



## Impacts of Malaria on Severe Anemia in Children Aged 6-23 Months Old from the Rural District of Kongoussi, Burkina Faso

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### ABSTRACT

**Background:** The present cross-sectional study was conducted to measure the population attributable risk (PAR) of severe anemia among children aged 6-23 months in the rural district of Kongoussi, in Burkina Faso. **Methods:** Socio-demographic, clinical, anthropometric, and biological data were collected from children and mothers. **Results:** In total, 671 children were included in the analysis, 50.4% of whom were male and 97.8% were breastfed. Only 5.8% of the children had adequate complementary feeding, 25.8% were wasted, and 23.5% stunted. Malaria affected about half (50.8%) of children; 39.3% had mild malaria and 11.5% had severe malaria. Children who were no longer breastfed were more likely to have malaria [OR = 3.98 (1.11-14.2),  $P = 0.022$ ] than those who were breastfed. Fever in the last fortnight [OR = 1.49 (1.07-2.08),  $P = 0.019$ ], current fever [OR = 4.30 (2.39-7.76),  $P < 0.001$ ], and presence of splenomegaly [OR = 2.68 (1.54-4.67),  $P < 0.001$ ] were also positively associated with malaria. Anemia and severe anemia had a prevalence of 96.8% and 24.4%, respectively, and were associated with both mild and severe malaria. Body mass index of mothers [OR = 1.82 (1.06-3.12),  $P = 0.029$ ], diarrhea in the last fortnight [OR = 1.70 (1.06-2.71),  $P = 0.027$ ], stunting [OR = 1.54 (1.01-2.34),  $P = 0.045$ ], and splenomegaly [OR = 2.93 (1.70-5.06),  $P = 0.045$ ] were other independent factors associated with severe anemia. The PARs of severe anemia due to mild and severe malaria were 22.1% (6.1%-35.4%) and 22.0% (11.6%-27.7%), respectively. **Conclusion:** Given the high frequency of anemia and severe anemia in this rural malaria-endemic area, interventions are required that consider the important contribution of malaria to anemia and aim to prevent infection.

**Keywords:** Malaria; Severe anemia; Children; Impact; Burkina Faso

### Introduction

Micronutrient deficiencies remain a major public health concern in developing

countries because of their high prevalence in children, their significance for child morbidity and

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mortality and their long-term consequences. The consequences include stunting, poor mental and cognitive development, vulnerability or exacerbation of disease, mental retardation, blindness, and general loss in productivity and potential (Bailey *et al.*, 2015, Black, 2003, The World Bank, 2006, UNICEF and MI., 2004, United Nations, 2004). Iron deficiency, which can lead to anemia, is the most prevalent micronutrient deficiency worldwide (Kassebaum, 2016, Lopez *et al.*, 2016, World Health Organization, 2001). By the 1990s, it was seen as little more than a debilitating nuisance. Today, lack of iron is known to impair the normal mental development of 40% to 60% of the developing world's infants (Balarajan *et al.*, 2011, UNICEF and MI., 2004). Anemia is a widespread public health problem with major consequences for human health as well as social and economic development (Brabin *et al.*, 2003, Brabin *et al.*, 2001). The most dramatic health effect of anemia is the increased risk of child mortality (Brabin *et al.*, 2003, Crawley, 2004). The relative risk of death (if hemoglobin values are < 70 g/l) is 4.3 compared to normal hemoglobin values (110 g/l), and hemoglobin values < 50 varies from 3.5 to 12.0 (Crawley, 2004).

The main cause of anemia is iron deficiency, but infectious diseases, especially malaria, are important factors contributing to the high prevalence of anemia in many populations (Brabin *et al.*, 2003, Crawley, 2004, DeLoughery, 2017, Lopez *et al.*, 2016). It is likely that the relative importance of each of these causes varies by context and location. The extent to which malaria can cause severe anemia is important to know before designing interventions that aim to reduce anemia in malaria endemic countries.

