonatal outcomes (i.e. neonatal near misses plus early neonatal deaths). We also determined the case/fatality ratio (calculated as the ratio between neonatal near-miss cases and each neonatal death), together with the mortality index (calculated as the number of early neonatal deaths divided by the number of infants with severe neonatal outcomes). We stratified the countries according to the level of HDI estimated in 2012 by the United Nations Development Programme (very high, high, moderate, and low), and calculated the previously mentioned indicators by HDI country strata.

This analysis was conducted using STATA 11.2 (Statistics/Data Analysis; Statacorp LP, College Station, TX, USA, 1985–2009), EPI-INFO 3.5.3 statistical package (Centers for Disease Control and Prevention, Atlanta, GA, USA), Microsoft EXCEL 2007 and REVIEW MANAGER 5.0 Review Manager (RevMan) (Nordic Cochrane Centre, Copenhagen).

Results

From the WHOGS, a total of 277 706 liveborn infants were included in this analysis (2042 early neonatal deaths and 275 664 infants alive at hospital discharge or on the seventh day of life). From the WHOMCS, a total of 309 644 liveborn infants were included in this analysis (2850 early neonatal deaths and 306 794 infants alive at hospital discharge or on the seventh day of life). The summary analysis flow is illustrated in Figure 1. Several combinations of pragmatic markers of neonatal severity were developed and tested using the WHOGS data set. Table 1 presents the DA of three sets of pragmatic markers of neonatal severity selected to illustrate the relationship between these markers and the prediction of early neonatal deaths. Table S3 and Figure 2 present the relationship between early neonatal mortality and stratified categories of birthweight, gestational age, and Apgar score at 5 minutes. Considering the accuracy, prevalence, mortality, and heterogeneity, set 1 of the severity markers (i.e. Apgar score at 5 minutes less than <7, birthweight <1750 g, and gestational age <33 weeks) was selected to integrate the proposed neonatal near-miss definition.

Based on the WHOMCS data set, Table 2 presents the accuracy profile of pragmatic markers of severity, management markers of severity, and the combined set (pragmatic or management markers of severity). The pragmatic set showed a similar accuracy profile in the WHOMCS as compared with the accuracy profile observed in the WHOGS data set. Combining pragmatic and management markers of severity resulted in improved accuracy over the pragmatic markers alone for the prediction of early neonatal deaths, as shown in Table S4 (Diagnostic accuracy of selected markers of severity in the prediction of early neonatal deaths among all liveborn infants). The frequencies of individual pragmatic and management markers of severity (stratified by survival status, near-miss cases, and early neonatal deaths) are presented in Table 3, together with the mortality rates associated with each severity marker. The presence of any pragmatic or management marker identified 72.5/1000 among liveborn infants with a mortality rate within this group of 10.5%. Any intubation during the first week of life and need of cardiopulmonary resuscitation or use of vasoactive drug were associated with high mortality rates. Table 4 presents the number of liveborn infants, early neonatal deaths, neonatal near-miss cases, infants with severe neonatal outcomes, and the case/fatality ratio or mortality index (with relevant health indicators) according to HDI level. The case/fatality ratios decrease as the HDI decreases.

Discussion

This analysis studied various combinations of markers of neonatal morbidity for the identification of neonatal near-miss cases. The combined use of pragmatic and management markers of severity showed a very good performance as predictors of early neonatal deaths. Considering the methodological aspects of the development of near-miss definitions, the survivors of life-threatening conditions presented characteristics warranting the status of appropriate proxies of early neonatal deaths, and could be labelled as neonatal near-miss cases. Indicators derived from this analysis illustrated the strong connection between quality of care (evaluated by early neonatal mortality index and the case/fatality ratio) and the development of the country (measured by the 2012 HDI).[22]

A number of scoring systems have been developed to assess prognosis, quality of care, and to allow comparisons between health care services; however, most of these scoring systems may not be routinely applicable in developing or under-resourced settings.[7,23–27] The main constraint to the application of these systems is the need for more detailed and complex information, often requiring laboratory facilities. In this context, an accurate, pragmatic, and easily applicable indicator for assessing the quality of maternal, perinatal, and neonatal care, to be applied in health facilities and health systems, could be useful.[21] We believe that the use of the near-miss approach in neonatal health is a step forward in the direction of an innovative tool to improve the quality of antenatal, intrapartum, and postnatal care.

The WHOGS and WHOMCS produced large maternal and perinatal health databases, with information obtained from several countries around the world. One of the strengths of this analysis is the fact that the pragmatic

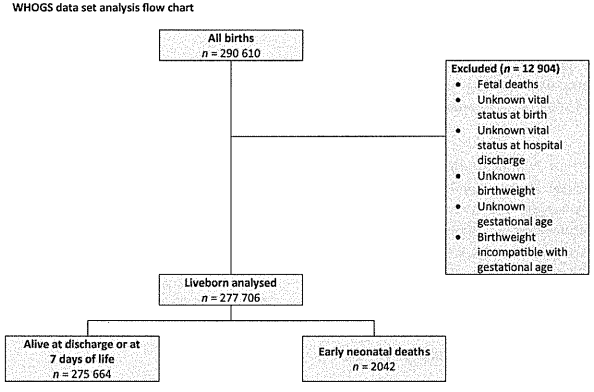

Figure 1. The analysis flow.

markers of severity were identified in the WHOGS database and then tested in an independent population using data from the WHOMCS. Some limitations should be acknowledged, however. These studies are facility-based, and may not be representative of a proportion of pregnant women and babies from areas where the coverage of institutional births is low; in addition, this data set might be biased towards larger and more equipped facilities, which may over-represent more complicated deliveries, and the collected sample may not represent the overall population at the country level. A second limitation is the source of data within health facilities, i.e. routine hospital records, which can lead to missing or misrecorded data. Another limitation is the relative paucity of data related to neonatal characteristics and care in the WHOGS database, mostly because the primary research questions of these studies were generally related to maternal health. The Apgar score at 5 minutes of life, gestational age, and birthweight were among the few neonatal characteristics available for analysis in the WHOGS study database; however, the WHOMCS study collected data on an expanded set of neonatal variables related to the management of complications that allowed the development of a more comprehensive and robust set of markers of severity. It is important to note that data on gestational age were obtained from medical records and reflected at each setting the best available method for gestational age estimation (i.e. in many settings this could be only the fundal height or weight at birth, if other methods such as ultrasound or reliable maternal information were not available).

Management markers of severity are essentially composed of life-saving interventions (e.g. surfactant, intubation, etc.). In some settings, these life-saving interventions may not be available, and the omissions of such life-saving interventions are likely to contribute to increased mortality. This should not compromise the applicability of the proposed definition in settings where some of the management markers are not available, because the performance of the health service can be assessed by the ratio between survivors and non-survivors (case/fatality ratio). In settings with poor quality of care, there are fewer survivors per neonatal death, and the case/fatality ratio can complement the information provided by early neonatal mortality. In settings where lower neonatal mortality rates are observed or in individual health facilities (where the number of neonatal deaths may provide insufficient information), reviewing near-miss cases as part of a clinical audit can function as a complementary source of information for understanding the performance of health services and identifying issues related to quality of care.

Only intrahospital early neonatal mortality was assessed in this analysis. Thus, the observed survival, particularly for infants at very early gestational ages, and among those born with very low birthweight, may not reflect the survival at the end of the full neonatal period. It is relevant to consider that the development of the near-miss concept is centred in neonates surviving severe perinatal and neonatal conditions, and this analysis assessed outcomes within the first postpartum week. The use of the near-miss concept in neonatal health might also be important to predict later developmental problems related to the life-threatening conditions to which these neonates were exposed. More research should be fostered to understand the impact of these neonatal life-threatening conditions in long-term survival and disabilities.

Table 1. Diagnostic accuracy profiles for prediction of early neonatal death and other characteristics of selected sets of pragmatic markers of neonatal morbidity (n = 277 706)*

	Set 1 Apgar <7 or Birthweight <1750 g or Gestational age <33 weeks	Set 2 Apgar <5 or Birthweight <1500 g or Gestational age <31 weeks	Set 3 Apgar <7 or Birthweight <1500 g or Gestational age <30 weeks
Sensitivity	79.1% (77.3–80.8)	62.0% (59.9–64.1)	72.6% (70.6–74.5)
Specificity	96.5% (96.4–96.5)	98.7% (98.6–98.7)	97.4% (97.4–97.5)
Positive likelihood ratio	22.3 (21.7–23.0)	46.9 (44.7–49.1)	28.3 (27.7–29.4)
Negative likelihood ratio	0.22 (0.20–0.24)	0.39 (0.36–0.41)	0.28 (0.26–0.30)
Diagnostic odds ratio (95% CI)	103.1 (92.5–114.9)	121.7 (110.6–133.8)	100.7 (91.1–111.3)
Prevalence	3.5%	1.3%	2.5%
Mortality	14.2%	25.8%	17.3%
Heterogeneity**	0%	18%	98%

*Calculated using the data set of the WHO Global Survey on Maternal and Perinatal Health (2004–2008).
**Statistical heterogeneity between severity markers, assessed by the I^2 test.

As learned from the maternal near-miss experience, audit processes of near-miss cases contribute to highlight specific issues and help to prioritise the implementation of effective interventions for improving maternal health care.[14] We believe that the assessment of medical records of neonatal near-miss cases in addition to neonatal death cases would function similarly to maternal near-miss audit processes, and would facilitate the selection and performance evaluation of interventions for improving perinatal health.

Lastly, the neonatal near-miss approach represents a simple and easily applicable tool for the quality assessment of perinatal health care, independently of the development level where the health institution is located. The calculation of proposed neonatal near-miss indicators enables an objective analysis of the performance of a health facility. Another advantage of this approach is to allow comparison of the performance of health facilities at different points in time and within the same country. Comparison of perinatal health services between countries with different development levels might be of use to assess the effectiveness of complex interventions, which might require the evaluation of softer outcomes instead of neonatal mortality.

