Factors contributing to preventing malaria in children aged 3 to 59 months after the first cycle of seasonal malaria chemoprevention in Tenkodogo Health District of Burkina Faso, July 2020: A prospective cohort study

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ABSTRACT

Background: The incidence of malaria in children under 5 years in Burkina Faso was 163 per 1000 with a case fatality of 1.5% in 2018. Despite the implementation of several strategies, malaria incidence increased in Tenkodogo Health District after the seasonal malaria chemo prevention (SMC) in 2018. We conducted a study to identify the factors contributing to malaria prevention in children after the first cycle of the seasonal malaria chemoprevention of 2020 in Tenkodogo Health District. **Methods:** We conducted a prospective cohort study, from June 5 to September 5, 2020 in Tenkodogo Health District, among children aged 03 to 59 months. We employed cluster sampling and selected 847 eligible children. Sociodemographic characteristics of children and their mothers/caregivers, SMC adherence and malaria incidence in the 28 days SMC were collected. The presence of long-lasting insecticide-treated mosquito net (LLNs) in the household was noted when the mother or the babysitter reported having one. Data collectors were able to confirm cohabitation with animals either from their presence in the household or from the residues of their feces. A questionnaire was used, and implemented documents review for data collection. We used Epi info 7 for calculating averages and proportions and carried out multivariate logistic regression. **Results:** The overall level of SMC adherence was 90.02%. During the 4-week follow-up, malaria incidence was 99.76 cases per 1000 children, increasing from 15.43 to 34.44 cases per 1000 children from the first to the fourth week after the first cycle of SMC. Advice from community health workers was a protective factor against malaria in children (aRR= 0.41; 95% CI [0.22; 0.77]). **Conclusion:** There was a gradual increase in malaria incidence after the first SMC cycle. Receiving advice from community health workers was a protective factor against malaria after the first cycle of SMC. Measures to strengthen the advice by community health workers are needed to reduce this incidence of malaria in children after first cycle of SMC in Tenkodogo Health District.

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Introduction

Malaria remains one of the main challenges of public health, although significant progress has been made [1]. Globally in 2022, there were an estimated 249 million malaria cases and 608 000 malaria deaths in 85 countries [2]. According to the World Health Organization (WHO), African region bears a disproportionate share of the malaria burden, accounting for 94% of malaria cases (233 million) and 95% (580 000) of malaria deaths [2]. Twenty-nine countries accounted for 95% of malaria cases globally. Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%), Mozambique (4%) and Niger (3%) accounted for about 51% of all cases globally [1]. There are five Plasmodium parasite species that cause malaria in humans and two of these species *Plasmodium falciparum* and *Plasmodium vivax* pose the greatest threat. *Plasmodium falciparum* is the deadliest malaria parasite and the most prevalent on the African continent. *Plasmodium vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa [2].

In Burkina Faso, the incidence was higher in children with 1,631 cases per 1000 inhabitants compared to 591 for the general population in 2018 [3]. In the same year, malaria was the main reason for consultation in basic health facilities (41.3%), the main reason for hospitalization (21.4%), and the first cause of death (16.4%) in medical centers and hospitals [3]. Several interventions have been implemented in recent years by the national malaria control programme to reduce the burden of malaria. These interventions include: intermittent preventive treatment (IPT) with sulfadoxine-pyrimethamine in pregnant women during antenatal consultations, periodic national campaigns for the universal distribution of long-lasting insectide-treated mosquito nets (LLINs) every three years, indoor spraying in some pilot districts, seasonal malaria chemoprevention (SMC) campaigns since 2014, initially localized to a few districts and then generalized to all districts in 2019, community malaria management and malaria awareness and communication activities [4].

Among these strategies, seasonal malaria chemoprevention (SMC) for children aged 3 to 59 months is one of the most important, effective, inexpensive and safe strategies [5]. It is defined as "the intermittent administration of a complete course of treatment with an antimalarial drug during the high transmission season of malaria to avoid the disease[6]. The goal of SMC is to maintain therapeutic concentrations of antimalarial drug in the blood during the period, when the risk of contracting malaria is higher. It is expected to administer at least four cycles of sulfadoxin pyrimethamin plus Amodiaquin (SP+ AQ) treatment in one-month intervals to children aged 3 to 59 months in areas of high seasonal malaria transmission [5].

