Evidence-based practices to reduce maternal mortality: a systematic review

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ABSTRACT

Background To achieve the World Health Organization’s Millennium Development Goal of reducing maternal mortality by three-quarters by 2015, a strong global commitment is needed to address this issue in sub-Saharan Africa where the risk to women is greatest. A comprehensive international effort must include both clinical and community-based interventions. In sub-Saharan Africa where the majority of women deliver babies at home without a trained attendant, the national plans must rely predominantly on community-level interventions.

Methods and results This study compiles the Cochrane reviews whose outcome measure is maternal mortality. Nine reviews documented the effectiveness of specific drugs given during pregnancy while six reviews demonstrated that particular drug regimens and procedures actually increase maternal death. Two of the Cochrane reviews found no significant difference in maternal mortality risk due to antioxidant use or in training traditional births attendants.

Conclusions The dearth of evidence highlights the need for increased focus on clinical and community-based interventions that are feasible in sub-Saharan Africa. This cannot be accomplished without a stronger commitment to reducing maternal mortality by global health practitioners and researchers.

Keywords health promotion, primary care, public health

Introduction

More than half a million women and girls die each year as a result of pregnancy, childbirth and related complications. The lifetime risk of maternal death is more than 200 times greater for women in poor countries compared with women in Western Europe and North America. About 99% of maternal deaths occur in the 53 low-income countries defined as having a gross national income per capita (GNI) per capita of US$905 or less. More than 60% of these countries are in sub-Saharan Africa.1,2 Every 4 years, almost one million African mothers die from preventable pregnancy-related risks while women in wealthy nations give birth with very little risk of death. The tragedy of a woman dying in childbirth extends beyond her own death, devastating her infant, her other children, her family and the community. Commitment is needed among global public health leaders to identify best practices in reducing maternal mortality, and to fund and implement programs with strong evidence of effectiveness in and translate the best interventions for dissemination to countries and communities that are disproportionately affected.

Background

Maternal death is defined as ‘the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes’.3 The World Health Organization (WHO) is committed to achieving the Millennium Development Goal of reducing maternal deaths by three-quarters by the year 2015. Despite the global commitment to reduce the maternal mortality ratio by 5.5% each year, the current rate of decline is <0.4% per annum.4 The worldwide maternal mortality ratio was 400 per 100 000 live births in 2005. At the current rate of decline, it will take more than 188 years to meet the goal of 100 per 100 000 live births. ‘Of the estimated total of 536 000 maternal deaths worldwide in 2005, developing countries accounted for 99% (533 000) of these deaths. Slightly more than half of the maternal deaths (270 000)
occurred in the sub-Saharan Africa region alone. In Africa where the maternal mortality rate is 684 per 100 000 live births, millions of young women will experience preventable deaths before the goal is met. A stronger commitment is needed to save these lives. The global public health community should hasten in researching and identifying effective interventions which are culturally relevant, cost-effective and acceptable to sub-Saharan communities. These efforts will help meet the Millennium Development Goal of reducing maternal mortality.

**Causes and risk factors**

Almost 75% of maternal deaths are caused by direct complications as follows:

- Hemorrhage (25%),
- Infection (15%),
- Unsafe abortion (13%),
- Eclampsia (very high blood pressure leading to seizures) (12%),
- Obstructed labor (8%).

The high rates of death to women during pregnancy, childbirth or in the immediate postpartum period are due to complex influencing factors relating to health care delivery (access to skilled health care, blood transfusions, anesthesia, sterile conditions and essential drugs) and social factors (poverty, the role of women, education and empowerment of women, religion). According to the WHO, unavailable, inaccessible, unaffordable or poor quality care are the factors that are fundamentally responsible for so many maternal deaths.

**Medical interventions/community-level interventions**

Medical interventions occur in clinical settings and can include primary (supplements during pregnancy), secondary (early detection and treatment of risk) or tertiary prevention (treating obstetrical emergencies and complications). Medical interventions have a wide reach in high-income countries where nearly all infants are delivered in hospitals with trained medical providers. The Lancet Maternal Survival steering group published a series of five articles about maternal survival in 2006. Their key messages included the importance of focusing on maternal death rather than morbidity as an outcome where the mortality burden is high. A clear message from this series of articles is that focus on the intrapartum period is essential to end the epidemic of maternal deaths. Interventions such as prenatal care, postpartum care, family planning and safe abortion are justified after near birth interventions are already in place. They also assert that the single interventions with strong evidence are only effective at reducing MMR in populations if they are part of component packages that are distributed widely.

