SEASONAL VARIATION IN THE RISK AND CAUSES OF MATERNAL DEATH IN THE GAMBIA: MALARIA APPEARS TO BE AN IMPORTANT FACTOR

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Abstract. An increase in maternal mortality risk during peak malaria transmission in endemic countries is thought to implicate malaria in maternal deaths. The purpose of this study was to evaluate changes in risk and causes of maternal death in relation to the malaria season at the main referral hospital in The Gambia. During the malaria season, there was a 168% increase in the maternal mortality ratio (MMR), a three-fold increase in the proportion of deaths due to anemia, and an eight-fold increase in the anemia MMR. Apart from a 5.4-fold increase in eclampsia, there was no significant change in the contribution of other causes of death. It is estimated that malaria may account for up to 93 maternal deaths per 100,000 live births.

INTRODUCTION

Concern about unacceptably high maternal mortality ratios (MMRs) in developing countries led to the launching of the Safe Motherhood Initiative in 1987 with the main focus on obstetric factors such as hemorrhage, pre-eclampsia/eclampsia, puerperal sepsis, obstructed labor and abortions. However, recently increasing interest has been shown in the potential contribution of malaria to maternal mortality in endemic countries. One method has been by assessing variation in maternal mortality risk with periods of increased malaria transmission.

The purpose of this study was to determine whether the risk of maternal mortality and or the causes of maternal death varied with the malaria season at the main referral hospital in The Gambia. The study also provided an opportunity to determine the extent to which the previous Safe Motherhood Initiative goal of a 50% reduction of the MMR by the year 2000 was achieved in the hospital.

MATERIALS AND METHODS

The Gambia is located on the west African Atlantic coast and is bordered by Senegal to the north, east, and south. There are two climatic seasons, a long dry season from November to June and a short rainy season from July to October. Malaria is endemic with peak transmission during and shortly after the rainy season. More than 90% of pregnant women receive antenatal care with 70% of them having four or more visits. The Royal Victoria Hospital (RVH) is the main referral hospital in the country and more than 85% of pregnant women in Banjul deliver there. Only 3.4% of pregnant women receive antimalarial prophylaxis during pregnancy (Department of State for Health, Banjul, The Gambia, unpublished data).

Maternal deaths during the period from January 2001 to December 2002 were identified from the maternal mortality register maintained in the maternity unit of the Royal Victoria Teaching Hospital. The register was opened in August 2000 and includes women who died while pregnant or up to 42 days after pregnancy. Women who died as a result of abortions, accidents, or intentional injuries are not included. Cause of death is assigned based on clinical findings supported by laboratory results where available. Anemia was defined clinically by degree of pallor. Patients with severe anemia were marked pale (paper white). When available, a hemoglobin concentration of less than 7 g/dL also defined severe anemia.

The number of births during the same period was obtained from delivery registers in the central records office. The births and maternal deaths were grouped into two periods, January to August and September to December. The latter period corresponded to peak malaria transmission time and part of the rainy/farming season. During this period, malaria parasitemia rates among adults increase from approximately 10% in September to 21% in October and peak at 45% in November before decreasing to 30% in December, 10% in January, and 3% in May. Thus, parasitemia rates at the peak of malaria transmission in October and November are 7–15 times the basal rate in the non-malaria season.

The MMR was calculated as number of maternal deaths per 100,000 live births. Seasonal variations in risk and causes of death were assessed using the chi-square test. Relative risk (RR) is also presented, with 95% confidence intervals. The MMR and causes of death from January 1991 to December 1992 at the same hospital were obtained from a published report and are also presented. The study protocol was reviewed and approved by the Department of State for Health (Banjul, The Gambia).

RESULTS

Maternal mortality ratio. The number of births in 2001–2002 and 1991–1992 were similar, but there was an increase in the number of maternal deaths in 2001–2002 (Table 1). This resulted in a 52.3% increase in the MMR in 2001–2002 compared with 1991–1992 (P = 0.005).

Causes of death. The only significant change was the increase in deaths due to anemia in 2001–2002 (Table 2). There was a four-fold increase in the proportion of maternal deaths due to anemia to 32% in 2001–2002 from 8% in 1991–1992 (RR = 4.0, 95% confidence interval = 1.8–9.0, P = 0.0002) and a six-fold increase in the MMR due to anemia in 2001–2002 (P = 0.000003).

Anemia accounted for 77.9% of the 52% increase in the MMR in 2001–2002 compared with 1991–1992. This is based on the formula \[ \text{anemia MMR 2001–2002} = \text{anemia MMR 1991–1992} + \left( \frac{\text{anemia MMR 2001–2002} - \text{anemia MMR 1991–1992}}{\text{MMR 2001–2002} - \text{MMR 1991–1992}} \right) \times 100 = \left( \frac{300}{385} \right) \times 100. \]
TABLE 1

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Total births</td>
<td>11,936</td>
<td>11,327</td>
<td>1.0 (1.0–1.0)</td>
</tr>
<tr>
<td>Live births</td>
<td>10,882</td>
<td>10,590</td>
<td>1.0 (1.0–1.0)</td>
</tr>
<tr>
<td>Maternal deaths</td>
<td>122</td>
<td>78</td>
<td>1.6 (1.3–2.0)</td>
</tr>
<tr>
<td>Maternal mortality ratio</td>
<td>1,121</td>
<td>737</td>
<td>1.5 (1.4–2.0)</td>
</tr>
</tbody>
</table>

‡ From Hoestermann and others.‡
† P = 0.005.