Started in Burkina Faso in 2014 with 07 districts, SMC covered 65 districts in 2018 and all 70 districts of the country in 2019. It consists of four separate cycles of 4 weeks during the high transmission season of malaria from July to October every year. The first dose of SP-AQ during each cycle is administered in a supervised manner by Community Distributors (CDs). The second and third doses are given to parents for home administration for the last two days at the same hour.

The major finding from routine malaria data in Burkina Faso, in recent years, shows a "significant" decrease in the number of malaria cases among children under 5 years of age, within two weeks after a SMC passage and then a "rebound" for the two weeks before the next pass [7]. Some studies on malaria incidence after intermittent preventive treatment (IPT) of malaria noted that IPT provides substantial protection against malaria in children already protected by an Insecticide-Treated Bednet [8] and the prevalence of malaria decreased in the implementation district of Kita in Mali [9]. On the otherhand, despite the introduction of seasonal malaria chemoprevention (SMC) in the Magaria district of Niger, malaria incidence remained high [10]. There are few studies that have looked at malaria incidence and its associated factors a few weeks after the first cycle of SMC campaign.

This study was conducted in 2020 to determine the malaria incidence and associated factors in children aged 03 to 59 months within 28 days of the first SMC cycle of year 2020 in Tenkodogo Health District in Burkina Faso.

Methods

Study setting

The study was implemented in the health district of Tenkodogo, located in the Boulgou province. It covers three (03) communes, comprising one (01)

urban (Tenkodogo with 06 sectors and 92 villages) and two rural (Bagré: 8 villages and Bissiga: 23 villages). There are fifty-five (55) farming hamlets. Tenkodogo is the capital of Boulgou Province and of the East-Center Region. It has an area of 1990 Km2. It is bordered by the health districts of Koupela to the north, Fada to the northeast, Ouargaye to the east, Bittou to the south, Garango to the west, and Zabré and Manga districts in the southwest. The population of the health district in 2020 was estimated at 261,732 inhabitants, according to a projection of the general census of population and housing (RGPH) of the year 2006. In 2018, children under the age of 15 accounted for almost half of the population (47.84%) and women of reproductive age (23.75%). The population density was estimated in 2019 at 124 inhabitants per km^2. The crude birth rate was 40.7 per thousand inhabitants, the fertility rate was 83.6 per thousand among women aged 15-49 and 57 children out of 1000 live births die before their first birthday in Boulgou province in 2018 [11]. The average household size was six people according to the same census. It is a relatively young population with significant migratory movements internationally and in the sub-region.

Study design

We conducted a prospective cohort study. Study period: The study period was from 5 June to 5 September 2020.

Sample size and sampling technique

The sample size (n) was calculated from the following formula, using the OPEN EPI software:

$$\frac{Npq}{\frac{d^2}{1{,}96^2}(N-1)+pq}$$

where deff=design effect (deff=2 because clusters were formed in both rural and urban areas and children were included through a two-level sampling (village for the first level and household for the second)), N= population size, p=estimated proportion of compliance of SMC in Tenkodogo district, p=50% because the relative status of SMC compliance is not known in Burkina Faso, d=desired absoluted precision (d=0,05). We retained the accuracy level at 0.05. The cluster effect was 2. We calculated n = 762. In anticipation of possible lost follow-up or non-respondents, a 10% increase in size 762/(1-0.1)was achieved; giving us a total of 847 children, aged 3-59 months to investigate.

The health district of Tenkodogo was randomly selected from the list of 70 districts in Burkina Faso. The districts were arranged alphabetically and then a serial number from 1 to 70 was assigned to each. Excel software was used to generate a random number between 1 and 70. The number generated corresponded to the chosen district.

