Malaria Journal

RESEARCH

Open Access

High incidence of clinical malaria among asymptomatic *Plasmodium falciparum* infected children receiving SMC with sulfadoxine-pyrimethamine and amodiaquine (SP + AQ) in Koulikoro, Mali

Daouda Sanogo[1,2*], Mahamoudou Toure[1,2,4*], Moussa Keita[1,3,5], Fousseyni Kane[1,2,3], Soumba Keita[1,2], Ibrahima Sanogo[2,3], Sory Ibrahim Diawara[1,3,4], Cheick Oumar Tangara[1,2], Hamady Coulibaly[1,2], Bourema Cisse[1,2], Sidibé M'Baye Thiam[1,2], Mahamadou Diakite[1,2,3,5], Nafomon Sogoba[1,3,5] and Seydou Doumbia[1,2,3,4]

Abstract

Background Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine and amodiaquine (SP + AQ) involves the monthly administration of therapeutic doses to children under five years of age during periods of high risk of malaria in regions where malaria transmission is highly seasonal. Current SMC guidelines recommend administering the same treatment to both non-infected and asymptomatic *Plasmodium falciparum*-infected children. However, a critical knowledge gap remains the impact asymptomatic infection on the efficacy of SMC in preventing clinical malaria over a four-week period. This study aimed to evaluate the risk of clinical malaria and its association with children's infection status during SMC treatment.

Methods This study was conducted in the Koulikoro health district of Mali and focused on children under 10 years of age. A total of 726 children in 2019 and 1452 children in 2020 were randomly selected and followed throughout the SMC campaigns. The prevalence of asymptomatic *P. falciparum* infection was assessed in each round using microscopy prior to SMC drug administration. Children were passively monitored over a four-week period to record the incidence of clinical malaria. Data analysis was performed using R-Studio software. The risk of clinical malaria based on infection status was estimated through logistic regression analysis, and a Kaplan–Meier curve was used to compare survival times between infected and uninfected children. Proportions were compared using the Pearson Chi-square test, with statistical significance set at $p < 0.05$.

Results The average prevalence of asymptomatic *P. falciparum* infection was 11.0% across study years. Prevalence was notably higher among children aged 5 to 9 years old in 2019 ($p < 0.001$) and 2020 ($p = 0.016$). Asymptomatic infected children had a significantly higher risk of clinical malaria during both transmission seasons: 2019: (RR = 3.05,

*Correspondence:
Daouda Sanogo
sanogodd@icermali.org
Mahamoudou Toure
mah.toure@gmail.com
Full list of author information is available at the end of the article

CI [2.04–4.72]) and 2020 (RR = 1.43, CI [1.04–1.97]). Furthermore, the time to the first malaria episode was significantly shorter among infected children in both years ($p < 0.001$ for 2019, $p = 0.01$ for 2020).

Conclusion These findings demonstrate an elevated risk of clinical malaria in asymptomatic infected children during SMC implementation. Screening and treating *P. falciparum* infections prior to SMC administration could substantially enhance the effectiveness of this strategy in reducing malaria morbidity in endemic areas.

Background

Seasonal malaria chemoprevention (SMC) has been recommended by the World Health Organization (WHO) since 2012 for malaria prevention in children under five years of age in sub-Saharan African countries with highly seasonal transmission. The strategy involves the monthly administration of anti-malarial drugs over three days during periods of high malaria transmission, typically spanning three to five months each year [1, 2]. In Mali, SMC was initially deployed as pilot intervention in select regions from 2012 to 2015. By 2016, it was scaled up as a nationwide prevention strategy targeting children under five. Numerous studies have shown that SMC significantly reduces malaria-related morbidity, mortality and anaemia [1–5]. However, despite its proven effectiveness, malaria remains the most prevalent and fatal disease in Mali, with 3,204,275 confirmed cases and a fatality rate of 1.4% reported in 2022 by the National Malaria Control Programme (NMCP) [6]. Asymptomatic *Plasmodium falciparum* infections, characterized by the presence of parasites in the blood without clinical symptoms, are key challenge in malaria control. These individuals serve as reservoir for transmission, perpetuating the malaria burden.

Current WHO recommendations specify that only symptomatic children need to be tested for malaria using rapid diagnostic test (RDT) before receiving Sulfadoxine-pyrimethamine (SP) plus amodiaquine (AQ), while asymptomatic children are not routinely screened. Consequently, in malaria-endemic areas, many asymptomatic infections may persist undetected among children receiving SMC. Although asymptomatic infections can contribute to the development of anti-malarial immunity, they also play a crucial role in maintaining the chain of malaria transmission. Since the implementation of SMC as a community-based intervention, few studies have investigated its effectiveness in clearing theses subclinical infections, which act as reservoirs for ongoing transmission. While SMC is recognized as both a preventive and presumptive treatment, its limited ability to eliminate circulating parasite reservoirs raises concerns about its long-term efficacy. This study, conducted during the SMC campaign in the Koulikoro health district of Mali, aims to assess the risk of symptomatic malaria within four weeks following SMC round among eligible children. The findings provide critical insights into whether clearing asymptomatic infections prior to the start of the SMC campaign would enhance its impact in reducing malaria transmission in endemic regions.

Methods

Study sites

The study was conducted in the health district of Koulikoro, a tropical region in Mali located approximately 60 kms from the capital, Bamako. The district features diverse ecological patterns, resulting in varying lengths of the malaria transmission seasons, ranging from 4 to 5 months annually. A total of nine (9) villages were selected for the study, each equipped with a community health centre and representative of the different ecological zones:

- Dry area with short transmission season (3 months): Sirakorola, Chola, Monzombala.
- Area with a transmission season of approximately four months: Doumba, Sinzani, Koula.
- Riverine area with a transmission season lasting for five months: Gouni, Kenenkou and Kamani (Fig. 1).

