Occurrence of Onchocerciasis infection after decades of mass drug administration in the Western North Region of Ghana: The case of Sefwi Akontombra district

Derrick Adu Mensah
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Linda Batsa Debrah
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

John Boateng
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Monica Ahiadorme
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Jubin Osei-Mensah
Kumasi Centre for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Vera Serwaa Opoku
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Michael Agyemang Obeng
Kumasi Centre for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Eunice Kyaakyile Kuutiero
Kumasi Centre for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

John Opoku
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Abu Abudu Rahamani
Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Sarfowaa Amponsem

Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Prince Obeng

Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Charles Gyasi

Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Emmanuel Donawugube Kutu

Kumasi Centre for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Alexander Yaw Debrah (yadebrah@yahoo.com)

Department of Medical Diagnostics, Faculty of Allied Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

Research Article

Keywords: Prevalence, Onchocerciasis, Nodule, Microfilaria, Mass Drug Administration, Ivermectin, Sefwi Akontombra

Posted Date: September 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1925871/v2

Abstract

Background

Onchocerciasis is the world's second leading cause of infectious blindness and a major public health problem in many parts of the world, including Ghana, with severe impact on the skin also. Mass drug administration (MDA) with ivermectin began in the Sefwi Akontombra district of the Western North Region of Ghana in 1994. The aim of this cross-sectional study was to evaluate the impact of about three decades of MDA on onchocerciasis and its clinical manifestations by investigating the current nodule and microfilaria (MF) prevalence in the Sefwi Akontombra district using established protocols.

Methodology

This cross-sectional study had participants examined for signs of dermal/skin onchocerciasis and palpated, and those with ≥ 1 palpable sub-cutaneous nodule had skin snips taken from the left and right iliac crests for later parasitological (microfilariae) assessment. Logistic regression models were used to identify independent predictive and risk factors significantly associated with nodule and MF prevalence.

Results

A total of 1980 participants from 25 communities in three sub-districts were recruited. Compliance to the MDA intervention in the district was 93.7%. The study recorded *Onchocerca* nodule prevalence of 35.4% (N = 701), out of which 31.5% (N = 221) were MF positives, with district community microfilariae load (CMFL) and geometric mean intensity of 0.25 MF/ss and 0.26 MF/ss respectively. Adawu, the central community among the 25 surveyed recorded the highest CMFL (0.77 MF/ss)— with 14 communities being hypoendemic and 11, mesoendemic for the onchocerciasis infection. The overall estimated district onchocerciasis MF prevalence was 11.2%, making the district hypoendemic. Of the 17 participants who presented with dermal symptoms, acute papular onchodermatitis (41.2%) was the most prevalent. Age, ivermectin intake and gender were the independent predictive factors significantly associated ($p < 0.05$) with onchocerciasis in the district.

Conclusion

Despite decades of ivermectin administration in the district, the MF prevalence in the district was > the 1% threshold required for elimination. As the focus of the Ghana Onchocerciasis Control Programme has changed from control to elimination, MDA should be intensified in areas with MF prevalence > 1%. Though the district's CMFL was far below the 5.0 MF/ss public health problem threshold, macrofilaricidal drugs should be explored to complement the microfilaricidal ivermectin.

Background

Onchocerciasis caused by *Onchocerca volvulus* is a neglected tropical devastating filarial disease that affects the skin and sometimes permanent damage to the eyes causing blindness [1, 2]. This disease is often referred

to as river blindness due to damage the eyes sustain in severe infections and its association with occurrence along rivers and streams. This skin filarial disease is transmitted from person to person by the repeated bites of infected blackflies (*Simulium* spp.) that breed in fast-flowing rivers and streams close to fertile agricultural lands in remote villages [2–3]. This has in certain situations led to such lands being abandoned for fear of the disease [4].

Microfilariae (MF) produced by the adult worms migrate to the skin, eyes and other organs leading to intense pruritus [5]. This has caused 14.6 million skin diseases and 1.15 million vision loss according to a 2017 data by World Health Organization (WHO) [3]. Skin inflammation and changes such as acute and chronic papular onchodermatitis, sub-cutaneous nodules, loss of elasticity, depigmentation and atrophy of the skin and epilepsy are some of the clinical manifestations of the disease [3–4, 6].

Globally, onchocerciasis infection as estimated in 2017 was 20.9 million with Africa, Yamen and the Americas (Brazil and Venezuela) being at high risk of infection [3]. The disease exhibits three different levels of endemicity in areas where it is mostly prevalent. Endemicity classification of communities based on *Onchocerca* MF prevalence can be defined as hyperendemic (MF prevalence > 60%), mesoendemic (MF prevalence between 35–60%) and hypoendemic (MF prevalence < 35%) [7]. According to WHO, and as reported, over 99% of infected people live in about 31 African countries including Ghana [3, 8]. Currently, there is no vaccine for the prevention of onchocerciasis but there are ongoing studies for possible vaccine candidates with promising results [3, 9]. Over the decades, various control programmes have been implemented to reduce the transmission of onchocerciasis infections. The implementations of the strategies of the WHO's Onchocerciasis Control Program – OCP (1974–2002) and the Africa Programme for Onchocerciasis Control – APOC (1995–2015), have resulted in considerable reduction in disease burden [10]. Strategies included vector control interventions in West Africa targeting potential breeding sites of the blackflies through mass spraying with insecticides, together with mass drug administration (MDA) [3, 8].

The strategic plans of the WHO has earmarked onchocerciasis for elimination by 2025 [11]. As part of the efforts to bring the infection under control and possible elimination, MDA since 1987 has played pivotal roles since its implementation in endemic countries. To interrupt transmission, WHO recommends directly observed treatment coverage of ≥ 80% with 200μg/kg ivermectin (IVM) annually or biannually for 10–15 years— and ivermectin has demonstrated to be an effective microfilaricidal drug over the years which reduces the development of skin and ocular diseases that results from the impact of the infection [3, 12].

In spite of IVM's ability to kill efficiently MF in the skin, it has very little effect on the survival and longevity of the adult worm but in turn reduces fecundity [13–14]. The effectiveness of MDA programme in disease interruption depends much on the compliance level of the people in taking the recommended drugs. A study by Arndts *et al.* indicated that compliance to MDA in the Upper and Lower Denkyira districts in Ghana has not been effective and that many (> 50%) had not/had infrequently taken part in the MDA [15], although the MDA since 2001 has been implemented in those districts. More so, sub-optimal efficacy of IVM and/or IVM resistance in humans has been reported in onchocerciasis patients in Ghana where despite multiple treatments with IVM, microfilaridermia persisted [16–18]. This, in addition to many other factors may contribute to the persistence of the onchocerciasis infection.

A recent review on onchocerciasis control in Ghana (1974–2016) by Biritwum *et al.*, showed that there has been a significant decrease in the prevalence of the infection from 69.13% in 1975 to 0.72% in 2015 [10]. Similarly, the mean community MF load (CMFL) had decreased from 14.48 MF/skin snip in 1975 to 0.07 MF/skin snip in 2015. Again, the therapeutic coverage had increased from 58.5–83.8% – with nearly 100 million IVM tablets distributed between 1997 and 2016. The review also revealed that the nodule and MF prevalence in the Western Region as at 2008 was 2.89% and 3.57% respectively [10].

However, data on the current prevalence of onchocerciasis in the Western North region (formerly part of Western region) since the inception of MDA to fight against the infection is scanty, obsolete and not robust. Also, there has not been any reported data on the prevalence of onchocerciasis in the Sefwi Akontombra district (formerly under the Sefwi Wiawso district) since its creation and subsequently an evaluation of the impact of MDA in eliminating the infection from the district. Annual MDA is reported to have begun in the district in the year 1994 and biannual treatment since 2018 as indicated by the disease control office. Considering that there has been almost three decades of IVM administration, it would be expected that the district achieves an interruption of disease transmission. Hypothetically, reduction in the number of infections is much dependent on continuous administration of IVM but this was curtailed in the advent of the COVID-19 pandemic. The WHO on 1st April, 2020 recommended for the postponement of MDA due to an ongoing COVID-19 pandemic [19]. Upon this new development, MDA was not carried out in Ghana in that year (2020) and this may to some extent affect the interruption of infection. Therefore, our study sought to investigate the current microfilaridermia and nodule prevalence of onchocerciasis in the Sefwi Akontombra district in the Western North Region of Ghana. The study also purposed to determine reasons for the persistence of the infection in the study district.