Conclusion

Newborn infants presenting selected markers of severity and surviving the first neonatal week could be considered as neonatal near-miss cases. This definition and criteria may be seen as a basis for future applications of the near-miss concept in neonatal health. The neonatal near-miss concept represents an additional tool to complement the assessment of burden and quality of perinatal care. These tools can be used to inform policy makers on how best to

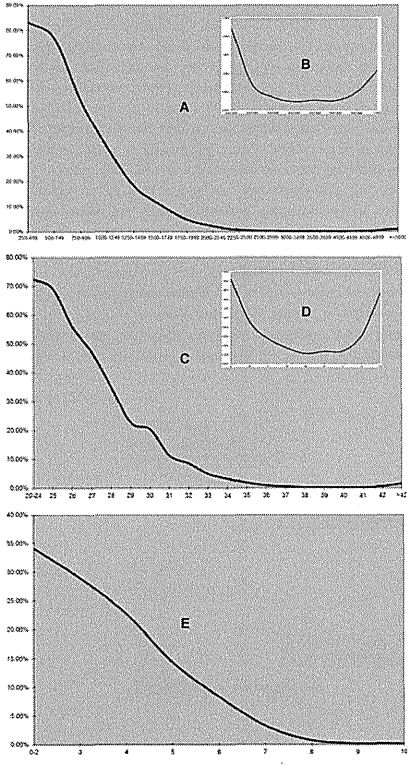

Figure 2. (A) Early neonatal mortality rates (ENM, %) by birth weight (in grams). (B) Detail on ENM from 2000 g to 5000 g. (C) ENM (%) by complete gestational week. (D) Detail on ENM from 35 to 42 complete weeks. (E) ENM (%) by Apgar score at 5 minutes of extra-uterine life.

apply scarce resources for improving the quality of care and reducing neonatal mortality.

Disclosure of interests

The authors declare no competing interests.

Contribution to authorship

CP and JPS designed the analysis. CP performed the analysis and drafted the article. All authors contributed to and approved the final version of the article.

Table 2. Diagnostic accuracy profiles of severity markers for early neonatal death among liveborn infants (n = 309 644)*

		Early neonatal death	
		+	–
Pragmatic set (any pragmatic marker of severity) (Set 1: Apgar< 7 or birthweight <1750 g or gestational age <33 weeks)	+	2208	11 587
	–	642	295 207
Sensitivity (95% CI)		77.5% (75.9–79.0%)	
Specificity (95% CI)		96.2% (96.2–96.3%)	
Positive likelihood ratio (95% CI)		20.5 (20.0–21.1)	
Negative likelihood ratio (95% CI)		0.23 (0.22–0.25)	
Diagnostic odds ratio (95% CI)		87.6 (80.1–95.9)	
Management set (any management marker of severity)	+	2252	16 421
	–	598	290 373
Sensitivity (95% CI)		79.0% (77.5–80.0%)	
Specificity (95% CI)		94.7% (94.6–94.7%)	
Positive likelihood ratio (95% CI)		14.8 (14.4–15.1)	
Negative likelihood ratio (95% CI)		0.22 (0.21–0.24)	
Diagnostic odds ratio (95% CI)		66.6 (60.8–73.0)	
Combined set (any pragmatic or management marker of severity)	+	2645	22 458
	–	205	284 336
Sensitivity (95% CI)		92.8% (91.8–93.7%)	
Specificity (95% CI)		92.7% (92.6–92.8%)	
Positive likelihood ratio (95% CI)		12.7 (12.5–12.9)	
Negative likelihood ratio (95% CI)		0.08 (0.07–0.09)	
Diagnostic odds ratio (95% CI)		163.4 (141.6–188.4)	

*Calculated using the data set of the WHO Multicountry Survey on Maternal and Newborn Health (2010–2011).

Details of ethics approval

The WHOGS (protocol ID, A25176; date of approval, 25 April 2003) and WHOMCS (protocol ID, A65661; date of approval, 27 October 2009) were conducted following ethical clearance from the Scientific and Ethical Review Group of the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Geneva, Switzerland. Both studies were independently reviewed by the relevant review board(s) of each country.

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Table 3. Frequency of severity markers among liveborn infants (n = 309 644)*

	Severe neonatal outcomes** n (‰)	Neonatal near-miss cases n (‰)	Early neonatal deaths n (‰)	Mortality rate %
Pragmatic set (any pragmatic marker of severity)				
Apgar score at 5 minutes <7	8033 (25.9)	6745 (21.8)	1288 (4.2)	16.0
Birthweight <1750 g	6099 (19.7)	4456 (14.4)	1643 (5.3)	26.9
Gestational age <33 weeks	4438 (14.3)	3424 (11.1)	1014 (3.3)	22.8
Any pragmatic marker of severity	13 795 (44.6)	11 587 (37.4)	2208 (7.1)	16.0
Management set (any management marker of severity)				
Use of therapeutic intravenous antibiotics	13 496 (43.6)	11 952 (38.6)	1544 (5.0)	11.4
Nasal CPAP	4772 (15.4)	3874 (12.5)	898 (2.9)	18.8
Any intubation (anytime within the first week)	3970 (12.8)	2811 (9.1)	1159 (3.7)	29.2
Use of phototherapy in the first 24 hours	3434 (11.1)	3222 (10.4)	212 (0.7)	6.2
Cardiopulmonary resuscitation	2961 (9.6)	1598 (5.2)	1363 (4.4)	46.0
Use of any vasoactive drug	1890 (6.1)	1176 (3.8)	714 (2.3)	37.8
Use of anticonvulsants	1441 (4.7)	1166 (3.8)	275 (0.9)	19.1
Surfactant administration	1366 (4.4)	1075 (3.5)	291 (0.9)	21.3
Use of any blood products	980 (3.2)	802 (2.6)	178 (0.6)	18.2
Use of steroids to treat refractory hypoglycaemia	895 (2.9)	736 (2.4)	159 (0.5)	17.8
Any surgery	247 (0.8)	216 (0.7)	31 (0.1)	12.6
Any management-based marker of severity	18 673 (60.3)	16 421 (53.0)	2252 (7.3)	12.1
Combined set (any pragmatic or management marker of severity)	25 103 (81.1)	22 458 (72.5)	2645 (8.5)	10.5

*Calculated using the data set of the WHO Multicountry Survey on Maternal and Newborn Health (2010–2011).
**Calculated by the sum of neonatal near-miss cases and early neonatal deaths.

Table 4. Number of liveborn infants, early neonatal deaths, neonatal near-miss cases, infants with severe neonatal outcomes, and case/fatality ratio (with relevant health indicators: ratios per 1000 live births in brackets) according to the HDI of the country, with data from WHOMCS (n = 309 644)

	Overall	Countries with very high HDI	Countries with high HDI	Countries with medium HDI	Countries with low HDI
Number of liveborn infants	309 644	30 397	67 247	88 979	119 388
Number of early neonatal deaths (per 1000 live births)	2850 (9.2)	79 (2.6)	390 (5.8)	882 (9.9)	1334 (11.2)
Number of neonatal near-miss cases* (per 1000 live births)	22 458 (72.5)	1187 (39.0)	5096 (75.8)	7345 (82.5)	7880 (66)
Number of infants with severe neonatal outcomes** ;(per 1000 live births)	25 308 (81.7)	1266 (41.6)	5486 (81.6)	8227 (92.5)	9214 (77.2)
Case/fatality ratio (mortality index***)	8:1 (11.3%)	15:1 (6.2%)	13:1 (7.1%)	8:1 (10.7%)	6:1 (14.5%)

Missing data with tabulation of HDI and early neonatal death: 3633.
*Calculated based on the presence of any pragmatic or management marker of morbidity or the occurrence of an early neonatal death.
**Severe neonatal outcome: early neonatal deaths plus neonatal near-miss cases.
***Mortality index: number of early neonatal deaths divided by the total number of severe neonatal outcomes.

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Supporting Information

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

Box S1. Operational definitions.

Table S1. Countries participating in the WHOGS and WHOMCS, stratified by HDI, with the total number of live births and respective percentages.

Table S2. Neonatal near-miss cases, early neonatal death, severe neonatal outcome, and case/fatality ratio, by country.

Table S3. Relationship between Apgar score at 5 minutes, birthweight, and gestational age with early neonatal mortality (n = 277 706).

Table S4. Diagnostic accuracy of selected markers of severity in the prediction of early neonatal deaths among all liveborn infants (n = 309 644). ■

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Original article

Pregnancy and childbirth outcomes among adolescent mothers: a World Health Organization multicountry study

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Objective To investigate the risk of adverse pregnancy outcomes among adolescents in 29 countries.

Design Secondary analysis using facility-based cross-sectional data of the World Health Organization Multicountry Survey on Maternal and Newborn Health.

Setting Twenty-nine countries in Africa, Latin America, Asia and the Middle East.

Population Women admitted for delivery in 359 health facilities during 2–4 months between 2010 and 2011.

Methods Multilevel logistic regression models were used to estimate the association between young maternal age and adverse pregnancy outcomes.

Main outcome measures Risk of adverse pregnancy outcomes among adolescent mothers.

Results A total of 124 446 mothers aged ≤24 years and their infants were analysed. Compared with mothers aged 20–24 years, adolescent mothers aged 10–19 years had higher risks of eclampsia, puerperal endometritis, systemic infections, low birthweight, preterm delivery and severe neonatal conditions. The increased risk of intra-hospital early neonatal death among infants born to adolescent mothers was reduced and statistically insignificant after adjustment for gestational age and birthweight, in addition to maternal characteristics, mode of delivery and congenital malformation. The coverage of prophylactic uterotonics, prophylactic antibiotics for caesarean section and antenatal corticosteroids for preterm delivery at 26–34 weeks was significantly lower among adolescent mothers.

Conclusions Adolescent pregnancy was associated with higher risks of adverse pregnancy outcomes. Pregnancy prevention strategies and the improvement of healthcare interventions are crucial to reduce adverse pregnancy outcomes among adolescent women in low- and middle-income countries.

