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MALJ-D-21-00646 Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data Malaria Journal

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Thank you very much for your review of manuscript MALJ-D-21-00646, 'Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data'.

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Malaria Journal

Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data --Manuscript Draft--

Manuscript Number:	MALJ-D-21-00646
Full Title:	Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data
Article Type:	Research
Abstract:	Introduction : The COVID-19 pandemic and its collateral damage severely impact health systems globally and risk to worsen the malaria situation in endemic countries. Malaria is a leading cause of morbidity and mortality in Ghana. This study aims to analyze routine surveillance data to assess possible effects on the malaria burden in the first year of the COVID-19 pandemic in the Northern Region of Ghana. Methods : Monthly routine data from the District Health Information Management System II (DHIMS2) of the Northern Region of Ghana were analyzed. Overall outpatient department visits and malaria incidence rates from the years 2015 to 2019 were compared to the corresponding data of the year 2020. Results : Compared to the corresponding periods of the years 2015 to 2019, overall visits and malaria incidence in pediatric and adult outpatient departments in northern Ghana decreased in March and April 2020, when major movement and social restrictions were implemented in response to the pandemic. Incidence slightly rebounded afterwards in 2020 but stayed below the average of the previous years. Data from inpatient departments. In pregnant women, however, malaria incidence in outpatient departments increased after the first COVID-19 wave. Discussion : The findings from this study show that the COVID-19 pandemic affects the malaria burden in health facilities of Ghana, with declines in in- and outpatient rates. Pregnant women may experience reduced access to intermittent preventive malaria treatment and insecticide treated nets, resulting in subsequent higher malaria morbidity. Further data from other African countries, particularly on community-based studies, are needed to fully determine the impact of the pandemic on the malaria situation.

1	1	Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis
1 2 3	2	of routine surveillance data
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43 44 45	18	Abstract
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48 49 50	20	health systems globally and risk to worsen the malaria situation in endemic countries. Malaria
50 51 52	21	is a leading cause of morbidity and mortality in Ghana. This study aims to analyze routine
53 54	22	surveillance data to assess possible effects on the malaria burden in the first year of the COVID-
55 56 57 58 59 60 61 62 63	23	19 pandemic in the Northern Region of Ghana.

 Methods: Monthly routine data from the District Health Information Management System II (DHIMS2) of the Northern Region of Ghana were analyzed. Overall outpatient department visits and malaria incidence rates from the years 2015 to 2019 were compared to the corresponding data of the year 2020.

Results: Compared to the corresponding periods of the years 2015 to 2019, overall visits and malaria incidence in pediatric and adult outpatient departments in northern Ghana decreased in March and April 2020, when major movement and social restrictions were implemented in response to the pandemic. Incidence slightly rebounded afterwards in 2020 but stayed below the average of the previous years. Data from inpatient departments showed a similar but more pronounced trend when compared to outpatient departments. In pregnant women, however, malaria incidence in outpatient departments increased after the first COVID-19 wave.

Discussion: The findings from this study show that the COVID-19 pandemic affects the malaria burden in health facilities of Ghana, with declines in in- and outpatient rates. Pregnant women may experience reduced access to intermittent preventive malaria treatment and insecticide treated nets, resulting in subsequent higher malaria morbidity. Further data from other African countries, particularly on community-based studies, are needed to fully determine the impact of the pandemic on the malaria situation.

43 Keywords

COVID-19, pandemic, malaria, sub-Saharan Africa, Ghana, Northern Region, health information system, surveillance, morbidity, routine data

7 Introduction

48 Malaria remains one of the leading causes of morbidity and mortality in sub-Saharan
49 Africa (SSA). It is responsible for nearly one quarter of all under five childhood deaths in this
50 region (1, 2).

The global spread of the coronavirus disease 2019 (COVID-19) was declared a Public Health Emergency of International Concern, which is the highest level of alarm, at the end of January 2020 (3). Many African governments responded rapidly to this threat by implementing control measures even before first cases were detected in their countries, comprising border closures, movement restrictions, social distancing and school closures (4). By November 2021, there were nearly 6.2 million COVID-19 cases reported from the WHO African Region, with about 152,000 deaths, mostly from the southern and northern rims of the continent (5). In the global context, SSA accounts for only about 2.5% and 3% of the overall reported COVID-19 morbidity and mortality, respectively, while it is home to 17% of the global population (6-8). This may be explained by factors such as a younger population, hotter climate, interferences with other infectious diseases, and especially lack of diagnostics and underreporting (9, 10). Ghana is among the countries with the highest reported COVID-19 cases (130,920) and deaths (1,209) in western and central SSA, as of November 2021 (8). COVID-19 vaccinations started in February 2021 but coverage in Ghana is still low with only 2.7% of the population fully vaccinated by November 2021 (11).

The socio-economic disruptions associated with the disease and the preventive measures present huge challenges for health systems and whole societies, especially in lowand middle income countries (12). In the highly malaria-endemic African countries, the progress made in malaria control during the last two decades is feared to be reversed by the side effects of the COVID-19 pandemic (13, 14).

This study aims to compare the malaria burden in the Northern Region of Ghana in the
first year of the pandemic to previous years to assess whether a reversal indeed occurred.

74 Methods

75 Study area

Ghana, with its population of about 31 million, lies in western SSA and has a relatively well functioning health care system (15, 16). Ghana is divided into 16 administrative regions. The Northern Region, with its capital city Tamale, had a population of 1.9 million in 2020. The socio-economic situation of the Northern Region is below the national average of the country and the region has the highest rate of mortality under the age of five years (17). The rainy season in northern Ghana, which is usually associated with an increase in the malaria incidence, lasts from May to October (18).

Malaria is highly endemic in Ghana; the country accounts for 2% of the global malaria morbidity and 3% of the malaria mortality (19, 20). In 2020, malaria was the cause of 34% of all outpatient attendances (21). Treatment expenditures for common diseases like malaria are covered by a health insurance (22).

The first two confirmed COVID-19 cases in Ghana were seen on March 12, 2020; two days later, all public gatherings were banned. Travel restrictions and border closures were implemented on March 22, 2020 and the country's major cities were placed under partial lockdown soon after. Schools were partially reopened on June 21, 2020 and borders were reopened to international airlines on September 21, 2020 (23). In Ghana, effects of the COVID-19 pandemic on malaria control interventions concerned the country's stock of artemisininbased combination therapies (ACT), the functioning of its insecticide-treated mosquito net (ITN) routine distribution, and the overall access to primary health care services and facilities (24).

97 Study design and data

This retrospective observational study uses monthly malaria morbidity data on the overall number of outpatients (interpreted as less severe cases) and inpatients (more severe cases). Additionally, all outpatient visits (including non-malaria related visits) are analyzed. Cases were extracted from the district health information management system II (DHIMS2) on demographic and health parameters of northern Ghana from January 1, 2015, to December 31, 2020. This system was implemented in 2007 with an update in 2012 and has improved the data quality and completeness since (25).

Malaria diagnosis was based either on the results of rapid diagnostic tests or microscopy.

Mid-year population estimates of the Northern Region of Ghana were also provided through the DHIMS2.

Analysis

The data have been processed with Microsoft Excel Version 16.52 and analyzed with Stata IC Version 16 (Statacorp, College Station, TX, USA). We have calculated and plotted monthly incidence rates of all outpatient visits and confirmed malaria cases for the year 2020 and as a comparison for the years 2015 to 2019 separately and combined using population figures of the Northern Region of Ghana. Additionally, we calculated incidence rate ratios with 95% confidence intervals (95% CI) comparing quarterly incidence rates of 2020 versus the combined rates of 2015 to 2019. The data allowed analyzing children under five years and pregnant women separately using the fraction of the under-five population (14% of the population) and the fraction of women between 15 and 45 years (23% of the population) as estimates of the respective population denominators (26).

Results

	Number	Percentage (%)
ou	tpatient department visits	

All	5,804,910	100
Malaria confirmed	2,278,296	39
Malaria confirmed among	454,779	20
children <5 years		
Malaria confirmed among	46,693	2
pregnant women		
h	ospital-admitted patients	
Malaria confirmed	295,465	100
Malaria confirmed among	165,313	56
children <5 years		
m	nean mid-year population	
Total population	1,842,701	100
Children <5 years*	257,978	14
Women aged 15 to 45*	423,821	23

Table 1: Description of the dataset

Table 1 presents a brief description of the dataset. Altogether 5.8 million outpatient department visits were reported between 2015 and 2020; 39% of those included a malaria diagnosis. Of all confirmed malaria cases, 20% were children under the age of five years and 2% were pregnant women. 295,465 patients were hospitalized with diagnosed malaria, 56% of those were children under the age of five years. The mean population of the years from 2015 to 2020 was 1,842,701 with 14% of children under the age of five years and 23% of women between the age of 15 and 45 considered as of possible childbearing age.