Methods

Ethics statement and approvals

This study was approved by the Committee on Human Research, Publication and Ethics (CHRPE) of the School of Medicine and Dentistry of the Kwame Nkrumah University of Science and Technology, KNUST, Kumasi, Ghana. Community leaders were consulted at the beginning of the study for their support and permission, and written approval was sought from the Western North Regional and the Sefwi Akontombra District Health Directorates. Written informed consent was voluntarily sought from all participants either by thumbprinting or signing before being enrolled in the study. Assents were completed for participants who were under 18 years (minors), with parents/legal guardians giving formal written consent for such volunteers/participants. The study was undertaken according to the principles and guidelines of the Helsinki Declaration of 1964, most recently amended in October 2013. This study is part of a larger ongoing trial: “Alternative treatment strategies using anti-Wolbachial drugs to accelerate elimination of Lymphatic Filariasis and Onchocerciasis (ASTAWOL) – sponsored by the European and Developing Countries Clinical Trial Partnership (EDCTP 2). The ethical approval number/code for the study is CHRPE/AP/337/20.

Study area/setting, site and population

The study was carried out in the Sefwi Akontombra district in the Western North Region (a newly created Region carved out of the then Western Region) of Ghana. Ghana on 27th December, 2018 held a referendum

which led to the creation of 6 more regions in addition to the 10 that already existed. This in consequence led to the creation of the Western North Region out of the Western Region [20]. The Sefwi Akontombra district lies in the North-Eastern part of the Western Region between Latitude 6^0 N and 6^0 30' N and Longitudes 2^0 45' W and 2^0 15' W. The district covers 3% of the Western Region land area (1,120 sq.km). It records high temperatures between 25^0C and 30^0C and falls within the tropical rainforest climatic zone. It is characterized by moderate to heavy rainfall between 1,524 mm and 1,780 mm per annum with heavy downpour in June-July and peaks in September-October. It is cut through by the Tano River together with other major tributaries like the Suhien, Kunuma, Sui and the Yoyo. The district in 2021 Ghana Population and Housing Census (PHC) had a population size of 70, 225. The population is mainly rural in nature with just an urban population of 8.8%. Agriculture plays a key role in the district's economy through the production of food crops along the Tano river body, palm trees and cocoa as the main cash crop. The district has a young population with just 4.1% of the population being adults of 60 years and above [21].

Study design and recruitment

The study employed a population-based cross-sectional study design with random community sampling technique which took place from November 2020 – April 2021. The district during the time of recruitment had administered ivermectin treatment for the interruption of infection transmission for about three decades since MDA began in the district. Prior to the recruitment, information was sent to the participating communities through information centers and also by the community health volunteers (CHV). A formal meeting was later held with community leaders and interested community members to explain the details of the study to them and questions appropriately addressed in both English, Twi and Sefwi (local language used by the people) languages as preferred by the participants. On the day of recruitment, informed consent was administered to those who were interested and willing to participate in the study. This was done in their local languages (Sefwi and Twi), as well as in English. Willing participants were asked to sign or thumbprint an informed consent form. Any individual ≥ 18 years who had stayed in the endemic community for ≥ 2 years and is mentally sound and could give consent (for adults) or consent on behalf of their wards (minors; <18 years) as parents or legal guardians— was deemed fit for inclusion. The exclusion criteria included any individual < 5 years who had stayed in the endemic community for < 2 years, not mentally sound and not ready to give consent.

A total of 2,019 participants from 25 communities in three sub-districts (Asantekrom, Kramokrom and Nsawora) all under the Sefwi Akontombra district were consented and enrolled into the study. An approved short-structured interview forms were used to collect demographics such as sex, age, number of rounds of IVM intake and number of years lived in the endemic area. This was assessed through participant interviewing, with interviews structured according to a predefined questionnaire which was administered by the investigators (research team) at a place far from the gathering, with participants assured of data safety and confidentiality of their responses [22]. To prevent MDA intake/treatment rounds recall bias, responses from participants were re-checked/cross-checked from the treatment records with the community health volunteers in the communities who have the MDA records for every household. This was done before the numbers were used in any analyses [22]. Individuals enrolled were given unique personal identification numbers for data collection, processing and laboratory results. Participants were then palpated and those with ≥ 1 palpable sub-cutaneous nodule had skin biopsies taken (snipped) from the left and right iliac crests for later parasitological assessment.

Palpation for Onchocercomata

Participants were physically examined and palpated by trained and experienced research scientists following standard procedures for the presence of onchocerciasis nodules (onchocercomata/sub-cutaneous nodules). The presence, size, number and site of onchocercomata identified were documented on a well-structured case report form. Nodules vary in size and the distinguishable features from other non-onchocerciasis nodules are that they are usually firm to touch, often flattened, bean-shaped, movable and non-tender. The presence of nodules likely suggests the existence of adult worms of *O. volvulus* [23]. Such participants were snipped for MF assessment.

Parasitological assessment (skin snipping and microscopy)

Skin snips (biopsies) were taken from the left and right superior iliac crests from only nodule positive individuals using Holth corneoscleral punch. For every individual, two (2) bloodless snips (left and right) of 1–3 mg skin were taken to determine microfilarial loads after both sides of the iliac crest of each person were disinfected with cotton wool soaked in 70% ethanol. Briefly, the skin biopsies were immersed and incubated in 100 µL of 0.9% physiological saline (sodium chloride) in a 24-well microtiter plate overnight for the emergence of MF from the skin. These were examined with inverted microscope by two independent experienced microscopists and the number of MF from both left and right snips counted. The 2 biopsies were then measured with an electronic mass balance and the arithmetic mean densities (load) of MF per mg of skin (left and right) for every individual determined. The wounds from the sites where the skin biopsies were taken were covered with a phlebotomy spot plaster to help avoid infection. Participants were advised to keep the area clean until the wound had healed [17–18].

Physical examinations for dermal Onchocerciasis

The study participants were further examined for signs of dermal/skin onchocerciasis and the results of these assessments were recorded in case report forms designed for the prevalence assessment. Dermal onchocerciasis, defined as any of the common skin manifestations of onchocerciasis such as lymphadenopathy, hanging groin, acute/chronic papular onchodermatitis, lichenified onchodermatitis, atrophic skin, depigmentation (leopard skin) and sowda (severe itching and skin darkening often confined to one limb) [24–25] were assessed during participant recruitment and findings recorded.

Parasitological indices/ Analysis plan

Nodule and MF prevalence assessment expressed as percentages were used to determine the degree of endemicity of onchocerciasis. Data for each community was expressed as the geometric mean intensities using antilogarithm of $[(\Sigma \log(x + 1))/n]-1$, where 'x' is the arithmetic mean of MF/mg of skin and 'n' being the number of participants assessed [26]. Community Microfilarial Load (CMFL) for individuals aged 20 years and older were also calculated as microfilariae per skin snip (MF/ss) (including MF counts of zero) using the adjusted geometric mean as the reference index of the intensity of infection [27–28].

Statistical analysis

Pearson Chi-square analysis was used to test for the association between demographic factors and infection status (nodule and MF). Independence of data were analyzed using bivariate and multivariate logistic

regression models (Crude and Adjusted odds ratio) to identify risk factors significantly associated with nodule and MF prevalence at a confidence level of 95%. Differences between independent continuous variables were assessed with the Mann-Whitney U test. Statistical significance was considered at p-value < 0.05. Data were captured using Microsoft Excel 2019. All analyses were done using SPSS version 25 and GraphPad Prism 9 for graphing data. All reported prevalence are estimates based on the voluntary participation in the study and not an epidemiological pre-defined sample size.

Results

Demographic distribution

A total of 2019 participants were examined from 25 study communities in the Sefwi Akontombra district of Ghana. However, 1980 participants were used in the analysis due to incomplete data from 39 participants. The 1980 participants had a mean age of 38.7 (± 13.4) years, with more than half (999, 50.5%) being females with majority in the age bracket of 34–44 years [Table 1]. The participants had lived in the study district for an average of 24.5 (± 12.9) years [Table 1].

Table 1
Distribution of age and gender among study participants in the Sefwi Akontombra district.