Keywords Adolescent pregnancy, adverse pregnancy outcomes, low birthweight, perinatal mortality, preterm birth.

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Introduction

Adolescent pregnancy is defined as pregnancy in girls aged 10–19 years. It is estimated that about 11% of births worldwide are to adolescents aged 15–19 years, and more than 90% of these births occur in low- and middle-income countries.[1] Giving birth during adolescence is not only a risk factor for adverse pregnancy outcomes, but also has a negative impact on the future well-being of the mother and infant.[2,3] Previous studies have reported an increased incidence of adverse maternal and perinatal outcomes, such as low birthweight,[4–7] preterm delivery,[4–7] perinatal death,[5,8] cephalo-pelvic disproportion[9,10] and maternal death.[6,11] However, there were conflicting findings from previous studies as to whether the adverse pregnancy outcomes among adolescent mothers were caused by their biological immaturity[4–6] or poor socio-environmental factors.[7,12,13] This may be explained by the heterogeneity between study settings, small sample size, especially for younger adolescents (i.e. ≤15 years), and the quality of medical services and women's social and cultural backgrounds. To evaluate pregnancy and childbirth outcomes among adolescent mothers, we used data from the World Health Organization (WHO) Multicountry Survey on Maternal and Newborn Health 2010–2011, which was conducted concurrently in 29 countries using a standard methodology. The aim of our study was to investigate whether adolescent mothers are at higher risk of adverse pregnancy outcomes compared with mothers aged 20–24 years after controlling for country and health facility effects and potential confounding factors.

Methods

Study design and data collection

The WHO Multicountry Survey on Maternal and Newborn Health was a multicountry, facility-based, cross-sectional study implemented from May 2010 to December 2011 across 29 countries in Africa, Asia, Latin America and the Middle East. A stratified multi-stage cluster sampling strategy was used to obtain samples from 359 health facilities from the capital city and two randomly selected provinces in each participating country. Methodological details of this survey have been published previously.[14,15] The study included all women who were admitted for delivery and with severe maternal outcomes (SMO) regardless of gestational age at the participating health facilities. Data were collected at individual and facility levels. At the individual level, data on demographic and reproductive characteristics, pregnancy and childbirth complications and their management, and maternal and newborn morbidity and mortality were collected before their discharge from hospital, or within 7 days after delivery, directly from medical records by trained medical staff. At the health facility level, data on the availability of obstetric and newborn services, laboratory tests and human resources were obtained.

Study population

The study population in this analysis was restricted to mothers aged 24 years or younger who gave birth to an infant of at least 22 weeks' gestation or with a birthweight of at least 500 g.

Exposure and potential confounding factors

The main exposure of interest in this study was the young maternal age, defined as mothers <20 years of age. Adolescents younger than 16 years have been shown to be at an increased risk of adverse pregnancy outcomes and were categorised separately from older adolescents (16–19 years).[5,6] It has also been suggested that girls who conceive shortly after menarche (<2 years after menarche, defined as low gynaecological age) are at an increased risk of adverse outcomes.[16] As menarche tends to start later in girls with poor nutritional and environmental conditions,[3] it was assumed that many adolescent mothers aged 16–17 years would have a low gynaecological age, and therefore it may not be appropriate to categorise them with older adolescents aged 18–19 years. Therefore, the maternal age was categorised into four groups: ≤15, 16–17, 18–19 and 20–24 years. The last group served as the reference group in all analyses. Categorisations of the demographic and reproductive characteristics used for adjustment corresponded to those shown in Table 1. Medical conditions during pregnancy and childbirth included severe anaemia, defined as haemoglobin (Hb) < 7 mg/dl, malaria or dengue, and others, such as the presence of any disease or injury affecting the heart, lungs, kidneys (except pyelonephritis) and liver. A coincidental condition describes an acute injury caused by external factors, such as violence, accident, poisoning or self-harm. The facility capacity index score was defined as the total score of essential and additional services provided by the selected health facilities. This index has been used in previous studies and is detailed elsewhere.[17]

Main outcomes and definitions

We assessed the following adverse maternal outcomes: caesarean section, pre-eclampsia, eclampsia, postpartum haemorrhage, puerperal endometritis, SMO and intra-hospital maternal death. Women with SMO were defined as maternal death or maternal near-miss cases; the latter describes women who presented with a life-threatening condition and nearly died, but survived pregnancy, childbirth or a pregnancy termination, and who were identified by clinical, laboratory and management markers.[18] Intra-hospital maternal deaths were defined as deaths that occurred on or before the eighth day postpartum.

We evaluated the following perinatal outcomes: low birthweight (live infant weighing <2500 g at birth), preterm delivery (live infant delivered at <37 weeks' gestation), stillbirths (macerated and fresh stillbirths), severe neonatal conditions (neonates presenting with any of the following conditions: birthweight <1500 g, gestational age <32 weeks and Apgar score at 5 minutes <7)[19] and early neonatal death. Intra-hospital deaths that occurred within 7 days after birth were classified as early neonatal deaths.

Table 1. Maternal characteristics and medical conditions by age group

	Total, *n* (%)	Maternal age, *n* (%)				
		≤15 years	16–17 years	18–19 years	20–24 years	*P*
No. of deliveries	124446 (100)	2206 (1.8)	9025 (7.3)	20948 (16.8)	92267 (74.1)	
Marital status						
Single	19728 (16.1)	1079 (49.3)	3524 (10.0)	5022 (24.4)	10103 (11.1)	<0.001
Education (years)						
None	16301 (14.1)	201 (9.7)	845 (9.9)	2490 (12.9)	12765 (14.9)	<0.001
1–6	18141 (15.7)	723 (34.9)	1952 (23.1)	3326 (17.2)	12140 (14.1)	
7–9	31251 (26.9)	1148 (55.4)	3431 (40.6)	5969 (30.9)	20703 (24.1)	
10–12	39861 (34.4)	–	2229 (26.4)	7087 (36.6)	30545 (35.5)	
>12	10216 (8.9)	–	–	473 (2.4)	9763 (11.4)	
Parity						
0	81928 (65.8)	2125 (96.3)	8262 (91.6)	16982 (81.1)	54559 (59.1)	<0.001
1	38877 (31.2)	69 (3.1)	732 (8.1)	3822 (18.2)	34254 (37.1)	
≥2	3641 (2.9)	12 (0.6)	31 (0.3)	144 (0.7)	3454 (3.7)	
Multiple birth	1487 (1.2)	13 (0.6)	69 (0.8)	205 (1.0)	1200 (1.3)	<0.001
Mode of delivery						
Vaginal	95351 (76.8)	1582 (71.9)	6941 (77.1)	16394 (78.4)	70434 (76.5)	<0.01
Caesarean section	28885 (23.2)	617 (28.1)	2067 (23.0)	4513 (21.6)	21688 (23.5)	
Previous caesarean section	7739 (18.2)	21 (25.9)	132 (17.3)	717 (18.1)	6869 (18.2)	0.295
Medical conditions						
Anaemia	1847 (1.5)	61 (2.8)	203 (2.2)	325 (1.6)	1258 (1.4)	<0.05
Malaria/dengue	163 (0.1)	8 (0.4)	23 (0.3)	30 (0.1)	102 (0.1)	<0.001
Other conditions*	546 (0.4)	12 (0.5)	46 (0.5)	102 (0.5)	386 (0.4)	0.597
Coincidental conditions**	350 (0.3)	23 (1.0)	62 (0.7)	85 (0.4)	181 (0.2)	<0.001

*Presence of any disease or injury affecting the heart, lungs, kidneys (except pneumonia and pyelonephritis) and liver.
**An acute injury caused by external factors, such as violence, accident, poisoning or self-harm.

We also assessed the coverage of health interventions by country group. Countries were stratified by country-level maternal mortality ratios (MMR), i.e. maternal deaths per 100 000 live births, into four groups: low (MMR < 20), moderate (MMR = 20–99), high (MMR = 100–299) and very high (MMR > 300) MMR countries.[20] Health intervention coverage was determined as the proportion of women who received essential interventions.

Statistical analysis

We performed the chi-squared test to assess the association between each of the maternal and neonatal characteristics and adolescent age, accounting for the clustering effect of the survey design, in which women were nested within facilities, and facilities within countries. We also undertook frequency comparisons between adolescent and adult mothers for demographic and reproductive characteristics, potentially life-threatening conditions per 1000 live births (i.e. maternal near-miss ratio, severe outcome ratio, intra-hospital maternal and neonatal mortality ratio) and intervention coverage.

To estimate the effect of young maternal age on pregnancy outcomes, we constructed multilevel logistic regression models with random effects for facilities and countries. The analysis was also adjusted for potential confounding factors, including maternal and health facility characteristics and country groups. The significance of the random effects was tested with a likelihood ratio test by comparing models nested within models with additional levels. Crude and adjusted odds ratios (AORs) with their 95% confidence intervals (CIs) were used to present the effects among mothers of <20 years of age compared with mothers aged 20–24 years. 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

The data of 314 623 women in total were collected from 359 health facilities in 29 countries by the WHO Multicountry Survey on Maternal and Newborn Health. We excluded deliveries with missing maternal age (935), missing birthweight and missing gestational age at birth (891) and pregnancies with an offspring birthweight of <500 g. If the birthweight was missing, we excluded pregnancies at <22 weeks of gestational age (500). This left a total of 312 297 deliveries retained in the analysis. Of these, a total of 32 179 (10.3%) deliveries occurred among adolescents aged 10–19 years, with a mean age of 17.7 years [standard deviation (SD), 1.3 years]. Figure 1 shows the number of adolescent births per 1000 deliveries in the participating countries of the WHO survey. Among the study population, the overall number of adolescent (i.e. ≤19 years) births was 103 per 1000 deliveries, and the highest occurrences of adolescent birth were in Nicaragua (288.2), Ecuador (233.8) and Angola (213.0), whereas the lowest were found in Japan (7.4), Qatar (19.4), India (29.3) and Vietnam (29.2). With further restrictions applied to mothers of ≤24 years of age, the sample size was 124 446, which consisted of 2206 (1.8%), 9025 (7.3%), 20 948 (16.8%) and 92 268 (74.1%) mothers aged ≤15, 16–17, 18–19 and 20–24 years, respectively.

