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# Malaria and anemia in children under 7 years of age in the western region of Côte d'Ivoire

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**Background:** Anemia is a major public health problem, affecting nearly one-quarter of the world's population. It is defined as a reduction in the hemoglobin level in the peripheral blood to below the normal threshold set for a particular population. Very often in the subtropics, helminths or malaria co-infect an individual, causing morbidities that vary by age and region. This study aims to characterize the type of anemia observed in children under 7 years of age infected with malaria in the western region of Côte d'Ivoire, to recommend a better strategy of care.

**Methods:** The study was carried out from March 2020 to May 2021 in 22 villages in Man, Tonkpi Region, with a cohort of 451 children, both male and female, aged from 3 months to 6 years. The children provided venous blood samples for the diagnosis and characterization of anemia (full blood count), and Giemsa staining (GS) (thick and thin smears) and rapid diagnostic tests (RDTs) were used for the diagnosis of malaria. Risk factors and morbidity profiles were assessed using a questionnaire. Logistic regressions models were employed to identify independent risk factors and morbidity patterns associated with *Plasmodium falciparum* mono-infection and co-infections.

**Results:** Of the 451 children who completed the study, 221 (49.0%) were female and 230 (51.0%) were male. The prevalence of anemia was 55.0%, distributed as 30.7% mild, 66.1% moderate, and 3.2% severe anemia. The characterization of anemia revealed that hypochromic microcytic anemia (HMA) was the predominant type, being found in 195 (78.63%) children. It was followed by normochromic microcytic anemia (29 children, 11.69%), normochromic normocytic anemia (14 children, 5.65%), and, finally, hypochromic normocytic anemia (10 children, 4.03%). The prevalence of malaria was 66.7% and 78.3% based on GS and RDTs, respectively. The closed association between malaria (*Plasmodium*) and anemia led to *P. falciparum* alone causing 56.7% of mild, 51.3% of moderate, and 37.5% of severe anemia in children.

**Conclusion:** Malaria infection was highly prevalent among children aged  $\leq 7$  years in both sex and in different age groups, although the number of

*Plasmodium* parasites present during infections was greatest in younger children. Similarly, the prevalence of anemia was high, with moderate anemia and HMA being more prevalent in children  $\leq 7$  years of age in the western region of Côte d'Ivoire.

#### KEYWORDS

anemia, prevalence, children under 7 years, malaria, Côte d'Ivoire

## Introduction

Parasitic infections such as malaria are common in the tropical and subtropical regions. They lead to high rates of morbidity and mortality, especially in children (1). In 2020, approximately 241 million people worldwide were infected with malaria, and an estimated 627,000 of these individuals died (2). Furthermore, the World Health Organization (WHO) African Region has been the most affected by malaria, accounting for 95% of malaria cases and 96% of malaria deaths worldwide. Children under 5 years of age in the same region accounted for approximately 80% of all deaths from malaria (3). Malaria is responsible for acute or chronic anemia in populations in the tropics (4). A 2022 WHO report on anemia estimated that the global prevalence of anemia was 39.8% in children aged 6–59 months and 29.9% in women of childbearing age (defined as women aged 15–49 years) (4). This equates to 269 million anemic children and over half a billion anemic women aged 15–49 years (4).

In Côte d'Ivoire, the prevalence of malaria in 2017 was estimated at 49% and 52% based on Giemsa staining (GS) of a thick blood smear and rapid diagnostic testing (RDT), respectively (5). The prevalence of anemia in 2019 among children aged 6–59 months was 72.2%, and among women of childbearing age it was 51% (6). In most cases, polyparasitism is the rule, and these conditions affect the same people, causing morbidities that vary by age and region (7, 8). Hence, it seems appropriate, even essential, to conduct research to treat these morbidities, which represent public health problems. This community-based research study aims to characterize the type of anemia observed in children under 7 years of age infected with malaria in Man, Tonkpi Region, in the western region of Côte d'Ivoire, to recommend a better strategy of care.

## Methods

### Study area and participants

This observational clinical research study was carried out from March 2020 to May 2021 in 22 villages in Man, Tonkpi

Region. The target sample size of 451 was calculated using Schwartz's formula:

$$n = z^2 \frac{p(1-p)}{e^2} * c$$

where  $p$  is the expected prevalence of anemia in the target population, estimated at 73.4% (9),  $e$  an accuracy of 5%,  $c$  a corrective coefficient for the cluster effect of 1.5, and  $z$  a confidence level of 95% ( $z = 1.96$ ).