Variable	**Mean**	**Standard Deviation (± SD)**	
Age (years)	38.7	13.4	
Years lived in endemic area	24.5	12.9	
Age Groups	Gender		
	Male, *N* (%)	Female, *N* (%)	Total, *N* (%)
12–22	137 (45.2)	166 (54.8)	303 (100)
23–33	178 (45.1)	217 (54.9)	395 (100)
34–44	280 (48.0)	303 (52.0)	583 (100)
45–55	290 (55.1)	236 (44.9)	526 (100)
≥ 56	96 (55.5)	77 (44.5)	173 (100)
Total	**981 (49.5)**	**999 (50.5)**	**1980 (100)**
N; number of cases examined			

Distribution of nodules and MF among study participants

The overall palpable nodule prevalence from the study district was 35.4% (N = 701), out of which 31.5% (N = 221) were MF positive. However, the overall estimated MF prevalence among the recruited study participants was 11.2% (221/1980). More males, 447 (45.6%) had *Onchocerca* sub-cutaneous nodules as compared to females; 254 (25.4%). This observation was also the same for MF prevalence in the study district (35.1% vs 25.2%) [Table 2].

Regarding the distribution of nodule status among age groups of participants, nodule prevalence was least among the 12—22-year age group (17.2%) and was significantly associated with the participants' age ($p < 0.001$). Notably, the highest MF prevalence was recorded among the 12–22-year age group (46.2%), with MF positivity significantly associated with age ($p = 0.015$) [Table 2]. Nodule positive participants were older as compared to the nodule negative participants ($p < 0.001$); however, the reverse was observed regarding MF status ($p < 0.001$) [Fig. 1].

Nodule and MF positivity were highest in males and in the age groups of 45–55 and 12 -22-years respectively [Fig. 2]. More than half of the participants (53.6%, N = 1062) had lived in the endemic area for ≥ 20, out of which 419 (39.5%) were nodule positive, with 126 (30.1%) being microfilaridermic [Table 2]. Significant association was found between number of years participants had lived in the endemic area and the acquisition of *Onchocerca* nodules ($p < 0.001$). However, this was not the case for MF positivity ($p = 0.312$) [Table 2]. Averagely, MF was more prevalent among participants with more nodulesand this differed significantly from the MF negative group ($p < 0.001$). [Fig. 3].

Table 2
Demographic characteristics of nodule and microfilarial status of the study participants in Sefwi Akontombra district.

Variable	*Category*	*Cases (%)*	*Nodule Status*			*Microfilaria (MF) Status*		
			Positive (%)	Negative (%)	p-value	Positive (%)	Negative (%)	p-value
Gender[a]	Male	981 (49.5)	447 (45.6)	534 (54.4)	< 0.001	157 (35.1)	290 (64.9)	0.007
	Female	999 (50.5)	254 (25.4)	745 (74.6)		64 (25.2)	190 (74.8)	
Age (years)[a]	12–22	303 (15.3)	52 (17.2)	251 (82.8)	< 0.001	24 (46.2)	28 (53.8)	0.015
	23–33	395 (19.9)	113 (28.6)	282 (71.4)		43 (38.1)	70 (61.9)	
	34–44	583 (29.4)	220 (37.7)	363 (62.3)		72 (32.7)	148 (67.3)	
	45–55	526 (26.6)	241 (45.8)	285 (54.2)		61 (25.3)	180 (74.7)	
	≥ 56	173 (8.7)	75 (43.4)	98 (56.6)		21 (28.0)	54 (72.0)	
Years lived[a] in endemic area	20 yrs.	918 (46.4)	282 (30.7)	636 (69.3)	< 0.001	95 (33.7)	187 (66.3)	0.312
	≥ 20 yrs.	1,062 (53.6)	419 (39.5)	643 (60.5)		126 (30.1)	293 (69.9)	
Total		**1980 (100)**	**701 (35.4)**	**1279 (64.6)**		**221 (31.5*)**	**480 (68.5)**	

[a] Pearson Chi-square test; *, Onchocerciasis prevalence based on only nodule positive participants

Palpable *Onchocerca* nodules were present among participants from all communities surveyed [Table 3]. Kwaku-Ofori (83.3%) and Nyamebekyere (50.0%) communities recorded the highest nodule and MF prevalences respectively. Measurement of community onchocerciasis endemicity based on MF prevalence revealed that fourteen (14) communities were hypo- (< 35%), with eleven (11) being mesoendemic (35% – 60%) for onchocerciasis. Findings from the current study showed that the study district, Sefwi Akontombra is hypoendemic for the onchocerciasis disease, and also had a geometric mean (GM) intensity of 0.26 MF/ss. Adawu (0.77 MF/ss) and Bopa-Nkwanta (0.02 MF/ss) communities recorded the highest and least GM/CMFL respectively. The district's CMFL was shown to be 0.25 MF/ss [Table 3].

Most of the participating communities (16) had a median IVM round of four as reported by the participants, with two (2) others having just five rounds as the maximum partaken MDA treatment by participants [Table 3]. With regards to community-based IVM compliance; two communities, Kwaku-Ofori and Mampong had all participants (100%) taking IVM ≥ 1 in the past. However, Bopa-Nkwanta had the least (75.0%) compliance to MDA among the study communities [Table 3].

Table 3
Community prevalence and Onchocerciasis status in the Sefwi Akontombra district.

Community	Cases	Nodule Positive N (%)	MF Positive N (%)	GM intensity MF/ss	CMFL MF/ss	IVM intake N (%)	Rounds of MDA, Median (Min-Max)
Adawu*	37	15 (40.5)	7 (46.7)	0.77	0.77	33 (89.2)	3 (0–4)
Amanfokrom*	51	17 (33.3)	8 (47.1)	0.39	0.39	39 (76.5)	3 (0–5)
Aprogya+	57	14 (25.6)	2 (14.3)	0.05	0.05	55 (96.5)	3 (0–5)
Asamoakrom+	34	14 (41.2)	3 (21.4)	0.07	0.06	27 (79.4)	4 (3–7)
Asamoano+	71	20 (28.2)	3 (15.0)	0.12	0.13	68 (95.8)	4 (2–7)
Asantekrom+	196	44 (22.4)	14 (31.8)	0.26	0.24	190 (96.9)	4 (1–7)
Asiekrom+	102	18 (17.6)	3 (16.7)	0.10	0.10	96 (94.1)	4 (0–8)
Bopa+	112	52 (46.4)	10 (19.2)	0.17	0.17	108 (96.4)	4 (1–8)
Bopa-Nkwanta+	36	10 (27.8)	2 (20.0)	0.02	0.02	27 (75.0)	3 (0–5)
Congo-Kusikrom*	107	43 (40.2)	21 (48.8)	0.48	0.41	99 (92.5)	3 (1–6)
Kofikrom+	108	37 (34.3)	9 (24.3)	0.08	0.08	106 (98.1)	4 (1–6)
Kojobikrom*	98	41 (41.8)	18 (43.9)	0.40	0.40	95 (96.9)	3 (0–8)
Kwaku-Ofori*	12	10 (83.3)	4 (40.0)	0.26	0.26	12 (100.0)	4 (1–5)
Mafiedu*	62	28 (45.2)	11 (39.3)	0.32	0.32	57 (91.9)	4 (1–8)
Mampong+	94	24 (25.5)	3 (12.5)	0.07	0.07	94 (100.0)	4 (1–6)
Manukrom*	99	44 (44.4)	17 (38.6)	0.28	0.28	95 (96.0)	4 (1–8)
Mensakrom*	57	23 (40.4)	8 (34.8)	0.17	0.10	54 (94.7)	3 (0–6)

Community	Cases	Nodule Positive N (%)	MF Positive N (%)	GM intensity MF/ss	CMFL MF/ss	IVM intake N (%)	Rounds of MDA, Median (Min-Max)
Ntom+	87	23 (26.4)	5 (21.7)	0.11	0.04	76 (87.4)	5 (1–10)
Nyamebekyere*	26	18 (69.2)	9 (50.0)	0.47	0.47	23 (88.5)	4 (2–6)
Nyamendae+	70	42 (60.0)	10 (23.8)	0.28	0.28	63 (90.0)	4 (0–8)
Obengkrom*	136	41 (30.1)	19 (46.3)	0.47	0.49	127 (93.4)	4 (1–10)
Oppongkrom*	53	22 (41.5)	9 (40.9)	0.25	0.25	50 (94.3)	4 (0–6)
Shed+	82	27 (32.9)	7 (25.9)	0.27	0.17	80 (97.6)	5 (1–8)
Sunkwa+	31	15 (48.4)	4 (26.7)	0.26	0.26	27 (87.0)	4 (1–5)
Wuruwuru+	162	59 (36.4)	15 (25.4)	0.22	0.23	155 (95.7)	4 (1–7)
Total	**1980**	**701 (35.4)**	**221 (31.5)**	**0.26**	**0.25**	**1856 (93.7)**	**5 (0–10)**

*, Mesoendemic communities; +, Hypoendemic communities; N, number of participants examined; MF, Microfilaria; GM, Geometric mean; CMFL, Community microfilarial load; IVM, Ivermectin; MDA, Mass Drug Administration; MF/ss, Microfilaria per skin snip

Distribution of dermal Onchocerciasis among study participants

From the 1,980 study participants examined, only 17 (0.9%) who were all microfilaridermic exhibited some forms of dermal/skin manifestations of onchocerciasis. Of the 17 participants, seven (41.2%) had developed acute papular onchodermatitis, whiles five each (29.4%) had atrophic skin and sowda. None of the 17 participants exhibited two or more conditions of the dermal onchocerciasis. Assessment of visual impairment/ocular defects due to onchocerciasis was not done.