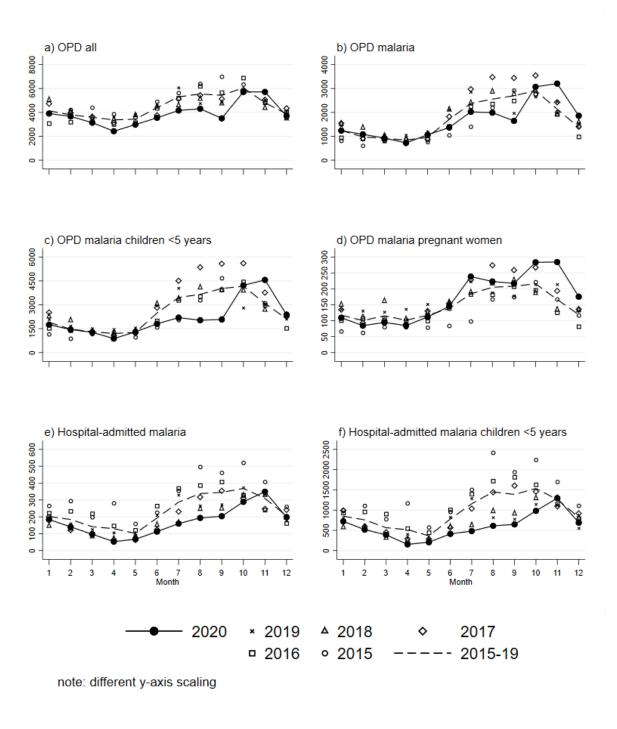


Figure 1: Reported monthly incidence rates per 100,000 of the Northern Region, Ghana for the years 2015 to 2020

Figure 1 presents the incidence rates of the different outcomes reported in the Northern Region of Ghana for the years between 2015 and 2020 separately as well as a combined rate for the period 2015 to 2019. All visits of the outpatient department (OPD) (see Figure 1a), including also non-malaria patients, have experienced a major decline in March/April 2020, the months where COVID-19 control measures were implemented in the country, and stayed low during the following months. After a further decrease in September 2020, the numbers increased again in October 2020 to the levels observed in previous years. This trend is similar but not as pronounced in the general malaria OPD visits (Figure 1b). In children under the age of five years, the decline in accessing OPD malaria health care is stronger, especially from June to September 2020 (Figure 1 c). In pregnant women, however, a different trend with an earlier increase, starting in June and exceeding previous year's levels, can be observed (Figure 1d). The 2020 numbers of the hospitally admitted malaria patients stayed below the previous standards from March to October 2020 (Figure 1e); and in accordance with the OPD figures, this trend is more pronounced in the children under five years population (Figure 1f).

Incidence rate ratios (IRR) depicting quarterly measures comparing the rates of 2020 to the combined rate of the years 2015 to 2019 are presented in table 2. General OPD visits were reduced in the 2nd and 3rd quarters of 2020 compared to the previous years (IRR 3rd quarter 0.736) with a return to previous standards at the end of the year. The same applies to the overall malaria cases (IRR 0.742 in the 3rd quarter) but with increases in the 4th quarter (IRR 1.265). Ambulatory malaria cases in children under five experienced stronger reductions compared to previous years with an IRR 0.566 in the 3rd quarter of 2020. These evolutions are not mirrored by the population of pregnant women with malaria infections, where no major reductions were observed during the first quarters of 2020 compared to previous years but with an earlier increase (IRR 1.481 in the 4th quarter). The situation is slightly different in malaria infected patients admitted to the hospital. The reductions in the 2nd and 3rd quarters of 2020 are more pronounced (IRR 0.548 for all ages in the 2nd quarter) and the numbers do not fully recover at the end of the year. Again, as for the outpatient population, this trend is more pronounced in children under five years of age (IRR 0.465 in the 2nd quarter).

Outcome	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
	1 st Quarter	2 nd Quarter	3 rd Quarter	4 th Quarter
	outpatie	nt department visits		
All	0.930	0.800	0.736	1.026
	(0.925-0.934)	(0.796 - 0.804)	(0.732-0.739)	(1.022-1.030)
Malaria	1.035	0.899	0.742	1.265
	(1.026-1.044)	(0.892-0.907)	(0.737-0.746)	(1.258-1.272)
Malaria children <5 years	0.956	0.806	0.566	1.190
-	(0.937-0.974)	(0.790-0.823)	(0.557-0.575)	(1.176-1.206)
Malaria pregnant women	0.865	0.957	1.136	1.481
	(0.815-0.918)	(0.905-1.011)	(1.091-1.182)	(1.424-1.540)
	hospita	l-admitted patients		
Malaria	0.799	0.548	0.574	0.946
	(0.780-0.817)	(0.531-0.565)	(0.563-0.586)	(0.930-0.962)
Malaria children <5 years	0.749	0.465	0.435	0.820
-	(0.726-0.773)	(0.445 - 0.486)	(0.422 - 0.448)	(0.800 - 0.839)

Table 2: Quarterly incidence rate ratios (IRR) with 95% confidence intervals (95% CI) comparing the incidence rates of 2020 with the combined incidence rates of the years 2015 to

Discussion

28 170 Since the beginning of the COVID-19 pandemic, several modelling studies have predicted negative collateral effects on the malaria burden in SSA, considering especially disrupted ITN campaigns and a limited access to antimalarial drugs. The study team of Weiss et al. created **172** nine scenarios for different reductions of ITN coverage and access to antimalarial medication **174** as well as regarding effects on malaria morbidity and mortality. As no ITN mass campaigns were scheduled for 2020 in Ghana, the worst-case scenario would have been a decline in access to antimalarials by 75% resulting in an increase of malaria morbidity and mortality by 12.6% ⁴⁵ 177 and 54.6%, respectively (13). Overall, the predicted public health relevant effects of the COVID-19 pandemic on malaria include shared clinical disease manifestations leading to **179** diagnostical challenges, disruptions of the availability of curative and preventive malaria commodities, significant effects on malaria programs, and in particular reduced access to malaria health services and health facilities in general (27). **181**

In this study, we observed a slight but significant decline in malaria incidence during the 2nd and 3rd quarter of 2020 (April to September), and only a rebound to the average levels

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 of previous years at the end of 2020. This pattern was visible in both, outpatient and inpatient settings, but more pronounced in the hospitalized population. The same applies to children and adults, where the reductions were also observed in both groups, but were more marked in children under five years of age. The marked decline in March/April 2020 can be explained by the extensive restrictions of movement and gathering and early stay-at-home advices for COVID-19-like symptoms unless these get severe. Such measures have likely supported the hesitancy to visit health facilities during the pandemic, which in turn poses a major risk for developing severe malaria (12, 28). The decline observed in March/April 2020 was even more remarkable in inpatients. This does not support our initial hypothesis, that in cases of more severe malaria manifestation, patients were still brought to health facilities and hospitalized, despite the pandemic. The findings from this analysis support the hypothesis, that the reported malaria burden in health facilities will shrink due to the effects of the COVID-19 pandemic in highly malaria-endemic countries (Heuschen et al. 2021). They also support results of the WHO World Malaria Report (12), and they agree with results of similar studies from other SSA countries classified as highly endemic for malaria, such as Sierra Leone, Uganda and the Democratic Republic of the Congo (29-32).

The distinct decrease of OPD visits in the health facilities of northern Ghana in September 2020 may also be explained by unusual heavy floods that started mid-August and could have further complicated the access to health services. Flooded land is a favorable habitat for Anopheles mosquitos, the malaria vector, what could have led to the observed increases of malaria incidence in October 2020.

Malaria incidence among pregnant women shows a different trend in northern Ghana. After a decline in reported malaria cases in April 2020, malaria figures have rebounded rapidly in this population and reached even higher levels compared to previous years. The most likely explanation of such an opposite trend would be the hesitancy of pregnant women to visit health

facilities. This is probably due to the fear of getting infected with COVID-19, combined with initial disruptions of the provision of intermittent preventive treatment in pregnancy (IPTp) to women in antenatal care (ANC) services as well as the disruption of routine distribution of ITNs (33). The disrupted access to and delivery of ANC services is likely to explain the malaria case trend in April. However, without IPTp and ITNs, more women were at risk for malaria thereafter, which can explain the subsequent rise in malaria cases over the following months. Also, many pregnant women probably have sought the missed ANC after the initial movement restrictions were lifted with subsequent malaria diagnosis.

