

# Mass Drug Administration Interruption by COVID-19 reportedly increases lymphatic filarial attacks, pains, and perceived increased lymphatic filarial infection transmission in rural Ghana

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## Research article

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# Abstract

## Background

Like all other diseases, the advent of the COVID-19 pandemic has been implicated to impact the elimination schedule and control of neglected tropical diseases such as human lymphatic filarial (LF) infections in endemic countries. However, it is unclear the extent to which delays in mass drug administration has affected people living with chronic lymphatic filarial pathology in rural Ghana as a result of the COVID-19 pandemic, and thus remain to be investigated.

## Method

To address this, a cross-sectional study where 133 LF participants from 8 LF-endemic communities in the Ahanta West District of Ghana were recruited to assess the impact of MDA interruptions as a result of COVID-19 among individuals presenting with the filarial pathology. Here, the chi-square test of independence was used as a statistical tool to assess the dependency: 1) between MDA interruption and filarial attacks 2) between MDA interruption and filarial-related pains 3) between MDA interruption and a perceived increase in LF transmission.

## Results

Study participants were asked whether the MDA interruption has affected them in any way. Here, 81% of the patients indicated yes, it had. In addition, we sought to investigate whether MDA interruption has resulted in increased filarial attacks and pains. At this, 68% of the study respondents reported an increase in filarial attacks. Similarly, 65% reported an increase in filarial-related pains. The study further reported that filarial attacks ( $B=14.997$ ,  $df=1$ ,  $p\text{-value} < 0.001$ ) and pains ( $a=11.773$ ,  $df=1$ ,  $p\text{-value} < 0.001$ ) are dependent on MDA interruption. Next, we further report that the perceived increase in LF transmission is dependent on MDA interruption ( $c=9.415$ ,  $df=1$ ,  $p\text{-value}=0.002$ ).

## Conclusion

In this study, MDA interruption is reported to increase filarial attacks, filarial-related pains, and a perceived LF transmission increase in the study communities. This study's findings are important and urgent, suggesting that sustained MDA interruption in LF-endemic communities could further worsen LF patients' plight as filarial attacks, pains, and transmission could increase. Therefore, the need to immediately identify alternative modes of MDA distribution in LF-endemic areas where mass treatment has been halted in the wake of COVID-19 to prevent an unwarranted surge in LF attacks, pains, and transmission.

## 1. Background

The COVID-19 global pandemic has affected every course of our lives. As of 21st November 2020, 55.6 million people have been infected with the SARS-COV2 virus, with 1.34 million reported dead globally (John Hopkins Coronavirus Update). Despite the gloomy projections by international health organizations about the exponential number of cases and associated mortality, the death rates in Ghana and many African nations have lagged behind many developed countries in Europe and the Americas. These estimates were justified by the high population densities and imperfect health systems in many African countries [1]. In addition, Africa's youthful population (median age 19.7 years versus 38.6 years in the US) could be attributed to the low prevalence and mortality given that most COVID-19 deaths occur in older people [2, 3]. While the low incidence rate and associated COVID-19 mortality in many African countries may seem positive news, under-reporting of cases due to fewer tests and incomplete documentation of actual causes of deaths have also been attributed to the low cases and mortality [4].

Like many other African nations, Ghana implemented early measures such as travel restrictions, closure of schools and other institutions, curfews on social gatherings such as congregational services. The country-wide restrictions have impacted several community health activities such as mass drug administration (MDA) with ivermectin and albendazole in Ghana, which operates a decentralized health system [5] for treating human filarial infections, including lymphatic filariasis (LF) and onchocerciasis. In Ghana, the majority of the implementation of health policies and interventions are carried out by community health facilities and community health workers.

Many LF patients remain asymptomatic; however, advanced LF, usually characterized by disfiguring swelling of the limbs, is common in endemic communities [6]. Most LF patients with advanced disease stages are immobile, unemployed, suffer seasonal filarial attacks associated with excruciating pain, and face lots of stigma from society [7, 8]. We previously revealed the negative impacts of financial constraints on LF pathology patients' quality of life [9]. In the wake of COVID-19, several countries had to shut down, including Ghana, in line with WHO guidelines to reduce the pandemic's spread [10]. While most countries in the developing world have lifted lockdown bans, and the resurgence of COVID-19 cases, especially in the West, presents a new challenge for most developing countries, which unfortunately rely heavily on foreign donor support. Together, it appears the rise in COVID-19 cases could potentially affect many vital sectors, especially health interventions such as mass drug administration programs in most low-and-middle-income countries. Thus, understanding how the COVID-19 pandemic could indirectly affect LF-control intervention strategies and the extent of its impact need to be urgently determined.