Table 1 shows the maternal characteristics and medical conditions during pregnancy by age group. Compared with mothers aged 20–24 years, adolescents were more likely to be single, less educated and nulliparous. The proportion of mothers with severe anaemia (Hb < 7 mg/dl) and coincidental conditions was significantly higher among all adolescents, whereas malaria and dengue were higher among younger adolescents aged ≤17 years.

The prevalence of adverse pregnancy outcomes varied by country among adolescents versus adult mothers aged 20–24 years (Tables S1 and S2). Table 2 shows the overall prevalence of adverse pregnancy outcomes among adolescents in participating countries. Pre-eclampsia, eclampsia, puerperal endometritis and systematic infections were significantly higher among adolescents than among adult mothers, whereas caesarean section was higher among younger adolescent mothers (≤15 years) than among adult mothers (27.9% versus 23.5%, respectively). The number of SMO cases per 1000 deliveries was insignificantly higher among all adolescent mothers relative to adult mothers.

Among all mothers with SMO, the most frequent complications were eclampsia (75.0%, 47.8%, 41.1% and 33.8% among mothers aged ≤15, 16–17, 18–19 and 20–24 years, respectively; $P = 0.006$). The prevalence of other complications was varied among mothers with SMO.

For perinatal outcomes, a significant increase in the prevalence of preterm delivery and severe neonatal conditions with decreasing maternal age, compared with adult mothers aged 20–24 years, was observed. The increased prevalence of other perinatal outcomes was not significant and is presented in Table 2.

Table 3 shows the coverage of essential interventions among the study population. The total coverage of prophylactic antibiotics for caesarean section, parenteral antibiotics for systemic infections and therapeutic uterotonics was 86.2%, 77.9% and 93.1%, respectively, with no significant differences among maternal age groups. However, despite the higher coverage of prophylactic uterotonics, all adolescent mothers had significantly lower coverage than adult mothers aged 20–24 years (91.4%, 92.7% and 94.4% among mothers aged ≤15, 16–17 and 18–19 years, respectively, versus 95.4% for adult mothers). The coverage of antenatal corticosteroids for preterm births at 26–34 weeks was noticeably lower and the overall coverage was 48.1%, ranging from 28.4% to 52.3% across the maternal age groups, with significantly lower coverage among the youngest age group. Similar trends were observed for prophylactic uterotonics and antenatal corticosteroids for preterm births at 26–34 weeks among moderate to high MMR country groups, but not in the very high MMR country group (Table S3).

Table 4 presents the results of multilevel logistic models of adverse outcomes among adolescent mothers. After adjustment for country- and facility-level effects and covariates, AOR for caesarean sections among mothers aged <20 years was significantly lower than among mothers aged 20–24 years. Although adolescent mothers had a lower risk of pre-eclampsia, the risk of eclampsia was 1.85, 1.88 and 1.55

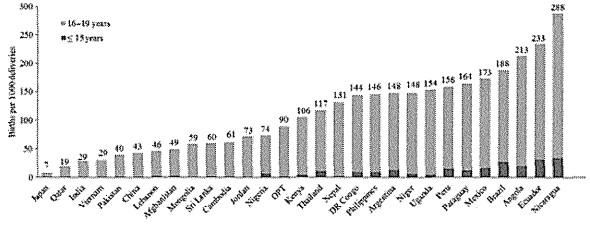

Figure 1. Number of adolescent births per 1000 deliveries in participating countries in the World Health Organization (WHO) 2010–2011 Multicountry Survey. DR Congo, Democratic Republic of Congo; OPT, Occupied Palestinian Territory.

Table 2. Prevalence of adverse pregnancy outcomes by maternal age

Outcome	Total, *n* (%)	Maternal age, *n* (%)				
		≤15 years	16–17 years	18–19 years	20–24 years	*P*
Number of deliveries	124446 (100)	2206 (1.8)	9025 (7.3)	20948 (16.8)	92267 (74.1)	
Maternal outcomes						
Caesarean section	28885 (23.2)	617 (27.9)	2067 (22.9)	4513 (21.5)	21688 (23.5)	0.004
Pre-eclampsia	2398 (1.9)	84 (3.8)	221 (2.5)	419 (2.0)	1674 (1.8)	<0.001
Eclampsia	547 (0.4)	23 (1.0)	81 (0.9)	139 (0.7)	304 (0.3)	<0.001
Postpartum haemorrhage	1438 (1.2)	18 (0.8)	127 (1.4)	232 (1.1)	1061 (1.2)	0.134
Puerperal endometritis	151 (0.1)	10 (0.5)	22 (0.2)	43 (0.2)	76 (0.1)	<0.001
Systemic infections*	503 (0.4)	14 (0.6)	69 (0.8)	111 (0.5)	309 (0.3)	<0.001
Severe maternal outcomes** (ratio)	582 (4.6)	12 (5.4)	46 (5.1)	107 (5.1)	417 (4.5)	0.648
Eclampsia	216 (37.1)	9 (75.0)	22 (47.8)	44 (41.1)	141 (33.8)	0.006
Haemorrhage	254 (43.6)	1 (8.3)	20 (43.5)	37 (34.6)	196 (47.0)	0.009
Systemic infections	66 (11.3)	NR	11 (23.9)	11 (10.3)	44 (10.6)	0.027
Others	83 (14.3)	3 (25.0)	7 (15.2)	11 (10.3)	62 (14.9)	0.444
Maternal severity score***	2.5 (±2.7)	1.5 (±0.9)	2.7 (±3.1)	2.1 (±2.3)	2.6 (±2.7)	0.530
Maternal severity index****	8.8% (±21.7)	0.1% (±0.2)	11.1% (±23.6)	5.7% (±18.3)	9.6% (±22.5)	0.455
Maternal near miss***** (ratio)	479 (3.8)	12 (5.4)	36 (4.0)	89 (4.2)	342 (3.7)	0.501
IHMM****** (ratio)	103 (0.8)	NR	10 (1.1)	18 (0.9)	75 (0.8)	0.554
Perinatal outcomes						
Low birthweight (<2500 g)	14594 (12.3)	308 (14.6)	1071 (12.4)	2441 (12.2)	10774 (12.3)	0.357
Preterm delivery (<37 weeks)	8610 (7.3)	235 (11.2)	743 (8.6)	1524 (7.7)	6108 (7.0)	<0.001
Neonatal severe conditions*******	2536 (2.1)	72 (3.6)	239 (2.7)	467 (2.3)	1758 (1.9)	<0.001
Stillbirths	2375 (1.9)	50 (2.3)	202 (2.2)	382 (1.8)	1741 (1.9)	0.108
IHENM********	1171 (1.0)	31 (1.4)	84 (1.0)	223 (1.1)	833 (0.9)	0.053

Numbers and rates are shown for severe maternal outcomes (SMO), maternal near miss (MNM) and intra-hospital maternal mortality (IHMM); for other entries, numbers and percentages are shown. NR, not reported.
*Systemic infections includes pneumonia, peritonitis and post-operative abdominal infections.
**SMO includes MNM and IHMM.
***The maternal severity score is calculated as the number of markers of organ dysfunction.
****The maternal severity index is defined as the probability of maternal death among women with severe maternal outcomes.
*****Maternal near miss is an event in which a woman survives a life-threatening complication during pregnancy, childbirth or termination of pregnancy.
******IHMM refers to the intra-hospital death of a liveborn baby during the first 8 days after delivery.
*******Neonatal severe conditions refer to a liveborn baby with one of the following conditions: birthweight < 1500 g, <32 gestational weeks at birth or a 5-minute Apgar score of <7.
********Intra-hospital early neonatal mortality (IHENM) refers to the death of a liveborn baby during the first 7 days after delivery.

times higher among adolescent mothers aged ≤15, 16–17 and 18–19 years, respectively, compared with adult mothers. Higher risks of puerperal endometritis and systemic infections were observed among all adolescent age groups, with no significant differences among mothers aged 16–17 years for puerperal endometritis and ≤15 years for systemic infections. The risk of SMO was not significant among adolescent mothers aged ≤15, 16–17 and 18–19 years: 1.13 (95% CI, 0.59–2.18), 1.03 (95% CI, 0.72–2.18) and 1.10 (95% CI, 0.86–1.41), respectively. Additional adjustment for medical conditions during pregnancy, e.g. chronic and acute diseases, severe anaemia, malaria and coincidental conditions and stratified analysis for parity, did not alter the risks of adverse maternal outcomes among adolescents (data not shown).