Recruitment of study cohort

This study builds on a prior community-based study that assessed the efficacy of seasonal malaria chemoprevention (SMC) in children aged 3 months to 9 years. The target population consisted of children eligible for SMC (specifically those aged 3 months to less than 10 years). Following a census enumeration in each village, the total population across the nine villages was approximately 27,867 with 6326 and 6638 children eligible for SMC in 2019 and 2020, respectively. Each selected site was supported by a community health centre managed by a physician, ensuring access to healthcare for study participants.

Sampling

Before the start of the SMC season, parents, or guardians of children under 10 years of age who were eligible for SMC were invited to provide voluntary consent. Only children whose parents/guardians completed and signed the consent form were enrolled in the study and assigned

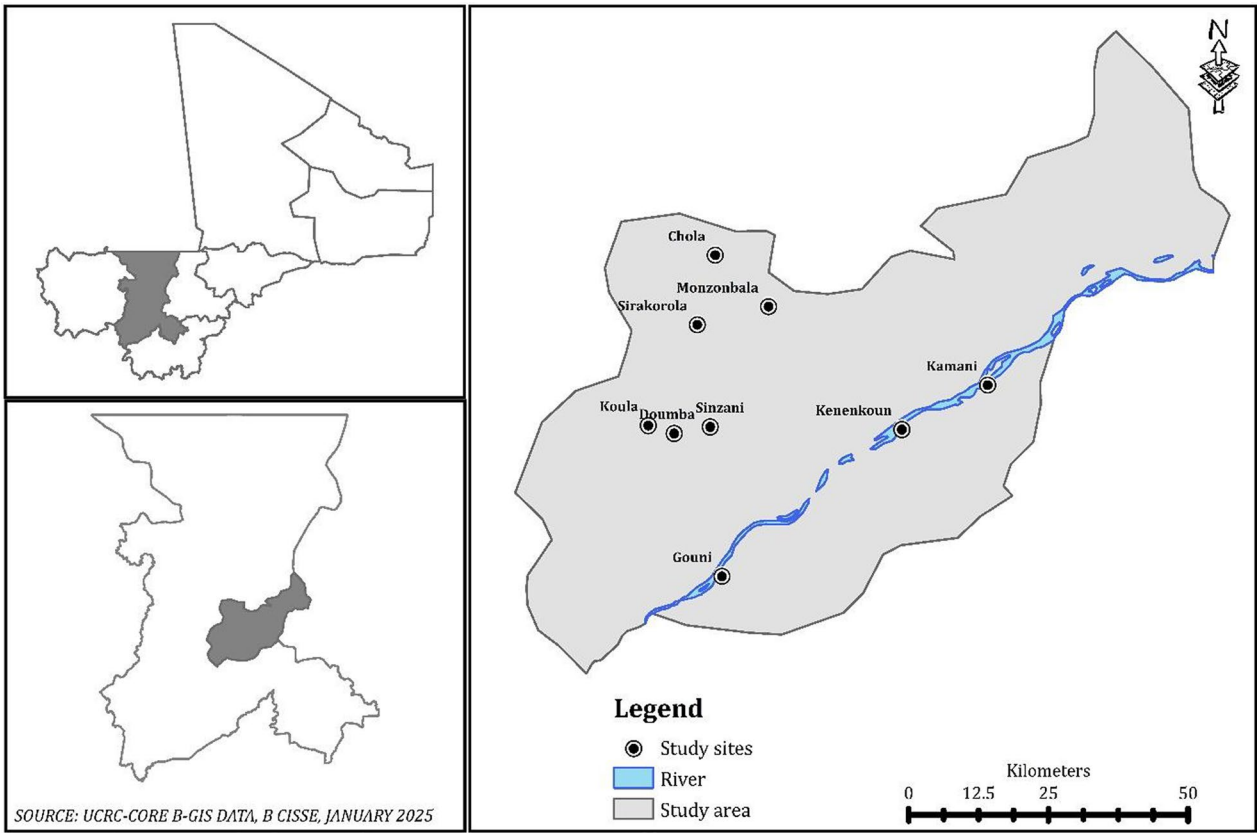

Fig. 1 Study site

a unique identifying number. A subsample of 726 children in 2019 and 1452 in 2020, was randomly selected using a rigorous stratified random sampling design. Villages were stratified by ecological zones to ensure the sample represented the diverse malaria transmission contexts within the Koulikoro health district. Within each village, a list of eligible children was compiled, and participants were randomly selected through a proportional sampling based on the size of the eligible population in each village. This process ensured that the sample reflected the relative population sizes across the villages. All selected participants were tested for asymptomatic *P. falciparum* infection using microscopy.

The sample size in 2020 was doubled compared to 2019 to improve statistical power. Monthly sample sizes were derived from the initial sample, accounting for the monthly variation of malaria burden in the study area (Fig. 2).

Follow-up and passive cases detection

Asymptomatic *P. falciparum* infection was assessed using thin blood smears only prior to SMC drug administration. Before enrollment children were carefully screened for clinical symptoms following NMCP guidelines. Children presenting with fever or a history of fever within the preceding 48 h were tested using a rapid diagnostic test (RDT). Those with a positive RDT results were excluded from the study and referred to the centre's medical director for appropriate treatment.

For blood smear preparation, finger-prick blood samples were air-dried, stained with 2% Giemsa for 30 min, and examined under an optical microscope with a 100 × oil immersion lens. A smear was deemed negative after reviewing of at least 100 fields. Each smear was independently examined by two experienced microscopists. Results were considered discordant if one microscopist reported a positive result and a negative result, and in such cases, a third microscopist resolved the discrepancy.