Ghana had already achieved high levels of ITN coverage, and no ITN mass campaign was planned for 2020 (12). However, the routine distribution of ITNs, which is usually done in health facilities during ANC sessions and in primary schools, needed to be adapted to the COVID-19 measures, which included school closure from March 2020 until January 2021 (34, 35). Also the seasonal malaria chemoprevention intervention for children and the annual indoor residual spraying of insecticides, which both require physical contact between the health workers and the community, needed to be modified (36, 37). As another consequence of the COVID-19 pandemic, the provision of rapid diagnostic tests for malaria is fragile, which may have led to under-diagnosis of cases (38). Finally, reports of hesitancy to visit health facilities due to fear of getting infected with COVID-19 are still common (33, 38). Last but not least, the malaria health care workers capacities were limited due to frequent reassignments to the control of COVID-19, to stigmatization or absence following quarantine, or to the development of COVID-19 disease or even death (13, 35, 39).

This study has strengths and limitations. A strength of the study is that the data represent a whole year of follow-up into the pandemic, which provides a more comprehensive picture of the effects compared to the previous studies with much shorter study periods. Limitations are that the surveillance system itself may have been affected by the pandemic, with a bias in the

reported numbers. Moreover, it is not clear if the quality of surveillance data is fully comparable during the five years observed. Finally, much more people with malaria symptoms may have switched to self-medication during the pandemic, which may also have an albeit unknown effect on the malaria figures. In conclusion, this study shows that the COVID-19 pandemic has been accompanied by a reduced malaria incidence in northern Ghana's health facilities. Further data from other African countries and in particular data from community-based studies are needed to fully judge the impact of the pandemic on the global malaria situation. **Declarations** Ethics approval and consent to participate No ethical approval and consent to participate was required as only secondary data have been used. Consent for publication No consent for publication was required (only secondary data used). Availability of data and material The datasets used and/or analyzed in this study are available from the corresponding author on reasonable request. **Competing interests** The authors declare that they have no competing interests.

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Authors' contributions

AAM and MNA were responsible for the data collection. AH, VW and OR performed the data analysis. AH wrote the first draft under the supervision of OM, AAM and MNA supported the data interpretation. All authors read, reviewed and approved the final manuscript.

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Reviewer Recommendation and Comments for Manuscript Number MALJ-D-21-00646				
Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data				
	Original Submission Hamzah Hasyim			
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Reviewer Comments to Author

The COVID-19 pandemic's impact on malaria burden in Northern Ghana is examined. Northern Ghana DHIMS2 monthly data analysis Outpatient visits and malaria rates from 2015 through 2020. Pediatric and adult outpatient visits declined in Northern Ghana in March and April 2020. However, it was remained below average in 2020. Inpatient data followed the same pattern. Post the first COVID-19 wave, malaria incidence among pregnant women rose. This study found that the COVID-19 pandemic reduces the malaria burden in Ghanaian health facilities, both in and outpatient rates. A lack of intermittent malaria prophylaxis or insecticide-treated net use increases malaria morbidity. In addition, more data from other African countries is needed to assess the pandemic's impact on malaria.

However, the study's organization and content should be updated. The methodologies were incomplete. So far, I've provided feedback on the title

Reviewer Confidential Comments to Editor:

The reviewer was intrigued by the research.

This study demonstrates that the COVID-19 pandemic and its effects may worsen malaria in endemic areas. This study examines the COVID-19 pandemic's impact on the malaria load in Northern Ghana.

An analysis of Northern Ghana DHIMS2 monthly data Comparing 2015 to 2020 outpatient visits and malaria incidence rates. Pediatric and adult outpatient visits in Northern Ghana decreased in March and April 2020 compared to 2015-2019. 2020 saw an uptick, although it was still below normal. Inpatient data followed the same pattern as outpatient data. After the first COVID-19 wave, malaria incidence in pregnant women increased. Malaria load has decreased in Ghanaian health institutions due to the COVID-19 pandemic. Malaria morbidity rises because pregnant women cannot use intermittent malaria prophylaxis or insecticide-treated nets. Further data from other African nations are required to analyze the pandemic's impact on malaria properly.

However, The structure and content of the study should be revised. As given, the methods lacked sufficient information. I have given my feedback in title and abstract, introduction, methods, results, discussion, and other information.

After Major revisions, I recommend the manuscript be published in the Malaria Journal.

Below is the paper's recommendation.

Attachments:

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MALJ-D-21-00646 "Impact of the COVID-19 pandemic on malaria cases in health facilities in northern Ghana: a retrospective analysis of routine surveillance data" Original Submission

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Below is the paper's recommendation.

Comments to Author:

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However, the study's organization and content should be updated. The methodologies were incomplete. So far, I've provided feedback on the title and abstract as well as the introduction, methods, results, discussion, and others.



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MALJ-D-21-00646 "Impact of the COVID-19 pandemic on malaria cases in health facilities in northern Ghana: a retrospective analysis of routine surveillance data" Original Submission

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MALJ-D-21-00646

Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data

Methods, Results and conclussions of this study do not answer the objective: "In the highly malaria-endemic African countries, the progress made in malaria control during the last two decades is feared to be reversed by the side effects of the COVID-19 pandemic. This study aims to compare the malaria burden in the Northern Region of Ghana in the first year of the pandemic to previous years to assess whether a reversal indeed occurred". The passive case detection of malaria cases performe by the Health Information Management Services is not reliable to compair malaria incidence rates of the two periods: pre-COVID-19 (2015-2019) and during the COVID-19 pandemic (2020). The COVID-19 restrictions, mentioned by the authors, during the year 2020 could cause an underreporting of malaria cases making unreliable the reported malaria incidence, especially for outpatients. In addition, objective of the study does not agree with the title. Therefore, I have deep concern about the manuscript as it currently stands.

In spite of the before mentioned, in my opinion the manuscript has importan information related with possible side effects of the COVID-19 pandemic on the report of malaria in the Health Information Management Services of Ghana. Taking into account this, the manuscript must be modified as follows before it would be consider for a pair review:

Objective

The aim of the study should be changed. The new aim should be adressed to describe the posible effects of the COVID-19 restrictive measures on malaria case reports (not on incidence of cases) by the Health Information Management Services of Northen Ghana. For instance: The aim of the study was to describe the effects of the COVID-19 pandemic restrictions on routine surveillance data recording for malaria in the Norther Region of Ghana.

Title

The title must be modified according to the new objective.

Introduction

(a) To add a brief epidemiological description of malaria in Ghana, including the population groups (pregnant woman and children under 5 years old) described in the study.

(b) To mention the expected effects of the COVID-19 restrictions on the Health Information Management Services regarding malaria case reporting and the possible effects on malaria incidence (stock of antimalarial drug and vector control program activities).

(c) Research question should be clearly state.

(d) A research hypothesis for the study should be added.

Materials and method

(a) Study área. The authors should include an epidemiological description for malaria (total of all cases) and COVID-19 of the Northen región of Ghana. Information could be summarise in a graphic.

(b) Authors should justified the presentation of malaria cases by outpatients and inpatients, as well as for pregnant woman and children under 5 years old. In addition, Why malaria mortality was not included inthe study?.

(c) Restrictions applied in Northen Ghana to control the COVID-19 pandemic should be described in detail and should include, if possible, the starting and ending dates of each restriction measure. Author may include the information in a timeline and to add this in figure 1.

(d) Authors should also describe in detail changes in control actions agaisnt malaria suspected to be linked to CIVID-19 restrictions such as stock of antimalarial drug, functioning of the vector control program (routinary distribution of ITN), and overal access to primary health care services and facilities. These information shoud be summarize comparing the pre-COVID-19 (2015-2019) and COVID-19 pandemic (2020) periods, including, as much as possible, starting and ending dates and any measure of magnitude. For example, in the routinary distribution of ITN the anual covering with

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ITN and proportion of households with al least one ITN may be reported. (e) Analyses. (i) data on monthly incidence rate of malaria for the period 2015-2019 should be summarized using a central tendency measure (for example, mean or median) and a dispersion measure (CI 95% or low and upper quartiles). All graphics in Figure 1 must be modify accordenly; (ii) For the incidence rate ratio, the authors must include an statistical test (z-test) to confirm the null hypothesis that the incidence rates of 2020 vs the combine 2015-2019 are equal. The statistics of the test should be added to table 2.
Results
For a better understanding of the results the following changes are suggested:
 (a) To start the description of results, a text comparing the total anual mean report of malaria cases comparing the pre-COVID-19 (2015-2019) and COVID-19 pandemic (2020) periods should be added. This could identified in general any possible change in the malaria reporting. (b) A description of the pre-COVID-19 mean monthly variation in malaria reported cases should be added. (c) Figure 1, (i) A graphic comparing the total monthly mean report of malaria cases (outpatient and inpatients) comparing the pre-COVID-19 (2015-2019) and COVID-19 pandemic (2020) periods should be added; (ii) Graphic 1a (all patients) should be dropped because it is not relevant to the study. (d) Table 1. Summary of data should be Splited into pre-COVID-19 and COVID-19 pandemic periods. Mean total (outpatients+inpatients) anual malaria cases should be included in the tabla. (e) Table 2. What is the reason for presentation of the incidence rate ratios (IRR) data by quartery? It could be more appropriated to present the monthly IRR , to support the interpretation of figure 1.
Discussion
The discussion should be modified according to the changes in the previos sections.
Additional coments
Captions of figures and tables are not clear and need to be rewrited. Captions should describe tables and figures in such way that not reading of the test is necessary to understand then.
Close

