THE EPIDEMIOLOGY AND BURDEN OF \textit{PLASMODIUM FALCIPARUM}-RELATED ANEMIA AMONG PREGNANT WOMEN IN SUB-SAHARAN AFRICA

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Abstract. The paucity of precise information on the burden of malaria among pregnant women has hampered effective lobbying for the inclusion of preventive strategies against malaria in Safe Motherhood Initiatives. This article reviews the evidence on the coincidental risks of malaria and anemia in Africa and attempts to estimate the probable burden of malaria-related severe anemia in this susceptible group. Twenty-six studies on hemoglobin levels in all-parity pregnant women throughout this region could be matched with a malaria parasite ratio in children < 15 yr old (a measure of the intensity of transmission). In areas with no malaria, the mean hemoglobin levels were markedly higher than those found in areas with stable malaria transmission, though changes with increasing intensity of transmission were unclear. Eighteen studies from areas with stable malaria transmission in sub-Saharan Africa suggested that the median prevalence of severe anemia in all-parity pregnant women is approximately 8.2%. Assuming that 26% of these cases are due to malaria, it is suggested that as many as 400,000 pregnant women may have developed severe anemia as a result of infection with malaria in sub-Saharan Africa in 1995.

INTRODUCTION

In sub-Saharan Africa the causes of anemia during pregnancy are multifactorial. They include an iron- and folate-deficient diet and infections such as malaria, hookworm, and increasingly human immunodeficiency virus (HIV). Most of these conditions are preventable through increased awareness by the community and through access to affordable interventions. Both international donors and national governments must prioritize investment in overall health service delivery. This is particularly true in resource-constrained sub-Saharan Africa. There is an increasing move to provide credible evidence-based estimates of disease risk and burden for the setting of health priorities.\textsuperscript{1} It is generally accepted that in malaria-endemic areas, \textit{Plasmodium falciparum} is a major contributor to anemia in pregnancy. Nevertheless, a systematic review of the evidence and its relationship to disease burden is lacking. These lacunae have hampered effective lobbying for the inclusion of malaria prevention in the new Safe Motherhood Initiatives.\textsuperscript{2}

This article reviews the available evidence on the coincidental risks of anemia and malaria among pregnant women in sub-Saharan Africa.

METHODS

Anemia in pregnant women and malaria endemicity. A literature search was undertaken for data on anemia in pregnant women in sub-Saharan Africa. MEDLINE and CAB HEALTH were searched with combinations of the following keywords: anemia, hemoglobin, anemic, PCV, hematocrit and pregnancy, pregnant women, and Africa. Manual searches of predigital journals for the major tropical journals were also made for possible data sources. The bibliographies of all articles collected were checked for additional references. All studies that recorded the mean hemoglobin or packed cell volume (PCV) and/or severe anemia (as defined below) in a sample of pregnant women > 30 yr were extracted from the literature and included in the analysis. Where possible, the data were summarized separately for all parities, primigravidae, and multigravidae. For each data point, the date of survey, gestational age at assessment, measurement technique, description of study, and cutoff for severe anemia were recorded. The exact location of each study was recorded as longitude and latitude using a combination of ENCARTA (World Atlas, Microsoft, 1998) and topographical maps.

One commonly used measure for the intensity of malaria transmission is the cross-sectional prevalence of infection among asymptomatic children below 15 yr of age (malaria parasite ratio). The exact locations of the anemia surveys were used to find corresponding data on malaria parasite ratio. As far as possible, these studies were matched by location and date of survey.

Differences in the hemoglobin values by parity groups and malaria endemicity were expressed as medians with upper and lower quartiles. Significant differences were tested using a 1-tailed Mann-Whitney \textit{U} test in SPSS (Release 7.0, SPSS Inc., Chicago, IL 1989–1995).

Measuring anemic status. One of the problems in assimilating the evidence of an impact of malaria on anemia in pregnancy is the heterogeneity in the techniques used to measure anemia, the parameter measured (hemoglobin or packed cell volume [PCV]), and the cutoff used. For the purposes of this analysis the following assumptions were made. Severe anemia was defined as a hemoglobin < 7 g/dL or < 8 g/dL or a PCV < 30% or < 25%. Mean PCV values (in earlier studies denoted as hemocrit values) were converted to mean hemoglobins by applying the constant factor of 0.3.\textsuperscript{3} All techniques for measuring hemoglobin and PCV were included except the use of the Talquist method and pallor to define anemia. Most studies measuring PCV used microhemocrit centrifugation, but the techniques used for hemoglobin ranged from the very simple portable Hemoglobinometers through to the more complex Cyanmethemoglobin method.