Children aged 3 months to < 7 years were enrolled and provided blood samples for the diagnosis of anemia and malaria. Study participants belonged to different ethnic groups (Akan, Gour, Mandé, Krou, and others from neighboring countries such as Burkina Faso, Mali, and Guinea), resided in a rural area, had similar lifestyle patterns, and had parents who earned their living mostly as farmers or commercial traders.

### Sociodemographic

Sociodemographic data, including age, sex, height (to the nearest cm), weight (to the nearest 0.5 kg), and parents' profession, were also collected using a questionnaire administered to each enrolled participant who provided a signed written informed consent or gave a fingerprint (if illiterate).

### Blood collection

A total of 2 ml of venous blood was drawn in the morning into ethylenediaminetetraacetic acid (EDTA)-treated evacuated tubes from each of the 451 consented study participants. Blood samples were kept on ice until they were transported to the central laboratory at the *centre hospitalier régional* (CHR), Man, for the hematology testing [i.e., full blood count (FBC)].

In addition, approximately 10–20  $\mu$ l of blood was collected from the children's pricked fingers for use in malaria RDTs.

## Malaria microscopy and malaria rapid diagnostic test

### > Malaria microscopy

Approximately 10  $\mu$ l of the 2 ml of venous blood that was collected in the EDTA-treated tube was used to prepare GS thick and thin blood smear on a single slide for the count of malaria parasitemia (10, 11). The slides were analyzed and quality controlled by well-trained and experienced laboratory technicians. Slides were considered positive when asexual forms and/or gametocytes of any *Plasmodium* species were observed on the blood film. Parasite density per microliter of blood was determined by the number of malarial parasites per 200 leukocytes on a thick blood film, assuming a white blood cell (WBC) count of 8000 leukocytes/ $\mu$ l of blood and then transformed into malaria parasite density by multiplying by a factor of 40. Malaria parasite density was classified as low (< 5,000 parasites/ $\mu$ l of blood) or high ( $\geq$  5,000 parasites/ $\mu$ l of blood) (10, 11).

The GS (thick and thin blood smear) slides were scored as negative or positive. Positive scores were further classified as *Plasmodium falciparum*, *P. malariae*, *P. vivax*, or *P. ovale*, or as undetermined if the technician experienced difficulty clearly identifying the species.

### > Malaria rapid diagnostic test

About 10–20  $\mu$ l of blood collected from the child's pricked finger was tested for malaria using an RDT, using the plastic capillary tube provided in the RDT kit, as per manufacturer instructions (Humasis Malaria Pf/Pan Antigen Test; Humasis Co. Ltd, Humasis, South Korea). The result was scored as negative (i.e., no *P. falciparum* detected) or mixed (i.e., *P. falciparum* and other species of *Plasmodium* detected).

## Hemoglobin determination and classification of anemia

The FBC was measured using the URIT 3000 PLUS analyzer (URIT Medical Electronic Co. Ltd, Guilin, China). The results were printed and analyzed further, and characterized on the basis of the mean corpuscular hemoglobin (MCH) (normal value 27–31 pg) and the mean corpuscular hemoglobin concentration (MCHC) (normal value 33–36 g/dl) as either *normochromic* or *hypochromic*, and on the basis of the mean cell volume (MCV) (normal value 80–100 fl) as *normocytic*, *microcytic*, or *macrocytic*.

Anemia was classified, depending on age and sex, according to hemoglobin (Hb) concentration, as per WHO guidelines ([www.who.int/vmnis/indicators/haemoglobin.pdf](http://www.who.int/vmnis/indicators/haemoglobin.pdf)) (12). Thus, children aged from 3 months to 6 years with a Hb level of < 11 g/dl were

considered anemic, and those with a Hb level of  $\geq$  11 g/dl were considered normal (non-anemic). Anemia was also categorized as mild if the Hb level was < 10 g/dl, as moderate if Hb level was between 7 g/dl and 10 g/dl, and as severe if the Hb level was < 7 g/dl. The samples were further characterized based on the MCH and MCHC as either *normochromic* or *hypochromic*, and based on MCV as being *normocytic*, *microcytic*, or *macrocytic*.