Beyond national indicators: Adapting the Demographic and Health Surveys program to inform the sub-national malaria intervention⁴ policy better Beyond national indicators: Adapting the Demographic and Health Surveys program to better inform subnational malaria intervention policy

Ifeoma D. Ozodiegwu DrPH^{1*}, Monique Ambrose PhD², Katherine E. Battle DPhil², Caitlin Bever PhD², Ousmane Diallo MD PhD¹, Beatriz Galatas PhD³, Manuela Runge PhD¹, Jaline Gerardin PhD¹

¹Department of Preventive Medicine, Northwestern University, Chicago IL USA

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Authors' Authors' contribution

Ifeoma D. Ozodiegwu - Conceptualization, writing and revising manuscript drafts Monique Ambrose - Conceptualization and editing manuscript drafts Katherine Battle - Conceptualization and editing manuscript drafts Caitlin Bever - Conceptualization and editing manuscript drafts Ousmane Diallo - Conceptualization and editing manuscript drafts Beatriz Galatas - Conceptualization and editing manuscript drafts Manuela Runge - Conceptualization and editing manuscript drafts Jaline Gerardin - Conceptualization, writing and revising manuscript drafts

Conflict of interest statements and consent for publication

The authors declare no competing interest and have approved the manuscript for submission

Funding source

There was no funding source for this viewpoint. Additionally, none of the authors received payment from any pharmaceutical company or other agency to write this article

Availability of data

All data used in this work are publicly available. DHS is available for download from https://dhsprogram.com/. ACT watch data is available for download from https://dhsprogram.com/. ACT watch data is available for download from https://malariaatlas.org/actwatch/

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Abstract

In malaria-endemic countries, prioritizing intervention deployment to areas that need the most attention is crucial to ensure continued progress. Global and national policy-makers increasingly rely on epidemiological data and mathematical modelling to help optimize health decisions at the sub-national level. The Demographic and Health Surveys (DHS) Program is a critical data source for understanding subnational malaria prevalence and intervention coverage, which are used for parameterizing country-specific models of malaria transmission used for parameterizing country-specific models. However, data to estimate indicators at finer resolutionmore acceptable resolutions indicators are limited, and surveys questions have a narrow scope. We use examples from the Nigeria DHS to highlight gaps in the current survey program design, and w. We propose additional questions and expansions to the DHS sampling strategy that would advance the data analyses and modelled estimates that inform national policy recommendations. Collaboration between the DHS program, national malaria control programs, the malaria modelling community, and funders is needed to address the highlighted data challenges.

Introduction

The growing spatial and temporal variability in malaria risk,^{1–3} increasing diversity in malaria control tools,⁴ and limited funding availability is precipitating the need for malaria-endemic countries to adopt intervention policies that move away from a one-size-fits-all approach to one that is specifically tailored to their sub-national context. The Global Technical Strategy for malaria (GTS) recommends that targeted strategies be country-led.⁵ The High Burden to High Impact (HBHI) initiative further describes how each country can drive its strategy with its own data, including routine health facility reporting, national household surveys, and post-campaign assessments that collect information on current gaps in intervention coverage.⁶ Mathematical modelling can be used to integrate these data sources together to predict the impact of possible subnational intervention strategies and explore whether achieving a malaria strategies<u>trategies</u> malaria target is feasible.

Many malaria control programs are now choosing to target interventions at the district level (second administrative level, admin-2), given that this is an operationally feasible unit at which intra-provincial heterogeneity is captured. Monthly reports from health facilities provide routine surveillance data that can be aggregated up to districts. Routine data is used to identify malaria trends and needs at the local level,^{7,8} as-recommended by the GTS. Aside from issues of data quality and delayed reporting, these datasets only include individuals who seek treatment at reporting health facilities, and they provide no insight into individuals who live in less-accessible

areas or who seek treatment from private and informal health care sectors. The incomplete view of malaria incidence and treatment provided by routine reporting can result in biased estimates of population burden and access to care.

National surveys such as the Demographic and Health Surveys (DHS) and the Malaria Indicator Surveys (MIS) supplement routine surveillance by providing representative estimates of malaria prevalence and intervention coverage. Here, <u>""DHS"-"</u> is used to encompass both DHS and MIS surveys. Because data from the DHS program is easily accessible, analyses by National Malaria Control Programs (NMCPs) and the research community generate insight into spatial and temporal differences in malaria indicators, which allow data-driven prioritization of intervention deployment and serve as parameters for mathematical models. Nonetheless, the DHS survey presents with several deficiencies, discussed in the adjoining section, which limit understanding of the impact of interventions and identification of coverage gaps.

NMCPs increasingly consider outputs of mathematical models when planning sub-national malaria strategy, including making decisions about expansion of chemoprevention and choosing from a set of vector control strategies. To address related questions, epidemiological models must capture for each subnational area its historical trends in transmission, current patterns of exposure, and intervention coverage for each subnational area. Given the limitations of routine surveillance, NMCPs and modellers use the DHS to understand the subnational malaria context. Here, we highlight how DHS data are utilized by mathematical models and suggest improvements that would enhance both modelling and data analysis efforts from NMCPs to facilitate informed decision-making.

DHS data is useful for national policy-making, but parameterizing subnational malaria transmission models is challenging

Models of malaria transmission used for national strategic planning are informed by household survey data on intervention coverage, transmission intensity, and malaria burden. To set subnational intervention coverages, models rely on DHS measures of treatment-seeking rates for febrile illness among children under five, insecticide-treated nets (ITN) usage at the household level and for different age groups, and coverage of intermittent preventive treatment in pregnancy (IPTp). Modelled transmission intensity can then be calibrated to capture DHS measures of the *Plasmodium falciparum* parasite rate in children under the age of five (*Pf*PR₀₋₅).

Estimates of malaria prevalence and intervention coverage from the DHS are only meant to be representative at a state or provincial level (Figure 1 and 2). To help NMCPs stratify and plan operations, howeverHowever, to help NMCPs stratify and plan operations, models must capture

data at finer spatial scales than admin-1. Parameterizing mathematical models at these fine spatial scales requires either directly using DHS household cluster data, which are underpowered to measure malaria indicators at admin-2 and displaced to protect <u>participant's-participants'</u> confidentiality,⁹ or inferring admin-2-level values via geospatial models.^{10,11} Both options introduce additional assumptions and sources of uncertainty.

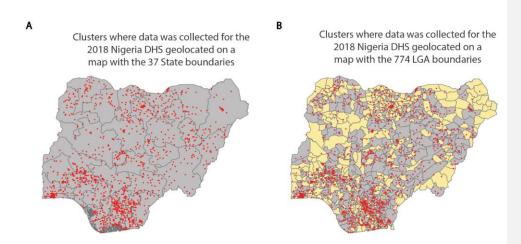


Figure 1. A) State-level (admin-1) map of Nigeria with red dots representing clusters where DHS data collection was conducted in 2018. <u>Number A number</u> of clusters in state boundaries range from 20 to 54 with a median of 36. B) Local government area (LGA)-level (admin-2) map of Nigeria with red dots representing clusters where DHS data collection was conducted in 2018. LGAs colored in yellow are areas where <u>an</u> estimation of malaria indicators will be challenging because they contain zero or one cluster. Number of clusters within LGA boundaries ranged from zero to 11 with a median of two. 103 LGAs had no clusters.

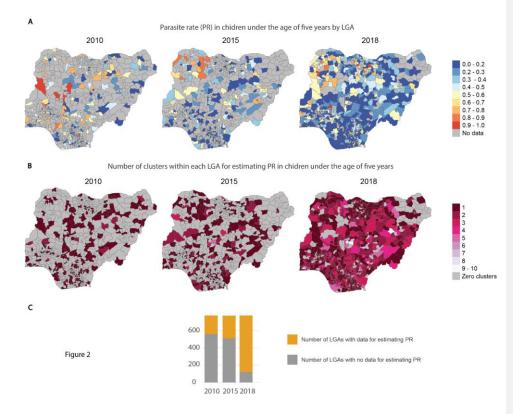


Figure 2. A) PfPR₀₋₅ according to 2010, 2015, and 2018 Nigeria DHS. The LGA prevalence values depicted are not representative for the population per LGA, as DHS is not powered at the LGA level. B) Number of clusters located within each LGA boundary used to estimate PfPR₀₋₅ in each DHS year. Many LGAs contain zero DHS clusters, although geographic coverage improved substantially in the most recent DHS. C) Number of LGAs with and without PR data. LGAs without data were 558 in 2010, 510 in 2015 and 121 in 2018, out of 774 total LGAs.