The focus of community-level interventions is generally primary prevention and may include distribution of vitamins and supplements to all pregnant women in the community. Others have focused on training community health workers or traditional birth attendants to recognize the early warning signs of pregnancy risks and refer mothers for clinical care. Community-level interventions also occur prior to pregnancy by reducing the risk factors and indirect causes for adverse pregnancy outcomes. Mothers who begin their pregnancies with anemia, malaria, tuberculosis, diabetes or malnutrition are at highest risk; therefore, interventions to eliminate these indirect causes of maternal mortality in the community are essential. Risk factors such as the extremes of maternal age, short intervals between pregnancies, and lack of formal education also need to be addressed at the community-level. Unsafe abortions account for 67 900 maternal deaths annually (13% of total maternal mortality). These deaths are preventable by providing safe, accessible abortion care as well as by addressing ‘restrictive abortion legislation, lack of female empowerment, poor social support, inadequate contraceptive services and poor health service infrastructure’. Community-level interventions are especially necessary in low-income countries where the majority of infants are delivered at home and often without the support of a trained birth attendant.

Medical interventions are an essential component of comprehensive national plans to reduce maternal mortality since the highest risk patients need to be referred to hospitals and clinics for emergency, life saving, drugs and medical procedures. A comprehensive national program to reduce maternal deaths should include support for both clinical and community-level interventions. This paper identifies the clinical and community-level interventions that have been established as effective in reducing maternal mortality and that could be employed in sub-Saharan Africa.

**Methods**

To find effective interventions and policies that could be used in sub-Saharan Africa, a systematic review of published literature was conducted. This paper describes the first stage of analysis: examination of the Cochrane reviews with the specific outcome of maternal death. The Cochrane Collaboration promotes the search for evidence-based health care by producing and disseminating systematic reviews of clinical trials and other studies of interventions.

A search was conducted using ‘maternal mortality’ as key word and limited to the publication years from 1998 to 2008,
which resulted in 390 titles of Cochrane reviews (see Fig. 1). Two hundred and fifty titles clearly indicated that the outcomes measured were related to infant or fetal mortality and morbidity and were thus excluded from the compilation. After further screening the abstracts of the remaining 139 reviews, those that represented protocols rather than actual reviews and reviews with outcomes of infant or fetal mortality or morbidity were excluded. Seventy-six full text reviews were examined. The Cochrane reports clearly indicate the outcome of analysis in the index, and this allowed for the exclusion of 55 reviews which did not include maternal death as a specific outcome. Two additional reviews were excluded because they had been withdrawn from the Cochrane database. The results of the remaining 19 Cochrane reviews are compiled below and not re-analyzed since strict protocols were implemented in including clinical trials in the existing analyses.

**Results**

A mineral supplement (calcium supplements), a class of drugs (antihypertensive) and five drugs prescribed for specific high-risk conditions in pregnant women were shown to reduce the risk of maternal death (see Table 1). Specifically, calcium supplements given during pregnancy prevented hypertensive disorders, related disorders and ultimately maternal death. The risk of severe hypertension and subsequent maternal death was reduced by administering any antihypertensive drug to pregnant women with mild to moderate high blood pressure. Dexamethasone, a corticosteroid prescribed for HELLP syndrome (Hemolysis, elevated liver enzymes and low platelets), reduced maternal deaths. Ketanserin and Nifedipine administered for very high blood pressure in pregnancy also reduced the risk of maternal death. Magnesium sulfate prescribed for pre-eclampsia or eclampsia significantly reduced the risk of maternal death.

Five of the Cochrane reviews demonstrated an increase in risk of maternal death with the administration of particular drugs to high-risk pregnant women (see Table 2). Specifically, antiplatelet agents prescribed for preventing pre-eclampsia and its complications, beta-blockers prescribed for mild hypertension, and Prostaglandins and Misoprostol prescribed for preventing postpartum hemorrhage all increased the risk of death to pregnant women. The procedure amniotomy, which is the intentional artificial rupture of the amniotic membrane during labor, also increased the risk of maternal death.
Two of the Cochrane reviews looked at several studies and interventions which did not significantly alter maternal mortality outcomes (see Table 3). The studies found that the use of antioxidants to prevent pre-eclampsia did not reduce or increase the risk of death and training traditional birth attendants did not significantly reduce the maternal mortality ratios in the one study that met the inclusion criteria.

