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EVALUATION OF LYMPHATIC FILARIASIS AFTER TWO ROUNDS OF MASS DRUG ADMINISTRATION IN LAU LOCAL GOVERNMENT AREA OF TARABA STATE NIGERIA

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ABSTRACT
This study was undertaken to evaluate the effects of Mass Drug Administration (MDA) on *Wuchereria bancrofti* (microfilariae) after two rounds of combined Ivermectin and Albendazole distribution. A total of 221 participants were recruited in three communities in Lau Local Government Area of Taraba State by convenience sampling method. Questionnaires and physical examinations were used to assess clinical manifestations associated with the infection. Blood samples were collected by finger prick method and stained with Giemsa stain for examination to establish the presence of *W. bancrofti* while immunochromatographic card test was performed to determine the presence of filarial antigen in serum. Previous data were used to determine the pre-drug prevalence of the parasite. The results showed that the drug did not significantly reduce the clinical manifestations reported among the patients. The microfilariae prevalence and microfilaria mean density after two rounds of drug administration was 19.5% and 1.49%, while the pre- MDA prevalence and microfilaria mean density was 27.8% and 2.44% respectively. There was a statistically significant decrease of microfilaria prevalence ($P<0.05$) after two rounds of MDA. There was no significant effect of MDA by age, sex and occupation-related microfilariae prevalence in the study area. In conclusion, the study reveals that microfilaria prevalence and load decreased after two rounds of MDA of combined Ivermectin and Albendazole distribution amongst the studied populations. Routine evaluation of the MDA is required to assess the impact of the drug for the eventual elimination of the infection.

KEYWORDS: *Wuchereria bancrofti*, Mass Drug Administration, Prevalence, clinical manifestations, microfilaria,

INTRODUCTION

Lymphatic filariasis (LF) is a neglected tropical disease caused by the following parasitic nematodes, *Wuchereria bancrofti*, *Brugia malayi* and *B. timori*. These parasites are transmitted by many species of mosquitoes in four genera, *Anopheles*, *Culex*, *Aedes* and *Mansoni* (WHO, 2013). The distribution, ecology, biology and transmission potential of these mosquitoes vary greatly. However, in sub-Sahara Africa only *Anopheles funestus*, *Anopheles gambiae*, and *Culex quinquefasciatus*, transmit *Wuchereria bancrofti* (WHO, 2013). Lymphatic filariasis does not directly cause death but it is recognized as the second leading cause of permanent and long term disability worldwide (Addiss, 2011). The symptoms of chronic disease generally appear in adult males more often than females and include damage to the lymphatic system, arms, legs or genitals, which causes significant pain, wide-scale loss of productivity as well as social exclusion (WHO, 2013).

The Global Burden of Disease (GBD) by World Bank (WHO, 2013) showed an estimated LF prevalence rate of 3.4%. It is estimated that there are about 1.2 billion people who are at risk of the disease in the 83 countries (20% of the world population), and over 128 million people are infected or diseased (McCarth *et al.*, 2012). About 76 million people in the world are estimated to be suffering from the hidden disease or subclinical renal, respiratory, lymphatic and genital complications associated with LF (Tyrell, 2013). Of the 128 million people infected globally by LF, 91% of them are due to *W. bancrofti* while *B. malayi* and *B. timori* account for the other 9% burden (Addis, 2011).

In Africa, 34 countries are endemic, and Nigeria was rated as the third most endemic country with lymphatic filariasis in the world after India and Indonesia. It was reported that 22.1% of the Nigerian population is thought to be infected, with 66% of people at risk of being infected. Nigeria is believed to bear the highest burden of LF, with an estimated 80 to 120 million people at risk (WHO, 2011; Hotez *et al.*,.2012).

In endemic communities, LF is most prevalent in the rural and slum areas, predominantly affecting the poor in rural communities (Okon *et al*., 2010). Nigeria was rated as the third most endemic country with lymphatic filariasis in the world after India and Indonesia

(WHO, 2011; Hotez *et al*., 2012). It was reported that 22.1% of the Nigerian population is thought to be infected, with 66% of people at risk of being infected (Eigege *et al*., 2013). There is a significant burden of lymphatic filariasis in Nigeria, as findings in some parts of Taraba state have a prevalence between 21.1% and 30.02% (Badaki, 2013; Obadiah *et al*., 2018).