After adjusting for country- and facility-level effects and covariates, risks of preterm delivery (<37 weeks of gestational age), low birthweight infants (<2500 g) and severe neonatal conditions were significantly higher among all adolescent age groups, with the highest risk observed among the youngest age group (low birthweight: AOR = 1.17; 95% CI, 1.01–1.37; preterm delivery: AOR = 1.60; 95% CI, 1.37–1.87; severe neonatal conditions: AOR = 1.56; 95% CI, 1.20–1.70). A high risk of stillbirth was found among all adolescent age groups, but the risk was significant only among adolescent mothers aged 16–17 years (AOR = 1.32; 95% CI, 1.11–1.57). The risk of intra-hospital early neonatal mortality was significantly higher among all adolescent mothers compared with adult mothers (data not

Table 3. Intervention coverage by maternal age

Medical interventions	Total, *n* (%)	Maternal age, *n* (%)				*P*
		≤15 years	16–17 years	18–19 years	20–24 years	
Prophylactic uterotonic	117989 (95.0)	2011 (91.4)	8343 (92.7)	19727 (94.4)	87908 (95.4)	0.0007
Therapeutic uterotonic	1339 (93.1)	18 (100)	123 (96.9)	212 (91.4)	986 (92.9)	0.120
Prophylactic antibiotics for caesarean section	24907 (86.2)	534 (86.5)	1757 (85.0)	3847 (85.2)	18769 (86.5)	0.427
Parenteral antibiotic for systemic infections	392 (77.9)	10 (71.4)	53 (76.8)	86 (77.5)	243 (78.6)	0.919
Magnesium sulfate for eclampsia	493 (90.1)	19 (82.6)	78 (96.3)	128 (92.1)	268 (88.2)	0.077
Antenatal corticosteroids for preterm birth (26–34 weeks)	1655 (48.1)	27 (28.4)	117 (39.4)	236 (38.6)	1275 (52.3)	<0.001

Intervention coverage was determined as the proportion of women who received the essential intervention divided by all women who were eligible for that intervention.

shown). After further adjustment for birthweight and gestational age at birth, the risk decreased and became statistically insignificant. The results of adverse perinatal outcomes were not altered after additional adjustment for eclampsia (data not shown).

Discussion

Main findings

By using a large multicountry dataset, we have described the pregnancy outcomes among adolescent mothers in 29 countries. Controlling for country- and facility-level effects, and co-variates at the individual level, such as marital status, educational attainment, parity and multiple births, as well as for the capacity of the health facility and the maternal mortality rate by country, we found higher risks of eclampsia, puerperal endometritis and systemic infections and lower risks of caesarean section and pre-eclampsia among adolescent mothers compared with mothers aged 20–24 years. The risk of SMO was higher among adolescents than non-adolescent mothers; however, the differences were not significant. We observed higher risks of adverse perinatal outcomes with decreasing maternal age, but not for adverse maternal outcomes. Our results showed that adolescent pregnancy was independently associated with increased risks of low birthweight, preterm delivery and severe neonatal conditions, and an increased risk of intra-hospital early neonatal death was partially explained by the preterm delivery among infants born to adolescent mothers. Coverage of antenatal corticosteroids for preterm births at 26–34 weeks was significantly lower among adolescent mothers, despite the fact that they are at an increased risk of preterm delivery.

Strengths and limitations

To our knowledge, this is the most recent and largest multicountry study undertaken to assess pregnancy outcomes among adolescent mothers. There has been controversy regarding the association between young age and adverse pregnancy outcomes. Reasons for this could include the inconsistent definition of adolescents across the field, age-related reference groups, the small sample size and failure to adjust for known confounders. As our study included a large sample size, we categorised adolescent mothers into three age groups (≤15, 16–17 and 18–19 years), and obtained a sufficient number of adverse outcomes in each age group to estimate the risk of young maternal age. In our analysis, we selected mothers aged 20–24 years as the reference group, consistent with previous studies,[5,6,21] and have taken into account contextual factors, such as country and health facility, socio-demographic characteristics and medical conditions during pregnancy, to describe the biological effect on adverse outcomes.

This study has several limitations. First, the estimation of adverse risks could be biased as this study was implemented in large health facilities, mainly located in urban settings, which had the capacity to perform caesarean sections. An overestimation of risks may exist when high-risk adolescent mothers are referred to these facilities; however, the majority of low- and middle-income countries are known to have low institutional delivery rates and a higher proportion of adolescent pregnancies in rural areas. In addition, adolescent mothers are more likely to seek out smaller hospitals, or have deliveries outside of hospitals.[3] Therefore, an underestimation of adverse risks is more likely to exist, which may limit the generalisability of the results. Second, it is likely that residual confounding exists in our analyses. We attempted adjustment for the socio-demographic and reproductive factors available in this survey; however, we did not have any information on key risk factors for adverse outcomes, including antenatal care[13] and smoking,[22] which may dilute risk estimates, as adolescent mothers tend to have inadequate antenatal care and a higher smoking rate than adult mothers. We tried to

Table 4. Risks of adverse birth outcomes among adolescent mothers compared with mothers aged 20–24 years

Outcome	Maternal age at delivery								
	≤15 years			16–17 years			18–19 years		
	OR	AOR	95% CI	OR	AOR	95% CI	OR	AOR	95% CI
Adverse maternal outcomes									
Caesarean section delivery	1.26**	0.79	0.65–0.89***	0.97	0.69	0.65–0.73***	0.89**	0.77	0.74–0.80***
Pre-eclampsia	2.14***	0.92	0.69–1.22	1.35***	0.73	0.61–0.86***	1.10	0.81	0.71–0.92**
Eclampsia	3.18***	1.85	1.14–2.98*	2.74***	1.88	1.41–2.50***	2.02	1.55	1.25–1.95***
Postpartum haemorrhage	0.70	0.67	0.40–1.09	1.22	1.07	0.86–1.32	0.96	0.91	0.77–1.07
Puerperal endometritis	5.52***	2.73	1.29–5.78*	2.96***	1.35	0.79–2.31	2.49***	1.66	1.10–2.50*
Systemic infections	1.90**	1.22	0.71–1.17	2.29***	1.69	1.26–2.27***	1.58***	1.35	1.07–1.71*
Severe maternal outcomes****	1.20	1.13	0.59–2.18	1.12	1.03	0.72–2.18	1.13	1.10	0.86–1.41
Adverse perinatal outcomes									
Low birthweight(<2500 g)	1.21	1.17	1.01–1.37*	1.01	1.15	1.05–1.25**	0.99	1.10	1.04–1.17**
Preterm delivery (<37 weeks)	1.67***	1.60	1.37–1.87***	1.26***	1.34	1.23–1.47***	1.11*	1.18	1.11–1.27***
Neonatal severe conditions*****	1.75***	1.56	1.20–2.01**	1.41***	1.27	1.09–1.48**	1.17*	1.16	1.04–1.30**
IHENM******	1.57*	1.36	0.86–2.15	1.04	1.05	0.79–1.39	1.18	1.18	0.98–1.41
Stillbirth	1.21	1.23	0.89–1.70	1.19	1.32	1.11–1.57*	0.96	1.03	0.91–1.17

Three-level structure random effects regression models were used to obtain adjusted odds ratios (AORs): individual (level 1), facility (level 2) and country (level 3).
At the individual level, adverse maternal outcomes were adjusted for marital status, education, parity and multiple births. For the analyses, additional adjustments were made for congenital malformation in stillbirths and preterm births, gestational age for low birthweight, and gestational age and birthweight for intra-hospital early neonatal mortality (IHENM).
All analyses were adjusted for facility capacity score at the facility level.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.
****Severe maternal outcomes include maternal near miss and intra-hospital maternal mortality.
*****Neonatal severe conditions refer to a liveborn baby with one of the following conditions: birthweight <1500 g, <32 gestational weeks at birth or a 5-minute Apgar score of <7.
******Intra-hospital early neonatal mortality (IHENM) refers to the death of a liveborn baby during the first 7 days after delivery.

use appropriate and inappropriate education for age, as maternal education is closely related to maternal age. However, in our data, adult mothers had more inappropriate education than adolescents, possibly because, in recent years, school enrollment and attendance have increased among younger mothers in many countries.[23] We considered the interaction between age and parity, and, after performing an analysis stratified by parity, we found that the results were no different.

Interpretation

In this study, we found that adolescent mothers had a lower risk of pre-eclampsia and a higher risk of eclampsia, with eclampsia being the leading cause of SMO. A recent study in the USA has suggested that the risk of pre-eclampsia among adolescents is increased by maternal obesity and excessive gestational weight gain.[24] The majority of our study population were from low- and middle-income countries, where malnourishment is prevalent among adolescents[25]; therefore, the risk of pre-eclampsia may be lower than in adults, as observed in a similar secondary analysis of adolescent pregnancy outcomes using the WHO Global Survey.[10] Limited access to antenatal care and a lack of prevention and treatment interventions for pre-eclampsia and infections during pregnancy among adolescents could be possible explanations for the higher risk of eclampsia, puerperal endometritis and systematic infections. However, a conclusion could not be drawn from our study in this regard because of an absence of data on antenatal care and interventions administered during pregnancy.

We also observed a significant low coverage of prophylactic interventions for postpartum haemorrhage, prophylactic antibiotics for caesarean section and antenatal corticosteroids for preterm delivery in countries with high and very high maternal mortality rates, which suggests the existence of inequality in effective interventions and may place adolescents at greater risk of adverse outcomes. Previous studies have shown that adequate antenatal care reduces the risks of pregnancy complications among adolescent mothers and their infants,[12,13,26] and the risk of maternal mortality was not significantly higher than in mothers aged 20–24 years.[27]

In this study, all adolescent mothers were more likely to have a vaginal delivery and had a lower risk of caesarean section, which was consistent with previous studies.[7,28] However, this result should be interpreted carefully. It has been suggested that adolescents are at an increased risk of obstructed labour and caesarean section indicated for cephalo-pelvic disproportion because of the immaturity of their pelvic bone. However, it is important to note that practitioner policy or maternal request, as well as limited access or availability of caesarean section among adolescents, may influence the mode of delivery.[9,10] Although adolescent mothers had a lower risk of caesarean section after adjusting for confounding factors, higher caesarean section rates (21.6–28.1%) may increase the risk of adverse birth outcomes for the next pregnancy and require special care (repeat caesarean section or vaginal birth after caesarean section).[29]

Consistent with previous studies,[6,8,30–33] we found significantly higher risks of low birthweight and preterm delivery, with the magnitude of risk decreasing as age increased. Previous studies have also suggested that these risks among adolescent mothers are associated with biological immaturity independent of poor socio-economic status, smoking and inadequate antenatal care.[6,32,34] Feto–maternal competition for nutrients is a common explanation for the higher risk of delivering low birthweight infants in adolescent mothers.[16] Gynaecological immaturity (i.e. short cervix [≤25 mm] and small uterine volume) and susceptibility to subclinical infections increase the risk of preterm delivery among adolescent mothers.[35]

Our study suggested that the higher risk of early neonatal death was partly explained by the poor socio-demographic factors and prematurity of infants born to adolescent mothers, which was consistent with previous studies.[7,21]

Our study found higher risks of adverse birth outcomes among adolescent mothers, suggesting that adolescent pregnancy prevention is crucial. As early marriage (<18 years) and sexual debut have been reported to be determinants of adolescent pregnancy, government policies to control marital age, and early education on sex and contraception, are fundamental to prevent adolescent pregnancies.[1]

Conclusions

In this study, we identified increased risks of maternal and perinatal adverse outcomes among adolescent mothers after adjustment for country- and facility-level effects and potential confounding factors. Coverage of essential interventions was significantly lower among adolescent mothers. These findings underline the importance of the further implementation of pregnancy prevention strategies and the improvement of healthcare interventions to reduce adverse birth outcomes among adolescent women in low- and middle-income countries.