Compliance to Ivermectin (IVM) treatment

All study communities reported having MDA with IVM implemented and being carried out in their communities. The participants reported receiving the yearly IVM treatment through the Community Health Volunteers (CHVs) for ≥ 20 rounds. The overall compliance level of the Sefwi Akontombra district regarding treatment with IVM in response to MDA intervention was 93.7% (N = 1856), with individuals having taken IVM for at least once. An average IVM treatment round distribution of 5 (0–10) was recorded, with compliance among gender showing that both males and females equally adhered to MDA (50.0%). Further to this, 7.1% (N = 71) of females and

5.4% (N = 53) of males had never taken IVM in the past, 81.0% (N = 809) and 80.6% (N = 791) of all females and males respectively had taken it at least once (1–5) and 11.9% (N = 119) of females and 14.0% (N = 137) of males had taken > 5 rounds. Nevertheless, there was no significant association between gender and IVM compliance nor the number of rounds taken ($p = 0.118$ and 0.141 respectively). The 45–55 and ≥ 56-year age groups were the most compliant (98.3%), with compliance rate being significantly associated with age ($p < 0.001$). Individuals who had lived in the endemic communities for ≥ 20 years showed a greater degree of MDA compliance, with 97.5% (N = 1035) having taken MDA ≥ 1 and 81.4% (N = 864) participating in 1–5 treatment rounds [Table 4]. Though majority (93.7%) of the participants had taken IVM ≥ 1, only 12.9% had taken > 5 rounds albeit having stayed in the filarial endemic area for an average of 24.5 (± 12.9) years. Thus, as the treatment rounds increased, participation in the MDA program reduced.

The study also revealed that 6.3% (N = 124) of the participants had never taken part in MDA for a number of reasons [Table 4]. Leading reasons for non-adherence bordered on fear of adverse events and the misconception of the drug being meant for sick people. Others expressed reasons due to pregnancies, being absent during MDAs, refusal to take the drugs and not being in good health [Fig. 4].

Table 4
Compliance of participants to Ivermectin treatment in Sefwi Akontombra district.

Variable	*Category*	*Cases (%)*	*IVM intake (MDA)*			*Number of IVM rounds taken (MDa)*			
			Compliance	**Non-compliance**	**p-value**	**0**	**1–5**	**> 5**	**p-value**
Gender[a]	Male	981 (49.5)	928 (94.6)	53 (5.4)	0.118	53 (5.4)	791 (80.6)	137 (14.0)	0.141
	Female	999 (50.5)	928 (92.9)	71 (7.1)		71 (7.1)	809 (81.0)	119 (11.9)	
Age[a]	12–22	303 (15.3)	267 (88.1)	36 (11.9)	< 0.001	36 (11.9)	265 (87.5)	2 (0.7)	< 0.001
	23–33	395 (19.9)	349 (88.4)	46 (11.6)		46 (11.6)	340 (86.1)	9 (2.3)	
	34–44	583 (29.4)	553 (94.9)	30 (5.1)		30 (5.1)	487 (83.5)	66 (11.3)	
	45–55	526 (26.6)	517 (98.3)	9 (1.7)		9 (1.7)	412 (78.3)	105 (20.0)	
	≥ 56	173 (8.7)	170 (98.3)	3 (1.7)		3 (1.7)	96 (55.5)	74 (42.8)	
Years lived[a] in endemic area	20 yrs.	918 (46.4)	821 (89.4)	97 (10.6)	0.001	97 (10.6)	736 (80.2)	85 (9.3)	< 0.001
	≥ 20 yrs.	1,062 (53.6)	1035 (97.5)	27 (2.5)		27 (2.5)	864 (81.4)	171 (16.1)	
Total		**1980 (100)**	**1856 (93.7)**	**124 (6.3)**		**124 (6.3)**	**1600 (80.8)**	**256 (12.9)**	

[a] Pearson Chi-square test; MDA, Mass Drug Administration; IVM, Ivermectin

Bivariate modeling analyses for Onchocerciasis infection in Sefwi Akontombra district

Binary logistic regression analyses (modelling) were done for gender, age, years lived in endemic area, IVM intake (compliance) and number of rounds of IVM intake to determine the variables fit to be included in the multivariate model which independently predicts the chances of an individual being infected with *Onchocerca volvulus*. From the bivariate model, all variables included showed statistically significant associations ($p < 0.05$) with *Onchocerca* nodules [Table 5]. Except for years lived in endemic area ($p = 0.312$), all other variables in the bivariate modelling were also significantly associated with onchocerciasis MF infection ($p < 0.05$) [Table 6].

Multivariate modelling analyses of independent predictors of onchocerciasis infection in the Sefwi Akontombra district

Variables that were significantly associated with *Onchocerca* nodules and MF infection in the bivariate analysis were entered into the multivariate model to determine factors that exclusively and independently predicted the odds of an individual developing onchocerciasis infection. From the model, gender, age and IVM intake (MDA) stood out as independent predictors for the infection with the latter being significantly predictive of only MF infection (p = 0.013). A male individual was twice more likely to develop *Onchocerca* nodules as compared to a female [AOR = 2.388, CI = 1.967–2.898] and this was also the case for MF infection among participants [AOR = 1.620, CI = 1.144–2.295] [Tables 5 and 6]. Also, an adult in the 45–55-year age group had nearly four times increased odds of harbouring *Onchocerca* nodules referenced to individuals in the 12–22-year age group [AOR = 3.758, CI = 2.583–5.467] but this was not the case for MF infection [AOR = 0.446, CI = 0.236–0.836] [Tables 5 and 6]. Regarding IVM intake, individuals who were non-compliant to MDA were almost three times more likely to develop onchocerciasis infection compared to those in the compliant group [AOR = 2.938, CI = 1.259–6.856] [Table 6].

Table 5
Analyses of independent predictors associated with *Onchocerca* nodules in the Sefwi Akontombra district.

Variable	*Category*	*Cases (%)*	*Nodule Status*		COR [95% CI]	p-value	AOR [95% CI]	p-value
			Positive (%)	Negative (%)				
Gender	Male	981 (49.5)	447 (45.6)	534 (54.4)	2.455 [2.031–2.969]	< 0.001*	2.388 [1.967–2.898]	< 0.001*
	Female	999 (50.5)	254 (25.4)	745 (74.6)	1.000		1.000	
Age (years)	12–22	303 (15.3)	52 (17.2)	251 (82.8)	1.000		1.000	
	23–33	395 (19.9)	113 (28.6)	282 (71.4)	1.934 [1.226-2.800]	< 0.001*	1.961 [1.340–2.869]	0.001*
	34–44	583 (29.4)	220 (37.7)	363 (62.3)	2.925 [2.0771-4.120]	< 0.001*	2.874 [2.000-4.131]	< 0.001*
	45–55	526 (26.6)	241 (45.8)	285 (54.2)	4.082 [2.893–5.760]	< 0.001*	3.758 [2.583–5.467]	< 0.001*
	≥ 56	173 (8.7)	75 (43.4)	98 (56.6)	3.694 [2.418–5.644]	< 0.001*	3.258 [2.032–5.224]	< 0.001*
Years lived in endemic area	20 yrs.	918 (46.4)	282 (30.7)	636 (69.3)	1.000		1.000	
	≥ 20 yrs.	1,062 (53.6)	419 (39.5)	643 (60.5)	1.470 [1.220–1.771]	< 0.001*	1.023 [0.828–1.263]	0.835
IVM intake (MDA)	Compliance	1856 (93.7)	668 (36.0)	1188 (64.0)	1.000		1.000	
	Non-Compliance	124 (6.3)	33 (26.6)	91 (73.4)	0.645 [0.428–0.971]	0.036*	0.802 [0.483–1.332]	0.393
Number of rounds of IVM intake (MDa*)*	0	124 (6.3)	33 (26.6)	91 (73.4)	1.000		1.000	
	1–5	1600 (80.8)	553 (34.6)	1047 (65.4)	1.456 [0.965–2.198]	0.073	0.865 [0.647–1.156]	0.328
	> 5	256 (12.9)	115 (44.9)	141 (55.1)	2.249 [1.408–3.592]	0.001*	-	-