The Global Programme to Eliminate LF (GPELF) was launched in 2000 to eliminate LF as a public health problem by 2030 (WHO, 2011). The principal elimination strategy is to interrupt transmission by preventive chemotherapy, called Mass Drug Administration, which involves a combined dose of two (2) medicines given annually to an entire at-risk population in the following way: albendazole (400 mg) together with ivermectin (150–200 mg/kg) or with diethylcarbamazine citrate (DEC) (6 mg/kg) (WHO, 2011). These medicines have a limited effect on adult parasites but effectively reduce microfilariae from the bloodstream and prevent the spread of microfilaria to mosquitoes. Distribution is to entire communities where the prevalence of LF is equal to or more than 1% (WHO, 2010).

The socio-economic and psychological burden of the disease is enormous which include the direct cost of treatment, losses resulting from incapacitation and loss of labour (Stanton *et al*., 2017). Yet there is no comprehensive process to evaluate the progress of the impact of MDA based in the study area peculiarities. This present study was designed to monitor the effectiveness of MDA using parasite load evaluation, a physical examination for clinical manifestation associated with LF and antigenemiae presence as a monitoring tool for adoption**.**

The study area has Pre-MDA prevalence of 27.8% (Elkanah, 2006). This study main objective was to assess microfilaria prevalence and density amongst individuals that have received two rounds of MDA (FMOH, 2013) in the study area

Materials and methods

Study area

The three study sites are in Lau Local Government Area of Taraba State, Nigeria comprising of Appawa located at 9° 6' 52.704" N11° 31' 36.2064" E, Lube- 9° 14' 14.3952" N11° 40' 29.2584" E, and Garin Bako - 9° 9' 13.0356" N11° 34' 57.2772" E. (Figure 1). The communities are
Comprise of thatched mud huts as the major housing, the selection of the study site was based on the base-line prevalence and the administration of MDA.