Burkina Faso is a developing country located in West Africa, with 18,450,494 (INSD, 2015) inhabitants. It is a poor country classified on the Human Development Index as 182<sup>nd</sup> out of 189 countries in the world with a score of 0.434 (UNDP, 2019). The health situation is characterized by high mortality and morbidity rates largely attributable to infectious and parasitic

diseases (Donnen P *et al.*, 2005). The death rate of children under five is 184% (202 % in rural areas). Burkina Faso is a malaria-holoendemic country. In 2002, malaria represented 31% of health service visits, 40% of hospitalizations, and 45% of causes of death among children under five. The nutrition situation of children under five is marked by high prevalence of stunting, at 24.9. Anemia as measured by hemoglobin level <110 g/l affects 91.5% of children under five (93.6% in rural areas, 99.4% in children aged 10-11 months) (Ministry of health, 2020). The objective of this study was to determine the population attributable risk (PAR) of severe anemia among children aged 6-23 months in the rural district of Kongoussi, one of the poorest districts in the country.

### Materials and Methods

*Study area:* Kongoussi is a rural district located 115 km north of Ouagadougou, the capital of Burkina Faso. There are 211,551 inhabitants distributed in 245 villages. It is a young population; 17.7% of whom are children under five years of age, and 31.3% comprises children aged 5-14 years. The main economic activities are agriculture and animal husbandry. As in most of Burkina Faso, the climate is of the Sudanese type, including two unequal seasons which alternate between the influence of Saharan winds (dry season from October to May) and monsoons (rainy season from June to September). Total rainfall is about 500 mm per year. Such minimal rainfall has consequences, such as poor soil which is not favorable to agriculture, and little availability of water. Among children aged 6-23 months, the prevalence of wasting was 26.3% according to a previous study (Ouedraogo *et al.*, 2008). The prevalence of anemia, severe anemia, vitamin A deficiency, and zinc deficiency was respectively 99.6%, 31.0%, 17.3%, and 21.6% (Donnen P *et al.*, 2005). Among anemic children, hypo-chromic anemia, which is more likely to be nutritional anemia, represented 65.1% of cases (DeLoughery, 2017, Lemeshow and Robinson, 1985). The health system is comprised of a larger hospital at the district level, the Medical Center with Surgical

antenna (CMA), controlling referrals from a first recourse level hospital system made up of 26 Centers of Health and Social Promotion (CHSP) and 111 Primary Health Posts (PSP). These structures operate thanks to teams led by a physician for the CMA, a nurse for the CHSP, and a community health worker for the PSP.

*Study design:* A cross-sectional study was implemented from August to September 2016 in the district of Kongoussi. A total of 671 children aged 6-23 months were recruited from 30 villages (89.5% of the desired sample size of 750 children: 30 clusters of 25 children). The villages were the same as selected in an earlier cross-sectional survey, using the “probability proportionate to size” cluster sampling derived from the Expanded Program on Immunization (EPI) surveys method (Donnen P *et al.*, 2005). The sample size was determined to enroll enough subjects who met the study criteria (Hemoglobin  $\geq 70$  g/l and  $< 110$  g/l) for inclusion in a community-based micronutrient supplementation trial. The analysis included the total population screened for enrollment into the trial. Clinical, anthropometric, and biological measurements were performed on children and mothers, and a questionnaire was addressed to mothers.

*Data collection:* The questionnaire records included demographic and socio-economic data, as well as child feeding and caring practices, and morbidity. Mothers’ education refers to their past formal school attendance. Mothers’ activities were recorded as income-generating activities. Agriculture and domestic activities which involve all mothers were not considered in this definition, since these activities concern almost all mothers. Shop keeping, market gardening, artisanal goldmining, gainful domestic job, pottery, sewing, weaving, and hairdressing were considered as income-generating activities. The child’s age was recorded from their health-book or from birth and immunization registers obtained from the PSP or the CHSP. Mothers were asked about breastfeeding and complementary feeding in the last 24 hours as well as morbidity (diarrhea, fever

and cough) in the last fortnight.