Disclosure of interests

None of the authors have a conflict of interests.

Contribution to authorship

TG wrote the article and performed the data analysis. EO, NM and RM contributed to the data analysis and the writing of the manuscript. ML, PL, JZ, BY, MT, LS, OT, JV and JPS contributed to the 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 World Health Organization Ethical Review Committee (A65661, date: 27 October 2009) and the relevant ethical clearance mechanisms in all countries.

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Supporting Information

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

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Table S1. Distribution of adverse maternal outcomes by maternal age and regions defined by the maternal mortality rate (MMR).

Table S2. Proportion of adolescent deliveries and adverse maternal outcomes by country.

Table S3. Intervention coverage by maternal age and country group. ■

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Original article

Education and severe maternal outcomes in developing countries: a multicountry cross-sectional survey

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Objective To assess the relationship between education and severe maternal outcomes among women delivering in healthcare facilities.

Design Cross-sectional study.

Setting Twenty-nine countries in Africa, Asia, Latin America, and the Middle East.

Population Pregnant women admitted to 359 facilities during a period of 2–4 months of data collection between 2010 and 2011.

Methods Data were obtained from hospital records. Stratification was based on the Human Development Index (HDI) values of the participating countries. Multivariable logistic regression analyses were conducted to assess the association between maternal morbidity and education, categorised in quartiles based on the years of formal education by country. Coverage of key interventions was assessed.

Main outcome measures Severe maternal outcomes (near misses and death).

Results A significant association between low education and severe maternal outcomes (adjusted odds ratio, aOR, 2.07; 95% confidence interval, 95% CI, 1.46–2.95), maternal near miss (aOR 1.80; 95% CI 1.25–2.57), and maternal death (aOR 5.62; 95% CI 3.45–9.16) was observed. This relationship persisted in countries with medium HDIs (aOR 2.36; 95% CI 1.33–4.17) and low HDIs (aOR 2.65; 95% CI 1.54–2.57). Less educated women also had increased odds of presenting to the hospital in a severe condition (i.e. with organ dysfunction on arrival or within 24 hours: aOR 2.06; 95% CI 1.36–3.10). The probability that a woman received magnesium sulphate for eclampsia or had a caesarean section significantly increased as education level increased ($P < 0.05$).

Conclusions Women with lower levels of education are at greater risk for severe maternal outcomes, even after adjustment for key confounding factors. This is particularly true for women in countries that have poorer markers of social and economic development.

Keywords Education, health systems, human development index, inequity, near miss, severe maternal morbidity.

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Introduction

Launched in 2000, the Millennium Development Goal 5 (MDG 5) aimed for a three-quarter reduction in the maternal mortality ratio between 1990 and 2015. As 2015 approaches, increasing efforts have been made to improve maternal health. Despite a 47% decline in maternal mortality since 1990, it is unlikely that the MDG5 global target will be met.[1] An estimated 287 000 maternal deaths occurred in 2010, with nearly all (99%) occurring in low- and middle-income countries (LMICs).[2] The majority of these deaths are avoidable, and maternal mortality has been justly described as the starkest example of the disparities between the developed and developing world.[3,4] It is well recognised that one of the most powerful social determinants of health is education,[5–7] which is associated with a range of improvements in people's wellbeing, including infant and maternal health.[8–10]

Education has been shown to have a profound effect on a mother's use of maternal health services,[10] and a global analysis of predictors of maternal mortality showed that levels of female literacy and schooling were significantly associated with maternal death.[11] A recent WHO-led analysis of maternal outcomes following delivery in 23 LMICs showed that, compared against women with more than 12 years of education, women with no education had 2.7 times the risk of maternal mortality.[12]

Despite strong evidence that education is a powerful and modifiable determinant of maternal mortality and service use, there is no research examining the effect of education on other key maternal indicators, such as coverage of interventions and severe maternal outcomes, especially in terms of access to care. We conducted a secondary analysis of the WHO Multicountry Survey (WHOMCS) in order to assess the association of levels of education on access to health care and severe maternal outcomes among women delivering in health care facilities in 29 countries.[13]

Methods

The study protocol and methodology of the WHOMCS have been published previously.[13,14] In summary, it is a cross-sectional survey implemented in 359 health facilities from 29 countries, conducted between May 2010 and December 2011, including 314 623 women. A stratified, multistage cluster sampling approach was used to obtain a sample of facilities from two randomly selected provinces and the capital city of each country. The institutions sampled had to have over 1000 deliveries per year and the capacity to perform caesarean sections. Data were collected for 2–3 months depending on the annual number of deliveries per facility.

All women giving birth and with a severe maternal outcome, regardless of gestational age, during the data collection period were included. Women with severe maternal outcomes (SMOs) were defined by either maternal deaths or maternal near miss. Trained data collectors reviewed medical records during the study period and used this data to complete the paper data form at hospital discharge, transfer, or death. Information on the demographic and health characteristics, pregnancy, delivery, and maternal and perinatal outcomes of individual women were obtained from medical records. Data were then entered onto a web-based data management system.

Study population and variables

The key independent variable was education level, by quartiles created using the educational attainment variable in the survey, which collected years of formal education as a continuous variable. Initially, the database was examined and inconsistencies were addressed. The number and percentage of women by availability of the education variable was examined by country (Table S1). There was wide variation in the ranges of missing values, from <5% to more than 10%, and therefore we excluded countries if they had more than 10% of missing data for this variable. Education quartiles were developed for each country based on the years of formal education collected in the survey in each country (Table S2). The first quartile (Q1 or bottom 25%) was defined as the quartile with the lowest education, and the fourth quartile (Q4 or top 25%) was defined as the highest-educated quartile, using the XTILE function in STATA/SE 12.0 (Stata Corp LP, College Station, TX, USA). The highest quartile (top 25%) served as the reference group in all analyses performed.

According to the Human Development Index (HDI), countries were classified by the World Bank into four groups (very high, high, medium, and low), based on quartiles, thereby reducing the level of variation within each group, as shown in Table S3.[15] This index, first introduced in 1990, measures social and economic development by combining indicators of life expectancy, educational attainment, and income into a composite index.[15] As a result of missing data (>10% on education), Argentina and Japan were excluded, leaving Qatar by itself in the very high HDI category. We merged the very high and high groups to avoid a category containing just a single country. The background characteristics of the women included in the analyses were age, marital status, and number of pregnancies. The facility capacity index score was defined as the total score of essential and additional services provided by the selected health facilities, as explained elsewhere.[12,16]

Severe maternal outcomes were defined as maternal deaths and maternal near misses, identified by clinical, laboratory, and management markers. The variables related to access to healthcare facilities were defined as the presence of any organ dysfunction upon arrival or within 24 hours and dead upon arrival or within 24 hours.

Complications included in our analysis were haemorrhage, infections, hypertensive disorders, and complications related to abortion, ectopic pregnancy, and anaemia. Coverage of interventions (prophylactic oxytocin, therapeutic oxytocin, magnesium sulphate for eclampsia, prophylactic antibiotics for caesarean section, and parenteral antibiotics

for sepsis and systemic infections) was assessed among women who needed these specific interventions. Furthermore, caesarean sections, including caesarean section before labour, were assessed among delivering women.

Statistical analysis

We conducted multivariable regression analyses to assess the association between education level and severe maternal outcomes, including those related to access to healthcare facilities. The models were adjusted for non-independence at the facility level, and at the individual level adverse maternal outcomes were adjusted for maternal age, marital status, number of pregnancies, institutional capacity score, and HDI score of the country. Furthermore, this model was stratified by HDI groups. $P < 0.05$ was considered to be significant. Statistical analyses were conducted using STATA/SE 12.0 (Stata Corp LP).

Pearson's chi-square trend tests were conducted, taking into account the clustering effect of the survey design, to compare the coverage of interventions, access to caesarean section, and burden of complications by education quartiles.

Results

The WHOMCS collected data on 314 623 pregnant women in 359 facilities, who were admitted regardless of gestational age. Overall, 8.3% of responses were missing on the education variable, and we excluded these data (n = 25 872). Using 10% as a threshold for missing data on education, the case-wise deletion of countries led us to omit Afghanistan, Angola, Argentina, Brazil, Cambodia, Japan, Sri Lanka, and Uganda (n = 69 626). Analyses were conducted on 219 124 women from 261 facilities in 21 countries, all of which had ≤5% missing data on the education variable.

Table 1 summarises the background characteristics of the study population, classified by HDI groups. The majority of our study population was between the ages of 20 and 34 years (79%), with a partner (91%), and having had three or fewer pregnancies (81.6%). In our study population, 13.6% of the women had no education, with 26.4% of the women with no education being in the low HDI group. In terms of adverse maternal outcomes, women in low HDI group countries experienced the highest percentage of maternal near miss and maternal deaths: 1.1 and 0.28%, respectively.