In this study, we hypothesize that Ghana's lockdown and disruption of MDA due to COVID-19 could significantly affect filarial attacks, pains, and LF transmission increases in LF endemic communities.

## 2. Methods

To assess the impact of COVID-19 on the interruption of mass drug administration on individuals presenting with chronic filarial pathologies, we interviewed LF individuals using questionnaire instruments. The study was part of a larger study on skin microbiome ongoing in these selected communities. We obtained

### 3. Results

#### 3.1 Socio-demographics of study participants

A cross-sectional study design was employed where 133 LF participants from 8 LF-endemic communities in the Ahanta West District in the Western Region of Ghana were recruited. Of these, 103 representing (77%) were females, with the remaining were males. Approximately (68%) of the respondents were between the ages of 14 and 50, while the remaining were above 50 years. In terms of education level, 53% of the total respondents had no formal education, while the remaining 42% and 5% had primary and secondary education. Majority, (56%) of the study participants were into fishing-related activities in the fishing value chain, 2% artisans whereas 30% were into farming, with the remaining unemployed. Of note, some of the participants failed to respond to certain instruments accounting for the differences in demographic totals (see Table 1).

Table 1  
Demography of study participants

Age of Participant			Sex of Participant			Education			Employment of Participant		
Response	Frequency	Valid Percent	Response	Frequency	Valid Percent	Response	Frequency	Valid Percent	Response	Frequency	Valid Percent
20–30	16	13.3	Male	30	22.6	None	71	53.4	Unemployment	12	10.5
31–40	36	30.0	Female	103	77.4	Basic	56	42.1	Fishing	64	56.1
41–50	29	24.2	Total	133	100.0	Secondary	6	4.5	Farming	35	30.7
51–60	25	20.8				Total	133	100.0	Artisan	3	2.6
61–70	8	6.7							Total	114	100.0
71–80	3	2.5									
14–19	3	2.5									
Total	120	100.0									

#### 3.2 Impact of MDA interruption due to Covid-19 pandemic on LF patients

LF patients were asked whether the MDA interruption has affected them in any way. Here, 19% responded no, while 81% indicated yes, it had. Also, we sought to investigate the impact of the MDA interruption on filarial attacks. With this, 32% of respondents indicated no, whereas 68% answered yes. Given that most LF patients experience pains, we also assessed the MDA interruption's impact on LF pain. Majority, (65%) of the study participants reportedly experienced LF pains, while the remaining did not. Furthermore, we assessed the patients' perception of MDA interruption's potential effect on LF transmission. Here, 65% of the patients suggested that MDA interruption can drive LF transmission in the communities, while the remaining did not agree to this assertion, as shown in Table 2.

Table 2  
Participants response on the effect of MDA interruption and COVID-19 pandemic.

MDA INTERRUPTION DURING COVID 19 PANDEMIC			INCREASE IN LF ATTACKS DUE TO MDA INTERRUPTION			INCREASE IN PAIN IN LF PATIENT DUE TO COVID 19 PANDEMIC		
RESPONSES	Frequency	Valid Percent	RESPONSES	Frequency	Valid Percent	RESPONSES	Frequency	Valid Percent
No	25	18.8	No	42	31.6	No	46	34.6
Yes	108	81.2	Yes	91	68.4	Yes	87	65.4
Total	133	100.0	Total	133	100.0	Total	133	100.0

#### 3.3 MDA interruption reportedly increases LF attacks in LF-endemic communities

Having observed that MDA interruption affects LF attacks, we further investigated whether the reported increased LF attacks depended on the MDA interruption resulting from the COVID-19. We observed that increased LF attacks in LF-endemic communities depend on MDA interruption ( $\chi^2=14.997$ ,  $df = 1$ ,  $p\text{-value} < 0.001$ ) Table 3. Out of 133 study participants, 16 who indicated that MDA interruption had not affected them in anyway also stated that there had not been an increase in LF attacks. In contrast, 82 of the participants who indicated that MDA interruption had affected them also reported that there had been an increase in LF attacks. Furthermore, the study assessed the extent to which MDA interruption and LF attacks are associated. The results indicated a positive correlation between LF attacks and MDA interruption during the COVID-19 pandemics (Spearman rank correlation coefficient of  $r = 0.336$ ,  $p < 0.001$ ).