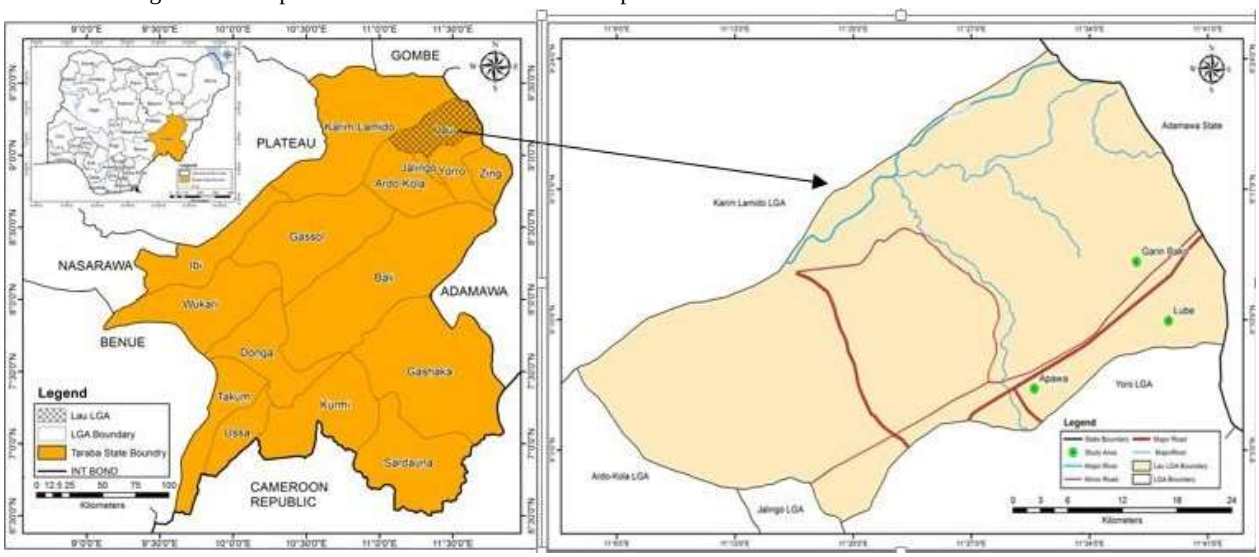

Figure 1. Study locations in Lau Local Government Areas of Taraba State

Ethical approval

Ethical clearance was obtained from the Ethical Committee (Ref: LLG/adm/036/VOL 1), Lau LGA, Taraba State, before the commencement of the study. Familiarization visits and meetings were held with district heads, religions leaders and health officers to explain the purpose, methods, scope and benefits of the investigation to the community, as well as obtaining informed consent.

Study design

The study was designed to evaluate the effect of the two rounds of MDA on the participants. Convenience sampling method was used by inclusion criteria to recruit the participants that received drugs in the two rounds of MDA and are residing in the community for more than five years. Physical examination for the infection was carried out; blood samples were collected to examine the filarial worms and rapid card test to assess the filarial antigen among the volunteered participants. The sample size was determined as described by Okoro (2014). Briefly,

$$n = \frac{Z^2pq}{L^2}$$

Where: n = is the sample size

Z = is the standard normal distribution at 95% confidence interval = 1.96

p = is the prevalence rate which is 19.5% (Badaki *et al.*, 2013) = 0.195

1-p = q = 1-0.195 = 0.805

L= is the allowable error, which is taken as 5% =0.05

Therefore, n= $(1.96)^2$ x 0.805 x 0.195/ 0.05^2 = 241.2 =**242**

A total of 221 that agreed to participate were recruited (the number of population recruited was less due to refusal to participate and the inclusion criteria) on a scheduled day as agreed during the familiarization and mobilization visit, informed oral consent of individuals who gathered at the agreed venue (Village head compound) were sought and obtained after the explanation of the procedures and the benefit of the study before blood samples were collected and were also examined for clinical signs and symptoms of filariasis as described by Akogun *et al.,* (2011). The inclusion criteria include those that received drugs in the two rounds of MDA and are residing in the community for more than five years. (Thiele *et al.,* 2016).

2.4 Blood collection

Blood samples were collected between 11 pm and 1 am (local time) by the finger-pricking method (WHO 2010). The left thumb was cleaned with methylated spirit-soaked cotton wool and disposable sterile blood lancet was used to prick the finger. A little pressure was then applied on the finger to ease the flows of blood. 2-3 drops of blood were placed on a clean, glass slide and edge of spreader use to make a thick blood film, which was then air-dried. A 100µl capillary tube in the Immunochromatographic Test card kit was used to obtained blood at the same time for ICT test (Weil *et al*., 2013).

2.5 Clinical examinations

The participants were examined for clinical manifestations including lymphoedema, hydrocoele, adenolymphoegitis, and itching. Physical examinations of males included the genitals, the legs and arms. The female examination was restricted to the legs, arms and breasts because of ethical reasons according to the International Society of Lymphology (WHO 2010).

2.6 Parasitological examination

In the laboratory, the air-dried blood smears were stained with 10% Giemsa's solution for 10 minutes and examined under a light microscope at x100 objective lenses. *W. bancrofti* were identified according to by the sheathed microfilaria without a caudal nucleus and the space between nucleus and body wall (Cheesbrough, 2010). Microfilariae (mf) were counted and recorded using counting chamber (Cheesbrough, 2010).