Variable	*Category*	*Cases (%)*	*Nodule Status*		COR [95% CI]	p-value	AOR [95% CI]	p-value
			Positive (%)	Negative (%)				

*, Statistically significant p-values ($p < 0.05$); COR, Crude Odds Ratio; AOR, Adjusted Odds Ratio; CI, Confidence interval

Table 6
Analyses of independent predictors associated with onchocerciasis microfilaria in the Sefwi Akontombra district.

Variable	*Category*	*Cases (%)*	*Microfilaria (MF) Status*					
			Positive (%)	Negative (%)	COR [95% CI]	p-value	AOR [95% CI]	p-value
Gender	Male	447 (63.8)	157 (35.1)	290 (64.9)	1.607 [1.140–2.266]	0.007*	1.620 [1.144–2.295]	0.007*
	Female	254 (36.2)	64 (25.2)	190 (74.8)	1.000		1.000	
Age (years)	12–22	52 (7.4)	24 (46.2)	28 (53.8)	1.00		1.000	
	23–33	113 (16.1)	43 (38.1)	70 (61.9)	0.717 [0.369–1.393]	0.326	0.731 [0.372–1.434]	0.362
	34–44	220 (31.4)	72 (32.7)	148 (67.3)	0.568 [0.307–1.048]	0.070	0.615 [0.329–1.149]	0.127
	45–55	241 (34.4)	61 (25.3)	180 (74.7)	0.395 [0.213–0.733]	0.003*	0.446 [0.236–0.836]	0.012*
	≥ 56	75 (10.7)	21 (28.0)	54 (72.0)	0.454 [0.216–0.953]	0.037*	0.578 [0.266–1.258]	0.167
Years lived in endemic area	20 yrs.	282 (40.2)	95 (43.7)	187 (66.3)	1.000		-	-
	≥ 20 yrs.	419 (59.8)	126 (30.1)	293 (69.9)	0.846 [0.613–1.170]	0.312	-	-
IVM intake (MDA)	Compliance	668 (95.3)	204 (30.5)	464 (69.5)	1.000		1.000	
	Non-Compliance	33 (4.7)	17 (51.5)	16 (48.5)	2.417 [1.197–4.878]	0.014*	2.938 [1.259–6.856]	0.013*
Number of rounds of IVM intake (MDa*)*	0	33 (4.7)	17 (51.5)	16 (48.5)	1.000		1.000	
	1–5	553 (78.9)	178 (32.2)	375 (67.8)	0.447 [0.221–0.905]	0.025*	1.523 [0.928–2.499]	0.096
	> 5	115 (16.4)	26 (22.6)	89 (77.4)	0.275 [0.122–0.618]	0.002*	-	-

Variable	*Category*	*Cases (%)*	*Microfilaria (MF) Status*					
			Positive (%)	Negative (%)	COR [95% CI]	p-value	AOR [95% CI]	p-value
*, Statistically significant p-values (p < 0.05); COR, Crude Odds Ratio; AOR, Adjusted Odds Ratio; CI, Confidence interval								

Discussion

Despite more than 40 years of concerted control efforts leading to significant reduction in onchocerciasis MF prevalence, the disease which has potentially severe impacts on the eyes and skin still remains endemic in some districts in Ghana as reported recently by Biritwum *et al.*, [10]. This present study is the first in determining the impact of MDA on the prevalence of onchocerciasis and its associated clinical manifestations in Sefwi Akontombra, a mesoendemic district in Ghana. Thus, the findings are important and can be used as a proxy regarding the directives of the Ghana onchocerciasis control programme (GOCP) towards the district, other surrounding districts with similar characteristics which are also endemic for the infection and the Western North Region at large.

In 2008, nodule and MF prevalence in the Western Region was estimated to be 2.89% and 3.57% respectively [10]. Findings from our current study in the Sefwi Akontombra district revealed an *Onchocerca* nodule prevalence of 35.4%. Out of this, 31.5% were MF positive— with an overall estimated MF prevalence among the total recruited study participants being 11.2%. This prevalence exceeded the WHO recommended < 1% threshold for MF and classifies the district as hypoendemic (MF prevalence < 35%) for the onchocerciasis infection [7]. However, 11 (44.0%) communities in the district were mesoendemic (MF prevalence 35% – 60%) for the infection. It is worth noting that the Sefwi Wiawso district (formerly in the Western Region and incorporated the Sefwi Akontombra district) was mesoendemic for onchocerciasis in 1980 before MDA with IVM begun [10]. Thus, the current hypoendemicity status of the district may be due to the impact of the continual MDA with IVM, supporting the frequently reported effectiveness of IVM as a potent microfilaricide [3]. Consequently, this observation suggests a general downward change in the state of the disease, although the current MF and nodule prevalence still remains high after many years of preventive chemotherapy with IVM. This seemingly high prevalence might be due to the one year break in MDA with IVM due to the COVID-19 outbreak [19].

Gender was found to be associated with harbouring of *Onchocerca* sub-cutaneous nodules and MF, with males being about two times more prone to the infection as compared to females. This may be due to the fact that the men are primarily farmers and they usually farm along the banks of the Tano River which also serves as breeding sites for the *Onchocerca*-infected *Simulium* flies. This in effect puts the men at higher risk of infective bites as compared to the women who are involved in food and cocoa cash crop merchandise and general trading [21]. More so, the differential exposure to bites of blackflies has also been shown to be dependent on the behaviour, occupation and clothing of different gender which vary from one culture to the other [29]. However, some other studies have found contrasting results as the prevalence of onchocerciasis in females in those areas were higher than the prevalence in males [30–31].

There has been a significant decrease in the prevalence of onchocerciasis infection in Ghana from 69.13% in 1975 to 0.72% in 2015, with mean community MF load (CMFL) decreasing from 14.48 MF/ss to 0.07 MF/ss in the same period [10]. The CMFL is the most important factor in the assessment of the endemicity of onchocerciasis [32]. Adawu, the most central community among the 25 surveyed communities in this study recorded the highest CMFL (0.77 MF/ss). This community due to its centrality remains the center of cocoa (the main cash crop) merchandise and commercial activities in the district. Thus, this finding (high CMFL) could be attributed to the fact that the community frequently received quite a number of inhabitants from the other areas and surrounding communities. The mean CMFL recorded in the district was 0.25 MF/ss which is higher than the 0.07 MF/ss reported by Biritwum et *al*., (2021) as the mean CMFL for Ghana as at 2015 [10]. This however can be regarded as acceptable, since onchocerciasis is considered a public-health problem only when the CMFL exceeds 5.0 MF/ss [33]. Nevertheless, considering that there has been almost three decades of continuous IVM administration, it would be expected that the CMFL will be reduced further than this. Reduction in the number of infections and subsequently the CMFL is much dependent on continuous administration of IVM but this was curtailed in the advent of the COVID-19 pandemic [19].