A medical practitioner examined mothers for goiter and made determinations based on the International Council for the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) definition and classification, and examined children for splenomegaly classified according to Hackett (Dunn *et al.*, 1992). The medical practitioner was also responsible for measuring axillary temperature ( $\pm 0.1$  °C) with an electronic, 32 to 43.9 °C range medical thermometer (MT 16 E1) which fit the European Instruction Requirement N° 93/42.

Anthropometrics measurements were performed on children and mothers by a nutritionist, in agreement with the WHO recommendations (World Health Organization, 2006). The children were weighed naked using an electronic 2 to 16 kg capacity baby scale (Seca 803 Clara Scale, Semur-en-Auxois, France) to the nearest 0.01 kg, and mothers with light dress by a mechanical 0 to 120 kg capacity scale to the nearest 0.10 kg. Recumbent length of children was measured with a horizontal locally made length board to the nearest 0.1 cm, and mothers with a vertical locally made gauge to the nearest 0.5 cm.

Capillary blood was obtained by lab technicians through a finger stick for hemoglobin measurement and malaria blood smear preparation. Hemoglobin was measured using a HemoCue® machine (Hemocue HB 201+, Angelholm, Sweden) to the nearest 1 g/l. Blood smear intending to detect malaria infection was stained with Giemsa at the local hospital laboratory and then read in duplicate. Discordant results underwent a third reading at the IRSS laboratory in Ouagadougou. The mean parasite density of the two concordant results of these readings was considered. Reading was performed for the specific parasite species’ density per microliter by counting against 500 white blood cells and multiplying by 16 (assuming 8000 white blood cells per  $\mu$ l of blood) (Spencer, 1986, Trape, 1985). If no parasite was seen in 400 fields on the slide, a negative result was declared.

**Definitions:** On the basis of the number of meals, complementary feeding was considered adequate in cases of at least 3 meals for children aged 12-23 months or at least two meals for children aged 6-11 months (Dewey and Brown, 2003). It was considered insufficient if the child received fewer than the above-mentioned numbers of meals in the last 24 hours.

Current fever was defined as axillary temperature  $\geq 37.5$  °C. Splenomegaly in children was transformed into a binary variable (presence or absence). Goiter was also transformed into a binary variable (visible goiter versus absence of or palpable goiter).

Children’s weights and heights were compared to the international reference curves of the WHO/NCHS and expressed as height-for-age z-scores (HAZ) and weight-for-height z-scores (WHZ). The  $-2$  cut-off points were used to define stunting (HAZ  $< -2$ ) and wasting (WHZ  $< -2$ ) (World Health Organization, 2006). Mothers’ body mass index (BMI) was computed as “weight (kg)/height (m)<sup>2</sup>”. BMI  $< 18.5$  defined underweight in mothers (Dewey and Brown, 2003). Malaria parasite count of less than 5000 per  $\mu\text{l}$  defined mild malaria while parasite count greater than or equal to 5000 per  $\mu\text{l}$  defined severe malaria (World Health Organization, 1999). In analyses regarding malaria, the presence of malaria versus absence of malaria was considered regardless of parasites count. Anemia was defined as hemoglobin level  $< 110$  g/l, with severe anemia defined as hemoglobin level  $< 70$  g/l (World Health Organization, 2001).