## Data management and analysis

Data were entered into a database using the double-entry system in EpiData version 3.1 (EpiData, Odense, Denmark). Inconsistencies were cleaned and, after validation, the data were exported for the analysis to SPSS version 20 [IBM Corp (13)] and Stata<sup>®</sup>, version 16 software (Stata Corp LP, College Station, TX, USA). Univariate analysis (chi-squared test), Wilcoxon rank-sum tests, and Kruskal–Wallis tests were used for comparison between groups. Logistic regression estimates were employed to identify independent risk factors and morbidity patterns associated with *P. falciparum* mono-infections and co-infections.

## Ethics consideration

This study was conducted after obtaining ethics clearance from the Comité National d'Éthique des Sciences de la Vie et de la Santé (CNESVS) de la Côte d'Ivoire (N/Ref 024-21/MSHP/CNESVS-km). Further permission to conduct the study was obtained from the chief of each village visited. In essence, the full study details (i.e., the aims, procedures, and potential risks and benefits) were explained to the physicians, nurses, and assistant nurses of each involved health center and the villagers before the start of the study.

Given that all the participants were minors, consent from one parent was sought and obtained before the study procedure was completed. Only voluntarily consented participants were included in the study. Treatment was made available free of charge to all sick participants. Those who were diagnosed with mild or moderate anemia, with or without malarial infection, received an ambulatory treatment of antimalarial or antihelminthic and/or anti-anemic treatment based on their Hb level (with treatment *via* ferric hydroxide polymaltose complex syrups), and their RDT and GS slide (thick and thin blood smear) results (with treatment *via* artemether/lumefantrine 20/120 or 40/240 tablets). Those who required further assistance were referred to the local health center.

Participants were informed that their information would be anonymized (confidential) by using a coding system instead of their names.

## Results

### Characteristics of the study populations

A total of 451 children from 22 villages were enrolled in the study, of whom 230 (51.0%) were male and 221 (49.0%) were female (Supplemental Table 1).

### Prevalence of anemic participants

Of the 451 children enrolled in the study, 248 (55.0%) were anemic and 203 (45.0%) were not anemic (Table 1). Further characterization of the observed anemia and its severity showed that 76 (30.7%) children had mild anemia, 164 (66.1%) had moderate anemia, and 8 (3.2%) had severe anemia. Female (56.1%) and male (53.8%) participants were equally affected by anemia. It was noted that anemia varied by age group, with

infants aged 3 months to 2 years (66.0%) being at a higher risk of anemia than older children (3 to 6 years; 28.1%). In addition, the majority of observed cases of anemia were of moderate severity (66.1%), with most of the remainder being classified as mild (30.7%) and severe disease being relatively uncommon (3.2%). Details are available in Table 1.

### Distribution of the type of anemia according to sex and age

The prevalence of each type of anemia did not vary by sex or age. Both sexes and the different age groups were almost equally affected. The only noted variation was the high prevalence of hypochromic microcytic anemia (78.63%), relative to normochromic microcytic anemia (11.69%) and normochromic normocytic anemia (5.65%). No case of macrocytic anemia was detected in the study (Table 2).

TABLE 1 Prevalence and intensity of anemia by sex and age, in the western region of Côte d'Ivoire, from March 2020 to May 2021.

	Tested ( <i>n</i> )	Anemics ( <i>n</i> )	% (95% CI)	$\chi^2$	<i>p</i> -value	Intensity of anemia		
						Mild	Moderate	Severe
<b>Sex</b>								
Male	230	129	56.1 (49.4 to 62.6)	0.23	0.633	34 (26.4)	93 (72.0)	2 (1.6)
Female	221	119	53.8 (48.1 to 59.5)			42 (35.3)	71 (59.7)	6 (5.0)
<b>Age group</b>								
3M–2Y	159	105	66.0 (58.1 to 73.3)	18.42	<0.001*	21 (20.0)	78 (74.3)	6 (5.7)
3–5Y	260	134	51.5 (45.3 to 57.8)			50 (37.3)	82 (61.2)	2 (1.5)
6–7Y	32	9	28.1 (13.7 to 46.7)			5 (55.5)	4 (44.4)	0 (0.0)
Total	451	248	55.0 (50.3 to 59.6)			76 (30.7)	164 (66.1)	8 (3.2)

$\chi^2$ , chi-squared test; %, prevalence; CI, confidence interval; M, month; p, probability; Y, year.