When we analysed the adverse maternal outcomes by the education levels of the women (Table 2), women in the lowest quartile (Q1) had consistently higher odds of experiencing severe maternal outcomes overall, as well as maternal near miss and maternal death. In the adjusted multivariable model, these associations remained significant for severe maternal outcomes (adjusted odds ratio, aOR, 2.07; 95% confidence interval, 95% CI, 1.46–2.95; $P < 0.001$), maternal near miss (aOR 1.80; 95% CI 1.25–2.57; $P < 0.001$), and maternal death (aOR 5.62; 95% CI 3.45–9.16; $P < 0.001$). In the adjusted model, the variables related to access to healthcare facilities showed that the odds of the presence of any organ dysfunction upon arrival or within 24 hours was twice as likely among women in the lowest quartile (Q1) versus women in the highest quartile (Q4) (aOR 2.06; 95% CI 1.36–3.10; $P < 0.001$). Furthermore, the women in the lowest education quartile (Q1) were more than five times as likely to die upon arrival, or within the first 24 hours of arrival, at a hospital than the women in the highest quartile (aOR 5.43; 95% CI 2.59–11.39; $P < 0.001$).

Table 3 shows the association between adverse maternal outcomes and educational level stratified by HDI groups. When stratified by HDI groups, education level was not significantly associated with experiencing severe maternal outcomes in the higher HDI countries. In contrast, for women in the lowest education quartile (Q1) living in countries classified under medium and low HDI groups, the odds of experiencing a severe maternal outcome were more than twice those of the women in the highest education quartile (Q4): aOR 2.36 (95% CI 1.33–4.17) and aOR 2.65 (95% CI 1.54–2.57), respectively. As shown in Table 3, these associations remain significant after adjustment for the other adverse maternal outcomes as well as for the indicators associated with access to healthcare facilities.

The burden of complications was highest among the women in the lowest education quartile (Q1). The women in this group accounted for 42% of haemorrhage cases, 44% of hypertensive disorders, 41% of infections, 48% of complications related to abortion or ectopic pregnancy, 41% of anaemia, and 42% of the other complications reported (Figure 1).

Table 4 summarises the coverage of interventions among women who needed them by education level. There were no statistically significant differences among women in different education levels for prophylactic antibiotics for caesarean section; however, therapeutic oxytocin for the treatment of postpartum haemorrhage and parenteral antibiotics for systemic infections had a downwards trend towards the highest education quartile (P = 0.007 and 0.02, respectively). The probability that a woman received magnesium sulphate for eclampsia significantly increased as education level increased (P = 0.001). When adjusted for other factors included in our multivariable modelling, only the association between magnesium sulphate coverage for eclampsia and higher levels of education remained significant (Q1 aOR 0.65; 95% CI 0.53–0.80; $P < 0.001$), whereas the association for the other groups attenuated. As shown in Table 5, among women in the study population who delivered by caesarean section, 27.2% of the women in the

Table 1. Background characteristics of the study population and adverse maternal outcomes, classified by HDI groups (n = 219 124)

	HDI groups 1 and 2 (very high/high) n (%)	HDI group 3 (medium) n (%)	HDI group 4 (low) n (%)	Total n (%)
Age				
<20 years	7224 (15.7)	7522 (7.7)	7848 (10.3)	22 594 (10.3)
20–34 years	32 365 (70.5)	81 089 (83.4)	59 657 (78.5)	173 111 (79.0)
≥35 years	6288 (13.7)	8506 (8.8)	8327 (11.0)	23 211 (10.6)
Missing	58 (0.1)	60 (0.1)	180 (0.2)	298 (0.1)
Marital status				
Without a partner	5831 (12.7)	8382 (8.6)	5164 (6.8)	19 377 (8.8)
With a partner	40 034 (87.2)	88 683 (91.3)	70 620 (92.9)	199 337 (91.0)
Missing	70 (0.1)	112 (0.1)	228 (0.3)	410 (0.2)
Number of pregnancies				
1 pregnancy	15 455 (33.7)	39 759 (40.9)	26 516 (34.9)	81 730 (37.3)
2–3 pregnancies	21 150 (46.0)	45 277 (46.6)	30 654 (40.3)	97 081 (44.3)
>3 pregnancies	9326 (20.3)	12 128 (12.5)	18 830 (24.8)	40 284 (18.4)
Missing	4 (0.01)	13 (0.01)	12 (0.02)	29 (0.01)
Years of formal education				
No education	695 (1.5)	8933 (9.2)	20 055 (26.4)	29 683 (13.6)
Primary (1–6 years)	6768 (14.7)	13 842 (14.2)	9810 (12.9)	30 420 (13.9)
Lower secondary (7–9 years)	45 521 (20.8)	20 573 (21.2)	14 025 (18.4)	45 521 (20.8)
Upper secondary (10–12 years)	72 811 (33.2)	34 277 (35.3)	22 100 (29.1)	72 811 (33.2)
Tertiary (>12 years)	40 689 (18.6)	19 552 (20.1)	10 022 (13.2)	40 689 (13.6)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Years of schooling by ranges				
Quartile 1 (Lowest)	18 386 (40.0)	25 857 (26.6)	20 055 (26.4)	60 103 (27.4)
Quartile 2	9822 (21.4)	33 132 (34.1)	21 770 (28.6)	71 144 (32.5)
Quartile 3	6612 (14.4)	18 636 (19.2)	24 165 (31.8)	47 188 (21.5)
Quartile 4 (Highest)	11 115 (24.2)	19 552 (20.1)	10 022 (13.2)	40 689 (18.6)
Facility capacity index: mean (SD)	67.3 (20.5)	58.5 (14.6)	49.5 (15.0)	57.2 (17.4)
Severe maternal outcomes				
No	45 550 (99.2)	96 554 (99.4)	74 993 (98.7)	217 097 (99.1)
Yes	385 (0.8)	623 (0.6)	1019 (1.3)	2027 (0.9)
Maternal near miss				
No	45 568 (99.2)	96 683 (99.5)	75 206 (98.9)	217 457 (99.2)
Yes	367 (0.8)	494 (0.5)	806 (1.1)	1667 (0.8)
Maternal death				
No	45 917 (99.96)	97 048 (99.87)	75 799 (99.72)	218 764 (99.84)
Yes	18 (0.04)	129 (0.13)	213 (0.28)	360 (0.16)

lowest education quartile (Q1) had a caesarean section, compared with 40.9% of the women in the highest education quartile (Q4) ($P < 0.001$). The same trend was observed for caesarean sections conducted before labour began: 9.8 versus 17.9% ($P < 0.001$). When adjusted for other factors included in our multivariable modelling, both of these associations remained significant (results not shown).

Discussion

Main findings

Our study showed that lower levels of maternal education are associated with women experiencing severe maternal outcomes, including maternal near miss and death. This relationship was stronger in lower HDI countries. Moreover, these women were more likely to present at healthcare facilities with worse health status compared with women with higher education levels. Additionally, we demonstrated that a number of interventions, such as coverage of magnesium sulphate for eclampsia and caesarean section, were more likely to be provided to women with higher education levels.

Strengths and limitations of the study

The WHOMCS is currently the largest study that has been conducted to explore the prevalence of severe maternal outcomes (including near-miss cases), using standardised

Table 2. Unadjusted and adjusted odds of adverse maternal outcomes, by education quartiles

	Number of women	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Adverse maternal outcomes			
Severe maternal outcomes (*n* = 191 804)			
Education Q4 (highest)	34 403	1.00	1.00
Education Q3	38 625	1.34 (0.95–1.89)	1.48 (1.05–2.07)*
Education Q2	41 219	1.21 (0.83–1.77)	1.20 (0.81–1.74)
Education Q1 (lowest)	77 557	2.10 (1.48–2.97)***	2.07 (1.46–2.95)***
Maternal near miss (*n* = 191 804)			
Education Q4 (highest)	34 403	1.00	1.00
Education Q3	38 625	1.27 (0.88–1.85)	1.40 (0.98–2.00)
Education Q2	41 219	1.11 (0.74–1.66)	1.09 (0.74–1.60)
Education Q1 (lowest)	77 557	1.82 (1.26–2.63)***	1.80 (1.25–2.57)
Maternal death (*n* = 191 804)			
Education Q4 (highest)	34 403	1.00	1.00
Education Q3	38 625	1.96 (1.12–3.41)*	2.43 (1.42–4.18)***
Education Q2	41 219	2.17 (1.20–3.92)*	2.51 (1.33–4.74)**
Education Q1 (lowest)	77 557	4.67 (2.83–7.68)***	5.62 (3.45–9.16)***
Adverse maternal outcomes related to access to a healthcare facility			
Presence of any organ dysfunction upon arrival or within 24 hours (*n* = 14 929)			
Education Q4 (highest)	2503	1.00	1.00
Education Q3	3057	1.11 (0.73–1.69)	1.21 (0.79–1.85)
Education Q2	3127	1.45 (0.98–2.14)	1.48 (1.01–2.20)*
Education Q1 (lowest)	6242	2.07 (1.38–3.09)***	2.06 (1.36–3.10)***
Dead at arrival or within 24 hours (*n* = 14 931)			
Education Q4 (highest)	2502	1.00	1.00
Education Q3	3058	1.72 (0.77–3.83)	1.99 (0.89–4.48)
Education Q2	3130	2.50 (1.12–4.50)*	2.45 (1.16–5.19)*
Education Q1 (lowest)	6241	5.34 (2.58–11.05)***	5.43 (2.59–11.39)***

The unadjusted odds ratios were adjusted for any clustering effect at the facility level. The adjusted odds ratios were adjusted for: maternal age; marital status; number of pregnancies, including current pregnancy; institutional capacity score; human development index of the country; and clustering at the facility level.
Levels of significance: *$P < 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$.

methodology of collection and analysis of data across 29 countries, which provided a large enough sample size, including a number of key variables, to conduct these analyses. Therefore, we were able to explore associations never studied before, such as severe maternal morbidity (near miss) and adverse maternal outcomes upon arrival at a healthcare facility, stratified by countries in different levels of economic and social development. Furthermore, instead of categorising education in terms of primary, secondary, etc., our analysis took into account the country-level differences by developing education quartiles for each country based on the years of formal education in each country.

