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Transmission potentials status of *Simulium damnosum* and willingness to comply with Ivermectin Treatment in Imo River Basin, Nigeria

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Abstract

Entomological, quantitative and qualitative data collection on willingness to comply with ivermectin treatment was conducted between May 2019 and March 2020 in Imo River Basin Nigeria. *Simulium damnosum* collected at Rivers Lolo and Ibii breeding sites by human-bait technique was assessed for transmission indices by standard methods. Structured questionnaires were used to ascertain compliance levels by communities (Umulolo and Amuro) and willingness to sustain the long-term ivermectin treatment. Entomologic indices (overall and specific for both sites) showed that infection, infective and parous rates were 0.7% (0.6% versus 0.7%), 0.0% (0.0% versus 0.0%), and 21.0% (22.3% versus 19.9%) respectively. Monthly biting rate (MBR) and monthly parous biting rate (MPBR) were 6,779.25 (3,291.75 versus 3,507.75) and 1,427.25 (770.0 versus 657.25) bites/person/month. Monthly transmission potentials (MTP) were zero indicative of no transmission. Of the 458 interviewed, 31.6% and 68.3% were males and females respectively. Among them, 66.8% were males and 67.4% were females treated before and 21 (14.5%) and 38 (121.1%) were high compliers. Sex did not affect the rate of compliance ($p > 0.05$). Age group 25 years and above (74.3%) had been treated before with 21.3% high compliers among age groups. Analysis of data revealed that age significantly affected the intake of drug ($p < 0.05$). On willingness to continue, 90.6% indicated that most people took the drug, 86.2% affirmed that most people will continue with the drug and 99.8% were personally willing to continue. The willingness to take the drug and response were not dependent ($p > 0.05$). Suggested ways to improve compliance were documented and findings discussed in the context of possible onchocerciasis elimination.

Keywords: Black flies, onchocerciasis, ivermectin treatment, willingness to continue, compliance

Introduction

Several studies in Africa ^[1, 2, 3] has confirmed *Onchocerca volvulus* transmission with mass drug administration as WHO recommended control strategy ^[4]. Ivermectin has a limited effect on the viability and reproductive capabilities of adult onchocercal worms. By practice repeated treatment is required to suppress the disease profile over time.

There are strong indications of elimination of onchocerciasis on the African continent ^[5, 6]. Despite this, there is need for updated data on vector transmission status in south eastern part of Nigeria, albeit a significant proportion are hyperendemic. The Nigerian Onchocerciasis Elimination Committee (NOEC) was launched in 2015 to help the country interrupt transmission of *O. volvulus* and stop MDA by 2025 ^[7].

Several studies on the impact of ivermectin therapy on the epidemiology of *O. volvulus* in both humans and black fly vectors have been conducted in some parts of south eastern Nigeria ^[8, 9, 10]. The caveat the recent studies point to the fact that the filarial worms are not properly identified. And the rate of infection speculative.

A major challenge for African programme for onchocerciasis control (APOC) is compliance with annual ivermectin therapy. Annual compliance studies to compliment elimination status have become possible and extremely desirable since workers are now lengthening the time frame for annual dosing from 15 to 25 or more years ^[11] and the coverage rate from 65% to 80% ^[12]. Published reports on community-directed treatment with ivermectin (CDTI) intervention have only centered on coverage with only few on compliance to annual ivermectin treatment.

This study presents the latest entomologic data and highlights the factors that necessitate individual's willingness to comply with annual ivermectin treatment and suggest ways to improve this compliance. The impact on *O. volvulus* transmission after 25 years of CDTI is demonstrated here.

Materials and Methods

Study sites and selection

The study sites (Ibii River and Lolo River) were from two rural communities (Umulolo and Amuro), Okigwe Local Government Area Imo State and the study was conducted from May 2019 to March 2020. These sites and their communities; Umulolo (Lat 05.85794⁰N and Long. 007.32566⁰E) and Amuro (Lat. 05.78808⁰N and Long. 007.26703⁰E) are drained by the Imo River, a known breeding site of the black fly vector. These communities fall outside the middle Imo River Basin as classified to be hyperendemic ^[13]. The inhabitants had benefited from yearly doses of ivermectin for over 20 years (included bi annual distribution which started in 2018). The study area and climatic details are described ^[14, 15].