Microfilaria density (mfd) was calculated as mfd = #mf/NI

Where:

#mf = number of microfilaria

NI = Number of individuals infected

2.7 Determination of infection by immunochromatographic card test

The OnSite filariasis IgG/IgM Combo Rapid Test (CTKBiotech, Inc.) is a highly sensitive and simple alternative test for the diagnosis of lymphatic filariasis. The principle of the card is a lateral flow of immunoassay for the detection and differentiation of IgG and IgM anti-lymphatic filarial parasites (*W. bancrofti)* in human serum, plasma or whole blood. The test was performed following the manufacturer's instructions using the 100-µl capillary tube blood. Collected blood was transferred from the capillary tube to the pad on the ICT test kit card and one drop of the accompanying diluents was then added to the pad. The results of each ICT test card were read after 15 minutes. A positive result showed two pink lines on the card's window, while a negative result was depicted by a single line (CTK Biotech, 2010). Test results together with the individual's ID number were recorded in a standard field format.

2.8 Data analysis

Statistical analysis was carried out using Epi-info 7 (Centers for Disease Control and Prevention, Atlanta, GA) and Statistical Package for Social Sciences (SPSS version 20).

Chi-square was used to determine if there were significant association at $p \leq 0.05$ in the variables (lymphoedema, hydrocoele, adenolymphoegitis and itching) and the relationship between demographic factors, clinical manifestations, microfilariae and antigenemiae. The odds ratio was used to determine the effect of the MDA and to compare the relationship between the pre-drug and post-drug administration prevalence in the studied area.

Results

Evaluation of MDA efficacy on clinical manifestations

The clinical manifestations indicative of LF among the recipients observed were lymphedema, hydrocele, ADL and itching (Table 1). The progression or decrease of the clinical manifestations among the participants was evaluated by an informal interview and direct examination.

A total of 31 participants were identified with lymphedema, hydrocele (8), itching (36) and ADL (28) (Table 1). Responses from Patients with lymphedema showed 32.3 % (10/31), hydrocele (14.3 %(1/8), itching (44.0(11/36) and ADL 32.1(9/28) respectively (Table 1). There was no statistical significant odd of decrease of clinical manifestations observed among patients with lymphedema, hydrocele and ADL (Odd Ratio <1.00), however, participants with itching showed odd of decrease (Odd Ratio > 1.00) among the studied population (Table 1).

Table 1. Participants' responses on the efficacy of MDA on clinical manifestations

Responses	Lymphoedema		Hydrocoele	Itching	ADL	Total
Reduced	10(32.3)	1(14.3)	11(44.0)	9(32.1)	31(30.1)	
Did not reduce	21(67.7)	7(85.7)	25(56.0)	19(67.9)	72(69.9)	
Total	31(30.1)	8(7.8)	36(35.0)	28(28.1)	103(100)	
P-value	0.420	0.260	1.000	0.971	0.151	
Chi value	0.651	0.531	0.050	0.001	0.068	
Odd Ratio	1.160	0.310	1.034	1.141	1.774	

Odd Ratio value: < 1.00 = no significant association; >1.00 = significant association, p value: P>0.05 = no significant association; p value: P< 0.05 = significant association

The overall evaluation showed that Mass Drug Distribution did not significantly reduce clinical manifestations indicative of LF in the study area P>0.05 (Table 1)

3.2 Microfilaria prevalence of Pre and post MDA with demographic factors

Microfilariae prevalence showed the same trend of prevalence decrease in age, sex and occupation from the pre to post MDA prevalence in the study area. Age group 41-50 years showed a higher decrease of microfilaria from 25% to 5% in after two rounds of MDA which were more significant than other age groups (Fig. 2). However, there was no statistically significant difference between the effects of MDA among the age groups in the study area. Microfilaria decrease in females (24.4 to 20.0 mf/10µL) while males showed no decrease (Fig. 2) but no statistically significant difference in the decrease of microfilaria load and gender (P>0.05).

There was decreased in the other individuals involved in occupations other than farming (Fig. 2). Nevertheless, there was no statistically significant difference in the decrease microfilaria load among all the participants involved in various occupations in the study area (P>0.05).