\*significant test at the threshold of 0.05.

TABLE 2 Distribution of the type of anemia according to sex and age in the western region of Côte d'Ivoire, from March 2020 to May 2021.

Type of anemia	Total ( <i>N</i> = 248)	Sex		Age group		
		Male ( <i>N</i> = 129)	Female ( <i>N</i> = 119)	3M–2Y ( <i>N</i> = 105)	3–5Y ( <i>N</i> = 134)	6–7 Y ( <i>N</i> = 9)
Hypochromic microcytic anemia	195 (78.63)	102 (41.13)	93 (37.50)	93 (37.50)	94 (37.90)	8 (3.23)
Normochromic microcytic anemia	29 (11.69)	17 (6.85)	12 (4.84)	7 (2.82)	22 (8.87)	0 (0.0)
Hypochromic normocytic anemia	10 (4.03)	2 (0.81)	8 (3.23)	3 (1.21)	6 (2.42)	1 (0.40)
Normochromic normocytic anemia	14 (5.65)	8 (3.23)	6 (2.42)	2 (0.81)	12 (4.84)	0 (0.0)
Macrocytic anemia	0 (0.0)	—	—	—	—	—

M, month; Y, year.

## Prevalence of anemic participants with malaria infection

### o Prevalence of malaria (rapid diagnostic test) by sex and age

Of the 451 children enrolled in the study, 233 (51.7%) were infected by *P. falciparum* and 120 (26.6%) by mixed species; 98 (21.7%) tested negative throughout using RDTs. Both sexes were almost equally infected (female 76.9% vs. male 79.6%), with younger children (66.7%) being infected less often than older children (84.6%).

Mono-infection with *P. falciparum* (51.7%) predominated, followed by co-infection with *P. malariae* (26.6%), and affected fewer males than females (ratio 1.6 vs. 2.4 respectively) (Table 3).

### o Prevalence of malaria (Giemsa staining – thick and thin blood smear test) by sex and age

The GS thick and thin blood smear on one slide could be carried out for only 288 (63.9%) participants. Of the 288 slides examined, 192 (66.7%) were positive and 96 (33.3%) were negative (Table 4).

There was no sex variation given that male participants (67.6%) were affected to almost the same extent as female participants (65.8%). Once again, the prevalence was higher among older children (aged 3–6 years) (77.8%) than among the youngest children (aged 3 months to 2 years) (58.3%), as shown in Table 4.

In terms of the mean parasite density *in contrario*, the study revealed that the youngest children (i.e., those aged 3 months to 2 years) had a higher level of parasitemia (11,105.4/μl of blood) than older children (aged 3–6 years) (2374.1/μl of blood) (Table 4).

Microscopic analysis indicated the presence of two *Plasmodium* species, which were identified as *P. falciparum* and *P. malariae*. Overall, 153 children were infected by *P. falciparum* (153/288, 53.1%), 13 by *P. malariae* (13/288, 4.5%), and 26 by a mixture (i.e., co-infection) of *P. falciparum* and *P. malariae* (26/288, 9.0%) among the examined slides of the infected persons (data not shown). It is important to emphasize that an RDT was carried out for each of the 451 participants, whereas the GS thick and thin blood smear was carried out for only 288 participants.

With regard to the severity of the anemia due to *P. falciparum* and *P. malariae* infections among the 248 anemic

TABLE 3 Prevalence of malaria (RDT) by sex and age in the Western region of Côte d'Ivoire, from March 2020 to May 2021.

	Tested*	Non-infected	Infected	% (95% CI)	$\chi^2$	p-value	<i>P. falciparum</i> infection	Mixed infection
<b>Sex</b>								
Male	230	47	183	79.6 (73.8 to 84.6)			113 (61.7)	70 (38.3)
Female	221	51	170	76.9 (70.8 to 82.3)	0.46	0.496	120 (70.6)	50 (29.4)
<b>Age group</b>								
3M–2Y	159	53	106	66.7 (58.8 to 73.9)			69 (65.1)	37 (34.9)
3–5Y	260	40	220	84.6 (79.6 to 88.8)			142 (64.6)	78 (35.4)
6–7Y	32	5	27	84.4 (67.2 to 94.7)	19.4	<0.001	22 (81.5)	5 (18.5)
<b>Total</b>	<b>451</b>	<b>98</b>	<b>353</b>	<b>78.3 (74.2 to 82.0)</b>			<b>233 (51.7)</b>	<b>120 (26.6)</b>

$\chi^2$ , chi-squared test; M, month; Y, year.  
\*RDT, rapid diagnostic test.