There was also a great deal of heterogeneity in the gestational age at which measurements were taken. In an attempt to minimize these differences, values were taken as close to term as possible.

Defining populations at risk of malaria-related severe anemia. An attempt is made to estimate the number of se-
vere anemia cases in pregnant women in sub-Saharan Africa that are due to malaria. The parameter values used for this analysis are summarized in Table 1. The population in sub-Saharan Africa (excluding the southern African countries of Botswana, Lesotho, Namibia, South Africa, Swaziland, and Zimbabwe) in 1995 that was exposed to stable malaria has been estimated at 447 million. These southern African countries have been excluded from the calculations, because aggressive vector control combined with active case detection and treatment artificially maintains a situation of virtual elimination of malaria risk. The estimate of 447 million was based on a climate-based model used to predict the likely occurrence of *P. falciparum* transmission, combined with interpolated models of population distribution. It must be noted that this population will be exposed to a wide range of transmission intensities, ranging from 1 infective bite every 2nd yr to several infectious bites every night. The number of pregnant women was assessed from the crude birth rate for sub-Saharan Africa (42 per 1,000 population; 1999 Population Reference Bureau, Washington, DC). This will represent an underestimate, because those women experiencing miscarriages and stillbirths are not included. The number of pregnant women with malaria-related severe anemia was determined from the prevalence of severe anemia in areas with stable malaria transmission (data presented below) and from the proportion of severe anemia cases due to malaria (based on the available evidence from cross-sectional and intervention studies reviewed below).

**RESULTS**

**Anemia and malaria endemicity.** Table 2 summarizes the data on anemia (mean hemoglobin and severe anemia) by parity and malaria endemicity in sites throughout sub-Saharan Africa. These data represent a total of 21 countries and 44 individual study sites throughout the continent (Figure 1).

A total of 24 studies from different localities in sub-Saharan Africa were identified that assessed the mean hemoglobin (g/dL) in pregnant women of all parities. Of these, 21 sites could be matched with a malaria parasite ratio, Packed cell volume values in pregnant women were available for 7 additional sites, 5 of which could be matched with a malaria parasite ratio (Table 2). One of these studies corresponded to 2 data points, mean PCVs, and parasite ratios for the wet and the dry season in Sikasso region of Mali.

The mean PCVs were converted into hemoglobins using the conversion factor of 0.3.

Figure 2 presents the relationship between mean hemoglobin in all-parity pregnant women and the malaria parasite ratio in the 26 localities. The relationship is markedly nonlinear, with those areas at very low or no risk of malaria having high but variable mean hemoglobins and with those at any risk having more consistent lower mean hemoglobin levels. From the data available, there appears to be no indication of decreasing hemoglobin levels with increasing endemicity as judged by the parasite ratio among children < 15 yr in the same areas. Taking only those 21 studies that reported hemoglobin, the median levels in those with no or very low risk (≤ 5% parasite ratio, n = 7) was 11.4 g/dL (11.0–11.6 lower and upper quartiles) compared to 10.1 g/dL (9.4–10.6) for those at any risk of malaria (n = 14; U = 0.5, P < 0.001). The difference was even greater when the altered PCV values were included: 9.7 g/dL (9.5–10.5; n = 8) compared to 11.6 g/dL (11.2–12.7; n = 19; U = 0.5, P < 0.001).

The data available on the relationship between the mean hemoglobin and parasite ratio for primigravidae only are more limited in number (n = 15) (Figure 3). As with the all-parity data, there is a marked difference in the mean hemoglobins between areas with and without stable malaria transmission. However, in primigravidae there also seems to be a decline in the levels of hemoglobin with increases in the parasite ratio. Although the number of studies is too small to make meaningful statistical comparisons, it is interesting to note that the median hemoglobins for parasite ratio groups of < 20%, 20–60%, and > 60% were 12.3 g/dL (11–13.4; n = 4), 10.1 g/dL (9.3–10.9; n = 7), and 9.2 g/dL (8.8–9.4; n = 4), respectively.

**The prevalence of severe anemia in areas with stable malaria.** A total of 18 studies from different localities in sub-Saharan Africa (excluding southern and northern Africa as shown in Figure 1) that experience a risk of malaria infection (childhood parasite ratio > 0%) reported the prevalence of severe anemia in women of all parities. The median of these studies was 8.2% (lower and upper quartiles: 4.5–10.3%). This compares to 11.3% (7.0–19.5%) for the median prevalence of severe anemia in primigravidae only (n = 8).