Within the district, we used two-stage cluster sampling to select the children for the study (**Figure 1**). For the first level, we performed a random selection of the cluster with Excel: Sectors and villages were considered clusters and listed alphabetically, with the size of their target population. After dividing the total population of children aged 3 to 59 months in Tenkodogo Health District (44,599) by 30 (cluster), we obtained a sampling step of 1487. Using Excel, we randomly generated a number between 1 and 1487. This number obtained corresponded to the rank of the first cluster and this number was 35 was. We applied this rank to select the first cluster and then used the sampling step for the selection of complementary clusters. For the second level, we randomly selected the households in the cluster. At the center of the cluster, we threw a pen, and the direction of the pen indicated the first household to be selected. Once inside the selected household, we proceeded to the exhaustive recruitment of children from this household meeting the inclusion criteria. Once the first household had been selected, we proceeded clockwise to select the next household, until we reached the maximum number of households required to have the desired number of children for this cluster. The mother/caregiver, with multiple children, responded for each child. The children targeted by our investigation who were absent when the investigators visited the concession were not retained.

Study population and eligibility criteria

The study population consisted of children aged 03 to 59 months in the Tenkodogo Health District and their parents/guardians of children. We included children aged 3-59 months, who received SP+AQ during the first cycle of SMC in July 2020, resided in the study area for at least one month, and wanted to stay there at least one month with the written consent of their parents/guardians. We excluded malaria illness children.

Data collection: variables, tools and techniques

Sociodemographic characteristics of study children and their mothers/caregivers, SMC adherence and malaria incidence in children in the 28 days, after taking SP+QA at the first cycle were collected. The presence of long-lasting insectide-treated mosquito net (LLNs) in the household, cohabitation with animals, presence of larval breeding sites, and advice from the community health workers to mothers during the first drug administration were also collected. Malnutrition and environmental conditions of the households were also collected.

A child was considered as adherent to SMC if he took Sulfadoxine + Pyrimethamine on Day 1, amodiaquine on Day 2 and Day 3 at the same time, and when he took the same drug in case of immediate rejection/vomiting. If one of these conditions was not respected, the child was considered as non-adherent. Malaria incidence was calculated as the proportion of new cases of malaria confirmed by rapid diagnostic test (RDT) during a period over the number of children followed. Presence of long-lasting insectide-treated mosquito net (LLINs) in the household was noted when the mother or caregiver declared having one. Cohabitation with animals was present when the data collectors saw animals living in the household with humans or from the residues of their feces. Larval breeding sites were present when data collectors saw them in stagnant water containers. Advice from the community health workers were collected by asking the mothers or caregivers if, during the first administration of SMC drugs, they received advice from community health workers on how to give the second or third dose of the malaria prevention drugs. The status of malnutrition was collected with a monitor by measuring the upper arm circumference of children (MUAC). We considered as child malnourished with an arm circumference under 125 mm. The environmental living was declared to be acceptable if there were no larval breeding sites and no cohabitation with animals. All these were independent variables.

The dependent variable was having malaria illness after SMC. Malaria was defined by the presence of fever (uncorrected axillary temperature greater than or equal to 37.5°C) or a history of fever in the last 72 hours, and the detection of plasmodium falciparum on microscopic examination by thick drop/blood smear or the positivity of the rapid diagnostic test (RDT) and/or the presence of signs of severity.

Data collection techniques consisted of interviews, literature review, and direct observation. Several data collection tools were developed, namely the questionnaire, the observation grid, and the literature review grid.

The questionnaire was administered face-to-face and consisted of the interviewer recording the interviewees answers on a paper form. Data collection was conducted by intermediate field epidemiology training program residents of cohort one in Burkina Faso. The initial data collection began the day after the first cycle of SMC ended. A second data collection took place two weeks after the initial collection. After the initial collection, the follow-up of the children in the cohort was provided by the community health workers of each village. The follow-up was done on day7, day14, day21, and day28. As a result, for children declared sick, data collectors were immediately informed by telephone by the community health workers. The data collectors also confirmed the child´s malaria diagnosis by reviewing the necessary forms (health record, primary health care facility consultation register). The control and supervision of community health workers was done by the health centers´ first managers. Health centers´ first managers supervised community health workers once a week during four week. Very sick children in community were cared for at the health center by the first managers and other members of the health center.

