

Risk of maternal mortality in women with severe anaemia during pregnancy and post partum: a multilevel analysis

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Summary

Background Anaemia affects as many as half of all pregnant women in low-income and middle-income countries, but the burden of disease and associated maternal mortality are not robustly quantified. We aimed to assess the association between severe anaemia and maternal death with data from the WHO Multicountry Survey on maternal and newborn health.

Methods We used multilevel and propensity score regression analyses to establish the relation between severe anaemia and maternal death in 359 health facilities in 29 countries across Latin America, Africa, the Western Pacific, eastern Mediterranean, and southeast Asia. Severe anaemia was defined as antenatal or postnatal haemoglobin concentrations of less than 70 g/L in a blood sample obtained before death. Maternal death was defined as death any time after admission until the seventh day post partum or discharge. In regression analyses, we adjusted for post-partum haemorrhage, general anaesthesia, admission to intensive care, sepsis, pre-eclampsia or eclampsia, thrombocytopenia, shock, massive transfusion, severe oliguria, failure to form clots, and severe acidosis as confounding variables. These variables were used to develop the propensity score.

Findings 312 281 women admitted in labour or with ectopic pregnancies were included in the adjusted multilevel logistic analysis, and 12 470 were included in the propensity score regression analysis. The adjusted odds ratio for maternal death in women with severe anaemia compared with those without severe anaemia was 2.36 (95% CI 1.60–3.48). In the propensity score analysis, severe anaemia was also associated with maternal death (adjusted odds ratio 1.86 [95% CI 1.39–2.49]).

Interpretation Prevention and treatment of anaemia during pregnancy and post partum should remain a global public health and research priority.

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Introduction

As many as half of all pregnant women in low-income and middle-income countries are diagnosed with anaemia,^{1,2} which affects 32 million pregnant women worldwide.² Women in low-income and middle-income countries are at increased risk of anaemia¹ because of the higher frequency of dietary iron deficiency, haemoglobinopathies, macronutrient deficiencies, and infections such as malaria, HIV, and hookworm infestation in those countries than in high-income countries.³ Anaemia has been associated with increased prevalence of ante-partum and post-partum haemorrhage.⁴

WHO has recognised anaemia as a global problem with serious consequence for mothers and their babies.⁵ Even though anaemia in pregnancy is readily treatable, data from several studies show an association between maternal anaemia and severe adverse maternal and perinatal outcomes.² The findings of these studies were not robust as a result of methodical limitations, including small sample sizes, use of surrogate outcome measures,⁶

inconsistent definitions of severe morbidity,⁷ and failure to adjust for relevant confounders. Thus, severe anaemia is strongly correlated with maternal morbidity secondary to known clinical and biological factors.⁸ Furthermore, the crucially important outcome of maternal death is often not reported or is reported with low precision because of the rarity of events⁹ in small and retrospective datasets.^{4,10} As a result, the relation between severe anaemia and maternal mortality is not well understood.

The absence of robust evidence of severe anaemia and maternal mortality could affect prioritisation of anaemia as an important condition in its own right. We assessed the association of severe anaemia with maternal mortality in a large, multicountry dataset gathered via standardised procedures.

Methods

Survey methods and participants

The WHO Multicountry Survey was a large, cross sectional study in which data were collected for all

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Research in context

Evidence before this study

Anaemia in pregnancy is associated with severe maternal morbidity and an indirect cause of maternal death across pregnant populations in both low-income and high-income settings.

We searched MEDLINE and Embase with the terms "anaemia", "anemia", "anae*", "anem*", "pregnancy", "pregnan*", "mother", "mortality", "death", and "maternal mortality" for observational studies published in any language before June 19, 2017. We also searched in WHO's study registry. We did not identify any large international analyses of the association between severe anaemia and maternal death, but noted several small national or regional studies with methodological limitations, such as small sample size, in which the small number of events prevented development of a robust model with adequate adjustment for known confounding variables.

Added value of this study

To our knowledge, ours is the first study to explore the independent association of severe anaemia with maternal

mortality. We noted an independent association to varying degrees in an ethnically and geographically diverse population. Because severe anaemia was recorded as a binary variable in our dataset (from the WHO Multicountry Survey), we could not examine whether a dose-response relationship exists between haemoglobin concentration and maternal mortality. Nonetheless, we identified an association that was present in several different regions and reproducible with different statistical techniques, even after adjustment for several known confounding variables.

Implications of all the available evidence

Irrespective of the cause, severe anaemia should be treated with vigour. Our findings support the use of haematological indices as outcome measures that are strongly associated with clinical outcomes. Our work also shows the need to prioritise the prevention and management of anaemia in pregnancy as a global public health and research priority.

delivery and severe maternal outcomes (ie, maternal death and maternal near-miss) with standardised methods at 359 health facilities in 29 countries across Latin America, Africa, the Western Pacific, eastern Mediterranean and southeast Asia between May, 2010, and December, 2011. The included countries were Afghanistan, Angola, Argentina, Brazil, Cambodia, China, Democratic Republic of the Congo, Ecuador, India, Japan, Jordan, Kenya, Lebanon, Mexico, Mongolia, Nepal, Nicaragua, Niger, Nigeria, Pakistan, Palestine, Paraguay, Peru, Philippines, Qatar, Sri Lanka, Thailand, Uganda, and Vietnam. They were chosen on the basis of their participation in the WHO Global Country Survey and on assessments of feasibility. Types of health-care facilities included government-funded regional and local hospitals, and community hospitals. Detailed explanations of the methods have been published previously.^{11,12}

The WHO Multicountry Survey was based on a stratified multistage cluster-sampling approach to obtain a global sample of pregnancy complications. Within each region, two randomly selected provinces and the capital city of each country were sampled. Within each capital city and province, seven institutions with more than 1000 deliveries per year and the capacity for caesarean deliveries were randomly selected (if there were fewer than seven eligible institutions, all eligible institutions were included). Data were collected for 2 months in institutions with more than 6000 deliveries per year data, and for 3 months in institutions with fewer than 6000 deliveries per year. In countries where fewer than 3000 deliveries were anticipated per year, data were gathered for 4 months at all centres. Health-care facilities were the primary sampling level of the WHO

Multicountry Survey, and thus individual level analyses could be affected by clustering.

The study population comprised all women giving birth in participating hospitals and their respective neonates; all maternal near-miss cases admitted to participating hospitals, irrespective of gestational age and delivery status; and all maternal deaths in participating hospitals, irrespective of gestational age and delivery status, during the data collection period. Those in whom severe outcomes were a result of miscarriage or ectopic pregnancy were also included. Data were gathered for all eligible individuals from admission to a health-care facility until 7 days post partum or post abortion, discharge, or death (whichever came first). Thus, complications that occurred before presentation, more than 7 days post partum, after discharge, or during a post-partum readmission were not recorded. Data were captured via a pre-tested individual data collection form. Trained data collectors reviewed medical records and abstracted data into the forms daily; there was no contact with eligible women. Clarification, when needed, was sought from clinical staff. Additionally, data collectors completed an institutional form in consultation with the head of the obstetric department, in which obstetric, neonatal, and intensive-care capacity, and capacity to identify a range of laboratory, clinical, and management severity indicators for mothers and neonates were captured. Data for both the individual and institutional forms were then entered into a web-based management system. Ethical approval for the original Multicountry Survey was granted by WHO's Ethical Review Committee, and was also sought in each contributing country. This specific analysis was approved by the

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