TABLE 4 Prevalence of malaria (Giemsa stained - thick and thin blood smear test) by sex and age in the Western region of Côte d'Ivoire, from March 2020 to May 2021.

	Tested*	Non-infected	Infected	% (95% CI)	$\chi^2$	p-value	DPM (95% CI)	Rank-sum/K-W	p-value
<b>Sex</b>									
Male	139	45	94	67.6 (59.2 to 75.3)			8904.9 (6237.3 to 11572.5)		
Female	149	51	98	65.8 (57.6 to 73.3)	0.11	0.739	5590.2 (3063.9 to 8116.6)	4.46	0.108
<b>Age group</b>									
3M–2Y	139	58	81	58.3 (49.6 to 66.6)			11,105.4 (7227.3 to 14,983.5)		
3–5Y	131	34	97	74.1 (65.7 to 81.3)			4661.1 (3257.0 to 6065.3)		
6–7Y	18	4	14	77.8 (52.4 to 93.6)	8.62	0.013**	2374.1 (-161.3 to 4909.6)	2.18	0.030**
<b>Total</b>	<b>288</b>	<b>96</b>	<b>192</b>	<b>66.7 (60.9 to 72.1)</b>			<b>7213.1 (5379.0 to 9047.1)</b>		

$\chi^2$ , chi-squared test; %, prevalence; CI, confidence interval; K–W, Kruskal–Wallis test; M, month; MPD, mean parasite density; p, probability; rank-sum, Wilcoxon rank-sum test; Y, year.  
\*GS thick and thin blood films; \*\*significant test at a threshold of 0.05.

children (164 mild, 76 moderate, and 8 severe), the RDT results showed that 56.7% (93/164) of the children with mild anemia were infected with *P. falciparum* and 20.7% (34/164) co-infected with *P. falciparum* and *P. malariae*, and 22.6% (37/164) tested negative. Similarly, 51.3% (39/76) of the children with moderate anemia were infected with *P. falciparum* and 32.9% (25/76) co-infected with *P. falciparum* and *P. malariae*, and 15.8% (12/76) tested negative. Finally, 37.5% (3/8) of the children with severe anemia were infected with *P. falciparum*, 50.0% (4/8) co-infected with *P. falciparum* and *P. malariae*, and 12.5% (1/8) tested negative among the severe cases (data not shown).

### o Association (univariate and multivariate) by sex and age analysis

In terms of the association between the *Plasmodium* species and other variables, such as type of anemia, sex, age, Hb levels, and severity of the anemia, the univariate and multivariate logistic regression results showed that there was no significant variation between malaria infection and sex, and that normochromic microcytic anemia was the only statistically significant type of anemia and was more prevalent irrespective of the *Plasmodium* species in children aged 3–5 years or older (OR<sup>a</sup> 2.75, 95% CI 1.72 to 4.41;  $p < 0.001$ ). Furthermore, females are more protected than males against mixed *Plasmodium* species infections (OR<sup>b</sup> 0.52, 95% CI 0.29 to 0.94;  $p = 0.030$ ) (Table 5).

## Discussion

This research article reports the findings of an observational community-based research study conducted in children between 3 months and 6 years of age in 22 villages in Man, Tonpki Region, Côte d'Ivoire. The overall prevalence of anemia shows that more than half of the children observed were anemic. Both sexes (males and females) were equally affected, although children aged 3 months to 2 years were affected slightly often more than older children (i.e., aged 3–6 years). In addition, mild and moderate anemia is more prevalent among the same age groups. These results are consistent with those reported in many low- to middle-income countries (LMICs), including Côte d'Ivoire (14, 15), and are far from the WHO's target goal for 2025 (16). In fact, our results are in line with what is reported by WHO in West Africa, which is that 51% of males and 49% of females of preschool age children are anemic (17). In terms of severity, although the trends from mild to severe are also shared, the prevalence in our study is higher for mild and moderate anemias than the WHO-reported prevalence in West Africa: males — 8% vs. 1.6% severe anemia, 50% vs. 72% moderate anemia, and 21% vs. 26.4% mild anemia; females — 5% vs. 7% severe, 59.7% vs. 48% moderate, and 35.3% vs. 22% mild, respectively (17).