Five of the Cochrane reviews found that it was not possible to measure variance in some of the studies because maternal death did not occur. These reviews were analyzed: antenatal daycare units versus inpatient care, any planned early birth versus expectant management for prelabor rupture of membranes at term, routine postnatal oral antihypertension therapy for prevention of postpartum hemorrhage, rectal misoprostol versus placebo and intravenous iron versus regular iron.

**Discussion**

**Main findings of this study**

This Cochrane review identified three medical, prevention strategies which were shown to produce significant improvements in maternal mortality:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>RR</th>
<th>95% CI</th>
<th>Studies</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo versus any antihypertensive drug (Abalos et al.11)</td>
<td>0.35</td>
<td>(0.33, 0.37)</td>
<td>Four</td>
<td>376</td>
</tr>
<tr>
<td>Calcium Supplementation (Hofmeyr et al.10)</td>
<td>0.17</td>
<td>(0.02, 1.39)</td>
<td>One</td>
<td>8312</td>
</tr>
<tr>
<td>Dexamethasone plus standard treatment versus standard treatment for HELLP syndrome (Matchaba and Moodley12)</td>
<td>0.33</td>
<td>(0.01, 7.65)</td>
<td>One</td>
<td>34</td>
</tr>
<tr>
<td>Ketanserin versus hydralazine for treating very high blood pressure (Duley et al.13)</td>
<td>0.32</td>
<td>(0.03, 2.96)</td>
<td>Two</td>
<td>124</td>
</tr>
<tr>
<td>Nifedipine versus prazosin for treating very high blood pressure (Duley et al.13)</td>
<td>0.32</td>
<td>(0.01, 7.73)</td>
<td>One</td>
<td>145</td>
</tr>
<tr>
<td>Magnesium sulfate versus placebo for treating pre-eclampsia (Duley et al.14)</td>
<td>0.54</td>
<td>(0.26, 1.10)</td>
<td>Two</td>
<td>10795</td>
</tr>
<tr>
<td>Magnesium sulfate versus diazepam for treating pre-eclampsia (Duley and Henderson-Smart15)</td>
<td>0.59</td>
<td>(0.37, 0.94)</td>
<td>Six</td>
<td>1336</td>
</tr>
<tr>
<td>Magnesium sulfate versus phenytoin for treating pre-eclampsia (Duley and Henderson-Smart15)</td>
<td>0.50</td>
<td>(0.24, 1.05)</td>
<td>Two</td>
<td>797</td>
</tr>
<tr>
<td>Magnesium sulfate versus lytic cocktail for treating eclampsia (Duley and Gulmezoglu17)</td>
<td>0.25</td>
<td>(0.04, 1.43)</td>
<td>Two</td>
<td>198</td>
</tr>
</tbody>
</table>

Outcome included maternal death and severe maternal morbidity.

Two of the Cochrane reviews looked at several studies and interventions which did not significantly alter maternal mortality outcomes (see Table 3). The studies found that the use of antioxidants to prevent pre-eclampsia did not reduce or increase the risk of death and training traditional birth attendants did not significantly reduce the maternal mortality ratios in the one study that met the inclusion criteria.

Five of the Cochrane reviews found that it was not possible to measure variance in some of the studies because maternal death did not occur. These reviews were analyzed: antenatal daycare units versus inpatient care, any planned early birth versus expectant management for prelabor rupture of membranes at term, routine postnatal oral antihypertension therapy for prevention of postpartum hemorrhage, rectal misoprostol versus placebo and intravenous iron versus regular iron.