Malaria indicators captured by the DHS are subject to seasonal variations in malaria transmission and human behaviour, which limit <u>the</u> understanding of malaria transmission intensity, ITN use, and comparability of yearly surveys. Parasite rate is typically at its-maximum during the rainy or peak mosquito-biting season and trend downwards in the dry season. Individuals use ITNs during the wetter months and reduce usage in the dryer months when mosquito activity is diminished.¹² Treatment-seeking behaviour can be affected by seasonal accessibility issues and seasonal demands on <u>parents' parents'</u> time, for example, agricultural needs during the wet season. Malaria indicators from DHS surveys conducted during the dry season months therefore Therefore, malaria indicators from DHS surveys conducted during the dry season

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months do not necessarily capture parasite rate, ITN use, and case management coverage in the peak transmission season. Surveys conducted in different seasons, even within the same DHS year, are not directly comparable without adjustment for the seasonality effect. NMCPs and modelers resort to other data sources with a narrower geographic scale to capture seasonal and temporal changes in malaria transmission, and to and accurately identify gaps in intervention coverage and areas of high prevalence and accurately identify gaps in intervention coverage and high prevalence areas.

The restriction of current questions to select age groups limit how informative the results are for driving country strategy and fors how informative the results are for driving country strategy and how informative the products are for driving country strategy and parameterizing models. For example, the DHS only tests children under the age of five for malaria infection, which, although important, is of limited utility for categorizing malaria transmission intensity in settings where more of the burden is in older children or adults. PfPR0-5 measured during implementation of seasonal malaria chemoprevention (SMC) may be particularly uninformative as PfPR is suppressed in this population and SMC coverage is not assessed in the DHS. Measurements of PfPR in older children can be more informative than PfPR0-5 even in high-transmission areas, as children above age two will have some immunity to clinical malaria, and hence less treatment with antimalarials,. Children above age two will have some immunity to clinical malaria, hence less treatment with antimalarials. Children above age two will have some immunity to clinical malaria, hence less treatment with antimalarials yet limited immunity to parasitemia itself.¹³ Some models therefore apply standardization algorithms to convert PfPR₀₋₅ to PfPR_{2-10.}¹⁴ While such algorithms have been validated in prior work,¹³ the extent of bias introduced by predicted *Pf*PR₂₋₁₀, especially in fine-scale models, is unknown.

A similar issue arises with using the DHS data to evaluate case management and treatment coverage for uncomplicated malaria, where questions are restricted to children under the age of five. NMCPs-therefore, therefore, know little about access to malaria treatment in older children, where burden is increasingly shifting.¹⁵ In the absence of case management information for uncomplicated malaria in older children and adults, modellers either assume homogeneous coverage by age or turn to site-specific research studies on treatment-seeking behavior.

Estimating case management rates from DHS data requires analyzing questions directed at a subset of DHS participants, which reduces the sample size and may introduce validity issues and inconsistencies. In the 2018 Nigeria DHS, effective case management coverage, that is the proportion of children under the age of five that received ACT given that they had a fever within the two weeks prior to the survey, who received ACT given that they had a fever within the two weeks prior to the survey, is the proportion of children under five that received ACT. They had a fever within the two weeks prior to the survey, is the proportion of children under five that received ACT. They had a fever within the two weeks prior to the survey, which was 22% at the national level. Disaggregated at the state level, ACT-related case management was remarkably low in many

areas. For example, the 2018 DHS suggests that febrile children were not treated at all with ACTs in Nasarawa, and only about 3 to 4% in Zamfara and Yobe (Figure 3A).

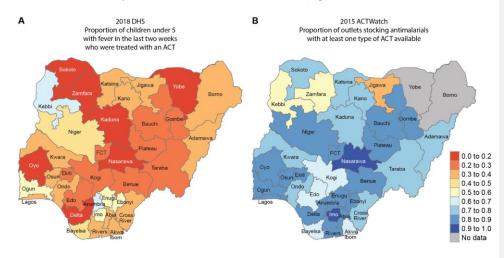


Figure 3. A) <u>Nigeria's-Nigeria's</u> 2018 DHS shows the proportion of children with fever in the two weeks preceding the survey that were treated by with an ACT. B) Proportion of outlets stocking antimalarials that had at least one type of ACT based on the 2015 ACTWatch survey^{16,17}. Maps share the same legend.

When these estimates were discussed with the Nigerian National Malaria Elimination Program, they indicated that the actual ACT use would likely be higher than those values seen in the 2018 DHS, and tseen in the 2018 DHS. The state level DHS estimates would not agree with their perceived ACT use in many parts of the country. This view is supported by the 2015 ACTWatch survey 2015 ACTWatch survey supports this view, ^{16,17} which indicated that most outlets stocking any antimalarials in individual states had at least one type of ACT for sale (Figure 3B). While the metrics are clearly different, the ACTWatch data suggests strong-intense penetration of ACTs across both the public and private health care sectors in Nigeria, and, together with the Nigerian program perspective, calls into question the 2018 DHS results that suggested extremely low rates of ACT treatment in some areas of Nigeria. This discrepancy of trends between access (ACTWatch) and use (DHS) metrics emphasizes the limitations of the current DHS sampling strategy to capture case management coverage among febrile children, who are few in number, and the need for a strengthened DHS data collection system that builds trust and meets NMCP needs.

The gaps that we have identified within the DHS sampling strategy and questionnaires do not diminish the immense contribution of the DHS program to evidence-based decision-making. However, when DHS measures do not adequately capture malaria indicators, or DHS data are out

of concordance with institutional knowledge and beliefs of intervention and treatment access and malaria risk behavior, deciding where to target interventions becomes more challenging and a data-driven approach nearly impossible.

Recommendations

Having outlined the major barriers to using the DHS for evidence-based subnational malaria strategic planning, we propose changes to the DHS surveys and sampling strategy to improve understanding of the malaria context at the relevant spatial scale of programmatic decision-making and drive more accurate predictions of the impact of targeted interventions.

- 1. Time DHS surveys to capture malaria indicators during the high-transmission season. Carefully timing the DHS survey to coincide with the high malaria transmission season and collecting data at the same time every year would improve estimation of malaria indicators, and comparability of yearly surveys, even at finer scales. Effective timing provides understanding of transmission intensity and intervention coverage at its peak periods and implies that a smaller sample size would be needed to accurately estimate malaria indicators estimate malaria indicators accurately. Hence, if the DHS retains a similar sampling strategy but conducts surveys only in the wetter months, malaria indicators will be more precisely estimated at both admin-1 and admin-2-level, and NMCPs can more reliably track indicator trends. If accessibility issues preclude peak-season surveys in some districts. In that case, a hybrid approach where isolated districts are surveyed at a different time of year may be necessary may be necessary at a different time of year.
- 2. Support malaria-endemic countries to conduct admin-2-level and/or monthly surveys. We hope to see the DHS support malaria-endemic countries in conducting more frequent and granular surveys at the admin-2 level. Increasing the spatial resolution of the survey to the admin-2 level will enhance the precision of survey estimates, and if these admin-2 surveys are done monthly, it would lead to excellent understanding of seasonal and temporal changes in parasite rate and intervention coverage. At the outset, priority could be given to districts in high-transmission areas where intervention targeting will be most beneficial, or surveys could be conducted only during high-transmission months. The frequency and scale of the surveys surveys' frequency and scale could be reduced if low spatial and temporal heterogeneity in malaria indicators are detected within neighboring districts. While we acknowledge that this comes with higher survey implementation costs for the DHS, this will vary for individual countries depending on several factors including coverage of the existing DHS survey, the number of admin-2 areas, and the target population sizes. The extra implementation costs will be relatively lower for some countries and possibly unfeasibly high in others. However, the potential savings from allocating resources to the most-at-risk population and thereby additional lives saved could serve as a justification for increased funding for the DHS to pursue a broader sampling strategy.