Table 3  
The association between the increase in LF attacks and MDA interruption

		Increase in LF attacks			Chi-square	P-value
		No	Yes	Total		
MDA interruption	No	16	9	25	14.997	< 0.001
	Yes	26	82	108		
	Total	42	91	133		

### 3.4 MDA interruption reportedly increases LF pains in LF-endemic communities

Most LF patients experience pains periodically and rely on MDA as the only source of relief. In the present study, we ascertained MDA interruption's impact on LF pain among the study participants. As described in Sect. 3.2, most of the participants reportedly experienced LF pains. We next interrogated whether MDA interruption primarily drove the reported increase in LF pains. Our results showed that increased LF pains depended on MDA interruption ( $\chi^2=11.773$ ,  $df = 1$ ,  $p$ -value < 0.001) Table 4. Out of 133 study participants, 16 who indicated that MDA interruption had not affected them in anyway also stated that there had not been an increase in LF pains. Of note, 78 of the study participants who indicated that MDA interruption had affected them also reported that there had been an increase in LF pains. We further observed that MDA interruption and LF pains were positively correlated with the Spearman rank correlation coefficient of  $r = 0.291$ ,  $p = 0.001$ .

Table 4  
The association between increase in LF pain and MDA interruption

		Has there been an increase in LF Pain?			Chi-square	P-value
		No	Yes	Total		
MDA Interruption	No	16	9	25	11.773	0.001
	Yes	30	78	108		
	Total	46	87	133		

### 3.5 MDA interruption reportedly increases perceived LF transmission in LF-endemic communities

In LF-endemic communities, MDA is the primary strategy used to interrupt transmission of the parasite. In this study, we assessed the perceived effects of MDA interruption on LF transmission. Having observed a perceived increase in LF transmission, we further evaluated the impact of MDA interruption on LF transmission, as shown in Sect. 3.2. Our results indicate that the perceived increase in LF transmission depends on MDA interruption ( $\chi^2=9.415$ ,  $df = 1$ ,  $p$ -value = 0.002) Table 5. In total, 15 out of 133 of the study participants who responded no to the question of "whether MDA interruption affected you in any way" also indicated that lack of MDA does not affect LF transmission. Instead, 78 of the participants who indicated that MDA interruption had affected them also reported a likelihood of increased LF transmission due to lack of MDA intervention. Here, we showed the extent to which MDA interruption and perceived LF transmission are associated. The results indicated a positive correlation between the two variables (Spearman rank  $r = 0.266$ ,  $p = 0.002$ ) described in Table 5.

Table 5  
The association between the increase in LF transmission and MDA interruption

		Do you think lack of MDA can increase LF transmission?			Chi-square	P-value
		No	Yes	Total		
MDA Interruption	No	15	10	25	9.415	0.002
	Yes	30	78	108		
	Total	45	88	133		

## 4. Discussion

With the advent of COVID-19, the MDA program in filarial endemic communities in Ghana have been halted in compliance with COVID-19 protocols of shelter in place and social distancing. This study observed more women with symptomatic LF than men, as shown by the demographic data. This observation is not uncommon as others have reported the same in other LF-endemic areas [8]. Similarly, most of the study participants were in their active years (50 years and below, 67.5%). Our findings corroborated previous studies with a high frequency of younger populations in endemic communities with LF morbidity [11, 12], thus presenting a unique challenge to the most endemic communities if adequate control measures are not quickly implemented.

In the present study, we observed increased LF attacks reported as a result of MDA interruption due to the COVID-19 pandemic among LF patients in south-western Ghana. MDA programs in filarial endemic regions rely on ivermectin and albendazole as the mainstay intervention against filarial infections [13]. Ivermectin is widely available, inexpensive, easy to administer, and has a wide safety margin [14]. Ivermectin is an effective macrocyclic lactone in reducing infection transmission. Thus, disruption of MDA activities could prolong timelines for LF elimination

[5]. Aside its microfilaricidal activities, ivermectin is reported to offer other benefits especially for people living with the end stage of the LF pathology, who are likely to be negative for the active infection by reducing filarial attacks [15]. In the current study area, ivermectin is distributed annually around March to control LF transmission. With the MDA interruption, the reported increased LF attacks could be worrying given the excruciating pain and discomfort associated with LF attacks [8], suggesting that urgent attention should be given to individuals suffering from human lymphatic filarial infections living in LF-endemic communities. Of note, this study's findings are important and urgent, suggesting that sustained interruption of the MDA interruption in endemic communities could further worsen the plight of these LF patients as filarial attacks could increase.

Next, MDA interruption was recounted to increase the frequency of LF pains experienced by the patients, and these pains were positively associated with MDA interruption during the COVID-19 pandemic. It is well-described that LF attacks are accompanied by pains [6]. Some LF patients do experience, which could be so high that victims would have to be admitted at the health facility to receive some form of relief [16, 17]. Unfortunately, with the increased cases of COVID-19, which burdens the local health facilities, more attention is given to individuals presenting with symptoms of SARS-COV-2, thus further frustrating the ability of LF pathology patients with attacks to visit the health facilities to receive the needed treatment.