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<th>n</th>
</tr>
</thead>
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<tr>
<td>Antiplatelet agents versus placebo (Duley et al.18)</td>
<td>2.57</td>
<td>(0.39, 17.06)</td>
<td>Three</td>
<td>257</td>
</tr>
<tr>
<td>Amniotomy (Smyth et al.22)</td>
<td>3.0</td>
<td>(0.12, 73.61)</td>
<td>Three</td>
<td>552</td>
</tr>
<tr>
<td>Beta-blocker versus placebo for treating mild to moderate hypertension (Magee and Duley19)</td>
<td>2.92</td>
<td>(0.12, 70.68)</td>
<td>Two</td>
<td>206</td>
</tr>
<tr>
<td>Prostaglandins for preventing post-partum hemorrhage (Gümezoglu et al., 200720)</td>
<td>1.46</td>
<td>(0.24, 8.81)</td>
<td>Two</td>
<td>2849</td>
</tr>
<tr>
<td>Sublingual misoprostol versus placebo preventing post-partum hemorrhage (Gümezoglu et al., 200720)</td>
<td>3.01</td>
<td>(0.12, 73.60)</td>
<td>One</td>
<td>661</td>
</tr>
<tr>
<td>Placebo versus Misoprostol preventing post-partum hemorrhage (Mousa and Alfirevic21)</td>
<td>1.38</td>
<td>(2.63, 0.007)</td>
<td>Two</td>
<td>398</td>
</tr>
</tbody>
</table>
reductions in maternal mortality. Dexamethasone, a cortico-steroid prescribed for HELLP syndrome,\textsuperscript{11} Ketanserin and Nifedipine, administered for very high blood pressure in pregnancy,\textsuperscript{12} and magnesium sulfate, prescribed for pre-eclampsia or eclampsia, significantly reduced the risk of maternal death.\textsuperscript{13,15,16} These drugs should be made available in local clinics and referral hospitals given their effectiveness in preventing maternal deaths.

What is already known on this topic

The core list of essential medicines includes the ‘minimum medicine needs for a basic health care system, listing the most efficacious, safe and cost-effective medicines for priority conditions’.\textsuperscript{29} Three of the four drugs proven to reduce maternal mortality are listed by the WHO as essential medicines.\textsuperscript{29} Ketanserin is not included in the list though it has been shown to reduce maternal mortality. Eclampsia and postpartum hemorrhage are not listed as priority conditions by the WHO although they are the most prevalent causes of maternal death.\textsuperscript{13,15,16} These drugs should be made available in local clinics and referral hospitals given their effectiveness in preventing maternal deaths.

What this study adds

One Cochrane review that included a clinical trial in sub-Saharan Africa, specifically South Africa,\textsuperscript{10} found that antihypertensives given to pregnant women with high blood pressure reduced the risk of maternal death. Pregnant women with diastolic blood pressure over 90 mmHg were given antihypertensive drugs in the second or third trimester of pregnancy in clinical settings. Global health researchers need to examine the feasibility of new strategies for widespread use of antihypertensives for pregnant women who do not receive medical/clinical prenatal care.

Limitations of this study

Only one review examined a community-based intervention, training of traditional birth attendants in Malawi,\textsuperscript{22} and found no significant effect in reducing maternal deaths. The 2 or 3 day training of traditional birth attendants did increase some important practices and improved measures for the infant such as: immediate feeding of colostrum, introduction of complementary foods and reduction in perinatal death, stillbirth and neonatal death. Intermediate maternal outcomes such as frequency of referral to a health facility for a complication of pregnancy during delivery or postpartum period and mean number of monthly and timely referrals were also significantly increased in the intervention areas. However, measures of severe maternal morbidity, such as obstructed labor, hemorrhage and sepsis, were not significantly reduced nor were maternal mortality. This may be attributed to the significantly higher frequency of obstructed labor among women living in intervention clusters compared with women living in control clusters. It is also important to note that the training of traditional births attendants did not include blood pressure measurement. High blood pressure is a risk factor for both hemorrhage and eclampsia, which account for 37\% of maternal deaths worldwide.

Conclusion

In sub-Saharan Africa where the majority of births are at home, effective community-based interventions are urgently needed. To reach the Millennium Development Goal of reducing maternal mortality by three-quarters by 2015, global public health programs need to make community-wide and nationwide progress. The evidence base of community-level and clinical interventions must be promptly developed and disseminated. There is an urgent need for more clinical trials and high-quality, evaluated, community intervention trials examining maternal death in low-income countries.
sub-Saharan African nations where the risk is highest. Failure to do so will subject millions of young African women and girls to premature and needless death.

References