- 3. Extend blood smear or rapid diagnostic testing (RDTs) to children up to the age of 10 years. As prevalence in the youngest children the youngest children's prevalence declines, testing of older children will be more informative for assessing malaria transmission intensity. In lower-transmission areas, collection of prevalence in adults will become necessary to identify remaining areas of sustained transmission for intervention targeting. Deprioritizing blood smears in favor of RDTs can help mitigate some of the added expense.
- 4. Adapt the DHS sampling strategy and survey questions to better capture data that inform estimation of treatment coverage. To obtain an improved estimate of treatment modalities, we recommend the DHS oversample children in selected high transmission settings where case management with ACT is particularly crucial to prevent death. The current DHS sampling approach may not provide accurate estimates of ACT treatment rates for malarial fevers, which lessens its utility in intervention planning. If recommendation #1 is adopted, the additional sample would not be substantial since the sampling frame for febrile children will be greatly significantly enhanced. Qualitative research is needed to better understandunderstand better how to word questions around care-seeking and access to effective treatment, as this could be a limiting factor in the accuracy of participant responses, and understanding where the cascade of care falls apart is necessary for identifying solutions to low treatment rates. Questions on case management urgently need to be extended to older children and adults, so that policy makers understand how symptoms and treatment dynamics vary by age, time, and transmission intensity their in country.
- 5. Add questions to the DHS to capture data on SMC coverage. In many areas with highly seasonal malaria transmission, SMC is a crucial intervention to reduce malaria incidence and mortality during the high-transmission season. DHS surveys implemented during peak transmission months would be well-positioned to measure SMC coverage, which is often challenging for NMCPs to calculate from doses distributed due to uncertain population denominators. Measuring SMC coverage will enable NMCPs to better assess implementation quality and to identify gaps and will allow models to generate more accurate predictions of the impact of SMC expansion or changes in scheduling.
- 6. Leverage the Service Provision Assessment (SPA) surveys to monitor malaria incidence and case management, even if at an aggregate level. The SPA surveys, which are part of the DHS portfolio of surveys, provide country-specific overviews of health service delivery. SPA surveys can be leveraged to obtain a snapshot of reported malaria incidence, severity, and case management modalities at the time of the DHS community surveys. This information can be very powerful: NMCPs can contextualize effective treatment results from the survey, and modelers can triangulate data from both surveys to capture and explain transmission dynamics.

7. Make the DHS dynamic and flexible to adapt to a changing intervention landscape. The landscape of malaria interventions is heterogeneous and can change with new strategic plans and pilots of intervention deployments. DHS design should be cognizant of local interventions. In areas where new interventions are introduced, survey questions related to the interventions can be asked only in those administrative units. Likewise, if interventions are discontinued in a particular locality, survey questions can be modified in response.

Conclusion

The DHS is already an invaluable tool for informing malaria intervention strategies and could be an even <u>greater_more significant</u> asset for subnational planning if the changes we propose are made to augment the existing DHS platform. We call for a dialogue between the DHS program experts, NMCPs, the malaria modeling community and funders to discuss existing data challenges and design a practical path for overcoming them. As countries move toward geographically tailored national strategies, the need for high-quality information is paramount, and t. The experience and technical expertise of the DHS program is essential to meet this need.

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Overall reflections and a summary of the research - for

Manuscript Number:	MALJ-D-21-00646
Full Title:	Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data
Article Type:	Research

Reviewer # HH

The research captivated the reviewer.

The COVID-19 pandemic's impact on malaria burden in Northern Ghana is examined. Northern Ghana DHIMS2 monthly data analysis Outpatient visits and malaria rates from 2015 through 2020. Pediatric and adult outpatient visits declined in Northern Ghana in March and April 2020. However, it was remained below average in 2020. Inpatient data followed the same pattern. Post the first COVID-19 wave, malaria incidence among pregnant women rose. This study found that the COVID-19 pandemic reduces the malaria burden in Ghanaian health facilities, both in and outpatient rates. A lack of intermittent malaria prophylaxis or insecticide-treated net use increases malaria morbidity. In addition, more data from other African countries is needed to assess the pandemic's impact on malaria.

However, the study's organization and content should be updated. The methodologies were incomplete. So far, I've provided feedback on the title and abstract as well as the introduction, methods, findings, and others.

Below is the paper's feedback.

Title and abstract

Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data.

The study's design has indicated a commonly used term in the title or the abstract. Besides, the abstract has provided an informative and balanced summary of what was done and what was found.

Introduction

In Background/rationale. This study has explained the scientific background and rationale for the reported investigation and has state-specific objectives; however, the reviewer doesn't see any prespecified hypothesis in the background/rationale session.

Methods

In the study design, this study has presented critical elements of study design early in the paper. This retrospective observational study uses monthly malaria morbidity data on the 99 overall number of outpatients (interpreted as less severe cases) and inpatients (more severe 100 cases). Furthermore, the paper has described the setting, locations, and relevant dates; however, it is needed, including recruitment, exposure, follow-up, and data collection periods.

In participants, please give the eligibility criteria and the sources and methods of selecting participants.

Variables clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable and in data sources/ measurement for each variable of interest, give data sources and details of assessment methods (measurement). Describe comparability of assessment methods if there is more than one group. In addition, please Describe any efforts to address potential sources of bias.

This study needs to explain how the study size was arrived at, and the study needs to explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Statistical methods.

- (a) Describe all statistical methods, including those used to control for confounding
- (b) Describe any methods used to examine subgroups and interactions
- (c) Explain how missing data were addressed
- (d) If applicable, describe analytical methods taking account of sampling strategy
- (e) Describe any sensitivity analyses.

Results

The authors have described well regarding results (report numbers of individuals at each stage of the study, give characteristics of study participants report numbers in each exposure category or summary exposure measures). In addition, the discussion summarises critical results concerning the study objective's limitations.

However, the reviewer did not see how the authors clarified which confounders were adjusted for and why they were included. Furthermore, it needed to discuss the study results' generalisability (external validity). In Participants give Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. Besides, give reasons for non-participation at each stage and consider using a flow diagram.

In Descriptive data, this study has given characteristics of study participants. However, is a need for information on exposures and potential confounders. Besides, please indicate the number of participants with missing data for each variable of interest.

In Outcome data, please report numbers in each exposure category or summary measures of exposure.

In Main results, please give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included. In addition, please report category boundaries when continuous variables were categorized, and if relevant, consider

translating estimates of relative risk into absolute risk for a significant period. Please report other analyses are done—e.g. analyses of subgroups and interactions and sensitivity analyses.

Discussion

Please summarise key results concerning study objectives.

This study has strengths and limitations. The limitations include the possibility that the pandemic impacted the surveillance system, resulting in a bias in reported numbers. Additionally, it is unknown whether the quality of surveillance data is comparable across the five years observed. Please discuss the limitations of the study, taking into account sources of potential bias or imprecision. Discuss both the direction and magnitude of any potential bias.

In the Interpretation section, please give a cautious overall interpretation of results considering objectives, limitations, the diversity of analyses, results from similar studies, and other relevant evidence and generalisability. Please discuss the generalisability (external validity) of the study results.

Other information

This study has given the source of funding that the funding of study from Anna-Katharina Heuschen acknowledges the support by the Else Kröner-Fresenius Stiftung within the Heidelberg Graduate School of Global Health. However, it is necessary to provide information about the funding sources, if applicable, the original research on which this article is based.

RESEARCH





Impact of the COVID-19 pandemic on malaria cases in health facilities in northern Ghana: a retrospective analysis of routine surveillance data

Anna-Katharina Heuschen^{1*}, Alhassan Abdul-Mumin², Martin Adokiya³, Guangyu Lu⁴, Albrecht Jahn¹, Oliver Razum⁵, Volker Winkler¹ and Olaf Müller¹

Abstract

Background: The COVID-19 pandemic and its collateral damage severely impact health systems globally and risk to worsen the malaria situation in endemic countries. Malaria is a leading cause of morbidity and mortality in Ghana. This study aims to describe the potential effects of the COVID-19 pandemic on malaria cases observed in health facilities in the Northern Region of Ghana.

Methods: Monthly routine data from the District Health Information Management System II (DHIMS2) of the Northern Region of Ghana were analysed. Overall outpatient department visits (OPD) and malaria case rates from the years 2015–2019 were compared to the corresponding data of the year 2020.

Results: Compared to the corresponding periods of the years 2015–2019, overall visits and malaria cases in paediatric and adult OPDs in northern Ghana decreased in March and April 2020, when major movement and social restrictions were implemented in response to the pandemic. Cases slightly rebounded afterwards in 2020, but stayed below the average of the previous years. Malaria data from inpatient departments showed a similar but more pronounced trend when compared to OPDs. In pregnant women, however, malaria cases in OPDs increased after the first COVID-19 wave.

Conclusions: The findings from this study show that the COVID-19 pandemic affects the malaria burden in health facilities of northern Ghana, with declines in inpatient and outpatient rates except for pregnant women. They may have experienced reduced access to insecticide-treated nets and intermittent preventive malaria treatment in pregnancy, resulting in subsequent higher malaria morbidity. Further data, particularly from community-based studies and ideally complemented by qualitative research, are needed to fully determine the impact of the pandemic on the malaria situation in Africa.

Keywords: COVID-19, Pandemic, Malaria, Sub-Saharan Africa, Ghana, Northern Region, Health information system, Surveillance, Morbidity, Routine data

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Background

Malaria remains one of the leading causes of morbidity and mortality in sub-Saharan Africa (SSA). Globally, there have been 627.000 malaria related deaths in 2020, 12% more than in 2019; 68% of these additional deaths

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were attributed to indirect consequences of the COVID-19 pandemic [1]. In Ghana, malaria is responsible for 10% of the overall mortality and nearly one quarter of all under five childhood deaths [1, 2]. The 2015–2020 Ghana Strategic Action Plan aimed to reduce the burden of malaria by 75.0% [3], but the COVID-19 pandemic could halt or even reverse the declining trends. In 2020, malaria was the cause of more than one third of all OPD attendances [4]; moreover 17.6% of OPD visits of pregnant women were due to malaria [5].