We also noted in this study that the prevalence of anemia among children aged < 5 years was higher (45.3%) than the global

TABLE 5 Association between plasmodial infections, demographic factors, and anemia in the Western region of Côte d'Ivoire.

	Association	OR (95% CI) <sup>a</sup>	<i>p</i> -value	OR (95% CI) <sup>b</sup>	<i>p</i> -value
<i>Plasmodium</i> species	Male	1.00		1.00	
	Female	0.86 (0.55 to 1.34)	0.497	0.91 (0.45 to 1.86)	0.807
	3M–2Y	1.00		1.00	
	3–5Y	2.75 (1.72 to 4.41)	<0.001*	3.38 (1.58 to 7.21)	0.002*
	6–7Y	2.70 (0.98 to 7.41)	0.054	4.43 (0.50 to 39.15)	0.180
	Hb < 11 g/dl	1.00		ND	
	Hb > 11 g/dl	0.56 (0.36 to 0.89)	0.013*	ND	
	Mild anemia	1.00		1.00	
	Moderate anemia	1.60 (0.81 to 3.19)	0.179	2.28 (1.06 to 4.89)	0.035*
	Severe anemia	2.02 (0.23 to 17.55)	0.525	4.11 (0.44 to 38.66)	0.217
	Non anemic	1.00		1.00	
	Hypochromic microcytic anemia	1.49 (0.93 to 2.37)	0.097	ND	ND
	Normochromic microcytic anemia	5.02 (1.15 to 21.80)	0.031*	3.04 (0.66 to 13.91)	0.152
	Hypochromic normocytic anemia	3.34 (0.41 to 27.01)	0.257	1.50 (0.16 to 13.4)	0.715
	Normochromic normocytic anemia	4.83 (0.61 to 37.80)	0.133	2.14 (0.26 to 17.71)	0.479
<i>P. falciparum</i> infection	Macrocytic anemia	ND	ND	ND	ND
	Male	1.00		1.00	
	Female	1.23 (0.85 to 1.78)	0.272	1.63 (0.95 to 2.76)	0.071

(Continued)

TABLE 5 Continued

	Association	OR (95% CI) <sup>a</sup>	p-value	OR (95% CI) <sup>b</sup>	p-value
	3M–2Y	1.00		1.00	
	3–5Y	1.57 (1.05 to 2.34)	0.026*	1.51 (0.87 to 2.60)	0.144
	6–7Y	2.87 (1.28 to 6.45)	0.011*	5.08 (0.95 to 27.02)	0.056
	Hb<11 g/dl	1.00		ND	
	Hb >11 g/dl	0.90 (0.62 to 1.31)	0.586	ND	
	Mild anemia	1.00		1.00	
	Moderate anemia	0.83 (0.48 to 1.43)	0.493	1.10 (0.61 to 1.99)	0.745
	Severe anemia	0.46 (0.10 to 2.07)	0.311	0.62 (0.13 to 2.93)	0.550
	Non anemic	1.00		1.00	
	Hypochromic microcytic anemia	1.02 (0.69 to 1.51)	0.917	ND	ND
	Normochromic microcytic anemia	2.60 (1.10 to 6.14)	0.029*	2.53 (1.04 to 6.15)	0.040*
	Hypochromic normocytic anemia	0.66 (0.18 to 2.41)	0.530	0.45 (0.12 to 1.74)	0.245
	Normochromic normocytic anemia	0.99 (0.34 to 2.93)	0.986	0.92 (0.29 to 2.84)	0.888
	Macrocytic anemia	ND	ND	ND	ND
Mixed <i>Plasmodium</i> infection	Male	1.00		1.00	
	Female	0.67 (0.44 to 1.02)	0.061	0.52 (0.29 to 0.94)	0.030*
	3M–2Y	1.00		1.00	
	3–5Y	1.41 (0.90 to 2.22)	0.135	1.42 (0.78 to 2.59)	0.257
	6–7Y	0.61 (0.22 to 1.70)	0.344	0.30 (0.03 to 2.84)	0.297
	Hb<11 g/dl	1.00		ND	
	Hb >11 g/dl	0.69 (0.45 to 1.06)	0.087	ND	
	Mild anemia	1.00		1.00	
	Moderate anemia	1.84 (0.97 to 3.49)	0.062	1.63 (0.83 to 3.21)	0.156
	Severe anemia	3.75 (0.84 to 16.67)	0.082	4.43 (0.92 to 21.35)	0.063
	Non-anemic	1.00		1.00	
	Hypochromic microcytic anemia	1.41 (0.90 to 2.21)	0.135	ND	ND
	Normochromic microcytic anemia	0.89 (0.34 to 2.32)	0.812	0.59 (0.22 to 1.57)	0.293
	Hypochromic normocytic anemia	3.41 (0.95 to 12.31)	0.061	2.94 (0.76 to 11.37)	0.119
	Normochromic normocytic anemia	2.56 (0.84 to 7.75)	0.096	1.54 (0.49 to 4.87)	0.462
	Macrocytic anemia	ND	ND	ND	ND