Study Design

This study was designed community-based cross sectional survey to assess the entomologic parameters and rate of compliance to annual ivermectin treatment and factors that can influence individual's willingness to continue the treatment. The researcher's team included parasitologists (CNU and CMU), Entomologists (AAA and BEB), optometrist, local health workers (nurses) and CDDs. The entomological study took place at the two river sites (Lolo and Ibii) in Umulolo and Amuro communities. The participants for treatment compliance were grouped into two the low compliers (those who had taken drug for less than 8 years) and high compliers (those who had taken the drugs for 8 years and above).

The study adopted cross sectional method through collection and analysis of quantitative and qualitative data that were evaluated by REMO as hyper endemic for onchocerciasis. An individual form was used to obtain respondents bio data which included household name/ code, age, sex, marital status, educational status, occupation, village code, number of years of residency in the village.

Ethical Clearance

Ethical review and clearance of the research protocol, research instruments and informed consent procedures were obtained from the Ethical Review Committee of the Department of Zoology, Imo State University Owerri. State Ministry of Health and Okigwe Local Government Health Unit approved the survey. Personal risk involvement and community benefit were explained to both person human attractants for black fly collection and other participants.

Preliminary Survey and Advocacy

The pre-disease survey logistics involved mobilization of the community-directed distributors (CDDs) and other research / field assistants. The communities with the vector collection sites (were selected on the basis of their hyper endemic status) are currently being treated with ivermectin.

Data Collection

Willingness to comply with annual ivermectin treatment was assessed with a well-structured questionnaires and

focus group discussion (FGD). Structured questionnaire was used to collect data from the community members, CDDs and community leaders on compliance rate and willingness to continue the treatment. The field assistants assisted in completing the questionnaires. Five hundred and sixty questionnaires were distributed with 458 returned. The issue of recall bias in the study (as most people do not remember easily beyond five years) was solved with treatment registers which compared respondent's claims on number of times the drug was swallowed. Where the treatment register fails, the claims were weighed with the reports of the CDDs. Individuals (10 men and 10 women) who volunteered and have been living in these communities for over 8 years formed focus group discussion participants. The rate of compliance was leveled on the number of times the drug was swallowed. Low compliers and high compliers denoted individuals who had taken the drugs for < 8 times and > 8 times respectively.

Collection of Adult Black flies

The human-bait catch method ^[16] was adopted along the bank of Lolo and Ibii Rivers from Amuro and Umulolo for black flies collections.

Black fly catches in each station was four times a month and fly fly catching lasted from May 2019 to March 2020. Black flies collection was done from 7:00am to 6:00 pm by black fly connectors working alternatively ^[17].

Speciation and Parity Status Assessment

Each fly caught was carefully put into a cold box filled with ice pack to prevent development of micro filarial before transporting them to laboratory. Flies were individually demobilised with chloroform and then placed on a clean grease slides containing a drop of physiological saline. They were identified on the basis of morphological characteristics. Parity status was determined following observations on the ovariole features ^[18].

Fly Dissection, Identification of Filarial species for Infection/ Infectivity and Entomological Parameters Calculation.

The standard method of ^[19] was adopted for dissection of black flies. Each black fly was dissected by teasing the head, thorax and abdomen separately in a drop of normal saline on a clean glass slides. The preparations were checked for the larvae of *O. volvulus* and the proportions of larval (L₁, L₂ and L₃) stages were recorded.

The black fly proportion and transmission of onchocerciasis status were quantified by two entomologic parameters; the monthly biting rates (MBR) and transmission potentials (TP). Walsh *et al.* ^[17] established methods were used to evaluate MBR and TP.

Data Analysis

Data from questionnaires were based on percentages and Chi Square. Two ways analysis of variance (ANOVA) were used for monthly densities and difference in entomological parameters were subjected to Chi Square test. Results were considered statistical significant when p-value was below 0.05.

Results

Of a total of 889[457/889 (51.4%) at Lolo and 432/889 (48.6%) at Ibii] black flies caught and dissected, 0.67%

(6/889) were infected with *O. volvulus*. The difference between the Vector proportion study between the two sites were comparable ($P>0.05$). The peak of MBR was September 585 bites/ person/ month and June 487 bites/ person/ month while the lowest MBR was in February. A comparison of the MBRs showed that there was a significant difference. While the months of September and June had the highest number of black flies than February. Insignificant differences existed in the biting rates between other months by LSD mean separation technique. At Ibi in Umulolo parous flies were 86 (19.9%), 3 (0.7%) were infected and no L3 was found. The monthly entomologic parameters at Lolo River in Amuro showed that a total of 22.1% were parous. 3 (0.6%) of the parous flies were infected and none had L3. Overall, proportion from both sites showed that the percentage flies parity rate were below 50% and MTP were zero (Table 1).