Ivermectin is known to reduce pains by inhibiting NF-kappa B's activity, a transcription factor, and MAP-kinases, which are known to drive inflammation [14, 18]. It has been demonstrated to have anti-inflammatory and immunomodulatory actions in several *in vitro* and animal models [14]. Not only do ivermectin-derivatives control nuclear transcription factors as indicated above, but there are also reports of its ability to suppress pro-inflammatory cytokine secretion (interleukin-1  $\beta$  and tumour necrosis factor- $\alpha$ , TNF- $\alpha$ ) by 30% and heightens the immunoregulatory cytokine interleukin (IL)-10, an *in vitro* model of lipopolysaccharide (LPS) induced-inflammation [18]. Furthermore, ivermectin-treated mice showed better survival rates with a decrease in pro-inflammatory cytokines, TNF- $\alpha$  and IL-1, IL-6 compared to controls following a lethal dose of LPS [19]. Interestingly, the therapeutic benefits of ivermectin works across all stages of LF pathogenesis [14]. This may be explained by ivermectin's multi-pronged effects, which range from direct parasite inhibition to immunomodulation to mitigation of cell access, as demonstrated by *in vitro*, *in silico*, and animal studies [14]. In addition, ivermectin has been demonstrated to show anti-viral activity, suggesting the potential use of this drug in LF endemic areas with high COVID-19 cases could have multiple benefits [27].

Furthermore, the present study also showed that individuals with LF pathology had a perceived LF transmission increase should MDA interruption continue for a long time. The findings confirm previous reports where a halt in MDA was projected to increase transmission in endemic areas and the frequency of filarial attacks and cases of other helminth infections such as lice [20]. It is important to understand the impact of COVID-19 on the transmission dynamics of lymphatic filariasis in endemic regions. While interruption of MDA in LF endemic communities could result in a resurgence of the disease [21], it can also provide several research opportunities to reassess the microfilarial levels before resuming the intervention, providing data that would otherwise be difficult to obtain.

Although not directly assessed, participants reported a perceived increase of LF transmission in endemic regions could also suggest their understanding of LF transmission and its causative agents. Previous studies have documented limited knowledge and perception of LF in endemic communities [22, 23]. Therefore the high frequency of individuals' perception of LF transmission may indicate the impact of health promotion and educational campaigns in endemic areas.

It is important to note that shift in attention, logistics, and human resources from filarial control program to COVID-19 control, while undoubtedly necessary, if not carefully reviewed, could be disadvantageous by denying individuals living in LF-endemic communities the opportunity of receiving timely anti-filarial treatment. Complexing the situation further is the similarity between malaria and LF infection symptoms, where both are characterized by increased body temperature (fever), headache, and chills [24]. Thus, based on this, many LF patients with these symptoms may be prevented from visiting local clinics, given the stigma associated with COVID-19 [25, 26].

## 5. Conclusion

The present study in Ghana is the first to document that MDA interruption is reported to increase LF attacks, LF-related pains, and the perceived increase of LF transmission in endemic communities. The findings herein are important and urgent. They offer insight into some of the indirect challenges posed by COVID-19 on LF and the need to quickly resolve and resume MDA intervention in other not to worsen the plight of LF patients living in endemic communities. The findings should inform policy regarding the management of filarial infections and other neglected tropical diseases during the COVID-19 pandemic.

## Abbreviations

MDA – Mass Drug Administrations

LF – Lymphatic Filariasis

WHO – World Health Organisation

TNF – Tumor Necrosis Factor

MAP - Mitogen-activated protein

LPS – Lipopolysaccharide

SARS-COV-2 – Severe acute respiratory syndrome coronavirus 2

IL – Interleukin

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# Declarations

## Ethical Approval and Consent to participate

The study was approved (CHRPE/AP/209/19) by the Committee of Human Research, Publications and Ethics, School of Medical Sciences and Dentistry, Kwame Nkrumah University of Science and Technology, KNUST, Kumasi, Ghana. Approval was also sought from Municipal Health Directorates at the Ahanta Nkwanta, Western Region, Ghana. The study protocols were explained to the participants and all participants consented to the study by signing or thumb printing the informed consent forms

## Consent for Publication

Not Applicable

## Availability of data and materials

Data sets will be made available upon request.

## Competing Interest

The authors declare no conflict of interest.

## Funding

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## Authors' contributions

AK conceived the idea and drafted the manuscript. SOA, EKA, JKY collected the data from the field. YDA, AK and SOA conducted the statistical analyses. EVSK and STA also read the manuscript critically and equally edited it. All authors approved the final version of this article

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