Our study found out that 6.3% of the 1980 participants had never taken part in MDA. This observation is lower compared to a study conducted in Nigeria in 2021 which reported a non-compliance rate of 35.4% [34] and may explain a possible increased awareness of the MDA program in Ghana. Our data also showed that IVM intake (MDA) was independently associated with MF status for onchocerciasis infection. Being non-compliant was nearly three times more likely to develop the infection as compared to being adherent. This explains the importance of the MDA program in interrupting the infection and therefore the need to ensure adherence among the eligible populations in affected communities. Participants who failed to comply to the MDA cited the fear of experiencing AEs (59.7%) due to IVM intake, and the drugs being meant for “sick” people (20.2%) as the main reasons for their failure to partake in the program. These responses were similar to that observed from a study carried out in the western region of Cameroon, but with the major reason for non-adherence being attributed to absence during the campaign [35]. Education, sensitization and awareness of the program should be strengthened to reduce the number of people who fail to comply as suggested in other studies [35–36]. This should stress on the importance of the program in breaking the cycle of the infection and the need for consistent participation in annual and biannual MDAs. In some cases, participants may have little to no knowledge regarding the effectiveness of IVM and in effect the importance of MDAs [35].

From the community MDA registers and according to the district disease control office, MDA compliance have been encouraging with an average of 85% of the participants claiming to have taken part in the MDA every year. This was consistent with our findings as the overall self-reported MDA compliance in the study district regarding IVM treatment was 93.7%. This is higher than the reported national MDA therapeutic coverage of 83.8% in 2016 [10]. These findings are also in agreement with a similar study conducted in Nigeria [34]. Looking at the high affirmative response of the participants to taking part in the annual/bi-annual MDA and the persistence of the infection in the district, a study on coverage and compliance needs to be done. This would ascertain the proportion of the participants who really consume the IVM tablets and those who do not (but still take the drug from the CHVs) as the high compliance may be mere MDA coverage and not necessarily consumption of the IVM tablets as reported elsewhere [37–38]. This was however not done in this study. Though majority (93.7%) of the participants had taken IVM ≥ 1, only 12.9% had participated in > 5 treatment rounds albeit having stayed in the filarial endemic area for an average of 24.5 (± 12.9) years. Thus, as the

treatment rounds increased, participation in the MDA program reduced. This observation is similar to that reported by Arndts *et al.* in a study which also sought to evaluate the impact of MDA on onchocerciasis levels in the Denkyira district of Ghana [15]. With ≥ 25 treatment rounds in the study communities, perennial non-compliance, treatment fatigue and apathy may have accounted for the lack of continual participation in the MDA program.

Despite the fact that IVM is a potent microfilaricidal drug, it has little to no adulticidal effect on the *O. volvulus* worm [3]. As established by Awadzi *et al.*, and in other studies, some people may show sub-optimal response to IVM treatment and may continue to produce viable MF [16]. This has translated into the persistence of microfilaridermia in some population, despite multiple treatments [16–18]. Thus, more effective drugs which are adulticidal in nature are needed to complement the actions of the existing microfilaricidal ones [39]. Doxycycline has emerged recently as a macrofilaricide due to its ability to deplete *Wolbachia* endosymbiont bacteria in both animal models and humans, eventually leading to the long-term sterility of the adult female *O. volvulus* filariae and ameliorating the clinical symptoms of the disease [39]. Logistics, duration of its administration (4–6 weeks), contraindications in children < 8 years, its usage on large scale basis [39] and the development of resistance to the antibiotic [40] are some of the challenges projected against the utilization of doxycycline as a macrofilaricide. Hence alternative drugs are needed. In this regard, all those who were found to be MF-positive were treated with 7–14 days of new anti-wolbachial drugs in a clinical trial funded by European and Developing Countries Clinical Trials Partnership (EDCTP 2). If proven efficacious against the adult worm, it will go a long way to reduce the prevalence of the disease in the district.

Acute papular onchodermatitis (41.2%) — an usual presentation in patients with MFs [24–25], was the most frequent dermal clinical symptom presented by the 17 participants with dermal onchocerciasis, followed by sowda and atrophic skin (29.4% each). A similar study in the middle belt of Ghana also found onchodermatitis as the most prevalent clinical manifestation [41]. Onchodermatitis and sowda are brought about by the intense pruritus generated by the inflammatory and antigenic reactions triggered by the migration of MFs under the skin, and this subsequently may lead to atrophic skin [5, 24–25]. In this present study, all the participants with dermal symptoms of onchocerciasis were microfilaridermic, positing a stronger link between microfilaridermia and dermal onchocerciasis. Averagely, the presence of MF was more prevalent among participants carrying more nodules and this differed significantly from the MF negative group ($p < 0.001$). This is consistent with the biology of the infection which elucidates that MF develops into adult filariae and resides in subcutaneous tissues as nodules. Thus, mostly the MF load in an individual is directly proportional to the nodule count [3, 39]. It must be mentioned that assessment of visual impairment/ocular defects due to onchocerciasis was not done in this study.

Again, age has been seen to play a role in the risk of the infection. From this study, age was significantly associated with onchocerciasis infection but patterns differed in MF and nodule status. The odds of developing *Onchocerca* nodules were about four times more likely for participants within the 45-55-year age group, compared to the 12-22-year group but this pattern was directly opposite to what was observed in MF status. Participants within this same age group (45–55 years) had almost a 50% reduced chance of having MF compared to 12-22-year group. These observations were not in agreement with a similar study done in Ethiopia which had as much as 10 times increased odds for the infection for people within ≥ 45 age group as compared to 15–24 years [42]. The MF prevalence in the 12—22-year age group was also the highest in our

study, contrary to other studies that observed lower levels in the younger population [42–43]. This may be attributed to the fact that adults in this setting are much more aware of the transmission cycle and therefore may likely protect themselves from the bites of the blackflies despite their regular outdoor activities. In addition, the study found a high IVM compliance rate together with the many years of IVM treatment which may also influence the low levels of MF in the older age groups as these formed the majority of our study population.

As the focus of the Ghana onchocerciasis control programme (GOCP) has changed from control to elimination [44], MDA has also been intensified in communities/districts with MF prevalence > 1%. GOCP and the National NTD Programme therefore, need to be recommended. Notwithstanding the above effort by the National NTD programme, there is an urgent need for research and development aimed at discovering new or repurposed anti-filarial agents which will augment ivermectin if global onchocerciasis eradication targets are to be achieved. Our ongoing trial "Alternative treatment strategies using anti-*Wolbachia* drugs to accelerate elimination of Lymphatic Filariasis and Onchocerciasis" will bring to light the possible utilization of macrofilaricides in a shorter duration in onchocerciasis elimination [45].

Conclusion

The study recorded *Onchocerca* nodule prevalence of 35.4% in the Sefwi Akontombra district, out of which 31.5% were MF positives albeit low MF burden, with CMFL and geometric mean intensity of 0.25 MF/ss and 0.26 MF/ss respectively. However, the overall estimated MF prevalence was 11.2%, making the district hypoendemic for the infection. The Covid pandemic and the one-year break in MDA prior to this study may account for the high MF prevalence. Age, IVM intake and gender were the independent predictive factors significantly associated with the onchocerciasis infection in the district. Though the district's CMFL was far below the 5.0 MF/ss stipulated public health problem threshold, the MF prevalence exceeded the WHO recommended < 1% threshold required for elimination. Adulticidal drugs should be explored to augment the microfilaricidal activities of IVM in eradicating the onchocerciasis infection.

List Of Abbreviations

MDA – Mass Drug Administration; **MF** – Microfilaria; **CMFL** – Community Microfilaria Load; **IVM** – Ivermectin; **APOC** – African Programme for Onchocerciasis Control; **OCP** – Onchocerciasis Control Programme; **WHO** – World Health Organization; **GOCP** - Ghana onchocerciasis control programme; **COVID-19** – Coronavirus Disease. **CHV** – Community Health Volunteers (CHV).

Declarations

Ethics approval and consent to participate

This study was approved by the Committee on Human Research, Publication and Ethics (CHRPE) of the School of Medicine and Dentistry of the Kwame Nkrumah University of Science and Technology, KNUST, Kumasi, Ghana. Community leaders were consulted at the beginning of the study for their support and permission, and written approval was sought from the Western North Regional and the Sefwi Akontombra District Health Directorates. Written informed consent was voluntarily sought from all participants either by thumbprinting or

signing before being enrolled in the study. Assents were completed for participants who were under 18 years (minors), with parents/legal guardians giving formal written consent for such volunteers/participants. The study was undertaken according to the principles and guidelines of the Helsinki Declaration of 1964, most recently amended in October 2013.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

Funding

This study is part of a larger ongoing trial: “Alternative treatment strategies using anti-Wolbachial drugs to accelerate elimination of Lymphatic Filariasis and Onchocerciasis” — funded by the European and Developing Countries Clinical Trial Partnership (EDCTP2) programme supported by the European Union (grant number TMA2018SF-2451-ASTAWOL) to AYD. The funder had no role in the study design, implementation, interpretation of data or publication of this work.