**Data analysis:** The data were double entered and validated using Epi-info version 6.04 (Center for Disease Control, Atlanta, GA), and analyzed using IBM SPSS 24. Univariate analyses were performed and percentages were compared with Pearson Chi-square. To evaluate the independent relationship of malaria and severe anemia, binary logistic regression was established through forward inclusion based on the likelihood ratio. Variables with p-values  $< 0.10$  in univariate analysis were considered in the adjusted logistic regression analysis. The first model included children’s

characteristics. The second model included the variables retained in the first model with the addition of mothers’ BMI which was the lone significant variable related to maternal status during univariate analysis. Variables retained in the second model entered in the final model in which interactions were tested (interaction between mothers’ BMI and children’s stunting as well as interaction between malaria status and splenomegaly). Adjusted ORs (aORs) with 95% confidence intervals (OR (95%CI)) were computed from the final model without interaction, and tested with the Wald Chi-square. The significance level of all tests was 0.05. Adjusted ORs for severe anemia were used to compute the PAR as **equation 1** (where Prev. is the prevalence of malaria and OR is the aOR for severe anemia) (Bruzzi *et al.*, 1985). The Wald Chi-square was involved in the calculation of the 95% confidence interval of the PAR as **equation 2** (where  $\chi^2$  is the Wald Chi-square).

$$PAR = \frac{[Prev(OR-1)]}{[Prev(OR-1)+1]}$$

**Equation 1:** Population attributable risk (PAR) calculation

$$95\% CI = \left[ 1 - (1 - PAR)^{\frac{1 \pm 1.96}{\sqrt{\chi^2}}} \right]$$

**Equation 2:** Confidence interval calculation.

**Ethical consideration :** The study received written ethical approval from the “Comité d’Ethique pour la Recherche en Santé” of the Ministry of Health of Burkina Faso. Informed written consent was obtained from caregivers before children’s inclusion in the study. Children observed with wasting during the survey were referred to the nearest district health center for treatment free of charge, and those seen with severe anemia underwent iron therapy for three months free of charge.

**Results**

Characteristics of mothers and children are presented in **Table 1**. Most mothers were illiterate (82.6%), and without income-generating activities

(61.1%). Among mothers, 11.2% had BMI < 18.5 kg/m<sup>2</sup>, and 26.8% had visible goiter.

Children's age ranged from 6.07 to 23.91 months with mean value ( $\pm$  standard deviation) of 13.6 ( $\pm$  4.9) months. Children were 50.4% male and 49.6% female. Almost all children (97.8%) were breastfed. Overall, 69.4% of children were receiving complementary feeding; however, only 5.8% of those children received adequate complementary feeding. Fever in the last fortnight affected 29.7% of children, and current fever was present in 10.9% of children. Malnutrition affected about one quarter of children (25.8% were wasted and 23.5% were stunted). Malaria affected about half (50.8%) of children, 39.3% of whom experienced mild malaria and 11.5% experienced severe malaria.

**Table 1** also presents crude ORs for the association of malaria (regardless of parasites count) with mothers and children's characteristics. Malaria was associated with breastfeeding and children who were not breastfed were more likely to have malaria than children who were breastfed with OR = 3.98 (1.11-14.2),  $P = 0.022$ . This association remains significant after adjustment for age and complementary feeding (results not shown). The other factors associated with high malaria frequencies were fever in the last fortnight

with OR = 1.49 (1.07-2.08),  $P = 0.019$ ; current fever with OR = 4.30 (2.39-7.76),  $P < 0.001$ , and presence of splenomegaly with OR = 2.68 (1.54-4.67),  $P < 0.001$ .

Hemoglobin levels ranged from 37 to 134 g/l with mean value ( $\pm$  standard deviation) of 81.5 ( $\pm$  16.2) g/l. Frequencies of anemia and severe anemia were 96.8% and 24.4%, respectively. Results of univariate analysis of severe anemia are presented in **Table 2**. Severe anemia showed significant associations with mothers' BMI, diarrhea in the last fortnight, fever in the last fortnight, cough in the last fortnight, current fever, splenomegaly, mild malaria, severe malaria, wasting, and stunting. After adjustment through logistic regression as presented in the **Table 3**, severe anemia remains significantly associated with mild and severe malaria. Children who had mild malaria were more likely to have severe anemia than children who did not have malaria. Children who had severe malaria were more likely to have severe anemia. The other independent factors associated with severe anemia were mothers' BMI, diarrhea in the last fortnight, stunting, and splenomegaly.