<sup>a</sup>Unadjusted OR.<sup>b</sup>adjusted OR.

CI, confidence interval; Hb, hemoglobin; M, month; ND, not determined; OR, odds ratio; Y, years.

\*Significant test at the threshold of 0.05 (p &lt; 0.05).

prevalence (42.0%) (18). Furthermore, 66.0% of the younger children aged 3 months to 2 years in our study were anemic, and exhibited the highest prevalence in terms of intensity (i.e., 5.7% severe and 74.3% moderate) among the stratified age groups. This alarming status can be explained by the fact that iron is a major factor in anemia in the first 46 months; the interval from conception of the fetus to 2 years of life is a critical window when nutritional needs must be met. If these needs are not met, children may experience morbidity or mortality (19). We noted that, among the stratified age groups, children in the age group  $\geq 6$  to < 7 years exhibited the highest prevalence of mild anemia (55.5%) and the lowest prevalence of moderate (44.4%) and severe anemia (0.0%). This may be explained by the fact that children of this age are likely to be spending most of their time running errands or playing outside in various environmental settings in which there

are additional foods, such as legumes, nuts and seeds, and fruits and vegetables, to be consumed in addition to their normal shared family food. These extra micronutrients may provide them with a healthy iron balance, reducing their absolute deficiency in iron. In fact, according to Gupta *et al.* in 2016, and the Physicians Committee for Responsible Medicine (PCRM)'s Guideline in 2022, iron deficiency anemia is usually preventable and highly treatable with the consumption of a fortified diet of whole grains, legumes, nuts and seeds, and fruits and vegetables (20, 21). Similar results were reported by Righetti *et al.*, in 2012 in Côte d'Ivoire, where 78.1% of infants were anemic (61% mild, 32% moderate, and 7% severe), compared with 46.8% of children (94.6% mild, 5.4% moderate, and 0% severe) (22).

The consequences of anemia are well established, and it has been reported several times that iron deficiency anemia affects

not only the intelligence of infants and children irreversibly, but also the rapid brain development, physical growth, and early learning capacity, with lifelong consequences on cognition that translate to the equivalent of a 5- to 10-point deficit in intelligence quotient (19, 23–28).

When the observed anemia was further characterized on the basis the MCH, MCHC, and MCV, the highest prevalence was te hypochromic microcytic anemia (78.6%) followed by normochromic microcytic anemia (11.69%). Indeed, iron deficiency is the most common cause of microcytic and hypochromic anemia (26). Iron deficiency anemia is classically described as a microcytic anemia and appears when the body's iron demand is not met by iron absorption from the diet. In most cases, microcytosis is the result of impaired Hb synthesis. Disorders of iron metabolism and protoporphyrin and heme synthesis, as well as impaired globin synthesis, lead to defective Hb production and to the generation of microcytosis and microcytic anemia (23, 29). Iron deficiency anemia has previously been reported in Côte d'Ivoire by Franziska et al., in 2001, with an estimated 50% prevalence (30), as well as elsewhere in other studies (14, 31–34).