Author contributions

AYD, LBD and JOM conceived and designed the study. AYD acquired the funding for the study. DAM, EKK, JOM, JO, VSO, EDK, MAO and ARA carried out the field/recruitment surveys. DAM, MAO, EKK, EDK, JO, MA, VSO, ARA, PO, JB, CG, SA, JOM, LBD and AYD worked on the laboratory investigations. DAM, CG, JB and MA did the data curation and formal analysis. The project administration was overseen by AYD, LBD, JOM and DAM. AYD, LBD and JOM supervised and validated the study. The first and original manuscript draft preparation was done by DAM, JB and MA. Review and Editing of the manuscript draft were done by AYD, LBD, JOM and DAM. All authors read and approved the final manuscript.

Acknowledgements

We are sincerely grateful to the chiefs and the entire population in all the surveyed communities for their permission and voluntary participation in this study. The authors are thankful to the Ghana Health Service and the Sefwi Akontombra District Health Directorate and all Community Health Volunteers (CHVs) for their support and all the facilities put in place during the surveys. Our greatest appreciation goes to the staff and students on the Filariasis project at the Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Kumasi.

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Figures

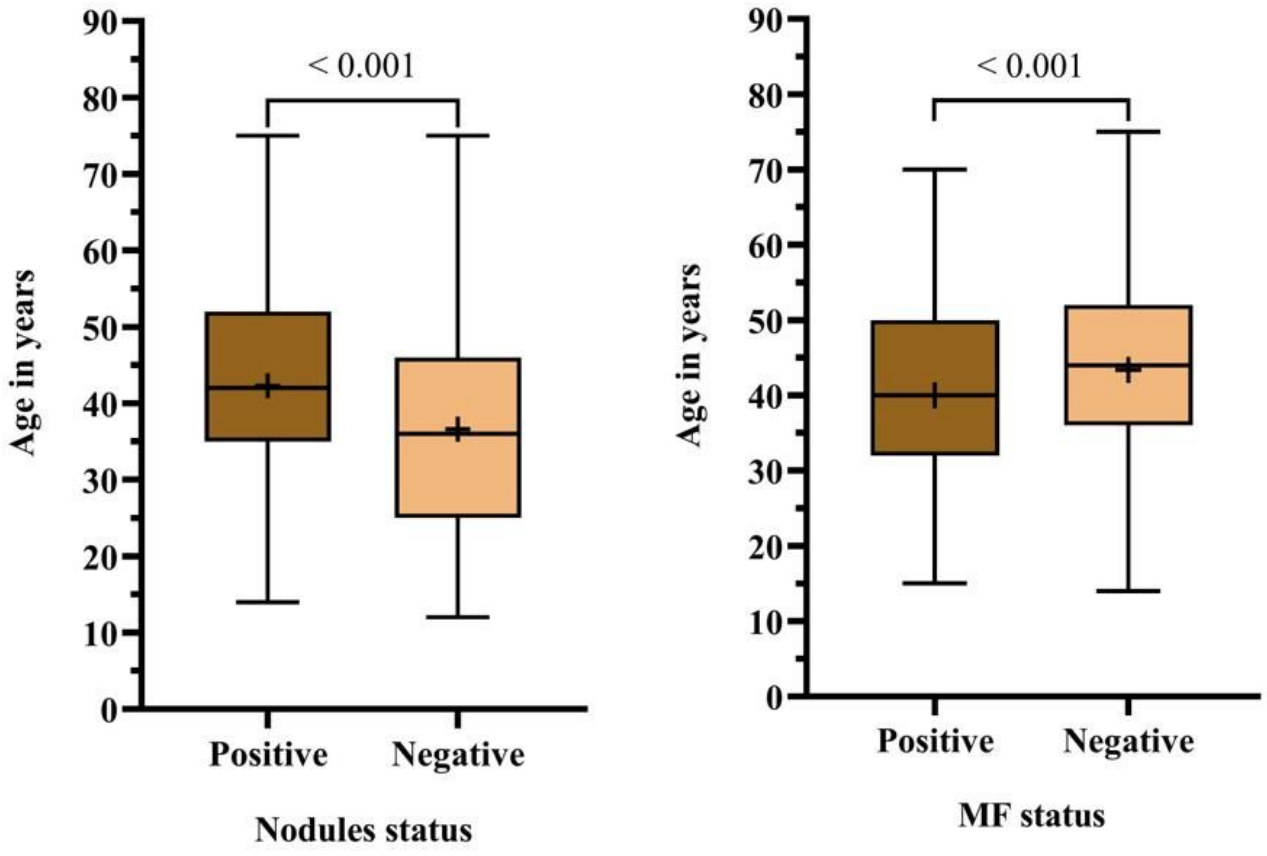

Figure 1

Age distribution among *Onchocerca* nodules and MF status.

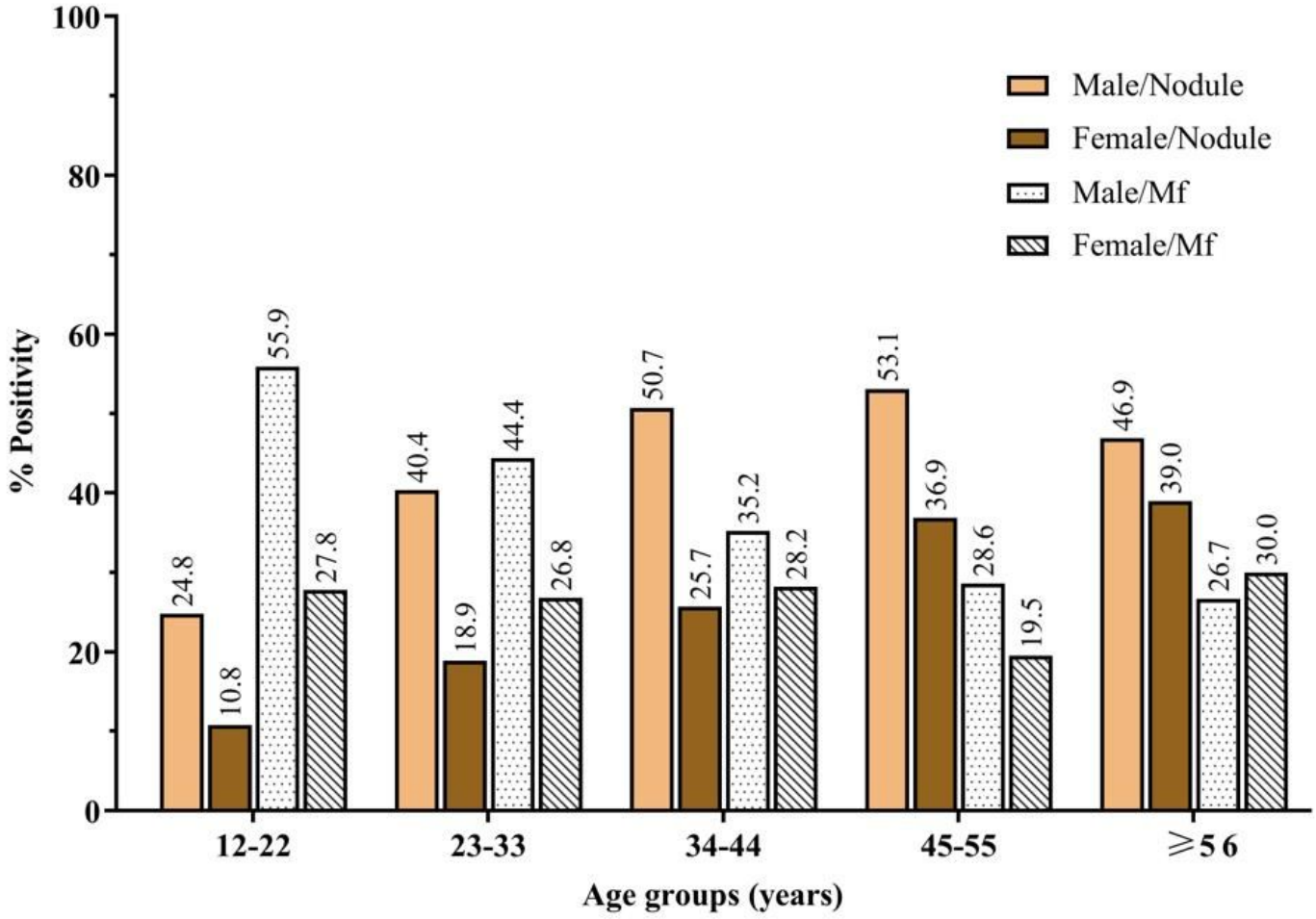

Figure 2

Distribution of *Onchocerca* nodules and MF among age groups and gender.