The PAR of severe anemia due to mild malaria and severe malaria were 22.1% (6.1%-35.4%) and 22.0% (11.6%-27.7%), respectively.

**Table 1.** Crude ORs for the association of malaria mothers and children's characteristics.

| Characteristics                      | n   | %    | Odds ratio (IC 95%) | P-value <sup>a</sup> |
|--------------------------------------|-----|------|---------------------|----------------------|
| <b>Mothers</b>                       |     |      |                     |                      |
| Age (y)                              |     |      |                     | 0.343                |
| ≤ 25                                 | 321 | 47.8 | 1                   |                      |
| > 25                                 | 350 | 52.2 | 1.16 (0.86-1.57)    |                      |
| Education level                      |     |      |                     | 0.912                |
| Primary and more                     | 117 | 17.4 | 1                   |                      |
| Illiterate                           | 554 | 82.6 | 0.98 (0.66-1.46)    |                      |
| Income-generating activity           |     |      |                     | 0.314                |
| Yes                                  | 261 | 38.9 | 1                   |                      |
| No                                   | 410 | 61.1 | 0.85 (0.63-1.16)    |                      |
| Body mass index (kg/m <sup>2</sup> ) |     |      |                     | 0.604                |
| ≥18.5                                | 596 | 88.8 | 1                   |                      |
| < 18.5                               | 75  | 11.2 | 0.88 (0.54-1.42)    |                      |
| Presence of visible goiter           |     |      |                     | 0.336                |
| No                                   | 491 | 73.2 | 1                   |                      |
| Yes                                  | 180 | 26.8 | 1.18 (0.84-1.67)    |                      |
| <b>Children</b>                      |     |      |                     |                      |
| Age (m)                              |     |      |                     | 0.358                |
| 6-11                                 | 293 | 43.7 | 1                   |                      |
| 12-23                                | 378 | 56.3 | 1.15 (0.85-1.57)    |                      |
| Gender                               |     |      |                     | 0.373                |
| Girls                                | 333 | 49.6 | 1                   |                      |
| Boys                                 | 338 | 50.4 | 0.87 (0.64-1.18)    |                      |
| Still breastfed                      |     |      |                     | 0.022                |
| Yes                                  | 656 | 97.8 | 1                   |                      |
| No                                   | 15  | 2.2  | 3.98 (1.11-14.2)    |                      |
| Complementary feeding                |     |      |                     | 0.570                |
| Adequate                             | 39  | 5.8  | 1                   |                      |
| Insufficient                         | 427 | 63.6 | 0.93 (0.46-1.88)    |                      |
| No complementary feeding             | 205 | 30.6 | 0.79 (0.37-1.64)    |                      |
| Diarrhea in the last fortnight       |     |      |                     | 0.481                |
| No                                   | 556 | 82.9 | 1                   |                      |
| Yes                                  | 115 | 17.1 | 0.87 (0.58-1.29)    |                      |
| Fever in the last fortnight          |     |      |                     | 0.019                |
| No                                   | 472 | 70.3 | 1                   |                      |
| Yes                                  | 199 | 29.7 | 1.49 (1.07-2.08)    |                      |
| Cough in the last fortnight          |     |      |                     | 0.453                |
| No                                   | 647 | 96.4 | 1                   |                      |
| Yes                                  | 24  | 3.6  | 1.37 (0.60-3.13)    |                      |
| Axillary temperature (°C)            |     |      |                     | <0.001               |
| < 37.5                               | 598 | 89.1 | 1                   |                      |
| ≥ 37.5                               | 73  | 10.9 | 4.30 (2.39-7.76)    |                      |
| Presence of splenomegaly             |     |      |                     | <0.001               |
| No                                   | 604 | 90.0 | 1                   |                      |
| Yes                                  | 67  | 10.0 | 2.68 (1.54-4.67)    |                      |
| Malaria status                       |     |      |                     | 0.094                |
| Absence                              | 330 | 49.2 | 1                   |                      |
| Mild malaria                         | 264 | 39.3 | 1.35 (0.95-1.91)    |                      |
| Severe malaria                       | 77  | 11.5 |                     | 0.299                |
| Wasting                              |     |      |                     |                      |
| No                                   | 494 | 74.2 | 1                   |                      |
| Yes                                  | 172 | 25.8 | 1.21 (0.85-1.73)    |                      |
| Stunting                             |     |      |                     | 0.299                |
| No                                   | 513 | 76.5 | 1                   |                      |
| Yes                                  | 158 | 23.5 | 1.21 (0.85-1.73)    |                      |