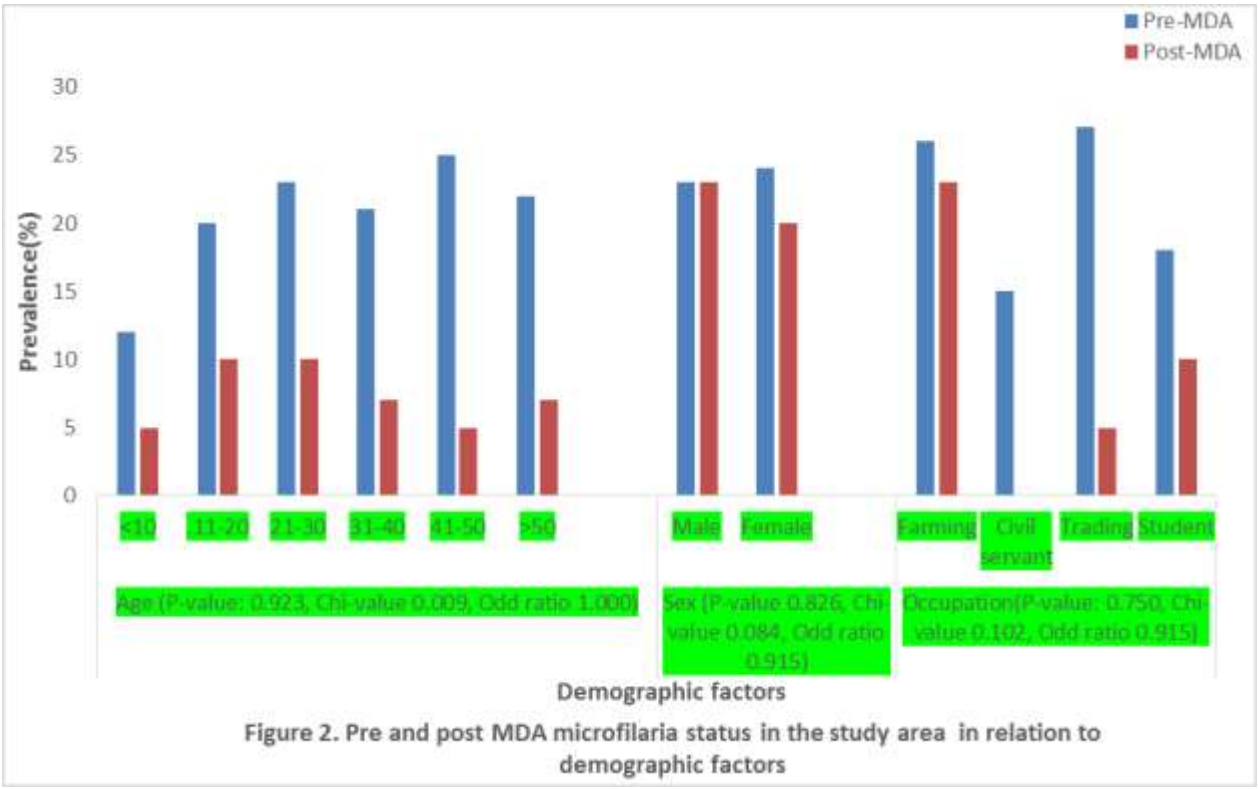

Figure 2. Pre and post MDA microfilaria status in the study area in relation to demographic factors

Figure 2. Comparison distribution of antigenemiae and microfilariae prevalence among MDA recipients

Microfilaria test and circulating filarial antigen test (CFA) are the recommended primary diagnostic tools in evaluating the impact of MDA (Weil 2006). In this study, ICT card test (CTK Biotech Inc.) was used to validate the microfilaria test carried out.

Antigenemiae prevalence of 28.5% was higher than the Microfilaria prevalence of 19.5% among the MDA recipients in the study area (Table 2). There was a statistically significant difference between the prevalence of antigenemiae and microfilaria among the MDA recipients (P<0.05).