Enrolled children were then followed through passive case detection (PCD) between SMC rounds, from July to November, i.e. up to four weeks after the last SMC round, to monitor the incidence of clinical malaria. Clinical malaria was defined as an axillary temperature ≥ 37.5 C or history of fever within the previous 48 h, accompanied by a positive RDT. Cases were identified through PCD at the community health center.

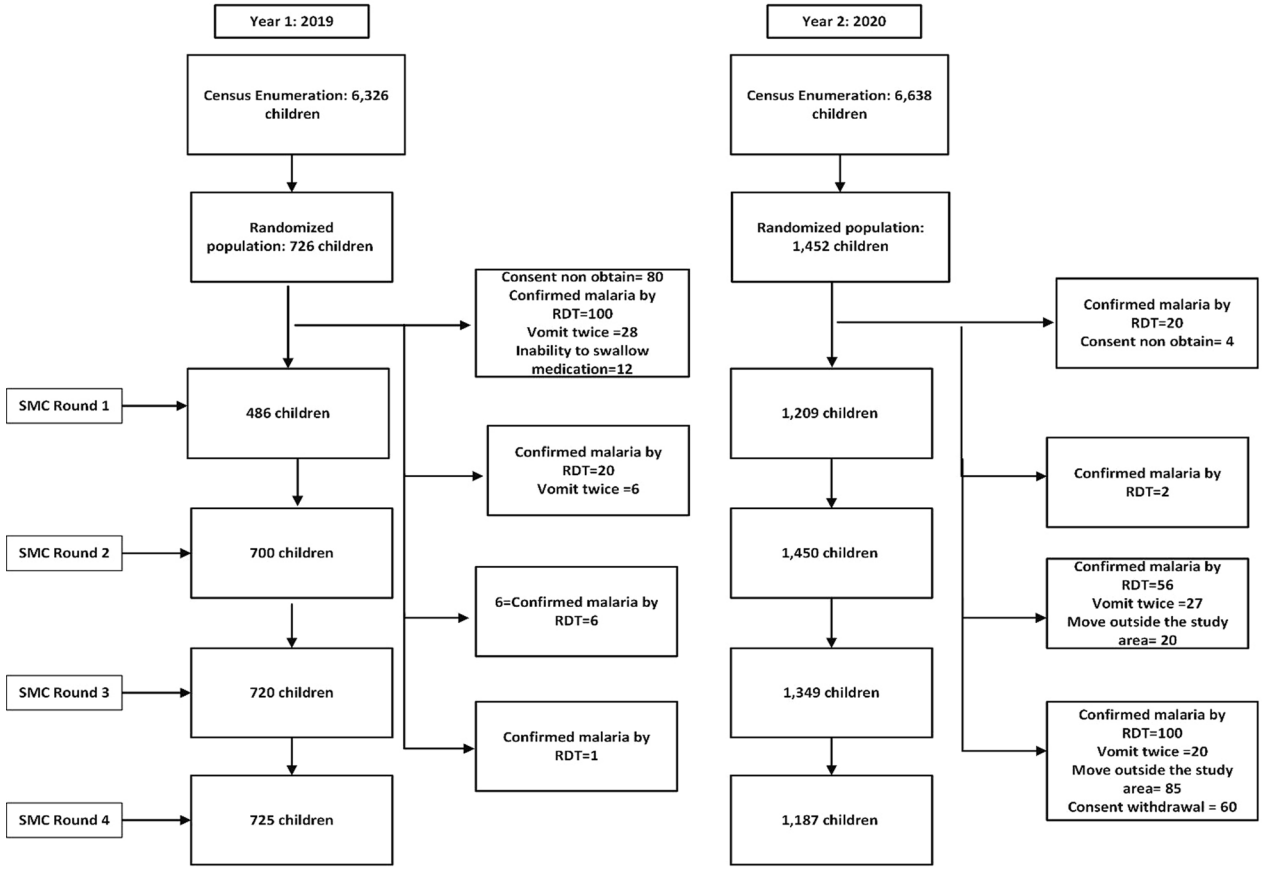

Fig. 2 Flowchart of participants recruitment and sample size distribution per SMC round

Data management and statistical analysis

Data collection was conducted using the electronic data capture Redcap platform, with daily synchronization to ensure accuracy and completeness. Data from Redcap were exported as Excel files for analysis in statistical program R version 4.2. Percentages were compared using the Chi-squared test, while logistic regression was applied to assess the risk of infection across groups. Statistical significance was determined at a p-value threshold of less than 0.05. The Kaplan- Meier method was employed to estimate the time to the first clinical malaria episode following SMC therapy, providing insights into survival probabilities over time.

Results

Descriptive characteristics of the study population

In 2019, children under five years old accounted for 52.9% (1394/2631) of the study population, while those aged 5–9 years old made up 47.1% (1.237/2.631). In 2020, the proportions shifted slightly, with children aged 3–59 months comprising 48% (2494/5195) and those aged 5–9 years constituting 52.0% (2701/5195) (Table 1).

The prevalence of *Plasmodium falciparum* asymptomatic infection by month, age group and year

In 2019, the prevalence of *P. falciparum* asymptomatic infection was 13.0%, 9.6%, 11.0% and 13.0% in July, August, September and October, respectively. For 2020, the prevalence rates were 11.0%, 15.0%, 8.2%, and 8.0% in the corresponding months (Fig. 3). The overall prevalence of malaria infection during the season was slightly higher in 2019 (11.65%) compared to 2020 (10.55%).