<sup>a</sup>: Chi square *test*.

**Table 2.** Measures of the association of severe anemia with characteristics of children and mothers (univariate analysis).

| Characteristics                      | n   | % Severe anemia | Odds ratio (IC 95%) | P-value |
|--------------------------------------|-----|-----------------|---------------------|---------|
| <b>Mothers</b>                       |     |                 |                     |         |
| Age (y)                              |     |                 |                     | 0.659   |
| ≤ 25                                 | 76  | 23.7            | 1                   |         |
| > 25                                 | 88  | 25.1            | 1.08 (0.76-1.54)    |         |
| Education level                      |     |                 |                     | 0.395   |
| Primary and more                     | 25  | 21.4            | 1                   |         |
| Illiterate                           | 139 | 25.1            | 1.23 (0.76-1.99)    |         |
| Income-generating activity           |     |                 |                     | 0.485   |
| Yes                                  | 60  | 23.0            | 1                   |         |
| No                                   | 230 | 25.4            | 1.14 (0.79-1.64)    |         |
| Body mass index (kg/m <sup>2</sup> ) |     |                 |                     | 0.013   |
| ≥18.5                                | 137 | 23.0            | 1                   |         |
| < 18.5                               | 27  | 36.0            | 1.89 (1.13-3.13)    |         |
| Presence of visible goiter           |     |                 |                     | 0.156   |
| No                                   | 127 | 25.9            | 1                   |         |
| Yes                                  | 37  | 20.6            | 0.74 (0.49-1.12)    |         |
| <b>Children</b>                      |     |                 |                     |         |
| Age (m)                              |     |                 |                     | 0.119   |
| 6-11                                 | 63  | 21.5            | 1                   |         |
| 12-23                                | 101 | 26.7            | 1.33 (0.93-1.91)    |         |
| Gender                               |     |                 |                     | 0.430   |
| Girls                                | 77  | 23.1            | 1                   |         |
| Boys                                 | 87  | 25.7            | 1.15 (0.81-1.64)    |         |
| Still breastfed                      |     |                 |                     | 0.418   |
| Yes                                  | 159 | 24.2            | 1                   |         |
| No                                   | 5   | 33.3            | 1.56 (0.53-4.64)    |         |
| Complementary feeding                |     |                 |                     | 0.376   |
| Adequate                             | 6   | 15.4            | 1                   |         |
| Insufficient                         | 105 | 24.6            | 1.79 (0.69-4.91)    |         |
| No complementary feeding             | 53  | 25.9            | 1.92 (0.72-5.42)    |         |
| Diarrhea in the last fortnight       |     |                 |                     | 0.009   |
| No                                   | 125 | 22.5            | 1                   |         |
| Yes                                  | 39  | 29.6            | 1.77 (1.14-2.73)    |         |
| Fever in the last fortnight          |     |                 |                     | 0.042   |
| No                                   | 105 | 22.2            | 1                   |         |
| Yes                                  | 59  | 29.6            | 1.47 (1.01-2.14)    |         |
| Cough in the last fortnight          |     |                 |                     | 0.046   |
| No                                   | 154 | 23.8            | 1                   |         |
| Yes                                  | 10  | 41.7            | 2.29 (1.00-5.25)    |         |
| Axillary temperature (°C)            |     |                 |                     | 0.003   |
| < 37.5                               | 136 | 22.7            | 1                   |         |
| ≥ 37.5                               | 28  | 38.4            | 2.11 (1.27-3.51)    |         |
| Presence of splenomegaly             |     |                 |                     | <0.001  |
| No                                   | 130 | 21.5            | 1                   |         |
| Yes                                  | 34  | 50.7            | 3.76 (2.24-6.30)    |         |
| Malaria status                       |     |                 |                     | <0.001  |
| Absence                              | 57  | 17.3            | 1                   |         |
| Mild malaria                         | 71  | 26.9            | 1.76 (1.17-2.66)    |         |
| Severe malaria                       | 36  | 46.8            | 4.21 (2.39-7.40)    |         |
| Wasting                              |     |                 |                     | 0.017   |
| No                                   | 110 | 22.3            | 1                   |         |
| Yes                                  | 54  | 31.4            | 1.60 (1.09-2.35)    |         |
| Stunting                             |     |                 |                     | 0.009   |
| No                                   | 113 | 22.0            | 1                   |         |
| Yes                                  | 51  | 32.3            | 1.69 (1.14-2.50)    |         |