Table 2: Distribution of Antigenemiae and microfilariae load among MDA recipients in the study area

Communities	No. Examined	Antigemiae) (%)	Microfilariae (%)	P-value	Chi value
Appawa	95	23 (24.2)	16 (16.8)	0.941	0.025
Lube	67	17 (25.3)	13 (19.4)	0.879	0.023
Garin Bako	59	23 (39.0)	14 (23.7)	0.904	0.015
Total	**221**	**63 (28.5)**	**43 (19.5)**	**0.914**	**0.015**

Pre-MDA and post-MDA status of the infection

The prevalence of the pre- MDA was 27.8% (Elkannah, 2006) while the post-MDA recorded 19.5% (Fig 3). There was a significant difference between the pre-MDA and post-MDA prevalence (OR= 1.6) after two rounds of the drug administration. The microfilaria count showed a decrease from 144 mf/10µL in the pre-drug prevalence to 44 mf/10µL after two rounds of MDA. Consequently, MFD showed a significant decrease from 2.44mf/10µL to 1.49mf/µL respectively after two rounds of MDA (Fig. 3).

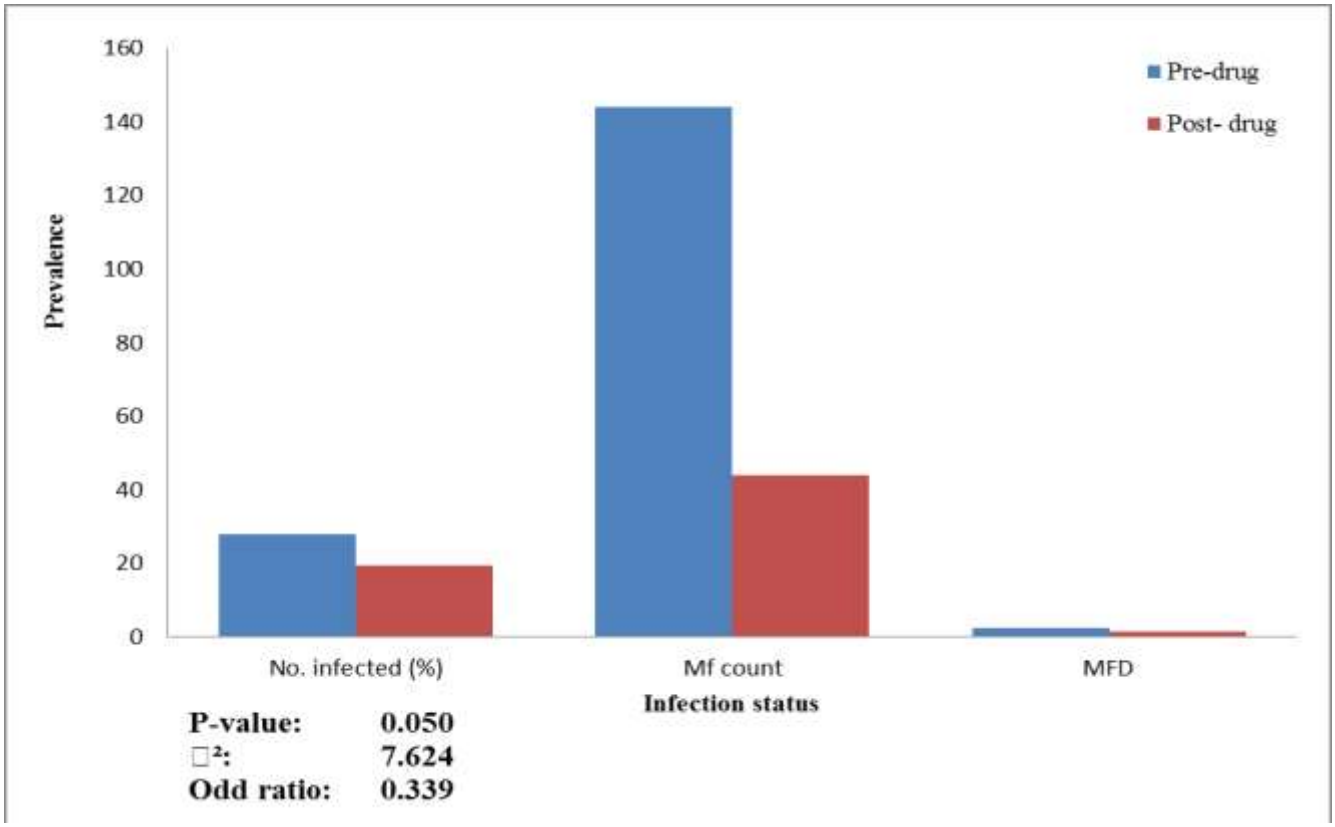

Figure 3. Microfilaria status in the Pre-and post-Mass Drug Administration in the study area.