The global spread of the coronavirus disease 2019 (COVID-19) was declared a Public Health Emergency of International Concern at the end of January 2020 [6]. Many African governments responded rapidly to this threat by implementing control measures even before first cases were detected in their countries, comprising border closures, movement restrictions, social distancing and school closures [7]. SSA accounted for only about 3.5% of the globally reported COVID-19 morbidity and mortality, mostly from the southern and northern rims of the continent, while being home to 17% of the global population [8]. This may be explained by factors such as a younger population, hotter climate, interferences with other infectious diseases, but especially lack of diagnostics and underreporting [9, 10]. Ghana was among the countries with the highest reported COVID-19 cases and deaths in western and central SSA, as of the end of 2020 [11]. COVID-19 vaccinations started in February 2021 but coverage in Ghana is still low with only 10% of the population fully vaccinated by February 2022 [12].

The socio-economic disruptions associated with the disease and the preventive measures present huge challenges for health systems and whole societies, especially in low- and middle income countries [13]. In the highly malaria-endemic African countries, the progress made in malaria control during the last two decades was feared to be reversed by the side effects of the COVID-19 pandemic [14, 15]. In the Ghanaian context, as no ITN mass campaigns were scheduled for 2020, the worst-case scenario presented in a modelling study by Weiss et al. could have been a decline in access to anti-malarial medication by 75%, resulting in an increase of malaria morbidity and mortality by 13% and 55%, respectively [14]. Overall, the predicted public health relevant effects of the COVID-19 pandemic on malaria include shared clinical disease manifestations leading to diagnostic challenges, shortages of anti-malarial medication, rapid diagnostic tests, preventive tools and personal protective equipment, decreasing quality of surveillance systems, and re-allocation of funds and professionals towards COVID-19 control activities [16].

This study aims to describe potential effects of the COVID-19 pandemic on malaria cases in health facilities

in the Northern Region of Ghana – a highly malaria endemic region. The research hypothesis that "lower access to health care services in combination with impaired malaria surveillance systems may have led to a lower number of reported malaria cases in highly endemic countries" will be investigated [16]. This hypothesis leads to the specific research question if the COVID-19 pandemic has led to less reported malaria cases in northern Ghana in 2020.

Methods

Study area

Ghana, with its population of about 31 million, lies in western SSA and has a relatively well functioning health care system [17, 18]. The Northern Region, with its capital city Tamale, had a population of 1.9 million in 2020. The socio-economic situation of the Northern Region is below the national average of the country and the region has the highest mortality rate in children under the age of five years [19].

Malaria is highly endemic in northern Ghana with a seasonal transmission pattern that is strongest between July and November. ITNs are a major malaria prevention strategy in Ghana; in 2019, about 74% of households owned at least one ITN and 52% of all households had at least one ITN per two people [20]. According to the state of the nation's health report 2018, the malaria prevalence in children under- five years in the Northern Region is 40%, the highest in Ghana [21]. Regarding the epidemiology of COVID-19, Ghana recorded the first cases in March 2020. The government responded immediately with the implementation of social gathering and travel restrictions as well as school closures. The country's major cities were placed under partial lockdown soon after. This lockdown started on March 30, 2020, and lasted for two weeks. Schools were partially reopened on June 21, 2020, and borders were reopened to international airlines on September 21, 2020 [22]. As at end of March 2021, the country had a total of 90,583 confirmed cases and 743 deaths [23]. These cases were clustered around two major waves in March-September 2020 and January-March 2021. The first wave coincided partly with the rainy season in the Northern Region, the time when the majority of cases of malaria in children and pregnant women are recorded [24].

In Ghana, effects of the COVID-19 pandemic on malaria control interventions concerned the country's stock of artemisinin-based combination therapy, the functioning of its insecticide-treated mosquito net (ITN) routine distribution, and the overall access to primary health care services and facilities [25].

Although the lockdown did not include the Northern Region directly, the other pandemic control measures including the 'stay at home unless absolutely necessary' campaign, suspension of OPD services in many hospitals and the general anxiety among the population, led to reduction in antenatal and child welfare clinic attendance. This situation could have further affected malaria control measures as the antenatal and child welfare clinics are two major service delivery points where education on malaria prevention, intermittent preventive treatment in pregnancy (IPTp) services and distribution of ITNs to children and pregnant women are carried out [26].

Study design and data

This retrospective observational study uses monthly malaria morbidity data on the overall number of outpatients (interpreted as less severe cases) and inpatients (more severe cases). Additionally, all outpatient visits (including non-malaria related visits) were analysed. Subgroup analysis was performed for the two groups at high risk for severe malaria manifestations, children under five years of age and pregnant women [1]. Cases were extracted from the *District Health Information Management System II* (DHIMS2) on demographic and health parameters of northern Ghana from January 1, 2015, to December 31, 2020. This system was implemented in 2007 with an update in 2012 and has improved the data quality and completeness since [27].

Malaria diagnosis was based either on the results of rapid diagnostic tests or microscopy.

Mid-year population estimates of the Northern Region of Ghana were also provided through the DHIMS2.

Analysis

The data have been processed with Microsoft Excel Version 16.52 and analyzed with Stata IC Version 16 (Stata-Corp, College Station, TX, USA). Monthly rates of OPD visits and confirmed malaria cases for the year 2020 and as a comparison for the years 2015–2019 separately as well as mean rates with 95% confidence intervals (95% CI) have been calculated and plotted using population figures of the Northern Region of Ghana. Additionally, quarterly rates are presented; rates of 2020 versus the combined rates of 2015–2019 have been compared with the z-test. The data allowed analysing children under five years and pregnant women separately using the fraction of the under-five population (14% of the population) and the fraction of women between 15 and 45 years (23% of the population) as estimates of the respective population denominators [28]. Malaria deaths have not been analysed due to low quality of the mortality data sets.

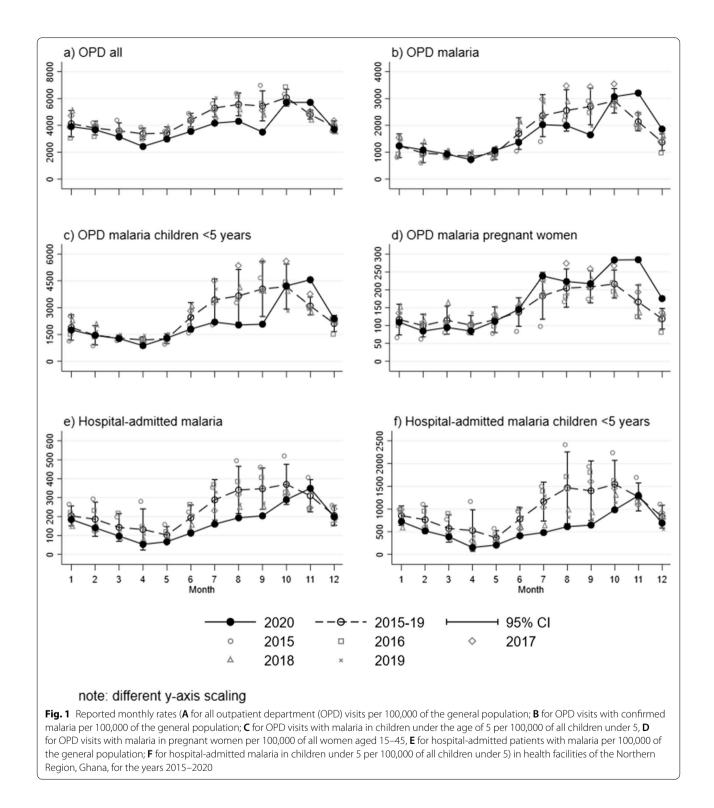
Results

Table 1 presents a brief description of the dataset. Altogether 5.8 million OPD visits were reported between 2015 and 2020; 39% of those were diagnosed with malaria. Of all malaria cases, 20% were children under the age of five years and 2% were pregnant women. 295,465 patients were hospitalized with diagnosed malaria, 56% of those were children under the age of five. The mean population in the Northern Region of Ghana of the years from 2015 to 2020 was 1,842,701.