**Table 3.** Measures of the association of severe anemia with characteristics of children and mothers (logistic regression analysis)

| Characteristics                              | n   | Odds ratio (IC 95%) | P-value |
|--|-----|---------------------|---------|
| Body mass of the mother (kg/m <sup>2</sup> ) |     |                     |         |
| ≥18.5  | 596 | 1                   |         |
| < 18.5                                       | 75  | 1.82 (1.06-3.12)    | 0.029   |
| Diarrhea in the last fortnight               |     |                     |         |
| No   | 556 | 1                   |         |
| Yes  | 115 | 1.70 (1.06-2.71)    | 0.027   |
| Stunting                                     |     |                     |         |
| No   | 513 | 1                   |         |
| Yes  | 158 | 1.54 (1.01-2.34)    | 0.045   |
| Presence of splenomegaly                     |     |                     |         |
| No   | 604 | 1                   |         |
| Yes  | 67  | 2.93 (1.70-5.06)    | 0.045   |
| Malaria status                               |     |                     |         |
| Absence                                      | 330 | 1                   |         |
| Mild malaria                                 | 264 | 1.72 (1.15-2.59)    | 0.009   |
| Severe malaria                               | 77  | 3.46 (1.97-5.99)    | <0.001  |

### Discussion

Among children aged 6-23 months old in the district of Kongoussi, 44.1% of severe anemic cases were attributable to malaria, and consequently, might be prevented with malaria management. The PAR was 22% for both mild and severe malaria. The potential of mild malaria to determine severe anemia (proxied by the aOR) was less strong than that of severe malaria, but the former occurs more frequently among children and thus equally contributes to severe anemia. The remaining 60% of severe anemia may be attributable to causes other than malaria. The relative importance of malaria may depend on the area under consideration and on the season in a given area due to seasonal variations of malaria transmission and of iron-rich food availability (children are provided with family meals starting at 6 months). The present study took place in the high transmission period of malaria but also at the best period of availability of fresh vegetables. Therefore, the importance of malaria could be high. This large contribution of malaria to severe anemia makes malaria a major cause of death among children, since severe anemia is one contributor to mortality. This underlines the great need for malaria interventions in this region. A previous study in the district of Kongoussi that