Age-specific prevalence revealed significantly higher rates of asymptomatic infection among older children (5 to 9 years) compared to children under five years. In 2019, the prevalence was 16.0% among older children versus 7.3% in younger children ($p < 0.001$). Similarly, in 2020, the prevalence was 12.0% among older children and 9.7% among younger ones ($p = 0.016$) (Fig. 4).

The overall incidence of clinical malaria according to asymptomatic *Plasmodium falciparum* carriage prior to SMC medications

In 2019, the average cumulative incidence of clinical malaria was significantly higher among asymptomatically

Table 1 Socio-demographic characteristics

Characteristic	2019					2020				
	July = 486	August, n = 700	September, n = 720	October, n = 725	Overall, N = 2,631	July, n = 1.209	August, n = 1.450	September, n = 1.349	October, n = 1.187	Overall, N = 5,195
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gender										
Male	253 (52.1)	371 (53.0)	396 (55.0)	377 (52.0)	1394 (52.9)	677 (55.9)	754 (52.0)	728 (53.9)	617 (51.9)	2753 (52.9)
Female	233 (47.9)	329 (47.0)	324 (45.0)	348 (48.0)	1237 (47.1)	532 (44.1)	696 (48.0)	621 (46.1)	570 (48.1)	2442 (47.1)
Age										
Under 5 y.o	252 (51.85)	399 (57.0)	382 (53.0)	377 (52.0)	1394 (52.9)	556 (45.90)	696 (48.0)	661 (48.9)	605(50.9)	2494(48.0)
5–9 y.o	234 (48.15)	301 (43.0)	338 (47.0)	348 (48.0)	1237 (47.1)	653 (54.1)	754 (52.0)	688 (51.1)	582 (49.1)	2701 (52.0)