Data analysis

A data entry tool was developed with Epi info software, version 7.2.3.1 by FETP residents. The questionnaire data was recorded in an Epi info data

entry screen . This was followed up with cleaning the database which consisted of finding and deleting duplicate records and completing missing data, and correcting outliers.

Analysis of the quantitative data was performed, using Epi info software, version 7.2.3.1. Descriptive statistics of the sample variables such as proportions were generated and presented in text, table and/or figure form. Bivariate analaysis was conduted and generated crude relative risks (cRR) and 95% confidence intervals (CI) of the different factors associated with malaria.

The comparison between qualitative variables was made using Pearson's chi-square test or Fisher's exact test if more than 20% of the expected values were ≤ 5. The level of significance was set at 0.05. Results were presented with a 95% confidence interval. Also, we used logistic regression model to identify independent variables associated with the outcome.

Ethical considerations

The study protocol was approved by the Burkina Faso national Research Ethics Committee (Number 2020-8-161). At the same time, and before the field phase, an authorization to collect data was issued by the Secretary General of the Ministry of Health and sent to the Regional Director of Health of the Central East, who forwarded it to the Chief Medical Officer of the Tenkodogo Health District. Participation in the study was conditional, on the participants providing written free and informed consent.

The confidentiality of the information collected and their anonymity by all stakeholders in this study was respected.

Results

Socio-demographic characteristics of the children surveyed and their mothers/caregivers

In our study, 50.59% (426/842) of children were male and 85.87% (723/842) were over 11 months of age. 65.8% (554/842) of the mothers and/or caregivers had no school education, and 97.39% (820/842) had a long-lasting insectide-treated mosquito net. Also, 57.96% (488/842) of children were in households with cohabitation of animals, and 48.1% (405/842) of children were in house with the presence of larval breeding sites (Table 1).

SMC adherence in children aged 3 to 59 months in Tenkodogo Health District at first cycle 2020

Adherence was 90.02% (758/842) and the first dose of SMC was supervised in 83.50% of cases (703/842).

Malaria incidence among children aged 3-59 months in Tenkodogo Health District after the first cycle 2020

During follow-up, 15.20% of children (128/842) became ill, of whom 84 had confirmed malaria, i.e. a confirmed malaria incidence of 99.76 cases per 1000 children. However, 11.71% (15/128) of sick children had suspected malaria (RDT not performed).

Confirmed malaria incidence increased from 15.43 per 1000 (n=13) to 34.44 cases per 1000 (n=29) from the first week to the fourth week after SMC (Figure 2).

Factors associated with malaria in children aged 03 to 59 months after taking SMC drugs at first cycle 2020

Children of mothers who received advice from community health workers during SMC administration were less likely to develop malaria compared to children who did not receive advice from community health workers (Crude RR=0.43 [0.24 '>0.24 - 0.75]). In multivariate analysis, children whose mothers had received advice from the community health workers during first administration of SP+AQ had a 59% decrease in the risk of developing malaria, compared to children whose mothers had not received advice (adjusted RR = 0.41 [0.22; 0.77'>0.22; 0.77]). The other variables were not statistically significant at multivariate level (Table 2).

Discussion

Overall adherence to seasonal malaria chemo prevention in the first cycle of our study was 90.02%. This proportion is good, according to the standards of Burkina Faso's national malaria control program,

which attests to the target of 90%[12]. This good compliance is explained by the strong support of the population for the strategy that has been implemented since 2017 in this health district and whose beneficial effects are observed by the populations. Our results are slightly higher than those found by Salissou in Niger, which found a level of adherence to treatment of 89.2% among children who received SMC [13].