Of the 458 interviewed, 145 (31.6%) were males and 313 (68.3%) were females. 66.8% and 67.4% males and females were treated before. 21(14.5%) and 38 (12.1%) were high compliers. The Chi Square (X^2) analysis showed that sex did not affect rate of compliance. Among ages, 25 years and above (74.3%) had been treated before with 77 (21.3%) high compliers. Analysis of data revealed that age significantly affected the intake of drug ($P<0.05$). Education and level of education contributed significantly to the consumption of the drug with the demographic location under statistical observations (Table 2). On willingness to continue with ivermectin drug 415 (90.6%) indicated that most people take the drug. 395 (86.2%) affirmed that most people will continue with the drug while 457 (99.8%) said that they were personally willing to continue with the drug if made available. The willingness to take the drug and response were not independent ($p>0.05$; Table 3). Suggestions on the ways to improve compliance are shown (Figure 1).

Table 1: Entomological parameters and proportions of filarial stages in black flies at two different sites in the study Area

Parameters	Lolo River	Ibii River	Total
Persons day worked	4	4	8
Total (%) flies caught	457 (51.4)	432(48.6)	889
Average daily catch per person	114	108	222
No (%) flies dissected	457(51.4)	432(48.6)	889
No (%) of parous flies	102(22.3)	86(19.9)	187
No (%) of Nulliparous flies	356(77.9)	346(80.1)	702
Total (%) of infected flies (L1 and L2)	3(0.6)	3(0.7)	6
Total (%) of infective flies (L3)	0(0.0)	0(0.0)	0
Monthly biting rate (MBR)	3,291.75	3507.75	6,779.25
Maximum monthly biting rate	585(September)	487(June)	997.5
Minimum monthly biting rate	112(February)	147(February)	289.0
Monthly parous biting rate (MPBR)	770.0	657.25	1427.25
Monthly transmission potential (MTP)	0	0	0

Table 2: Effects of Demographic features on compliance

Factors	No 458	No (%) treated before	No of high compliers	% compliance
Sex				
M	145	97(66.9)	21	14.5
F	313	211(67.4)	38	12.1
Age				
5-11	59	13(22.0)	0	0.0
12-24	37	05(13.5)	1	2.7
25+	362	269(74.3)	77	21.3
Education				
None	134	104(77.6)	19	14.2
Primary	202	113(55.9)	21	10.4
Secondary	112	57(50.9)	11	9.8

Table 3: Willingness to continue ivermectin treatment

Variables	Reasons		
	Yes (%)	No (%)	Don't know (%)
Most people take the drug	415(90.6)	27(5.9)	16(3.5)
Most people will continue	395(86.2)	0(0.0)	53(11.6)
Personally willing to continue	457(99.8)	0(0.0)	1(0.2)

Discussion

The study provided data set of filariasis transmission from the sites in the study area of Imo River Basin and willingness by the people to continue treatment intervention. Capture and dissection is non-insidious and advantageous means for probing the success of intervention. The ivermectin treatment intervention in the Imo River Basin has passed the estimated life expectancy of the worm 10-15 years ^[20] and demands evaluation by entomologic indices.

By WHO/APOC entomologic criteria for onchocerciasis stop MDA decision, infective rate in vector is $<0.05\%$ by sample size of at least 6,000. Unfortunately, we couldn't capture the required black fly proportion in the cause of our study. We created four capture sites within the selected sites by the rivers (Lolo and Ibii) with 4 days capture (7:00 am-6:00 pm) per month. In other words to attain the criteria, field activities ought to have increased, well beyond our logistic capacity. Improved or combined capture methods

are needed (probably by use of Esperanza window trap) if these current guidelines are to be made in the Imo River Basin as consented to by Nigerian Onchocerciasis Elimination Committee [21]. The trapping of 889 female *Simulium damnosum* might indicate that these rivers are moderately infested with black flies as reported elsewhere [13]. The regular and availability of human sources of blood meal and a suitable breeding and resting sites suggested occupational activities or residential proximity has been and will remain an endemic focus for the black flies [22].