There are several limitations. WHOMCS includes data that are limited to healthcare facilities; therefore, our results cannot be generalisable to the total populations in our study countries, where substantial proportions of women deliver at home. Even though we adjusted our models for a number of demographic and reproductive health-related variables, we did not have any information on some important factors such as economic status, place of residence (urban/rural), and history of antenatal care, contributing to residual confounding. We were therefore unable to sort out all of the potential factors leading to both poor educational attainment and higher adverse maternal health outcomes. Future analyses might also consider exploring the interactions between young age, nulliparity, and lower levels of education.

Interpretation

Health inequity is closely related to social determinants of health, where the burden of ill health is greatest in lower socio-economic groups.[17] A policy analysis highlighted that in six countries with marked progress in reducing maternal mortality, effective policies included investing in women's education.[1] In our study, the women in the lowest education

Table 3. Adjusted odds of adverse maternal outcomes, by education quartiles and Human Development Index (HDI)

	Very high/high HDI *n* = 32 692 Adjusted odds ratio (95% CI)	Medium HDI *n* = 86 606 Adjusted odds ratio (95% CI)	Low HDI *n* = 71 984 Adjusted odds ratio (95% CI)
Adverse maternal outcomes			
Severe maternal outcomes			
Education Q4 (highest)	1.00	1.00	1.00
Education Q3	0.76 (0.32–1.81)	1.91 (1.24–2.96)**	1.67 (1.01–2.75)*
Education Q2	0.76 (0.44–1.30)	1.90 (1.10–3.28)*	1.08 (0.57–2.05)
Education Q1 (lowest)	0.98 (0.50–1.93)	2.36 (1.33–4.17)**	2.65 (1.54–2.57)***
Maternal near miss			
Education Q4 (highest)	1.00	1.00	1.00
Education Q3	0.77 (0.33–1.79)	1.86 (1.16–2.99)**	1.47 (0.85–2.56)
Education Q2	0.79 (0.46–1.33)	1.63 (0.94–2.82)	0.93 (0.46–1.86)
Education Q1 (lowest)	0.98 (0.52–1.85)	1.82 (1.02–3.25)*	2.22 (1.22–4.04)**
Maternal death			
Education Q4 (highest)	1.00	1.00	1.00
Education Q3	0.73 (0.04–13.5)	2.09 (0.82–5.35)	3.19 (1.52–6.67)**
Education Q2	Omitted	3.54 (1.26–9.93)*	2.39 (1.07–5.35)*
Education Q1 (lowest)	1.77 (0.17–18.7)	6.09 (2.50–14.88)***	6.31 (3.45–11.51)***
	High HDI *n* = 2762	**Medium HDI *n* = 6749**	**Low HDI *n* = 5388**
Adverse maternal outcomes related to access to a healthcare facility			
Presence of any organ dysfunction upon arrival or within 24 hours			
Education Q4 (highest)	1.00	1.00	1.00
Education Q3	0.53 (0.18–1.58)	1.66 (0.91–3.06)	1.59 (0.94–2.69)
Education Q2	0.87 (0.44–1.71)	2.20 (1.14–4.24)*	1.48 (0.83–2.65)
Education Q1 (lowest)	0.71 (0.27–1.88)	3.80 (2.05–7.04)***	2.22 (1.36–3.62)**
Dead upon arrival or within 24 hours			
Education Q4 (highest)	1.00	1.00	1.00
Education Q3	0.47 (0.02–10.71)	1.81 (0.31–10.57)	3.07 (1.10–8.57)*
Education Q2	Omitted	5.77 (1.19–28.00)*	2.17 (0.92–5.15)
Education Q1 (lowest)	0.70 (0.06–8.32)	11.7 (2.57–53.50)***	5.06 (2.00–12.77)***

The models were adjusted for non-independence at the facility level, and at the individual level the adverse maternal outcomes were adjusted for: maternal age; marital status; number of pregnancies, including current pregnancy; and institutional capacity score.
Levels of significance: *$P < 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$.

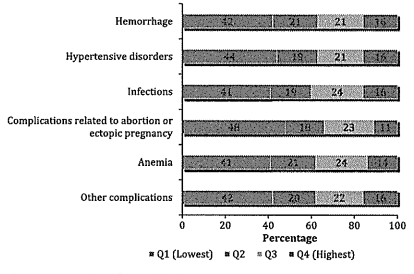

Figure 1. Burden of complications among women, based on their education levels (Q1, lowest; Q4, highest).

quartiles were significantly more likely to experience severe maternal outcomes, including maternal death. These findings were supported by a recent study from Bangladesh, where female education was a strong predictor of maternal mortality.[18] Our findings were also consistent with the results from the WHO Global Survey,[12] and showed a stronger relationship between educational levels and severe maternal outcomes, especially when comparing the lowest and highest educational quartiles within middle and low HDI country groups.

One of the possible underlying reasons for this strong relationship between education level and severe maternal outcomes is that less educated women might experience longer primary and secondary delays in deciding to seek and reach care, respectively.[19,20] Our current analysis

Table 4. Coverage of interventions among women who needed them, by education quartiles

Coverage of interventions	Q1 (lowest)% (95% CI)	Q2% (95% CI)	Q3% (95% CI)	Q4 (highest)% (95% CI)	Total	*P*
Prophylactic oxytocin (*n* = 218 012)	94.2 (92.2–95.8)	93.2 (90.2–95.3)	91.0 (86.5–94.1)	94.2 (91.4–96.2)	93.3 (90.9–95.1)	0.03
Therapeutic oxytocin (*n* = 3056)	89.3 (86.0–91.8)	89.6 (85.4–87.1)	82.5 (76.8–87.1)	81.5 (71.8–88.3)	86.7 (83.0–89.7)	0.007
$MgSO_4$ for eclampsia (*n* = 779)	88.8 (84.8–91.8)	82.9 (74.0–89.2)	70.8 (57.3–81.4)	93.4 (80.5–98.0)	85.0 (79.2–89.4)	0.001
Prophylactic antibiotics for caesarean section (*n* = 67 732)	86.5 (81.4–90.4)	88.3 (84.0–91.5)	85.0 (77.1–90.5)	90.5 (87.1–93.1)	87.4 (83.4–90.6)	0.12
Parenteral antibiotics for systematic infections (*n* = 628)	83.8 (74.6–90.2)	87.7 (74.1–94.7)	68.2 (40.9–86.9)	65.4 (40.2–84.1)	76.6 (55.8–89.4)	0.02

Coverage indicators were calculated as the proportion of the target population who received the intervention.

Table 5. Caesarean section rates among women delivering at study facilities, by education quartiles (*n* = 218 580)

Interventions	Education quartiles					
	Q1 (lowest)% (95% CI)	Q2% (95% CI)	Q3% (95% CI)	Q4 (highest)% (95% CI)	Total	*P*
Caesarean section	27.2 (25.0–29.6)	30.2 (27.7–32.9)	30.9 (27.7–34.1)	40.9 (37.5–44.4)	31.0 (28.7–33.4)	<0.001
Caesarean section before labour	9.8 (8.4–11.3)	11.7 (10.1–13.6)	12.5 (10.8–14.4)	17.9 (15.3–20.9)	12.2 (10.8–13.7)	<0.001

demonstrates that less educated women are indeed more likely to arrive at hospital presenting with organ dysfunction or death; however, a recent systematic review reports that focusing on the first two delays may mask the fact that many health facilities in developing countries are still chronically under-resourced and unable to effectively manage severe obstetric complications.[21] In our study, which included several types of healthcare facility in each country, the results further suggest that there is disparity between lower and higher education quartiles in terms of the coverage of evidence-based interventions, such as magnesium sulphate for the treatment of eclampsia, or a caesarean section, which in many cases is a life-saving surgery, indicating delays in receiving timely quality of care while at the healthcare facility. Therefore, assessing and improving the quality of care and management for these cases using tools such as the WHO Maternal Near-Miss Approach, or the Maternal Death Surveillance and Response, will be crucial.[13,22,23]

We stratified the analyses by HDI groups to further explore education level as an inequity factor in different settings. The level of education ceased to be a significant factor in relation to adverse maternal outcomes in the higher HDI countries. In contrast, the associations got stronger among middle and lower HDI level countries. This suggests that in countries with higher economic and social development, functioning healthcare systems can compensate for the inequality associated with educational attainment, whereas in less developed countries it still causes a discrepancy in terms of outcomes, access to services, and coverage of interventions such as caesarean section. It should be noted here that we did not have information on the indications for caesarean sections or emergency caesarean section status defined by decision or operation time.[24] Education is a marker of social development and inclusion, and although it is difficult to disentangle the intrinsic contribution of education to improved maternal outcomes in our analysis, it strongly indicates that less advantageous populations face additional barriers in reaching high-quality care.

Conclusion

Our study demonstrates that in countries that have poorer markers of social and economic development, education is a significant factor contributing to the disparities experienced by women delivering in healthcare facilities. It underlines that the countries with strong healthcare systems, which are ready to provide integrated, continuous, high-quality care, both as routine and in an emergency, are more likely to compensate for adverse outcomes faced by women with lower levels of education. In addition to ensuring universal education as a key policy, low-cost, effective interventions implemented within strengthened healthcare systems are needed to prevent maternal morbidity and mortality.

Disclosure of interests

We declare that we have no conflicts of interest.

Contribution to authorship

OT, JPS, MJH, CAS, and THO conceptualised the article and the analysis plan. OT conducted the analyses in collaboration with MJH and JPS, and OT wrote the first draft of the article. JPS, MJH, CAS, THO, JPV, GT, DQH, AMG, and LS contributed to the interpretation of the results and editing of the article. All authors read and approved the final version of the article.

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. Number and percentage of women by availability of the education variable by country.

Table S2. Sample sizes and ranges of years of education calculated by country and HDI groups.

Table S3. Country grouping by HDI. ■

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