Comparisons between the prevalence of severe anemia (< 7 or < 8 g/dL) in primigravidae and multigravidae from the same locality were only available for 4 sites under conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Crude birth rate for sub-Saharan Africa</td>
<td>42 per 1,000 population</td>
<td>1999 Population Reference Bureau</td>
</tr>
<tr>
<td>Prevalence of severe anemia in all parties from areas with stable malaria transmission in sub-Saharan Africa</td>
<td>8.2% (4.3–10.3%)</td>
<td>Present study</td>
</tr>
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<td>Percentage of severe anemia cases due to malaria</td>
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<tr>
<td>1) cross-sectional data</td>
<td>7.3%</td>
<td>Present study (Table 3)</td>
</tr>
<tr>
<td>2) chemoprophylaxis trial</td>
<td>26%</td>
<td>5 (Table 4)</td>
</tr>
</tbody>
</table>

* Excluding the southern Africa countries of Botswana, Lesotho, Namibia, South Africa, Swaziland, and Zimbabwe.

† Median (lower-upper quartiles).

**Table 1**

Parameter values for calculating the burden of malaria-related severe anemia among pregnant women in sub-Saharan Africa.

Parameter Value Reference
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Population residing in areas with stable malaria transmission in sub-Saharan Africa in 1995* 447 million 4
Crude birth rate for sub-Saharan Africa 42 per 1,000 population 1999 Population Reference Bureau
Prevalence of severe anemia in all parties from areas with stable malaria transmission in sub-Saharan Africa 8.2% (4.3–10.3%)† Present study
Percentage of severe anemia cases due to malaria
1) cross-sectional data 7.3% Present study (Table 3)
2) chemoprophylaxis trial 26% 5 (Table 4)
<table>
<thead>
<tr>
<th>Country</th>
<th>Location</th>
<th>Date</th>
<th>Definition of severe anemia</th>
<th>Parity</th>
<th>Mean hemoglobin</th>
<th>Prevalence of severe anemia (%)</th>
<th>Data source for anemia</th>
<th>Parasite ratio (%)</th>
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<td>10</td>
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<td>P</td>
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<td>Dar-es-Salaam</td>
<td>1971</td>
<td>&lt; 7 g/dL</td>
<td>A</td>
<td>9.25</td>
<td>55</td>
<td>20.3</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P</td>
<td>9.18</td>
<td>10.95</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>9.01</td>
<td>9.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moshi</td>
<td>1991–1994</td>
<td>&lt; 7 g/dL</td>
<td>A</td>
<td>9.69</td>
<td>7.01</td>
<td>57</td>
<td>32.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Muheza</td>
<td>1988–1991</td>
<td>&lt; 8 g/dL</td>
<td>A</td>
<td>14.84</td>
<td>59</td>
<td>80</td>
<td>60</td>
<td></td>
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<tr>
<td></td>
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<td>P</td>
<td>9.2</td>
<td>20.95</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>9.5</td>
<td>11.71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zanzibar</td>
<td>1989–1990</td>
<td>≤ 7 g/dL</td>
<td>A</td>
<td>9.33</td>
<td>61</td>
<td>51.2</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P</td>
<td>9.0</td>
<td>–</td>
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<td></td>
<td>M</td>
<td>9.4</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Gambia</td>
<td>Farafenni</td>
<td>1984–1987</td>
<td></td>
<td>MI</td>
<td>9.12†</td>
<td>63</td>
<td>63.7</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Uganda</td>
<td>Kampala</td>
<td>1964</td>
<td>&lt; 7 g/dL</td>
<td>A</td>
<td>1.11</td>
<td>65</td>
<td>18.1</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1965</td>
<td></td>
<td>A</td>
<td>10.74</td>
<td>–</td>
<td>67</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Makindye</td>
<td>1990s</td>
<td>&lt;30% PCV</td>
<td>A</td>
<td>7.45</td>
<td>68</td>
<td>37.3</td>
<td>69</td>
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</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>P</td>
<td>11.07†</td>
<td>6.49</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>7.83</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zambia</td>
<td>Mbarara</td>
<td>1990s</td>
<td></td>
<td>A</td>
<td>9.3</td>
<td>–</td>
<td>70</td>
<td>18.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kimpese</td>
<td>1989–1990</td>
<td>&lt; 7 g/dL</td>
<td>A</td>
<td>10.01</td>
<td>72</td>
<td>64.7</td>
<td>73</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>P</td>
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<td>7.50</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>2.82</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>Ubangi</td>
<td>1980s</td>
<td></td>
<td>A</td>
<td>9.54†</td>
<td>–</td>
<td>74</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lusaka</td>
<td>1970s</td>
<td></td>
<td>A</td>
<td>11.0</td>
<td>–</td>
<td>75</td>
<td>&lt; 5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nchelenge</td>
<td>1973</td>
<td></td>
<td>P</td>
<td>11.2</td>
<td>–</td>
<td>77</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Harare</td>
<td>1970s</td>
<td></td>
<td>A</td>
<td>11.6</td>
<td>–</td>
<td>78</td>
<td>&lt; 2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P</td>
<td>11.7</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A = all parities; P = primigravidae; M = multigravidae; I = data for multigravidae or primigravidae not given due to a sample size < 30; . = secundigravidae included in primigravidae; PCV = packed cell volume.
† Converted from PCV.
‡ Median value.
§ Mean hemoglobins by parity group were obtained from the author (Caroline Shulman).
¶ An earlier study by Verhoeff and others (1998) on a much smaller sample size showed an mean hemoglobin in primigravidae of 8.8 compared to 9.5 in multigravidae.
sis associated with malaria infection. Attributable fraction analysis
and 11.8), implying a 26% increased risk of severe anemia
study sites was 1.26 (range for individual sites between 1.08
a peripheral blood smear, though the absolute and relative
prevalence of severe anemia was greater in those women
infected with malaria than in those without
anemia in relation to malaria infection for all parities were identi-
ed. Of these, 3 also provided results for primigravidae only. In all cases, the
prevalence of severe anemia was greater in those women
infected with malaria than in those without
P. falciparum in a peripheral blood smear, though the absolute and relative
difference varied widely (Table 3).