took place in the dry season reported a very high prevalence of anemia (99.4%) and severe anemia (31%). Among anemic children, 65.1% had hypochromic anemia, indicating that these cases were likely iron deficiency anemia. The remaining 35% was attributable to other causes, including malaria (Donnen P *et al.*, 2005). The importance of malaria shown in this study is consistent with other studies that demonstrate the relationship between malaria and severe anemia, or the impact of malaria prevention on severe anemia in many sub-Saharan African areas. In a study in Kenya, a permethrin-treated bed nets intervention demonstrated a significant protective effect on severe anemia of 60% (37%-74%) although it did not fully control malaria (the protective effect on malaria parasitemia was 72% (95% CI : 62%-80%) (ter Kuile *et al.*, 2003). Across 29 studies, malaria control increased hemoglobin among children by, on average, 7.6 g/l (95% CI: 6.1-9.1), corresponding to a relative risk for hemoglobin < 110 g/l of 0.73 (95% CI: 6.4-8.1) and for hemoglobin < 8 g/l of 0.40 (95% CI: 0.25-0.55) (Korenromp *et al.*, 2004). Many studies have reported that malaria-infected children have lower hemoglobin status than uninfected children (Asobayire *et al.*, 2001, Cornet *et al.*, 1998, Desai MR *et al.*, 2005, Eliades MJ *et al.*, 2006, Friedman



*et al.*, 2005, Ong'echa JM *et al.*, 2006, Stoltzfus RJ *et al.*, 2000). The potential of malaria to lead to anemia is more important in young children than in older children. Some individual trials have found larger impacts on anemia in children aged 6–35 months than in older children. A study in Zanzibari showed that the association of hemoglobin and malaria exists among children aged < 30 months but not among children aged  $\geq$  30 months (Stoltzfus RJ *et al.*, 2000).

In the present study, the other factors independently associated with severe anemia were mothers' malnutrition, diarrhea in the last fortnight, stunting, and splenomegaly. Mothers' malnutrition and diarrhea likely lead to severe anemia through iron impairment. Diarrhea may increase nutrient loss (including iron) and decrease nutrient uptake (Lartey *et al.*, 2000). Mothers' malnutrition may contribute to anemia through insufficiency of breastfeeding because even if human milk is the optimal feeding mode for many reasons it contains relatively little iron and zinc, and its vitamin content can be compromised by maternal malnutrition (Brown *et al.*, 1998). However, the observed association between mothers' malnutrition and anemia is independent of breastfeeding. This may be due to the fact that the definition does not fully take the overall quantitative and qualitative dimension of breastfeeding into account. Furthermore, mothers' malnutrition may lead to anemia through pathways other than breastfeeding, such as suboptimal childcare practices, since mothers' condition is a resource of childcare practices. The cross-sectional design of this study does not allow a conclusion as to whether severe anemia is the consequence or cause of stunting. On one hand, severe anemia may be the cause of stunting, as iron deficiency has been demonstrated to be involved in growth faltering when the deficiency state is severe (Rivera *et al.*, 2003). On the other hand, stunting may determine the severity of malaria-associated anemia in African children (Friedman *et al.*, 2005, Verhoef *et al.*, 2002). Splenomegaly also remained associated with severe anemia in multiple

regression analyses in a study by Mogensen (Mogensen *et al.*, 2006).

The results show that breastfeeding has a protective effect against malaria. Recently in Cameroon, exclusive breastfeeding in young children was associated with lower prevalence of malaria (Asoba *et al.*, 2019). Moreover, an in vitro test that showed inhibitory factors of *Plasmodium falciparum* malaria parasite growth in breast milk is supportive of these results (Kassim OO *et al.*, 2000).

### **Conclusion**

These results underline the high frequency of anemia and severe anemia among young children in the rural district of Kongoussi. This high frequency may place anemia and severe anemia as major contributors to young children's death. There is a great need for urgent action aimed at reducing anemia among young children in this area. Interventions should include malaria prevention and treatment to allow a better impact on anemia.

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### **Authors' contributions**

Augustin Nawidimbasha Z assured data collection, data analysis and interpretation and contributed in the manuscript drafting. Hermann Zose O developed the study and contributed in data analysis and interpretation, the manuscript drafting, and its revision before submission. Alain H contributed in the revision of the final version of the manuscript before it was submitted.

### **Conflict of interests**

The authors declare that they have no competing interests.

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