DISCUSSION

The overall goal of Global Programme Lymphatic Filariasis (GPLF) is to eliminate the disease as a public health problem. Managing morbidity and preventing disability is integral to the elimination programme (WHO 2010). One of the objectives of this study was to evaluate the efficacy of MDA on clinical manifestation indicative to LF, the findings

showed that MDA only is not sufficient in reducing the infection among those suffering from the clinical burden.

The evaluation of the impact of MDA did not significantly halt the lymphoedema. This might be attributed to the lack or absence of basic lymphoedema management; principally hygiene and skincare (Cantey 2010). Therefore, alleviating suffering due to clinical manifestations by MDA cannot stand alone (WHO 2010). The study revealed that MDA did not alleviate participants suffering from hydrocoele. A similar study in India showed that managing morbidity of clinical manifestation of LF, especially Adenolymphoegitis which initiates filarial fever and increase acceptance and compliance with MDA among the patients will alleviate hydrocoele (Cantey 2010). Hence, MDA should be carried out alongside with morbidity management to assuage hydrocele. However, urogenital surgery is required (WHO 2010).

The episode of ADL among the participants in this study did not reduce after 2 rounds of MDA. Therefore, improved hygiene and care of the skin in the affected areas is required to alleviate the frequency of acute painful inflammatory episodes of adenolymphangitis (Addiss 2011).

In this study, the microfilaria prevalence was 19.5%; this is still above the threshold level of ≥1% prevalence (WHO 2010). The prevalence of microfilaraemia indicated a lower level of infection in the study areas compared to those reported from previous studies in Yorro (28.2%) in endemic areas in Taraba state (Badaki, 2010). Similarly, microfilarial density recorded in this study were as well lower (1.49) compared to (2.44) by Elkanah (2006). This shows that the combination of Ivermectin and Albendazole mass distribution in the study area was significantly effective after two rounds of MDA.

Age-specific distribution of prevalence among the participants showed a similar pattern of variation between pre-MDA and post-MDA. There was a decrease from the pre-MDA to post-MDA in all the age groups. The difference was not significant in gender, as only in the female that there was a slight reduction. There was no significant decrease in prevalence among the farmers in the study population from the pre-MDA to post-MDA (figure 2). This may be attributed to the environmental conditions where breeding sites of the vectors were observed in the study area, which may enhance transmission despite the MDA regime.

The study revealed that antigenemiae prevalence was higher than the microfilaria, it was expectedly high because rates decrease more slowly than the microfilariae (Yahathugoda *et al*.,2015).

There was a decrease in the microfilaria prevalence (19.7%) after annual two rounds of MDA against the previous study's prevalence (27.8%) which was before the distribution of the drug (Elkanah, 2006). There was also a significant decrease in the microfilaria density from 2.44 to 1.49. A study in Sri Lanka and Indonesia documented a decrease in prevalence from a baseline rate of 19% to 4.8% after five annual rounds of MDA (Yahathugoda *et al*., 2015).). The study, therefore, revealed the potential of the drug to eliminate the infection as public health importance.

CONCLUSION

The study revealed that two rounds of the annual MDA, may not be sufficient to significantly decrease clinical manifestations of Lymphatic filariasis such as lymphedema, hydrocele, itching and Adenolymphoegitis among the studied populations.

There was a significant decrease in both microfilaria prevalence and density in the studied populations. There was no significant effect of MDA by age, sex and occupation-related microfilariae prevalence in the study area.

It is therefore recommended that follow-up studies are required for proper monitoring and evaluation of the regime of MDA for the elimination of Lymphatic filariasis in the study area.

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Competing interest

The authors declare that they have no competing interest.

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