The combined prevalence or risk ratio for the 6 all-parity
study sites was 1.26 (range for individual sites between 1.08
and 11.8), implying a 26% increased risk of severe anemia
associated with malaria infection. Attributable fraction anal-
ysis suggests that 7.3% of all cases of severe anemia are
due to malaria infection (population attributable fraction)
(Table 3).

Effects of chemoprophyaxis/intermittent presumptive
treatment. There have been a number of intervention trials
that have monitored the impact of chemoprophyaxis/inter-
nittent presumptive treatment (IPT) on the prevalence of
severe anemia in pregnant women. Most of these studies
have focused on primigravidae (in 1 case including secun-
digravidae) (Table 4). The protective efficacy of antimalar-
ial chemoprophyaxis of these 4 studies ranges between 24%
and 55%. There are only 2 studies that record effects in all
parities, and these provide protective efficacies of 26%8 and
87%27 (Table 4). The latter seems an unlikely estimate, par-
cicularly because antimalarial treatment during pregnancy
was assessed retrospectively on the basis of questionnaires,
rather than prospectively as part of an intervention trial.

The burden of malaria in pregnant women in sub-Sa-
haran Africa. During the year 1995, a minimum of 18.8
million live births occurred in areas of stable malaria trans-
mission in sub-Saharan Africa. Assuming that this is the
minimum estimate of the number of pregnancies during
1995, and that 8.2% of pregnant women would have expe-
renced severe anemia, it seems reasonable to expect that at
least 1.5 million pregnant women in sub-Saharan Africa
would suffer from this condition in 1995.

We have used 2 estimates of the proportion of severe ane-
ia cases in pregnant women of any parity that can be at-
tributed to P. falciparum malaria: 1) the population attrib-
utable fraction from the 6 cross-sectional studies (7.3%: Ta-
ble 3), and 2) the population attributable fraction derived
from the chemoprophyaxis trial in Burkina Faso8 (26%: Ta-
ble 4). We therefore estimate that between 110,000 and
400,000 cases of malaria-related severe anemia may have
occurred among pregnant women in 1995 in stable malaria
transmission areas of sub-Saharan Africa.
An additional sensitivity analysis using the upper and lower quartiles for the prevalence of severe anemia (4.5–10.3%) suggests that the number of cases of malaria-related severe anemia could range between 200,000 and 500,000, assuming anemia could range between 200,000 and 500,000, assuming data source for the mean hemoglobin value: 1 = Addis Ababa (Ethiopia); 2 = Nouakchott (Mauritania); 3 = Harare (Zimbabwe); 4 = Kaduna (Nigeria); 5 = Dar-es-Salaam (Tanzania); 6 = Makindye (Kampala); 7 = Abidjan (Ivory Coast); 8 = Kilifi (Kenya); 9 = Zanzibar (Tanzania); 10 = Accra (Ghana); 11 = Zaria (Nigeria); 12 = Kimpese (Zaire); 13 = Chikwawa (Malawi); 14 = Asembo, Siaya, and Bondo (Kenya), 15 = Muheza (Tanzania). Five study sites measuring hemoglobin in all parities could not be matched with a malaria parasite ratio: Benin City (Nigeria),40 Nchelenge (Zaire); 77 Nangina (Kenya), 26 Banfora (Burkina Faso), 5 and Ebolowa (Cameroon).7