Despite the good overall treatment adhrence, a rebound of malaria was observed after SMC, with a gradual increase in malaria incidence from the first to the fourth week after SMC. This finding is similar to data from the epidemiological surveillance service at the level of the Burkina Faso malaria control program, which shows a gradual increase in malaria cases after the first week of each SMC cycle until the next cycle [7]. However, this situation is contrary to the one studied in vitro by researchers before the implementation of SMC. In fact, through the studies of Cisse B and Dicko A, researchers, no significant rebound in the clinical incidence of malaria in the year following the administration of SMC during initial studies in Senegal, Ghana, and Mali [8,14,15] was found. In addition, controlled studies have demonstrated protective efficiency against clinical malaria between 31% and 93% [16]. Also, after an evaluation of the implementation of seasonal malaria chemoprevention, it appeared that the administration of SMC reduced the risk of malaria measured by RDT during SMC campaigns in Burkina Faso from 2010 to 2017 [7]. This rebound of malaria after two weeks of administration of SMC in our situation could be explained by the reduced duration of the effectiveness of SMC in vivo, contrary to what is observed in vitro where we find a therapeutic efficiency of 4 weeks after the administration of preventive treatment.

Finally, the advice given by community health workers was a protective factor against the occurrence of malaria after SMC in children. This could be explained by the fact that the advice provided by the community health workers was beneficial and allowed mothers of children to follow good practices to have better malaria protection outcomes for children during the period of high malaria transmission. Furthermore, community health workers live in the same context as mothers and act as intermediaries with health workers. If the advice given by community health workers is successful, it means that their advice is in line with scientific knowledge and has a positive impact in malaria prevention, hence the need for good training of these actors in behaviour change communication before the start of SMC. This advice certainly has a positive impact on SMC compliance. However, the factors related to adherence are diverse and varied. Fatou Diawara et al. in Mali noted that forgetfulness was the main reason for non-adherence to treatment on days two and three [9].

This result suggest the positive role of community health workers in preventing malaria following SMC according to previous studies which found that the role and contribution of community health workers to the community management of the three commonest childhood illnesses have been proven to be quite crucial and successful especially in the rural areas that have limited access to health care [17-19].

Study limitations

The quality of the nets was not verified during the study. It can be possible that these nets may have wear and tears (aka holes) in them that may not be reported. Also, the data collector couldn´t verify if mother who said she slept last night on LLIN, had really slept on LLIN. They collected what the mothers said. This can be limits of our study. To mitigate some limits, the data collectors observed the environmental conditions in the household to verify the presence of larva gites or living of animals but didn´t enter in the houses.

Conclusion

The study on factors associated with the occurrence of malaria, after taking SMC, allowed us to identifiy a gradual increase in malaria incidence after the first passage of SMC; the advice given by community health workers to mothers of children was associated with the occurrence of malaria. This study underlines the importance of community health workers in the fight against malaria, but also reminds us the need to strengthen local communication actions with the beneficiaries of malaria control strategies in order to achieve the desired objectives of eliminating malaria. However, other studies may better assess the factors associated with the occurrence of malaria.

What is known about this topic

- Seasonal malaria chemoprevention protects children aged 3 to 59 months against malaria for 4 weeks after taking three daily doses of Sulfadoxine-pyrimethamine+ Amodiaquin

What this study adds

- Despite the chemoprevention of seasonal malaria, which protects children aged 3 to 59 months against malaria, during the first four weeks after taking the three daily doses of Sulfadoxine-pyrimethamine + Amodiaquin, our results show a progressive increase in the occurrence of malaria in children after two weeks of taking malaria chemoprevention and positive role of CHWs advice in preventing malaria following SMC

Competing interests

The authors declare no competing interest.

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Authors´ contributions

Yewayan Larba Berenger KABORE: conception of the study, data collection, data analysis, writing original draft, review and editing. Watton Rodrigue DIAO: conception of the study, data analysis, writing original draft. Denis YELBEOGO: review. Arouna KOIDIMA: conception of the study, data collection, writing original draft. Lassane KAFANDO: conception of the study, data collection, writing original draft. Frederic DIANDA: conception of the study, data collection, writing original draft. Noaga SAWADOGO: conception of the study, data collection, writing original draft. Jean-Baptiste OUEDRAOGO: conception of the study, data collection, writing original draft. Yamregma KABORE: conception of the study, collection collection, data analysis, writing original draft. Fréderic KAMBOU: conception of the study, collection collection, data analysis, writing original draft. Kodo ALBASSA: conception of the study, collection collection, data analysis, writing original draft. Salfo OUEDRAOGO: conception of the study, collection collection, data analysis, writing original draft. Brahima TRAORE: conception of the study, collection collection, data analysis, writing original draft. Pedwinde Hamadou SEOGO: review of the draft