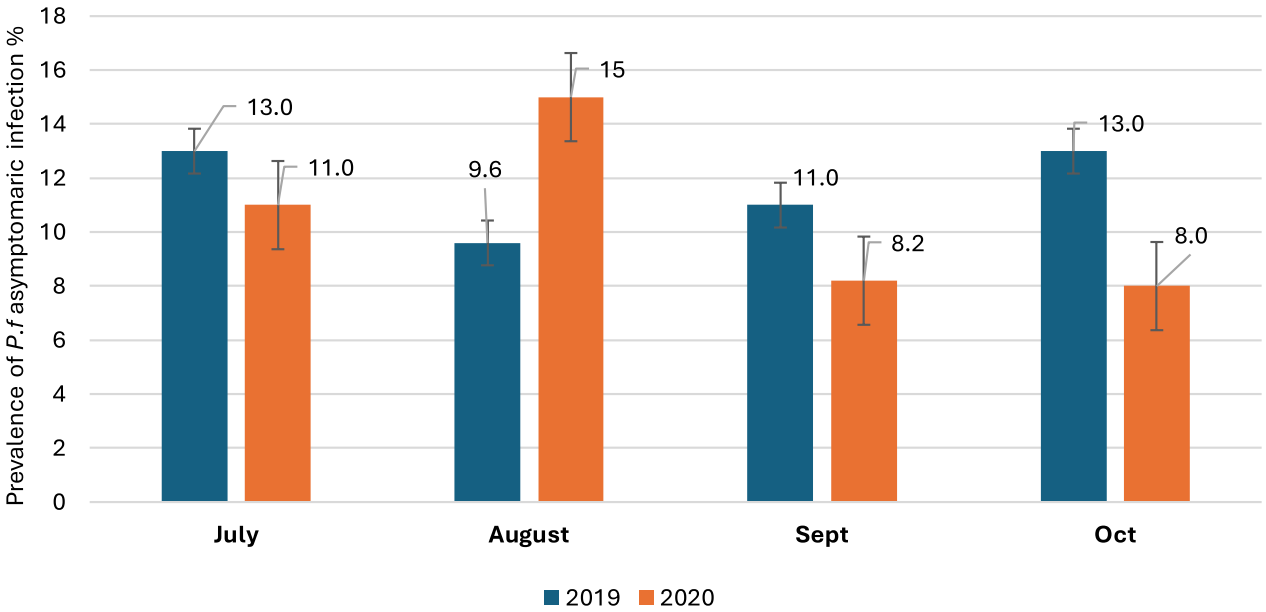

Fig. 3 Prevalence of symptomatic *P. falciparum* carriage by SMC round by year

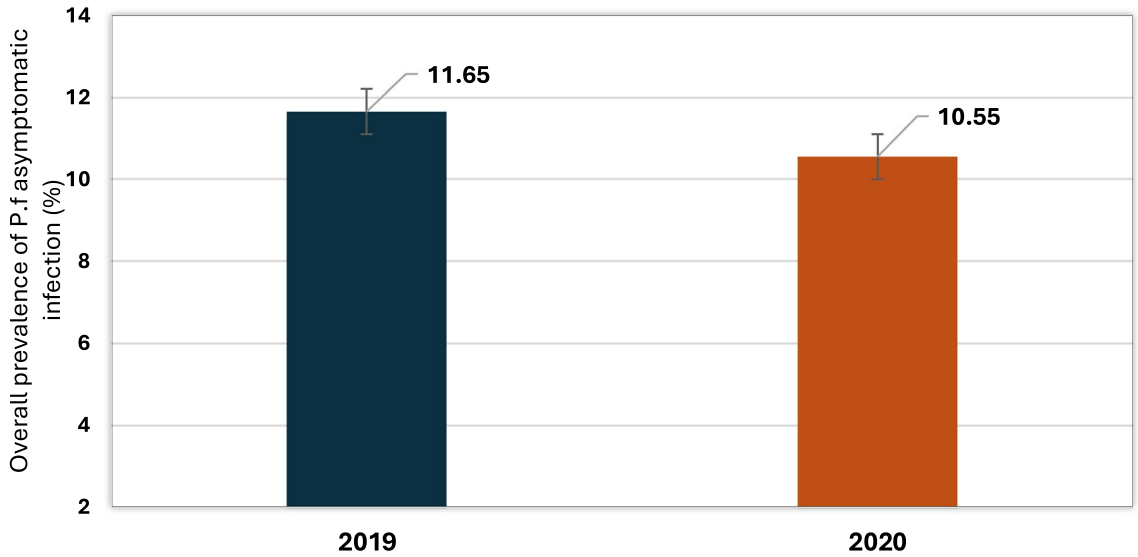

Fig. 4 Overall prevalence of asymptomatic *P. falciparum* carriage by year

infected children (23.58%) compared to uninfected children (7.47%) (RR = 3.16, 95% CI [2.49–40]; p < 0.001). Similarly, in 2020, the cumulative incidence of clinical malaria was 5.19% in asymptomatically infected children versus 3.60% in uninfected children (RR = 1.45; 95% CI [1.12–2.16]; p = 0.047) (Table 2).

The likelihood of becoming clinically symptomatic over time by asymptomatic statute before SMC

Survival curves between the two groups based on infection status prior to the first SMC treatment are presented in Figs. 5 and 6. Approximately 50.0% (2019) and 75.0% (2020) of infected children show up at the clinic within

Table 2 The overall incidence of clinical malaria according to asymptomatic *Plasmodium falciparum* carriage prior to SMC medications

Year of visit	*P. falciparum* Infection status before SMC by microscopy	Cumulative malaria Incidence per 100 during SMC season	RR 95% [IC]	p
2019	Uninfected children	7.47		< 0.001
	Infected children	23.58	3.16 [2.49–40]	
2020	Uninfected children	3.60		0.047
	Infected children	5.19	1.45 [1.12–2.16]	

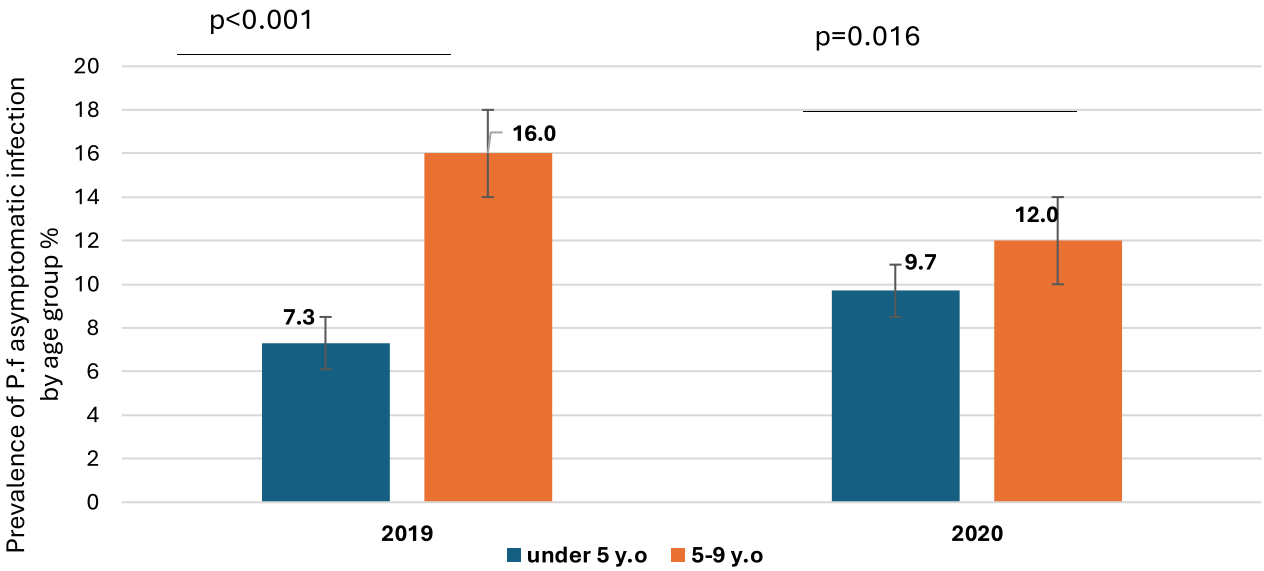

Fig. 5 Overall age specific prevalence of asymptomatic *P. falciparum* carriage per year