A more recent attempt to estimate the burden of malaria
on anemia in pregnancy have drawn upon randomized con-
trolled trials of chemoprophylaxis/IPT, and they suggest an
effect in primigravidae but not necessarily in multigravi-
dae.82 However, this review represented only 1 study that looked at protective effects on severe anemia (< 8 g/dL),
and this focused on primigravidae only (Shulman and others,
1999).81 This trial showed a protective efficacy of 39% in this
area, where prevalence of severe anemia is high (ap-
proximately 10% in all parities)21 and where malaria trans-
mission is intense, though seasonal (parasite rate of 49.2% in 0 to 9-yr-olds).22 It is unclear whether translating the re-
sults of a single study across the broad disease ecological
spectrum represented by malaria and anemia in Africa is
appropriate.

In this review, 26 studies on the levels of hemoglobin in
all parities, covering a wide range of intensities of malaria
transmission, were identified. The first observation from
these data was a clear and obvious association between the
overall hematological status of African pregnant women and
exposure to malaria infection (Figure 2). In areas with no
malaria, the mean hemoglobin levels were markedly higher
than those found in areas with stable malaria transmission.
The second observation from Figure 2 is that there is little
evidence to support decreasing mean hemoglobin levels in
pregnant women with increasing intensity of transmission.
This conclusion must be treated with some caution, because
anemia is clearly affected by a number of factors, which may
also not be independent. In addition, there is vast heteroge-
neity in the measurement techniques for both hemoglobin
and malaria parasite ratios, and there is no indication of the
true exposure of each woman from each study site. A slight-
ly different pattern may occur in primigravidae, where there
appears to be some decrease in hemoglobin levels, at least
at intense levels of malaria transmission (Figure 3). One of
the values of this type of meta-analysis is that it highlights

**DISCUSSION**

The most recent attempts to estimate the burden of malaria
on anemia in pregnancy have drawn upon randomized con-
trolled trials of chemoprophylaxis/IPT, and they suggest an
effect in primigravidae but not necessarily in multigravi-
dae. However, this review represented only 1 study that looked at protective effects on severe anemia (< 8 g/dL),
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1999). This trial showed a protective efficacy of 39% in this
area, where prevalence of severe anemia is high (approximately 10% in all parities) and where malaria trans-
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and malaria parasite ratios, and there is no indication of the
true exposure of each woman from each study site. A slight-
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appears to be some decrease in hemoglobin levels, at least
at intense levels of malaria transmission (Figure 3). One of
the values of this type of meta-analysis is that it highlights

