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ORIGINAL ARTICLE

Persistent 'hotspots' of lymphatic filariasis microfilaraemia despite 14 years of mass drug administration in Ghana

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Background: Among the 216 districts in Ghana, 98 were declared endemic for lymphatic filariasis in 1999 after mapping. Pursuing the goal of elimination, WHO recommends annual treatment using mass drugs administration (MDA) for at least 5 years. MDA was started in the country in 2001 and reached national coverage in 2006. By 2014, 69 districts had 'stopped-MDA' (after passing the transmission assessment survey) while 29 others remained with persistent microfilaraemia (mf) prevalence (≥1%) despite more than 11 years of MDA and were classified as 'hotspots'.

Methods: An ecological study was carried out to compare baseline mf prevalence and anti-microfilaria interventions between hotspot and stopped-MDA districts.

Results: Baseline mf prevalence was significantly higher in hotspots than stopped-MDA districts (p<0.001). After three years of MDA, there was a significant decrease in mf prevalence in hotspot districts, but it was still higher than in stopped-MDA districts. The number of MDA rounds was slightly higher in hotspot districts (p<0.001), but there were no differences in coverage of MDA or long-lasting-insecticide-treated nets.

Conclusions: The main difference in hotspots and stopped-MDA districts was a high baseline mf prevalence. This finding indicates that the recommended 5–6 rounds annual treatment may not achieve interruption of transmission.

Keywords: Lymphatic filariasis, Ghana, Hotspots, Mass drug administration, MDA

Introduction

Lymphatic filariasis (LF), also commonly known as elephantiasis, is a disabling and disfiguring disease resulting from damage to lymph vessels by microscopic larvae, microfilariae, which are transmitted to humans by mosquito bites. Lymph vessels and nodes are damaged by the parasites and may result in massive lymphoedema.[1,2]

LF is a widespread and a major public health problem in many developing countries with a warm and humid climate. According to WHO, over 120 million people are infected, and 40 million are disfigured or incapacitated by the disease.[3] It has a high prevalence in remote rural areas and disadvantaged peri-urban and urban locations.[4,5]

In 2000, WHO launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF), with an ambitious goal of eliminating LF in all disease-endemic areas by 2020. The major strategy recommended by GPELF was based on mass drug administration (MDA) of antifilarial medications that reduce microfilaraemia (mf) rates in communities to levels below those needed for sustained transmission by mosquitoes. The main GPELF strategy to interrupt transmission is MDA using combinations of two antifilarial medicines (albendazole plus either diethylcarbamazine or ivermectin) delivered once-yearly to entire eligible populations in endemic areas. The recommended regimen in sub-Saharan Africa is either diethylcarbamazine or ivermectin and albendazole for a minimum of 5 years with effective population treatment coverage (the goal is ≥65%). As the life expectancy of

adult worms is from 4 to 6 years, it is expected that disease transmission should be interrupted after five years of effective treatment coverage.[2,6,7]

Ghana is an LF endemic country with 98 endemic districts identified in 1999 by *Wuchereria bancrofti* antigen mapping. Implementation of MDA started in 2001 in 10 districts and reached national coverage by 2006. Out of the 98 endemic districts, 69 achieved interruption of transmission by 2014 with a prevalence of mf of <1%, and passed a transmission assessment survey, (referred to as 'stopped-MDA' districts); they have established post-MDA surveillance.[8] The remaining 29 districts have persistent transmission (>1% prevalence) after more than 11 years of drug distribution, despite high reported coverage, and are referred to as 'hotspot districts'. It is not clear why the hotspots persist, given the effectiveness of the drugs and reported high coverage in Ghana.

The number of rounds of MDA for interruption of transmission in endemic areas may depend on the initial prevalence of infection, initial intensity of transmission, efficacy of medicines, MDA drug regimen, compliance, combinations of parasite and vector species and density of vectors.[7,9] Other studies in Tanzania and Samoa have identified reasons for persistent mf prevalence. They include poor coverage of MDA and persistent non-compliance with medication by a section of the population.[10–14]

Thus, the aim of our study was to assess differences between hotspot and stopped-MDA districts that could be responsible for persistent mf prevalence of LF in Ghana after more than eleven rounds of MDA. Specifically, we mapped the impact of MDA from 2001–2016; compared the interventions undertaken in hotspot and stopped-MDA districts; and described the trend of mf prevalence in hotspot and stopped-MDA districts.