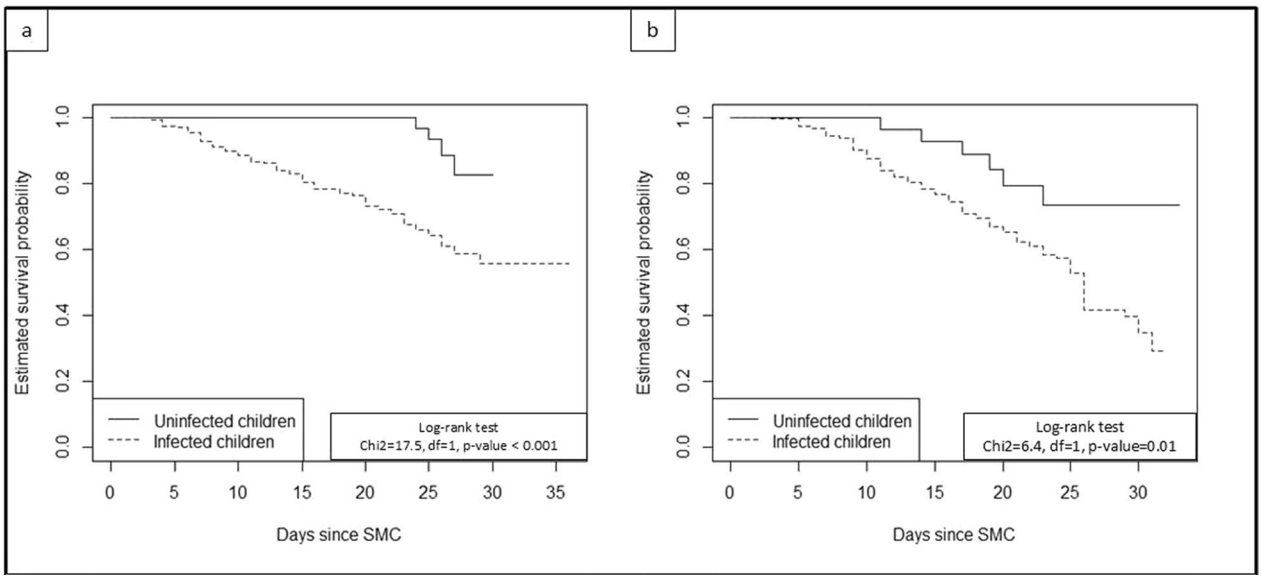

Fig. 6 Kaplan–Meier: the delay from SMC drug taking to clinical malaria occurring between infected and uninfected children in (**a**) 2019 and (**b**) 2020

four weeks with clinical malaria after receiving SMC treatment. In both years, children who were smear negative had a higher survival probability compared to those who were smear positive. Children who have taken the SMC and are infected are more likely to have clinical malaria than those who were not infected when they took the SMC ($p < 0.001$ in 2019 and $p = 0.01$ in 2020) (Fig. 6).

Discussion

Methodological approaches

SMC remains a crucial intervention for reducing malaria-related morbidity and mortality among target populations in areas with seasonal malaria transmission. However, asymptomatic *P. falciparum* carriage plays a significant role in sustaining malaria transmission and may hinder progress toward elimination [11–15]. As the SMC strategy does not recommend a test-to-treat approach for all eligible children, those without malaria-like symptoms at the time of SMC administration may receive SP + AQ while harbouring the parasite, often at low densities. This study investigated the risk of clinical malaria following SMC treatment, with a focus on the infection status of children under 10 years of age during two malaria transmission seasons.

The prevalence of asymptomatic malaria parasitaemia

The observed prevalence of *P. falciparum* asymptomatic infection indicates that while SMC is widely implemented with high coverage rates reported in countries such as Mali, a notable proportion of children receiving SMC treatment (approximately 11.0%) are already carrying *P. falciparum* asymptomatically. Research has shown a high prevalence of asymptomatic *P. falciparum* carriage in malaria-endemic regions [9, 11, 16–19]. Moreover, parasitaemia remains detectable in some children even after the administration of SP and AQ during SMC [20].

The prevalence of asymptomatic malaria parasitaemia was statistically higher among older children compared to those under five years of age, consistent with the age-shift in malaria prevalence and incidence reported in sub–Saharan Africa, where older children face a greater risk. Similar findings have been documented in The Gambia by Ahmad et al. [11], and in Mali by Tran et al. [21], Touré et al. [22]. and Coulibaly et al. [23].

Clinical malaria incidence following seasonal malaria chemoprevention drugs and asymptomatic malaria parasitaemia carriage

Asymptomatic *P. falciparum* infections prior to SMC delivery were significantly associated with a higher risk of clinical malaria within four weeks post-treatment, as demonstrated in this study. While the combination of SP + AQ remains effective for malaria prevention in Mali, it is not recommended as a first or second-line treatment by the NMCP. This limitation suggests that SP and AQ, by failing to clear the reservoir of asymptomatic infections, cannot fully prevent the progression to clinical malaria within the subsequent four weeks.

Survival analysis revealed a shorter time between SMC treatment and the onset of symptoms among children who were asymptomatically infected at the time of SP + AQ administration, compared to those without infection. The median time was 6.47 days versus 23.5 days in 2019 and 7.11 days versus 11.3 days in 2020 in infected and uninfected children, respectively. SMC's primary goal is to maintain optimal plasma concentration of SP and AQ for approximately four weeks, effectively preventing new infections during this period [2, 24].

However, the therapeutic efficacy of SP + AQ in endemic settings for *P. falciparum* has not been as thoroughly investigated since SMC implementation, in contrast to its well-established chemopreventive effectiveness [25–27]. Several factors may influence the limited protection observed in cases of asymptomatic parasitaemia. Malaria parasite sensitivity to SMC drugs and parasite load at the time of SMC treatment could affect drug metabolism and pharmacokinetics, leading to reduced prophylactic duration [20]. Additionally, the presence of asymptomatic infections might alter drug pharmacokinetics, potentially diminishing the effectiveness of SP + AQ.

Current data on this interaction are limited, underscoring the need for further studies to evaluate how asymptomatic parasitaemia impacts plasma concentrations of anti-malarial drugs and their efficacy.

In summary, the inability of SP + AQ to clear low density asymptomatic parasitaemia may be perceived as a treatment limitation, emphasizing the need for more effective drug regimens capable of targeting these infections [30–32].

Limitations of the study

The limitations of this study were: (1) the reliance on microscopy, which may have lower sensitivity compared to molecular methods, could underestimate the prevalence of asymptomatic infections, (2) the findings from the Koulikoro health district may not be generalizable to other settings with different malaria transmission dynamics and (3) the lack of knowledge on how the drugs behave in asymptomatic carriers because pharmacokinetic and pharmacodynamic measurements were not carried out. The third point is extremely important because the variability in drug absorption, metabolism, and clearance among infected children could influence the prophylactic efficacy of SMC. Thus, future studies

should incorporate these aspects to better assess the impact of asymptomatic infections on drug effectiveness.