From the data (albeit entomological incomplete), it was possible that skin mf available to the black flies has continued to decrease and this progressive decline impacted on transmission of onchocerciasis. The low results from the entomologic indices: infection rate (0.6% versus 0.7%), infectivity rate (0.0% versus 0.0%), parous rate (22.1% versus 19.1%), MBR (maximum 997.5 versus minimum 289.0) bites/ person/ month, MPBR (770.0 versus 657.25) bites/ person/ month and MTP (0.0 versus 0.0) L3H/ person/ month for the two sites were remarkable and indicated that ivermectin could suppress filarial transmission to the proportion where L3 will not be detected by dissection. The vector species probably exhibited limitation (vectors are efficient even at very low parasite densities), regulated by the peritrophic membrane. The greater the number of mf ingested, the smaller the percentage that reaches the haemocoel. Infected flies with low mf load have greater chances of survival and maintaining transmission of parasites [23]. Wanji *et al.* [24] have reported that percentage reduction was smaller in rainforest species compared to savannah species. Of interest was the MBR which is below the tolerable level of 1,000 bites/ person/ year. Also infectivity rates and MTP were zero indicative of non-transmission.

Infection of Onchocerciasis and lymphatic filariasis (LF) cross parts in many parts of Africa [25] and the stop MDA decision for one are known to be influenced by the transmission profile of the other. Despite our findings, Umulolo and Amuro communities are yet to meet the 2016 WHO criteria for interruption of onchocerciasis

transmission and stop ivermectin MDA [26]. We recommended that LF transmission be evaluated in these areas to ascertain the scope of cross-infection and result be used in support of a stop MDA decision for Imo River Basin. Interestingly, there was no evidence of any infective larvae in the vectors indication of absence or reduced skin mf in humans in the area which is consistent with our skin snip results.

The knowledge of the drug revealed that most respondents 'take the drug' and are willing to continue. More are willing to take ivermectin than before because the communities' distributors are part of them and understand them better. Government must ensure that the drug is available and procured early for distribution. Virtually every body interviewed was willing to continue with the drug as long as it is available. These individuals who are willing to take the drug must be maintained for the annual treatment objective to complete elimination of the disease. Health education (78.3%), house-to-house distribution (65%) and support to CDDs (63.3%) were the major suggestions on how to improve annual and long term compliance. Health education as strategy towards improving treatment have been well reported [27]. This calls for review on the existing education materials by taking into account those factors linked with low compliance and perceptual factors like benefits of treatments and challenges. Health education materials therefore should center on compliance especially on youths and children (5 years and above). Cupp *et al.* [6] had successfully interrupted transmission of *O. volvulus* in Abu Hamed and bi-annual treatment which started in 2018 is recommended to fill the gap between treatment beyond 90 days that may allow the effective transmission by the black flies [28]. Despite its rationale on logistics and cost, elimination at higher levels of community microfilarial load and less than the time i.e. with fewer treatment rounds has always been achieved.

Conclusively, the data confirmed continued decrease of skin mf acquisition by black flies vectors which was possible probably because most respondents "take the drug" and are willing to continue.

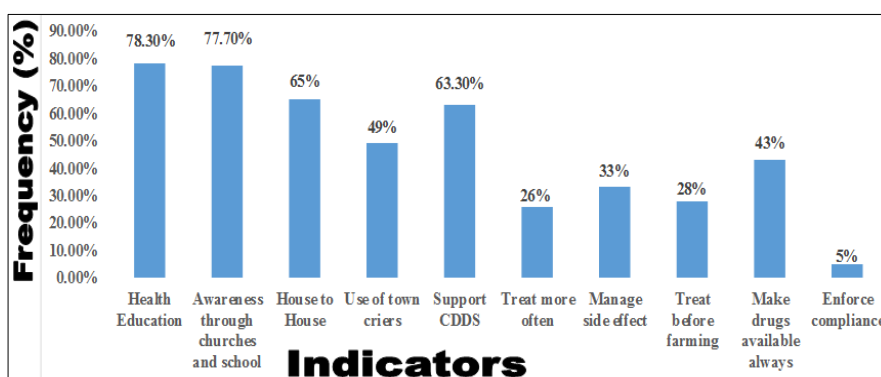


Fig 1: Suggested ways to improve compliance to Ivermectin treatment

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Authors' contributions

Conceived and designed the study: AAA, CNU, CMU. Collected the field data: AAA, IJI, ACC. Analyzed the data: IJI, NBE. Write the paper: AAA, AAA, CNU (review and editing). All authors have read and agreed to the published version of the manuscript.

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