Methods

Study design and setting

This was an ecological, descriptive study using routinely collected programme data.

General setting

Ghana is a West African country with an estimated population of 27 million in 2014.[15] There are 10 administrative regions with 216 administrative districts. The estimated 'at-risk population' for LF was 13.4 million in the 98 endemic districts. In 2014, the gross national income per capita was estimated at US$1590 and categorized by International Monetary Fund as a lower middle-income country.[16]

Ghana Neglected Tropical Diseases Programme

The Ghana Neglected Tropical Diseases Programme (NTD Programme) is under the Ghana Health Service and has adopted the WHO recommendation for LF elimination.[7] The MDA strategy has been implemented at the community level with the support of community drug distributors who are volunteers. There are 12 NTDs in Ghana, five of which use the preventive chemotherapy strategy through MDA. Among these five NTDs, three are targeted for elimination and include LF, onchocerciasis and blinding trachoma.

The 98 endemic LF districts are located in eight out of the 10 regions of the country. The programme starts by mapping and determination of baseline prevalence, and all endemic districts receive MDA. After MDA is implemented in a district, there is a midterm assessment after 2–3 years to assess the impact of MDA strategy. After 5 years of MDA implementation, a first pre-transmission assessment survey (Pre-TAS) is carried out in each sentinel site, which had been previously identified in every endemic district. Pre-TAS consists of collecting night blood samples from a minimum of 300–500 children of 5 years old and above. The prevalence is determined by the proportion of positive microfilariae cases among all the persons that are screened.

When prevalence is ≥1%, the district fails the Pre-TAS and MDA is continued for two or more years before the Pre-TAS is repeated. After ten years of MDA with persistent prevalence (≥1%) of mf, the district is considered a 'hotspot' by the Programme.

If the prevalence is less than 1%, a TAS is conducted to determine whether to stop or continue MDA as in WHO guidelines.[7] In Ghana, after the 2014 Pre-TAS, 29 districts remained 'hotspots'.

In addition to TAS, WHO recommends that endemic countries implement a post-MDA surveillance system in districts that have stopped MDA to complement TAS and avoid recrudescence.[8]

Apart from MDA, WHO recommends vector control including use of long-lasting insecticidal nets (LLINs) and indoor residual spraying.[2] These methods are not, however, part of the NTD Programme activities in Ghana but are part of the National Malaria Control Programme (NMCP). LLINs are distributed nationwide, but indoor residual spraying activities are carried out only in selected districts in the country and implemented by the NMCP.

Finally, for those persons who already manifest signs of the disease, elephantiasis and hydrocele, clinical case-management including surgery may be carried out to alleviate associated pain and suffering and correct some complications.

Process in conducting MDA

Ghana adopted the processes as set out in WHO guidelines in conducting MDA, which ensures that eligible persons are given the medicines using directly observed therapy strategy (DOTS).[17]

Study population

All 98 endemic districts, 29 hotspot and 69 stopped-MDA districts in 2014 were included in the study.

Data variables

Data collected for this study in each district were: MDA-status (hotspots and stopped-MDA districts), mf prevalence at baseline, midterm (defined as the mf prevalence available after 2–3 rounds of MDA), the most recent prevalence, number of rounds

of MDA, epidemiological coverage (defined as number of persons treated out of total at-risk population) and LLIN coverage (after 2010 nationwide distribution).

Data were collected from the electronic Excel 2016 database of NTD Programme and NMCP (Microsoft Corp., Redmond, WA, USA). Data from the Pre-TAS surveys were checked by a programme officer before being entered into the NTD Programme Excel database. Data were copied directly into a study Excel database to avoid data entry errors.