Conclusion

Asymptomatic malaria infections remain prevalent among children eligible to SMC in malaria-endemic areas, posing a substantial risk for clinical malaria. Children harbouring asymptomatic infections are at higher risk of progressing to clinical malaria during the transmission season. Implementing a mass drug administration (MDA) of efficient anti-malarials to clear parasite reservoirs before the first round of SMC campaigns could significantly reduce the disease burden and enhance the effectiveness of SMC in controlling malaria during the seasonal transmission periods.

Abbreviations

CI	Confidence interval
NMCP	National Malaria Control Programme
RDT	Rapid diagnostic test
SMC	Seasonal Malaria Chemoprevention
SP + AQ	Sulfadoxine-Pyrimethamine + Amodiaquine
RR	Relative risk
WAF ICEMR	West African International Center for Excellence in Malaria Research
WHO	World Health Organization

Acknowledgements

A special thank the WAF ICEMR program members, the community of Koulikoro, and Mali's NMCP and the Fogarty International Center of the National Institutes of Health of the United States for the support given to Dr Daouda Sanogo under Grant D43TW008652.The authors also thank Dr. Jamila Aboulhab, Special Advisor for Global Health, Collaborative Clinical Research Branch, Division of Clinical Research, NIAID/NIH, for her invaluable assistance in reviewing and improving the manuscript.

Author contributions

DS and MT conceived and designed the concept, DS performed the analysis and drafted the manuscript. DS, SK, IS and FK coordinated and carried out field activities. MT, MK, SID, MD, NS and SD performed critical review and revision of the manuscript. HC and ST were responsible for data management. All authors discussed the results and contributed to the final manuscript.

Funding

This study was supported by the National Institutes of Health Cooperative Agreements 3U19AI129387-03S1 for the International Center of Excellence for Malaria Research (ICEMR).

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The Ethic Committee of the University of Sciences, techniques, and Technologies of Bamako (USTTB) granted ethical approval for this study (N°2021/108/CE/FMPOS). All parents or guardians of individuals provided written informed permission. Furthermore, prior to the recruitment in the research, written consent was acquired from the children's parents.

Competing interests

The authors declare no competing interests.

Author details

[1]West African International Center for Excellence in Malaria Research (WAF ICEMR), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali. [2]University Clinical Research Center (UCRC), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali. [3]Malaria Research and Training Center (MRTC), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali. [4]Faculty of Medicine and Odontostomaotology (FMOS), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali. [5]Faculty of Pharmacy (Fph), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali.

Received: 20 June 2024 Accepted: 5 February 2025
Published online: 27 March 2025

References

1. WHO. World malaria report 2020: 20 years of global progress and challenges. Geneva: World Health Organization; 2020. https://cdn.who.int/media/docs/default-source/malaria/world-malaria-reports/world-malaria-report-2020-briefing-kit-fre.pdf.
2. WHO policy recommendation: seasonal malaria chemoprevention (SMC) for *Plasmodium falciparum* malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa. Geneva: World Health Organization; 2012. WHO/HTM/GMP/2012.02. https://apps.who.int/iris/handle/10665/337978.
3. Konaté D, Diawara SI, Touré M, Diakité SAS, Guindo A, Traoré K, et al. Effect of routine seasonal malaria chemoprevention on malaria trends in children under 5 years in Dangassa, Mali. Malar J. 2020;19:137.
4. Druetz T, Corneau-Tremblay N, Millogo T, Kouanda S, Ly A, Bicaba A, et al. Impact evaluation of seasonal malaria chemoprevention under routine program implementation: a quasi-experimental study in Burkina Faso. Am J Trop Med Hyg. 2018;98:524–33.
5. Diawara F, Steinhardt LC, Mahamar A, Traore T, Kone DT, Diawara H, et al. Measuring the impact of seasonal malaria chemoprevention as part of routine malaria control in Kita, Mali. Malar J. 2017;16:325.
6. Programme National de Lutte contre le Paludisme du Mali. Rapport Annuel 2022 sur le Paludisme au Mali. Bamako. https://pnlp.ml/.
7. Rasamoel P, Jambou R, Ralamboranto L, Raharimalala L, Roux J. Portage asymptomatique et accès palustre: un équilibre complexe. Arch Inst Pasteur Madagascar. 1998;64:45–7.
8. Frimpong A, Amponsah J, Adjokatseh AS, Agyemang D, Bentum-Ennin L, Ofori EA, et al. Asymptomatic malaria infection is maintained by a balanced pro- and anti-inflammatory response. Front Microbiol. 2020;11:559255.
9. Fontecha G, Maradiaga A, García J, Mejía-Torres R, Escober L, Matamoros J, et al. Asymptomatic malaria infections in an endemic city of Honduras. Hum Parasit Dis. 2016. https://doi.org/10.4137/HPD.S40183.
10. Bousema T, Okell L, Felger I, Drakeley C. Asymptomatic malaria infections: detectability, transmissibility and public health relevance. Nat Rev Microbiol. 2014;12:833–40.
11. Ahmad A, Mohammed NI, Joof F, Affara M, Jawara M, Abubakar I, et al. Asymptomatic *Plasmodium falciparum* carriage and clinical disease: a 5-year community-based longitudinal study in The Gambia. Malar J. 2023;22:82.
12. Babiker HA, Gadalla AAH, Ranford-Cartwright LC. The role of asymptomatic *P. falciparum* parasitaemia in the evolution of antimalarial drug resistance in areas of seasonal transmission. Drug Resist Updat. 2013;16:1–9.
13. Chen I, Clarke SE, Gosling R, Hamainza B, Killeen G, Magill A, et al. "Asymptomatic" malaria: a chronic and debilitating infection that should be treated. PLoS Med. 2016;13: e1001942.
14. Andrade CM, Fleckenstein H, Thomson-Luque R, Doumbo S, Lima NF, Anderson C, et al. Increased circulation time of *Plasmodium falciparum* underlies persistent asymptomatic infection in the dry season. Nat Med. 2020;26:1929–40.
15. Heinemann M, Phillips R, Vinnemeier C, Rolling C, Tannich E, Rolling T. High prevalence of asymptomatic malaria infections in adults, Ashanti Region, Ghana, 2018. Malar J. 2020;19:366.
16. Mabunda S, Aponte JJ, Tiago A, Alonso P. A country-wide malaria survey in Mozambique. II. Malaria attributable proportion of fever and