Seasonal variations. Maternal mortality ratio. There was a 168% increase (P < 0.000001) in the risk of maternal death during the malaria season (Table 3).

Causes of death. Table 4 shows that during the malaria season there was an eight-fold increase in risk of death for anemia (P < 0.000001) and a 5.4-fold increase for eclampsia (P = 0.008). The differences in the MMR due to hemorrhage (P = 0.6) and other individual causes of death were not statistically significant. Figure 1 shows the seasonality of maternal mortality risk and anemia-specific maternal mortality over five seasons. Both increased during the malaria season and decreased during the non-malaria season.

DISCUSSION

Two community-based maternal mortality surveys using the sisterhood method support the observation that anemia is the leading cause of maternal death in The Gambia. A recent nationwide survey of maternal mortality found that women were most likely (27%) to have features suggestive of anemia just before death (Department of State for Health, Banjul, The Gambia, unpublished data). Hemorrhage was the second commonest antecedent event. In a smaller localized study, anemia occurred in 22% of the women and was second only to hemorrhage (33%). The sisterhood method is an indirect method of obtaining population-based estimates of MMRs by asking a sample of women 15–49 years old how many of their sisters reached the age of 15 and how many of them died while pregnant, during delivery, or up to six weeks after the end of pregnancy.

Anemia is the main consequence of maternal mortality of women in malarious areas. Thus, the marked increase in the MMR due to anemia during the peak period of malaria transmission suggests that malaria is a significant factor in maternal deaths in The Gambia. An increase in malaria-related anemia during and following the rainy season has been reported elsewhere, and there has been increasing demonstration of the contribution of malaria to severe anemia.

In addition to malaria, nutritional deficiencies may increase the risk and severity of anemia during the rainy season as a result of food shortages at this time. Hookworm infestation is another potential etiologic factor because this period is also the farming season. A combination of these factors is most likely, especially for women with severe anemia, among whom the risk of death is greatest.

However, the 7–15-fold increase in parasitemia rates at the peak of malaria transmission appears to be of sufficient magnitude to explain the eight-fold increase in the anemia-specific MMR during the malaria season.

Severe anemia is a recognized cause of maternal death but the role of mild to moderate anemia is controversial. However, they may contribute to maternal deaths by limiting the ability to withstand hemorrhage including the usual blood loss associated with normal delivery. Anemia may also increase the risk of puerperal sepsis and the ability to recover from it. Similarly, both hemorrhage and septicaemia may worsen anemia.

Apart from an effect through anemia, malaria may contribute to maternal mortality by increasing the risk and severity of obstetric conditions such as pre-eclampsia/eclampsia and postpartum hemorrhage. In two west African countries, an increase in the incidence of eclampsia was observed during the rainy season when malaria transmission increases. In a third west African country (Senegal, which surrounds The Gambia on three sides), pre-eclampsia was commoner during the rainy season and associated with placental malaria. In the present study, there was a 5.4-fold increase in the MMR due to eclampsia during the malaria season.

Table 3

<table>
<thead>
<tr>
<th>Causes of maternal death</th>
<th>January–August MMR (number)</th>
<th>September–December MMR (number)</th>
<th>Relative risk September–December/January–August (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live births</td>
<td>6,486 (59.6)</td>
<td>4,396 (40.4)</td>
<td>1.5 (1.9–3.9)</td>
</tr>
<tr>
<td>Maternal deaths</td>
<td>43 (35.2)</td>
<td>79 (64.8)</td>
<td></td>
</tr>
<tr>
<td>Maternal mortality ratio</td>
<td>663</td>
<td>1,797</td>
<td></td>
</tr>
</tbody>
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* P < 0.000001.

Table 4
Seasonal variation in maternal mortality ratio due to anemia, eclampsia, and hemorrhage

<table>
<thead>
<tr>
<th>Causes of maternal death</th>
<th>January–August MMR (number)</th>
<th>September–December MMR (number)</th>
<th>Relative risk September–December/January–August (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>93 (6)</td>
<td>751 (33)</td>
<td>8.1 (3.4–19.2)</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>46 (3)</td>
<td>250 (11)</td>
<td>5.4 (1.5–19.3)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>247 (16)</td>
<td>182 (8)</td>
<td>0.7 (0.32–1.7)</td>
</tr>
</tbody>
</table>

* MMR = maternal mortality ratio.
† P < 0.000001.
‡ P = 0.005.

