Maternal anaemia and risk of mortality: a call for action

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Maternal anaemia is an important global health problem that affects about 500 million women of reproductive age.[1] Much is known about the consequences of anaemia during pregnancy, including the increased risks of low birthweight, preterm birth, perinatal mortality, and neonatal mortality.[2] Maternal anaemia also places the mother at increased risk of death during and after childbirth.[3] Severe anaemia can lead to circulatory decompensation, increased cardiac output, an increased risk of haemorrhage, and decreased ability to tolerate blood loss, leading to circulatory shock and death.[4,5] A review[3] of observational studies showed a linear association between maternal anaemia and death, with each 10 g/L increase in maternal haemoglobin associated with a 29% reduction in maternal mortality (odds ratio [OR] 0·71 [95% CI 0·60–0·85]).

In *The Lancet Global Health*, Jahnavi Daru and colleagues reaffirm the association of maternal anaemia with maternal mortality.[6] Their study makes important contributions to the field and emphasises the need to reduce anaemia during pregnancy and post partum. A unique feature of this study is the use of data from WHO's Multicounty Survey, which is one of the largest studies of severe complications in pregnancy and includes diverse data from 29 countries. The authors concluded that severe anaemia (defined as haemoglobin concentrations of <70 g/L) during pregnancy or post partum doubled the risk of maternal death in this population.[6]

Although this estimate is alarming, it is probably an underestimation. The authors potentially over-controlled for factors in the causal pathway, and compared women with severe anaemia with all other women, including those with mild or moderate anaemia and high haemoglobin concentrations. Haemoglobin was assessed during pregnancy or the first week post partum, but information about timing was not recorded, which is problematic. Without these data it is hard to establish, for example, whether post-partum haemorrhage led to severe anaemia, or whether severe anaemia during pregnancy increased the risk of post-partum haemorrhage. In view of the absence of data for timing, the authors developed a conservative model in which they adjusted for potentially confounding variables (including post-partum haemorrhage, sepsis, transfusion, shock, and admission to intensive-care units, among other factors). However, the possibility that some of these factors are on the causal pathway, which would attenuate the relation between maternal anemia and mortality, cannot be ruled out. For instance, if severe anaemia leads to circulatory shock and results in death, then adjustment for shock would reduce the estimated effect of anaemia. The true estimate probably lies somewhere between the adjusted OR of 2·36 (95% CI 1·60–3·48) and the crude OR of 43·35 (35·03–53·65).

The authors' analysis includes multiple models and sensitivity analyses. However, the cause of maternal mortality is complex and difficult to examine in cross-sectional surveys. Additionally, in the WHO Multicountry Survey, only severe anaemia is recorded. The inclusion in the control group of individuals at potentially heightened risk of mortality (ie, those with mild or moderate anaemia, or high haemoglobin concentrations) would also have attenuated the estimated effect of severe anaemia. In a Peruvian cohort,[7] women with haemoglobin concentrations greater than 145 g/L (OR 2·01 [95% CI 1·12–3·61]), between 70 g/L and less than 90 g/L (6·06 [3·16–11·6]), or less than 70 g/L (8·54 [2·06–35·42]) had increased odds of maternal mortality compared with those with haemoglobin concentrations of 110–45 g/L. Questions remain about the optimal haemoglobin cutoffs to identify pregnant people at risk for poor birth outcomes and how these cutoffs are influenced by timing of measurement.[8] Further research, including longitudinal surveillance that records continuous haemoglobin measurements throughout pregnancy and follows up women for longer post partum, could help to improve understanding of the relation between maternal anaemia and mortality.

The implication of Daru and colleagues' study is a call for action to address anaemia to reduce preventable maternal deaths. Even if this robust and conservative analysis underestimates the risk of death among women with severe anaemia, the risk remains unacceptability high.[6] These results emphasise that addressing maternal anaemia should be part of an integrated maternal health strategy to reduce maternal mortality. The WHO global targets call for a 50% reduction in anaemia in women of reproductive age by 2025 relative to 2010

prevalence.[9] Efficacious interventions, such as iron and folic acid supplementation,[10] are available, but they do not seem to be working at scale as evidenced by insufficient progress in reducing maternal anaemia.[1] The implementation of existing programmes needs to improve, and other approaches that reach women before conception and during pregnancy, such as mass fortification and home fortification, and that tackle non-nutritional causes of anaemia need to be developed. This study is a call to develop comprehensive strategies that address the diverse causes of anaemia across contexts to improve maternal and child health.

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