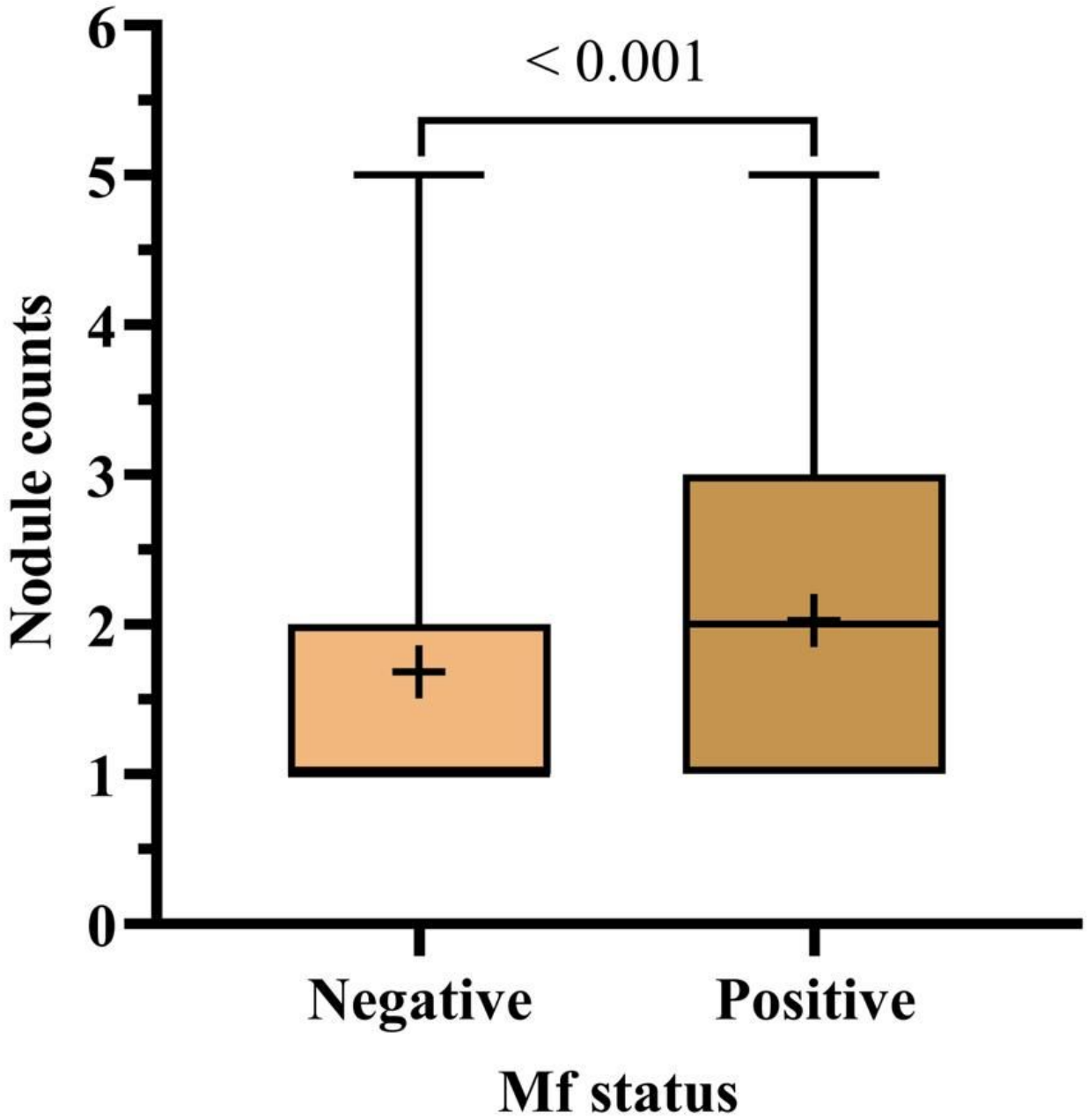

Figure 3

Onchocerca nodule count distribution against MF status.

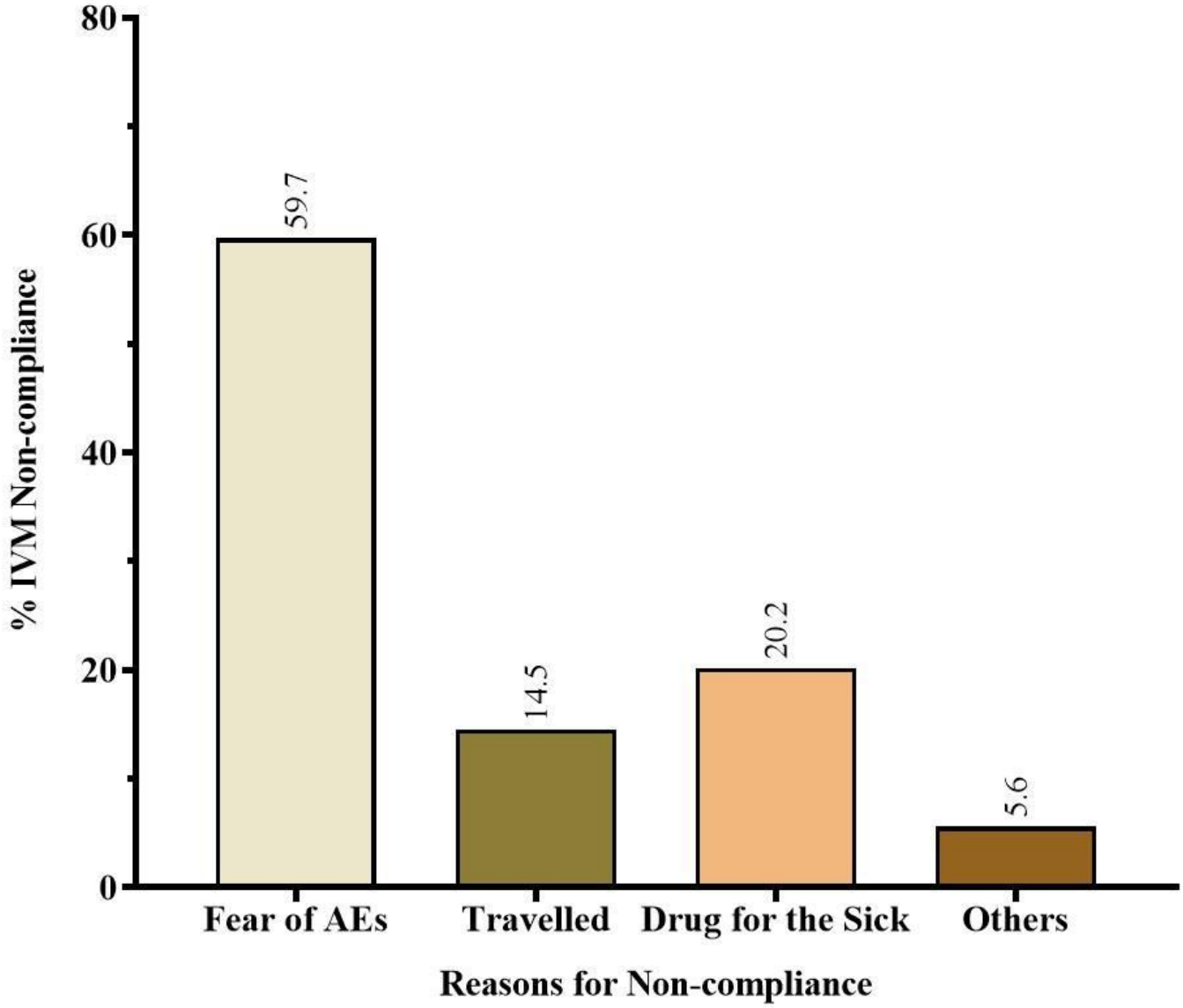

Figure 4

Reasons for non-compliance with ivermectin MDA.