TABLE 2

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<tr>
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</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>358 (39)</td>
<td>57 (6)</td>
<td>6.3 (2.7–14.9)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>221 (24)</td>
<td>170 (18)</td>
<td>1.3 (0.7–2.4)</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>129 (14)</td>
<td>66 (7)</td>
<td>2.0 (0.8–4.8)</td>
</tr>
<tr>
<td>Septicemia</td>
<td>64 (7)</td>
<td>104 (11)</td>
<td>0.6 (0.2–1.6)</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>55 (6)</td>
<td>85 (9)</td>
<td>0.7 (0.2–1.8)</td>
</tr>
<tr>
<td>Malaria</td>
<td>37 (4)</td>
<td>47 (5)</td>
<td>0.8 (0.2–2.9)</td>
</tr>
<tr>
<td>Uterine rupture</td>
<td>18 (2)</td>
<td>47 (5)</td>
<td>0.4 (0.1–2.0)</td>
</tr>
<tr>
<td>Others</td>
<td>239 (26)</td>
<td>161 (17)</td>
<td>1.5 (0.8–2.7)</td>
</tr>
</tbody>
</table>

* MMR = maternal mortality ratio.
† Adapted from Hoestermann and others.
‡ P = 0.000003.
During pregnancy, malaria is often unsuspected and because some degree of pre-existing immunity is retained look. Although pregnant women in endemic areas have been difficult essentially because malaria is often over-estimated to cause up to 33% of severe maternal anemia. Furthermore, peripheral blood films underestimate the link between malaria, obstetric disorders, and maternal death has been recommended.

There have been efforts to quantify the contribution of malaria to maternal morbidity and mortality with the expectation that this would provide evidence necessary to improve the effectiveness of advocacy to incorporate malaria-prevention strategies in Safe Motherhood Programs. This has been difficult essentially because malaria is often overlooked. Although pregnant women in endemic areas have higher rates of parasitemia and parasite density compared with non-pregnant women, infection is largely asymptomatic because some degree of pre-existing immunity is retained during pregnancy. Thus, malaria is often unsuspected and uninvestigated despite being associated with severe anemia, which is the main maternal consequence of malaria and the mechanism by which malaria causes maternal death in endemic areas. Furthermore, peripheral blood films underestimate the prevalence of malaria in pregnancy because the parasite is frequently sequestered in the placenta.

Quantifying the contribution of malaria to severe anemia remains a challenge. In one review article, the contribution of malaria to severe anemia was estimated as 7.3% based on six studies. However, this was thought to be an underestimate because those studies relied on peripheral blood films and did not account for placental malaria. An alternative figure of 26% based on one antimalarial prophylaxis trial in Burkina Faso was used to estimate that malaria might have caused severe maternal anemia in up to 400,000 women in sub-Saharan Africa in 1995. In Kilifi, Kenya, malaria has been estimated to cause up to 33% of severe maternal anemia.

These figures may not reflect the true situation in The Gambia, but in the absence of specific data provide an indication of the potential contribution of malaria to anemia and maternal mortality. In the present study, there were 358 anemia deaths in 100,000 live births. If 26% were due to malaria, the malaria-attributable mortality ratio will be 93/100,000 live births. This figure would conform to the hypothesis that when all-cause mortality exceeds 400/100,000 births, malaria-attributable mortality in endemic areas increases above 50/100,000 births.

There is also concern regarding the increasing incidence of malaria and malaria-related morbidity in sub-Saharan Africa and this study provides some evidence for such concern. There was a marked (four-fold) increase in the proportion of maternal deaths due to anemia, and a six-fold increase in the MMR due to anemia in this study compared with 10 years ago. Thus, anemia accounted for about 78% of the (52%) increase in the MMR at the hospital. Applying the 26% assumption again suggests that a rise in malaria-attributable mortality (through anemia) accounted for 20% of the increase in maternal mortality at the hospital in 2001–2002 compared with 1991–1992. Although, there was an increase in the number of deaths due to eclampsia and hemorrhage in the latter period, their proportions decreased and the difference in the MMR was not significant. Thus, the increase in anemia and potentially malaria was the major reason for the increase in risk of death in the latter period.

One of the advantages of hospital-based studies is the ability to obtain better information regarding the specific causes of death compared with community surveys using verbal autopsy. However, problems with classification cannot be completely excluded. In many cases, multiple conditions existed prior to death. In our register, an effort is made to assign the cause of death to anemia only in the absence of hemorrhage or septicemia. This may not be foolproof. Determination of cause of anemia was often incomplete prior to death and this prevented the establishment of a direct association between malaria and anemia.

Anemia appears to be the greatest barrier to maternal survival in The Gambia. Routine iron and folate supplementation is undertaken in the antenatal clinic, but there are suggestions it may be ineffective for a variety of reasons. The seasonal variation suggests that malaria plays a significant role in the etiology of anemia in pregnancy. Efficient blood transfusion services remain a challenge and the goal should be the prevention of anemia.

A comprehensive evaluation is required. This should determine the prevalence of anemia, assess seasonal variations, and evaluate the contribution of malaria and other etiologic factors. The availability of and compliance with iron and folate supplementation should be appraised and barriers to effective malaria control identified. A maternal mortality reduction strategy should be developed based on the evidence gathered. With the high antenatal attendance, universal coverage for an effective malaria and anemia control program is feasible. This in turn should lead to a significant reduction in maternal mortality.

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