Analysis

Data were transferred into EpiData Analysis software version 2.2.2.182 (EpiData Association, Odense, Denmark) for analysis. T-test and Wilcoxon test were used to compare means and medians, respectively, between the two groups. Level of significance was set at 5%. ArcGIS v10.3 (https://www.arcgis.com/) was used to develop the maps.

Results

Distribution of LF at baseline, following MDA implementation from 2001 to 2014 and the current status in 2016 are shown in Figures 1A, 1B and 1C. At baseline, all districts in Northern, Upper West and Upper East regions were endemic. The remaining endemic districts were located in Brong-Ahafo region in the middle belt of the country and the southern coastal area (Figure 1A). By 2014, 69 districts had become stopped-MDA after TAS were conducted. All these districts met critical-cut off points; the 29 others were declared hotspots. These were located in the Upper West, Upper East, Northern, Brong-Ahafo and Western regions (Figure 1B). By 2016, although 12 more districts had also become stopped-MD, no improvement was noticed in the north-western part of Ghana (Figure 1C).

Interventions undertaken in hotspot and stopped-MDA districts are presented in Table 1. There were slightly more MDA rounds in the hotspot areas, but there were no differences in the reported MDA coverage or LLIN distribution.

The trends of mf prevalence at baseline, midterm and most recent surveys in hotspot and stopped-MDA districts are shown in Figure 2. The mf prevalence at baseline was much higher in the hotspots than in stopped-MDA districts. However, even after three years of MDA implementation, there was a significant decrease in mf prevalence in hotspot districts; thereafter, the decrease in mf prevalence slowed.

Discussion

This study documents differences in mf prevalence between hotspots versus stopped-MDA areas during a programme of annual MDA in Ghana. It showed that hotspots persisted despite over 11 annual cycles of MDA. The mf prevalence at baseline was approximately 10-fold higher in hotspots than stopped-MDA districts but prevalence dropped sharply during the first few years of MDA in hotspots. No significant differences were observed in median coverage of MDA or average LLIN coverage, except that the number of MDA rounds were slightly higher in hotspot districts. We did not demonstrate any other obvious differences between the two contexts.

Despite the proven effectiveness of the MDA drugs,[18] we were not surprised by the persistence of mf in hotspot districts. According to WHO, at least five rounds of MDA may be sufficient for interruption of mf.[2,6,7] However, studies have shown that in areas with high mf prevalence, more than six rounds of MDA were required to achieve interruption with low epidemiological coverage.[10,19]

Other factors that may be responsible for the delay in mf interruption of transmission in high prevalent areas include poor compliance.[8] In this study, there seemed to be no differences in the reported MDA epidemiological coverage. Previous studies in Ghana have pointed out that data reported on epidemiological coverage may not be accurate (60%), however, this situation is not different between hotspots and stopped-MDA districts.[20] Poor compliance (44%) has been reported in a hotspot district in Ghana.[13]

Secondly, although LLINs were reportedly distributed equally among the hotspot and stopped-MDA districts, there was no documentation of their actual use. Thus, their direct contribution to interruption of transmission could not be determined.

The strengths of our study were that it covered all the endemic districts in the country. Additionally, the methods used to conduct mf prevalence surveys were well supervised and standardized. The study also adhered to The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[21]

However, there are some limitations. Because of the use of already collected data, we were not able to verify the accuracy of MDA uptake by the at-risk population. Lack of compliance has been identified in other studies as a major reason of persistent high mf prevalence.[12–14] One study from Nepal identified associated factors with non-compliance to MDA; these included advanced age, primary or less education, ever married, inadequate knowledge on the MDA drugs, inadequate awareness on MDA, no home visit by health workers during MDA and no trust in MDA drugs.[22] Furthermore, data on indoor residual spraying, which is another vector control measure, was not available.

This study has some implications for the programme. Districts with high mf prevalence at baseline will likely require more treatment rounds to reach the elimination targets compared to districts with low mf prevalence at baseline. More than the five recommended treatments will be required to achieve elimination in districts with high baseline mf prevalence. A study modelling impact and cost of bi-annual MDA against annual MDA in varied pre-control endemicity and coverage levels in India and West Africa concluded that bi-annual MDA was likely to shorten the duration and lower the cost required in conducting MDA for the elimination of LF in countries where this is possible.[23] This finding and conclusion could be considered in settings where baseline mf prevalence is high particularly for countries yet to start MDA in order to reach the 2020 elimination goal. Finally, drug resistance studies should be carried out to identify another potential reasons for the long duration required for interruption of transmission.