Figure 1 presents the case rates of the different outcomes reported from health facilities in the Northern Region of Ghana for the years 2015-20 separately as well as a combined rate for the period 2015 to 2019. All OPD visits (Fig. 1a), including also non-malaria patients, have experienced a decline in March/April 2020 (the months where COVID-19 control measures were implemented in the country) and stayed low during the following months. After a further decrease in September 2020, the numbers increased again in

Table 1Description of the dataset on outpatients and malaria patients recorded in northern Ghana health facilities during the years2015–2020

	Total number	Percentage (%)	
Outpatient department visits			
All OPD	5,804,910	100	
Malaria confirmed	2,278,296	39	
Malaria confirmed among children < 5 years	454,779	20	
Malaria confirmed among pregnant women	46,693	2	
Hospital-admitted patients			
Malaria confirmed	295,465	100	
Malaria confirmed among children < 5 years	165,313	56	
Mean mid-year population			
Total population	1,842,701	100	
Children < 5 years	257,978	14	
Women aged 15 to 45	423,821	23	



October 2020 to the levels observed in previous years. This trend is similar but not as pronounced in the malaria OPD visits (Fig. 1b). The decline in accessing OPD malaria health care is strongest in children under the age of five years, especially from June to September 2020 (Fig. 1c). In pregnant women, however, a different trend with an increase of malaria cases, starting in June and exceeding previous year levels, can be observed

(Fig. 1d). The 2020 numbers of the hospital-admitted malaria patients (March till October) stayed consistently below the numbers from previous years (Fig. 1e); and in accordance with the OPD figures, this trend is more pronounced in children under five years (Fig. 1f).

The rate ratios (RR), depicting quarterly measures comparing the rates of 2020 to the combined rates of the years 2015 to 2019, are presented in Table 2. General OPD visits were significantly reduced in the 2nd and 3rd quarters of 2020 compared to the previous years by up to 27%, with a return to previous standards at the end of the year. For the overall malaria cases only the 3rd quarter of 2020 experienced a decrease by 26%, but increases by 27% in the 4th quarter. Ambulatory malaria cases in children under five experienced stronger reductions compared to previous years by 43% in the 3rd quarter of 2020, and increases by 20% in the 4th quarter. These evolutions are not mirrored by the population of pregnant women with malaria infections, where no major reductions were observed during the first quarters of 2020 compared to previous years but with an earlier and stronger increase that reached 48% in the 4th quarter. The situation is slightly different in patients admitted to the hospital with malaria. The reductions in the 2nd and 3rd quarters of 2020 are more pronounced (46% and 43%) and the numbers recover at the end of the year but do not exceed previous levels. Again, as for the outpatient population, this trend is more pronounced in children under five years of age (64% in the 2nd, 67% in the 3rd quarter).

Discussion

The Covid-19 pandemic has major consequences on the functioning of health services and direct and indirect effects on the burden of various diseases [29, 30]. In this paper, effects of the pandemic on malaria case numbers in health facilities of northern Ghana, a region highly endemic for malaria, are described.

In northern Ghana, a slight but significant decline was observed in malaria cases during the 2nd and 3rd quarter of 2020. This decline is even more significant considering that the period coincides with the rainy season in northern Ghana (May-November) when usually the majority of malaria cases are recorded. Cases only rebounded to the average levels of previous years at the end of 2020. This pattern was visible in both, outpatient and inpatient settings, but more pronounced in the hospitalized population. The same applies to children and adults, where reductions were also observed in both groups, but were more marked in children under five years of age. The marked decline in March/April 2020 can be explained by the extensive movement and gathering restrictions and early stay-at-home advices for COVID-19-like symptoms unless these get severe. Such measures have likely supported the hesitancy to visit health facilities during the pandemic, which in turn poses a major risk for developing severe malaria [13, 31]. The decline observed in March/April 2020 was even more remarkable in inpatients. This does not support our initial hypothesis, that in cases of more severe malaria manifestation, patients were still brought to health facilities and hospitalized,

	RR ΔR p – value	1st quarter	2nd quarter	3rd quarter	4th quartei
Outpatient department visits	All visits	0.93 — 269.0 0.202	0.80 — 745.3 < 0.001	0.73 — 1448.2 <0.001	1.03 125.4 0.283
	All malaria	1.04 43.0 0.679	0.91 — 110.8 0.300	0.74 — 654.3 0.002	1.27 570.8 < 0.001
	Malaria children < 5 years	0.96 — 60.6 0.697	0.81 310.9 0.021	0.57 — 1614.5 <0.001	1.19 589.5 0.005
	Malaria pregnant women	0.87 14.2 0.269	0.96 4.4 0.709	1.14 27.6 0.127	1.48 80.7 <0.001
Inpatient department vistits	All malaria	0.79 — 36.8 0.139	0.54 — 65.1 0.008	0.57 139.7 < 0.001	0.94 —16.5 0.526
	Malaria children < 5 years	0.74 — 186.7 0.035	0.46 — 300.7 0.020	0.43 — 764.5 < 0.001	0.82 - 224.5 0.067

Table 2 Quarterly rate ratios (RR), rate differences (ΔR) and p – values comparing the rates of 2020 with the combined rates of the years 2015 to 2019 for outpatients and malaria patients in health facilities of northern Ghana

despite the pandemic. The findings from this analysis support the hypothesis, that the reported malaria burden in health facilities will shrink due to the effects of the COVID-19 pandemic in highly malaria-endemic countries [32]. They also support results of the WHO World Malaria Report [13], and they agree with results of similar studies from other SSA countries classified as highly endemic for malaria, such as Sierra Leone, Uganda and the Democratic Republic of the Congo [33–36].

The distinct decrease of OPD visits in the health facilities of northern Ghana in September 2020 could be explained by unusual heavy floods that started mid-August, which might have further complicated the access to health services. These floods have provided a favourable habitat for *Anopheles* mosquitoes, what could explain the observed increase of malaria cases in October 2020.

Malaria cases seen in health facilities among pregnant women show a different trend. After a decline in April 2020, cases have rebounded rapidly in this population and reached even higher levels compared to previous years. The most likely explanation of such an opposite trend would be the early hesitancy of pregnant women to visit health facilities. This is probably due to the fear of getting infected with COVID-19, combined with initial disruptions of the provision of IPTp to women in antenatal care (ANC) services as well as the disruption of routine distribution of ITNs [37]. The disrupted access to and delivery of ANC services is likely to explain the malaria case trend in April. However, without IPTp and ITNs, more women were at risk for malaria thereafter, which can explain the subsequent rise in malaria cases over the following months. Also, many pregnant women probably have sought the missed ANC with subsequent malaria diagnosis after the initial movement restrictions were lifted.

Ghana had already achieved high levels of ITN coverage, and no ITN mass campaign was planned for 2020 [13]. However, the routine distribution of ITNs, which is usually done in health facilities during ANC sessions and in primary schools, needed to be adapted to the COVID-19 measures, which included school closures from March 2020 until January 2021 [38, 39]. Also the seasonal malaria chemoprevention intervention for children and the annual indoor residual spraying of insecticides, which both require physical contact between the health workers and the community, needed to be modified [40, 41]. As another consequence of the COVID-19 pandemic, the provision of rapid diagnostic tests for malaria was fragile, which may have led to under-diagnosis of cases [42]. The main explanation for the lower number of malaria cases seen in health facilities was limited access to health facilities - public transportations were unavailable or unaffordable, and health facilities were closed or only provided reduced services [43, 44]. This is supported by findings from a study from Rwanda which showed that health facility visits for malaria decreased while community health services for malaria increased [43]. Finally, reports of hesitancy to visit health facilities due to fear of getting infected with COVID-19 were common [37, 42]. Last but not least, the malaria health care worker capacities were limited due to frequent reassignments to the control of COVID-19, to stigmatization or absence following quarantine, or to the development of COVID-19 disease or even death [14, 39, 45].

This study has strengths and limitations. A strength of the study is that the data represent a whole year of follow-up into the pandemic, which provides a more comprehensive picture of the effects compared to the previous studies with much shorter study periods. Also, the subgroup analysis of children under the age of five and pregnant women allows for a more complete picture. A major limitation is that the surveillance system itself may probably have been affected by the pandemic, producing a bias in the reported numbers. Massive underreporting could have falsified the observed trends and our conclusions. Moreover, it is not clear if the quality of surveillance data is fully comparable during the five years observed. The data from the Northern Region of Ghana may also not be representative for other malaria endemic areas in SSA, thus, the study has a limited external validity. Absenteeism in health facilities by people with malaria symptoms that have switched to self-medication or traditional medicine or that could not afford reaching official health care during the pandemic could also have had an albeit unknown effect on the malaria figures [46]. Especially in the first months of the pandemic, many people may have used malaria medication off-label to prevent and treat COVID-19 what may also have impacted the malaria situation [13].

Conclusions

This study shows that the COVID-19 pandemic has been associated with reduced overall outpatient visits and reduced malaria cases reported from northern Ghana's health facilities. Further data and qualitative explanations from Ghana and other SSA countries and in particular data from community-based studies are needed to fully judge the impact of the pandemic on the malaria situation on the African continent.

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Author contributions

MA provided the data sets; AH and VW performed the data analysis. AH wrote the first draft, VW did the methodological foundation, OR did the supervision. All authors read and approved the final manuscript.

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Availability of data and materials

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

Declarations

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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