Tables and figures

Table 1: Sociodemographic characteristics of children aged 03 to 59 months and their mothers or babysitters (n=842)

Table 2: Factors associated with malaria occurrence after first cycle of seasonal malaria chemoprevention in Tenkodogo District in 2020: Univariate and multivariate analysis

Figure 1: Sampling flow chart of the study

Figure 2: Malaria incidence by week children aged 03 to 59 months after first cycle of SMC in Tenkodogo, July 2020

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Table 1: Sociodemographic characteristics of children aged 03 to 59 months and their mothers or babysitters (n=842)		
Variables	**N**	**Proportion %**
Characteristics of children		
Sex		
Male	426	50,59
Female	416	49,41
Age		
12-59 months	723	85,87
3-11 months	119	14,13
Place of residence		
Urban	616	73,16
Rural	226	26,84
Sleeping under LLIN		
Yes	769	91,13
Not	73	8,87
Characteristics of mothers/caregivers		
Profession		
Farmer	353	41,92
Housewife	309	36,70
Merchant	87	10,33
Student	28	3,33
Official	14	1,66
Other	50	5,94
Educational attainment		
None	554	65,80
Secondary	140	16,63
Primary	104	12,35
Literate	38	4,54
Upper	6	0,71
Having LLIN		
Yes	820	97,39
Not	22	2,61
Characteristics of living environment		
Cohabitation with animals	488	57,96
Presence of larval breeding sites in the house	405	48,1
Presence of latrine	395	46,91
Presence of screens in the windows and doors Yes	10	1,2
No	831	98,7

Table 2: Factors associated with malaria occurrence after first cycle of seasonal malaria chemoprevention in Tenkodogo District in 2020: Univariate and multivariate analysis

Variables	Had malaria	No malaria	Univariate		Multivariate	
	Freq.(%)	Freq.(%)	cRR [CI; 95%]	*p-value*	aRR [CI; 95%]	*p-value*
Adherence to treatment						
Yes	72 (9,5)	686 (90,5)	0.62 [0.32 – 1.21]	0.16	0.68 [0.34; 1.34]	0.27
No	12 (14,29)	72 (85,71)	1		1	
Sex						
Male	43 (10,09)	383 (89,91)	1.02 [0.65 – 1.61]	0.9	0.63 [0.29; 1.36]	0.24
Female	41 (9,86)	375 (90,86)	1		1	
Age						
3-11 months	8 (6,72)	111 (93,28)	0.61 [0.28 – 1.30]	0.2	0.62 [0.29; 1.34]	0.23
12-59 months	76 (10,51)	647 (89,49)	1		1	
Place of residence						
Urban	59 (9,57)	201 (88,94)	1.17 [0.71 – 1.92]	0.52		
Rural	25 (11,06)	557 (90,42)	1			
Sleeping under LLIN						
Yes	77 (10,01)	692(89,99)	1.044 [0.4 – 2.36]	0.47		
No	7 (9,58)	66 (90,41)	1			
Occurrence of side effects						
Yes	5 (6,94)	105 (90,52)	0.93 [0.48 - 1.82]	0.84		
No	7 (9,58)	66 (90,41)	1			
Nutritional status						
Malnourished	1 (8,33)	11 (91,67)	0.81 [0.1- 6.41]	0.84		
Well nourished	83 (10)	747 (90)	1			
Educational attainment						
Uneducated	61 (10,30)	531 (89,70)	1.13 [0.68 - 1.87]	0.62		
Educated	23 (9,2)	227 (90,8)	1			
Difficulties in administering medications						
Yes	10 (10,41)	86 (89,58)	1.05 [0.52 – 2.12]	0.87		
No	74 (9,91)	672 (90,08)	1			
Living environment						
Acceptable[1]	41 (9,38)	396 (90,62)	1	0.55		
Not acceptable[2]	43 (10,61)	362 (89,38)	1.14 (0.73 - 1.8)			
Advice given by CHW to mothers during first administration						
Yes	65 (8,80)	673 (91,19)	0.43 [0.24 – 0.75]	0.003	0.41 [0.22; 0.77]	0.006***
No	19 (18,27)	85 (81,73)	1		1	
Dose 1 supervised						
Yes	68 (9,60)	635 (90,33)	0.82 [0.46 – 1.46]	0.25	1.22 [0.63; 2.35]	0.61
No	16 (11,51)	123 (88,49)	1		1	