**TABLE 3**

<table>
<thead>
<tr>
<th>Data source</th>
<th>Location</th>
<th>Definition of severe anemia</th>
<th>Sample size (infected/uninfected)</th>
<th>With malaria infection</th>
<th>Without malaria infection</th>
<th>Prevalence ratio†</th>
<th>Infected attributable fraction</th>
<th>Population attributable fraction†</th>
</tr>
</thead>
<tbody>
<tr>
<td>61</td>
<td>Zanzibar (Tanzania)</td>
<td>&lt; 7 g/dL</td>
<td>A</td>
<td>329 (158/171)</td>
<td>10.8%</td>
<td>9.9%</td>
<td>1.08</td>
<td>7.6%</td>
</tr>
<tr>
<td>21</td>
<td>Kilifi (Kenya)</td>
<td>&lt; 7 g/dL</td>
<td>P</td>
<td>73 (24/49)</td>
<td>13.9%</td>
<td>8.6%</td>
<td>1.62</td>
<td>38.1%</td>
</tr>
<tr>
<td>30</td>
<td>Chikwawa (Malawi)</td>
<td>&lt; 8 g/dL</td>
<td>A</td>
<td>3,668 (691/2,977)</td>
<td>28.1%</td>
<td>20.4%</td>
<td>1.52</td>
<td>27.4%</td>
</tr>
<tr>
<td>34</td>
<td>Mangochi (Malawi)</td>
<td>&lt; 30% PCV</td>
<td>P</td>
<td>801 (279/522)</td>
<td>37.6%</td>
<td>25.5%</td>
<td>1.77</td>
<td>32.3%</td>
</tr>
<tr>
<td>33</td>
<td>Lilongwe (Malawi)</td>
<td>&lt; 30% PCV</td>
<td>A</td>
<td>3,663 (1,630/2,033)</td>
<td>20.7%</td>
<td>18.3%</td>
<td>1.13</td>
<td>11.5%</td>
</tr>
<tr>
<td>5</td>
<td>Banfora (Burkina Faso)</td>
<td>&lt; 30% PCV</td>
<td>P</td>
<td>75 (19/56)</td>
<td>42.1%</td>
<td>3.6%</td>
<td>11.8</td>
<td>91.5%</td>
</tr>
<tr>
<td>Six studies combined</td>
<td></td>
<td></td>
<td>A</td>
<td>8,766 (2,648/6,118)</td>
<td>21.8%</td>
<td>17.3%</td>
<td>1.26</td>
<td>20.6%</td>
</tr>
</tbody>
</table>

* A = all parities; P = primigravidae; PCV = packed cell volume.
† The prevalence ratio (PR) is the proportion of infected women with severe anemia divided by the proportion of uninfected women with severe anemia; the infected attributable fraction is the percentage of infected women with severe anemia that is due to malaria ([PR − 1) / PR]; and the population attributable fraction is the percentage of severe anemia cases that are due to malaria infection ([S (PR − 1) / (1 + S (PR − 1))] where S is the proportion with malaria infection.)
gaps in our knowledge. There is a clear need to understand whether there are any associations between increasing levels of transmission and disease outcome, such as severe anemia, because this will have important implications for the impact of control interventions that reduce transmission, such as insecticide-treated bed nets. Further clarification of any differential effects in primigravidae and multigravidae is also required, as this may affect how these programs are targeted, with important consequences for overall cost.

The empirical evidence from cross-sectional studies on the association between malaria and anemia suggests that the effects are highly variable. A combined estimate for the proportion of severe anemia cases that could be attributed to malaria from the 6 studies of all-parity women was 7.3%. The accuracy of this value relies heavily on a correct diagnosis of malaria infection status. Because these studies defined infection status as the presence of parasitemia in a peripheral blood smear, it is probable that many women who harbored sequestered placcental infection were misclassified. It is therefore likely that 7.3% represents an underestimate of the proportion of severe anemia cases due to malaria. A more realistic value is represented by the protective efficacy achieved by chemoprophylaxis. There is only 1 prospective intervention trial that has assessed the impact for all parities, and it suggests that 26% of severe anemia cases could be due to malaria. The prevalence of severe anemia among pregnant women exposed to stable malaria transmission is estimated in this present review at approximately 8.2%. Given previous efforts to estimate populations exposed to the risk of stable malaria transmission in Africa, this combined evidence suggests that in 1995 as many as 400,000 pregnant women may have developed a severe anemia event as a result of malaria.

Severe anemia in pregnancy is associated with a high degree of physical and psychosocial morbidity. For instance, a recent study in Kilifi, Kenya, has shown that dizziness, breathlessness, and palpitations are 50–60% more frequent in pregnant women with severe anemia (<7 g/dL) compared with those with a hemoglobin of more than 9.9 g/dL. There is also good evidence that severe anemia increases the risk of maternal mortality. If one assumes a maternal mortality ratio for sub-Saharan Africa (excluding southern Africa) of 1,000 per 100,000 live births, this would translate to up to 10,000 malarial anemia-related deaths per year.

The more recent randomized control trials of 2 intermittent courses of sulfadoxine-pyrimethamine suggest that the incidence of severe anemia can be reduced by up to 48% in primigravidae and secundigravidae. Other chemoprophylactic data suggest an effect in all parities, and there are arguments that any pregnant woman infected with HIV would benefit from antimalarial treatment. Over and above the very obvious effects of malaria on low birth weight and subsequent infant mortality, the crude analysis presented here suggests that this affordable and operationally feasible intervention could potentially avert a significant burden of severe anemia and maternal mortality among pregnant women in sub-Saharan Africa.

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