Overall, the prevalence of malaria did not differ significantly between sex in our study (male 79.6% vs. female 76.9%) and the younger children were infected less than the older children (3 months to 2 years: 66.7%; 3–5 years: 84.6%; and  $\geq 6$  years: 84.4%). We also observed a high prevalence of anemia amongst the same sex (male 56.1% vs. female 53.8%) and in almost the same age groups (3 months to 2 years: 66.0%; 3–5 years: 51.5%;  $\geq 6$  years: 28.1%) and that was significantly associated with a high levels of *P. falciparum* infection, as previously reported (35, 36). In fact, the RDT results revealed 51.7% of *P. falciparum* infections, 26.6% of mixed infections and 21.7% negatives in both sex while the malaria Giemsa stained -thick and thin blood smear slides showed 53.1% *P. falciparum*, 4.5% *P. malariae*, 9.0% mixed infections made of *P. falciparum* and *P. malariae* and 33.3% of negatives). Our findings highlight the relationship between malaria and anemia, that is the malaria-associated decrease in Hb concentrations in infected individuals, which are in line with previously reported studies in Côte d'Ivoire (14, 32, 37), in other West African countries (28, 38), and globally (19, 36, 39–41).

The analysis of the prevalence of malaria either from the GS thin and thick blood smear tests or from the RDTs by sex indicates that there is no statistical significance on the sex basis ( $\chi^2 = 0.11$ ,  $p = 0.739$ , and  $\chi^2 = 0.46$ ,  $p = 0.496$ , respectively). This may be explained by the use of insecticide-treated nets (ITNs), long-lasting insecticidal nets (LLINs), and indoor residual spraying (IRS) by parents following the yearly country-wide National Malaria LLINs distribution program year, and also reported elsewhere by other authors (42–45).

However, when we consider the prevalence of malaria by age, there is a statistical significance ( $\chi^2 = 8.62$ ,  $p < 0.013$ , and  $\chi^2 = 19.4$ ,  $p < 0.001$ , respectively) indicating that the malaria parasites infect

younger children (3 months to 2 years) much less than older children (3–5 years and 6 to  $< 7$  years) (58.3% vs. 77.8%). Inversely, there is a low parasitemia in children aged 3 to 6 years compared to the children aged 3 months to 2 years (2374.1 vs. 11,105.4, respectively). This may be because of the maturity of the immune system of the children aged over 3 to 6 years compared with the youngest children (3 months to 2 years), with an immature immune system relying mainly on the mother's transmitted immune protection (maternal antibodies) or the presence of fetal Hb (HbF), which is protective and causes poor parasite growth, as previously reported (46–50). According to the study by Marete et al., these high variations in the parasitemia may be attributed to various factors, such as geographic locations, sociodemographics, genetic variations among these populations, utilization of malaria preventive measures, or the nutritional and immunity status among the infants (51).

Finally, the multivariate logistic regression analysis showed that female children are more protected than male children against the mixed *Plasmodium* sp. infection. We could not find any previously reported scientific evidence with regard to the age of our study population. Nevertheless, this protector effect may be because female children sleep in most cases under the impregnated mosquito nets (LLINs) with their mother, whereas male children tend to avoid the nets, mimicking their father.

Furthermore, it has also been reported that, given equal exposure, adult men and women are equally vulnerable to malaria infection, except for pregnant women who are at greater risk of severe malaria in most endemic areas (52).

Our study has some limitations. First, we did not measure serum ferritin levels to assess iron status or reticulocyte counts for confirming if the anemia is regenerative or not. Second, the small sample size led to some undetermined statistical analysis results. Finally, we did not assess the presence of other parasites that may have co-infected the same participant and caused the observed anemia.

## Conclusion

Based on our results, the prevalence of anemia among children aged  $< 7$  years is still high, with the moderate hypochromic microcytic anemia being the only statistically significant type of anemia and more prevalent (78.63%) irrespective of the *Plasmodium* species in children aged 3–6 years in the western region of Côte d'Ivoire. Furthermore, malaria infection was highly prevalent in both sex (66.7% by GS vs. 78.3% by RDT), with the *Plasmodium* parasites infecting the younger (aged 3 months to 2 years) children much less than the older children (aged 3–6 years). *P. falciparum* infection was more prominent in older children, who had the lowest infestation rate (parasitemia), than in the younger children, who had the heaviest infestation rate. Therefore, continued



and effective efforts are needed to improve the general health of the high-risk population.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving human participants were reviewed and approved by Comité National d'Éthique des Sciences de la Vie et de la Santé (CNESVS) de la Côte d'Ivoire. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## Author contributions

ME and KN contributed to the conception of the study, data analysis and interpretation, drafting of the manuscript, and agreed to be accountable for all aspects of the work. GC was involved in the data analysis of the manuscript. All authors contributed to the article and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/ftd.2022.957166/full#supplementary-material>

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