establishment of malaria case definition in children across different epidemiological settings. Malar J. 2009;8:74.
17. Vafa M, Troye-Blomberg M, Anchang J, Garcia A, Migot-Nabias F. Multiplicity of *Plasmodium falciparum* infection in asymptomatic children in Senegal: relation to transmission, age and erythrocyte variants. Malar J. 2008;7:17.
18. Akindeh NM, Ngum LN, Niba PTN, Ali IM, Ayem OLO, Chedjou JPK, et al. Assessing asymptomatic malaria carriage of *Plasmodium falciparum* and non-*falciparum* species in children resident in Nkolbisson, Yaoundé, Cameroon. Children (Basel). 2021;8:960.
19. Hayuma P, Wang C, Liheluka E, Baraka V, Madebe R, Minja T, et al. Prevalence of asymptomatic malaria, submicroscopic parasitaemia and anaemia in Korogwe District, north-eastern Tanzania. Malar J. 2021;20:424.
20. Somé FA, Bazié T, Ehrlich HY, Goodwin J, Lehane A, Neya C, et al. Investigating selected host and parasite factors potentially impacting upon seasonal malaria chemoprevention in Bama, Burkina Faso. Malar J. 2020;19:238.
21. Tran TM, Li S, Doumbo S, Doumtabe D, Huang C-Y, Dia S, et al. An intensive longitudinal cohort study of Malian children and adults reveals no evidence of acquired immunity to *Plasmodium falciparum* infection. Clin Infect Dis. 2013;57:40–7.
22. Touré M, Sanogo D, Dembele S, Diawara SI, Oppfeldt K, Schiøler KL, et al. Seasonality and shift in age-specific malaria prevalence and incidence in Binko and Carrière villages close to the lake in Selingué, Mali. Malar J. 2016;15:1251.
23. Coulibaly D, Guindo B, Niangaly A, Maiga F, Konate S, Kodio A, et al. A Decline and age shift in malaria incidence in rural Mali following implementation of seasonal malaria chemoprevention and indoor residual spraying. Am J Trop Med Hyg. 2021;104:1342–7.
24. WHO. Seasonal malaria chemoprevention with sulfadoxine–pyrimethamine plus amodiaquine in children: a field guide. Geneva: World Health Organization; 2013. https://apps.who.int/iris/handle/10665/85726. Accessed 10 Jun 2022.
25. Zongo I, Dorsey G, Rouamba N, Tinto H, Dokomajilar C, Guiguemde RT, et al. Artemether-lumefantrine versus amodiaquine plus sulfadoxine-pyrimethamine for uncomplicated falciparum malaria in Burkina Faso: a randomised non-inferiority trial. Lancet. 2007;369:491–8.
26. Zongo I, Dorsey G, Rouamba N, Dokomajilar C, Lankoande M, Ouedraogo J-B, et al. Amodiaquine, sulfadoxine-pyrimethamine, and combination therapy for uncomplicated falciparum malaria: a randomized controlled trial from Burkina Faso. Am J Trop Med Hyg. 2005;73:826–32.
27. Somé AF, Séré YY, Dokomajilar C, Zongo I, Rouamba N, Greenhouse B, et al. Selection of known *Plasmodium falciparum* resistance-mediating polymorphisms by artemether-lumefantrine and amodiaquine-sulfadoxine-pyrimethamine but not dihydroartemisinin-piperaquine in Burkina Faso. Antimicrob Agents Chemother. 2010;54:1949–54.
28. Chotsiri P, White NJ, Tarning J. Pharmacokinetic considerations in seasonal malaria chemoprevention. Trends Parasitol. 2022;3:673–82.
29. White NJ. Does antimalarial mass drug administration increase or decrease the risk of resistance? Lancet Infect Dis. 2017;17:e15-20.
30. Touré M, Shaffer JG, Sanogo D, Keita S, Keita M, Kane F, et al. Seasonal malaria chemoprevention therapy in children up to 9 years of age: protocol for a cluster-randomized trial study. JMIR Res Protoc. 2024;13: e51660.
31. Cairns M, Ceesay SJ, Sagara I, Zongo I, Kessely H, Gamougam K, et al. Effectiveness of seasonal malaria chemoprevention (SMC) treatments when SMC is implemented at scale: case–control studies in 5 countries. PLoS Med. 2021;18: e1003727.
32. Salman S, Griffin S, Kose K, Pitus N, Winmai J, Moore B, et al. Pharmacokinetic properties of conventional and double-dose sulfadoxine-pyrimethamine given as intermittent preventive treatment in infancy. Antimicrob Agents Chemother. 2011;55:1693–700.

Publisher's Note