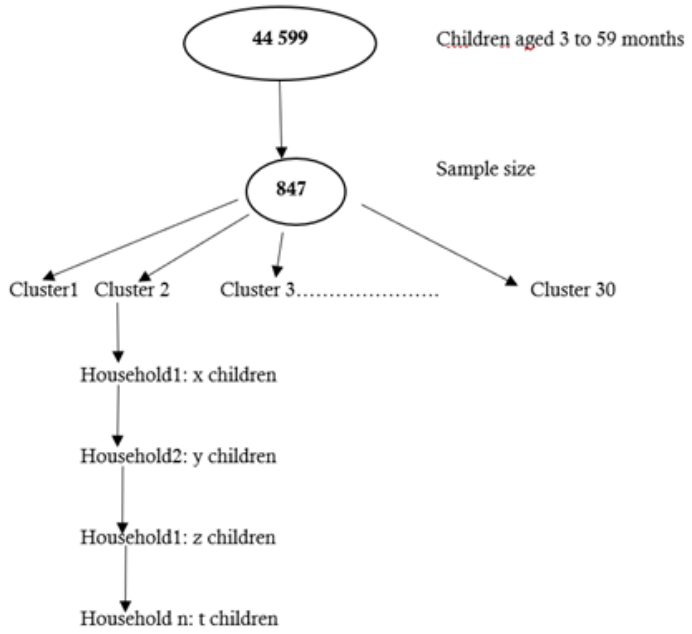

Figure 1: Sampling flow chart of the study

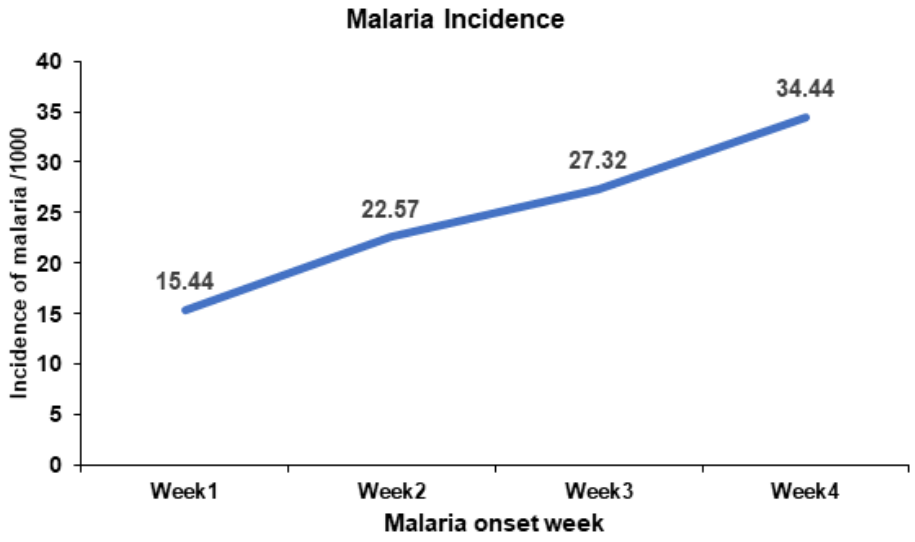

Figure 2: Malaria incidence by week children aged 03 to 59 months after first cycle of SMC in Tenkodogo, July 2020