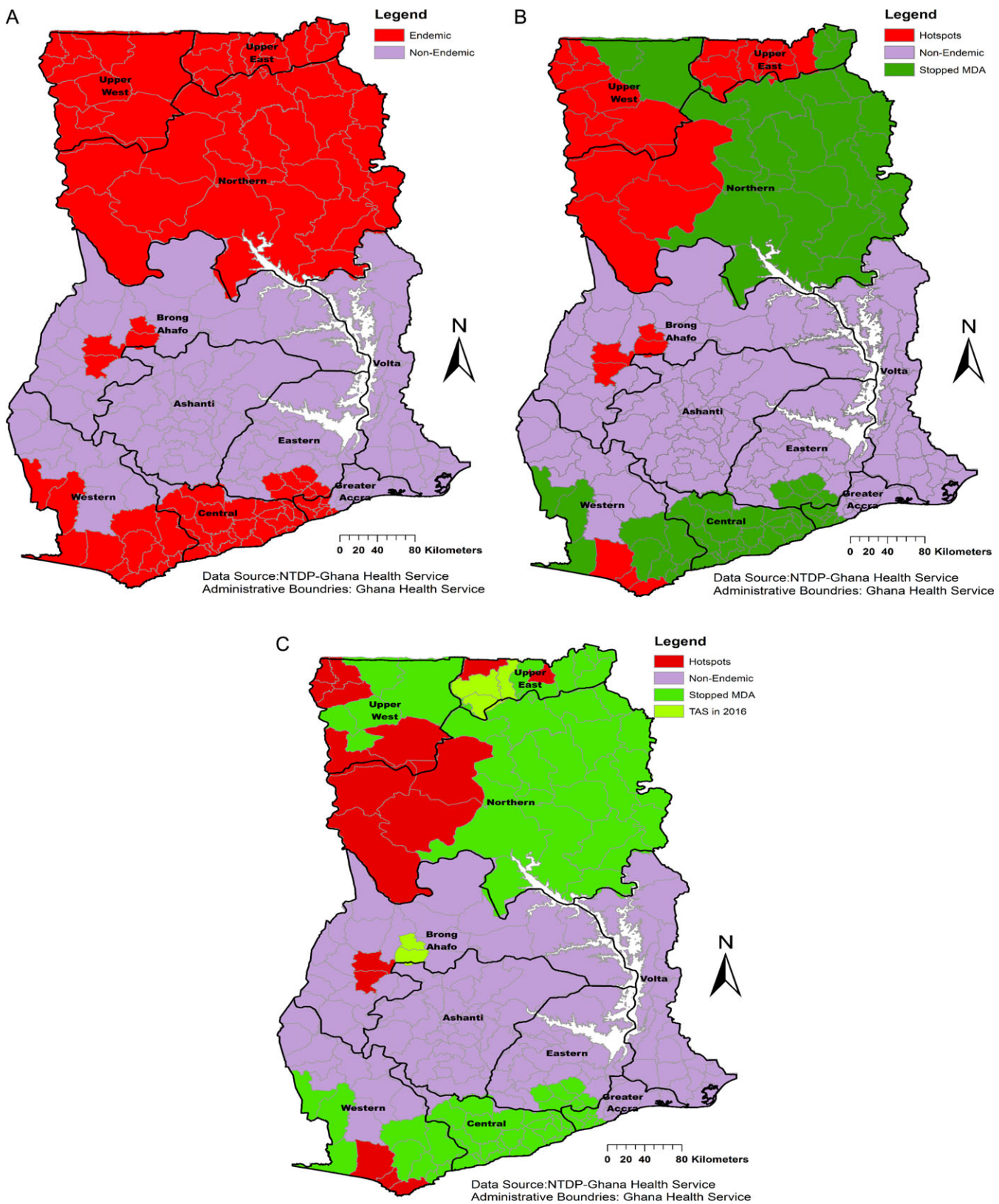

Figure 1. Lymphatic filariasis endemicity status, Ghana. (A) at baseline (2000–2004); (B) 2014; (C) 2016. MDA: Mass Drugs Administration; NTDP: Neglected Tropical Diseases Programme; TAS: Transmission Assessment Survey.

Table 1. Differences in interventions between hotspots and stopped MDA districts, Ghana, 2001–2014.

Factors	Hotspot districts	Stopped MDA districts	p-value
Average number of MDA rounds (SD)	11.5 (1.1)	10.2 (0.6)	<0.001
Median coverage of MDA (IQR)	75.4 (7.5)	77.5 (8.2)	NS
Average LLIN coverage (SD)	19.7 (1.5)	20.1 (12.2)	NS

Source of data: Ghana Health Service, Neglected Tropical Diseases Programme.
LLINs: long-lasting insecticidal nets; MDA: mass drugs administration; NS: not significant.

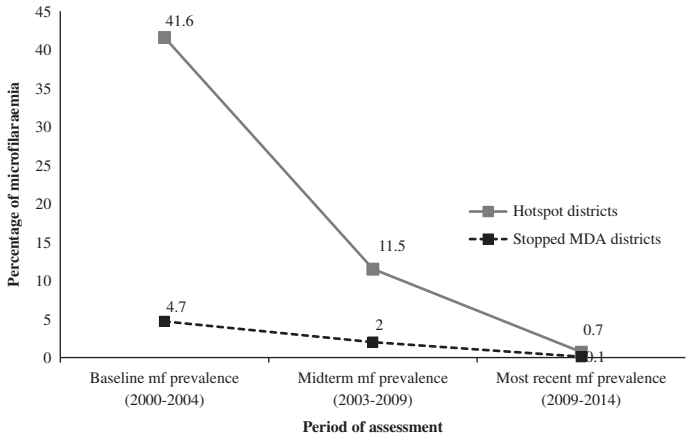

Figure 2. Lymphatic filariasis microfilaraemia prevalence trends in hotspot vs stopped mass drugs administration districts, Ghana, 2000–2014. MDA: Mass drugs administration; mf: Microfilaraemia.

Conclusions

Our study found that the main difference in hotspot and stopped-MDA districts was a high baseline mf prevalence. This may be indicative that more than the recommended five to six rounds of treatment may be required in areas with high baseline prevalence to achieve interruption of transmission. Improving compliance through strict MDA supervision may improve treatment coverage in hotspots areas. Modelling various treatment regimen indicate that increasing frequency of treatment may reduce duration required to interrupt transmission in high prevalence areas. Therefore, with effective compliance, bi-annual treatment in high endemic areas may be considered in reducing the duration of MDA to achieve interruption of transmission mf by 2020.

Authors' contributions: PY, NKB and JBK conceived the study; PY, NKB, SO, BA, SA, SGH, AR, KCT, BK and JBK designed the study protocol; PY, NKB, BKM, SO, EOM, OA, BA, ETH and AY carried out the epidemiological assessments; PY, NKB, SA, SGH, AR, KCT, BK and JBK carried out the analysis and interpretation of these data. PY, NKB, SA, SGH, AR, KCT, BK and JBK drafted the manuscript; PY, NKB, EOM, JBK, SA, SGH, AR, KCT, BK and JBK critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. PY, NKB, AR and JBK are guarantors of the paper.

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Competing interests: None declared.

Ethical approval: Permission to carry out the study was obtained from the NTD Programme of the Ghana Health Service. The study fulfilled the exemption criteria set by the Ethics Review Board (ERB) of Médecins Sans Frontières (MSF), Geneva, Switzerland, for a-posteriori analyses of routinely collected data and thus did not require MSF ERB review. It was conducted with permission from the MSF Medical Director, Operational Centre Brussels, Belgium. The study was also approved by the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. As this was a record review study, informed patient consent was not required.

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