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THE EPIDEMIOLOGICAL, ENTOMOLOGICAL AND SOCIO-ECONOMIC EVALUATION OF IVERMECTIN TREATMENT IN IMO RIVER BASIN, NIGERIA.

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ABSTRACT: *To assess the effectiveness of annual mass ivermectin treatment over 20 years in achieving elimination of onchocerciasis, we conducted a cross-sectional study between May 2021 and March 2022. A total of 540 individuals aged 5 years and above from rural farming communities selected were skin-snipped for dermal microfilariae (mf) by standard technique. Prospection of Simulium black flies was done at Lolo and Ibii Rivers. Structured questionnaires were used for the level of awareness, attitude and perceptions (KAP): onchocerciasis, vectors, treatment, drug compliance, benefits and socio-economy. Results revealed an overall mf prevalence of 12.8% and black fly infection rate (0.7%), infectivity and transmission potentials of (0.0%) indicative of non-transmission. These values contrasted with earlier reports in the range of 22%-68% for mf and 20.2%-48.2% infective rates suggesting the efficacy of mass ivermectin treatment in halting onchocerciasis. Participants had a high level of awareness about drug distribution. Benefits, dislikes and challenges of ivermectin were reported. We concluded that annual mass ivermectin treatment creditably reduced the microfilarial load and treatment in the study communities.*

KEYWORDS: Onchocerciasis transmission, Ivermectin distribution, Black fly vector infection, Socio-economy.

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INTRODUCTION

River Blindness or Onchocerciasis is an old disease scourge of many rural communities in Africa. The disease occurs through infection with the nematode parasite *Oncocerca volvulus* which is transmitted by the bites of infected black flies-*Simulium damnosum* (Crosskey 1981). The flies breed in fast-flowing streams and rivers (Vajime and Quillevere 1978); hence, individuals in areas that are located close to such places or within the flight range of the vector are usually at risk.

Nigeria alone accounts for the highest number of infected persons in the African continent (WHO 1995). Thirty-one of the existing 36 states of Nigeria and the Federal Capital Territory have meso to hyperendemic status. Out of the 774 local Government Areas in Nigeria about 416 are rated high priority for onchocerciasis control (NOCP 1996). Onchocerciasis causes hardship and leads to blindness, onchocerca skin disease (OSD), and manpower and economic losses (Nwoke et al 2006, Amazigo 1994). Control of onchocerciasis in Nigeria is presently through large-scale annual ivermectin therapy. This is sustained through Community-Directed Treatment of Ivermectin (CDTI) with support from the African Programme for Onchocerciasis Control, APOC (WHO/ TDR 2003). In Imo State, rapid epidemiological mapping of onchocerciasis (REMO) had placed the study areas in the hyperendemic zone (Nwoke et al 1994) and treatment with ivermectin had been ongoing from 1994 till date. The impact of onchocerciasis and transmission in Imo River Basin communities needs to be fully evaluated after repeated treatment. Accordingly, the study objectives were to (i) evaluate the effectiveness of ivermectin mass treatment by epidemiological method. (ii) ascertain the presence of *Simulium* species and transmission indices (iii) assess the knowledge, attitude, perception and rate of drug compliance as well as the socio-economy of the areas (production/productivity, interaction and health conditions of individuals and households). This paper gives an account of the epidemiological, entomological and socio-economic assessment of mass annual ivermectin treatment in parts of the middle Imo River Basin Nigeria.

METHODOLOGY

Study Areas

The communities involved were Amuro, Amano, Umulolo, Aku and Ihube, all located along the Imo River Basin area of Imo State Nigeria. They are all in Okigwe Local Government Area of Imo State. The area is located approximately between Latitude $5^{0}41^{1}$ and $6^{0}3^{1}$N and Longitude $7^{0}10^{1}$ and $7^{0}34^{1}$E. It is hilly with a lot of streams and rivers such as Ibii, Ugbi and Lolo Rivers. The exposure of rocks in the river belts or margins of these streams and rivers as well as enough trailing vegetation at certain periods of the year create favourable breeding sites for the vector (black fly). The villagers are exposed to the bites of the vector locally known as ‘NWAN MI’ (blood sucker) and consequently disease transmission is either by way of occupational exposure (farming, fishing, wine tapping etc) or residential nearness.

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Study Villages

The LGA onchocerciasis and the Carter Center Owerri provided a list of villages that have been under mass ivermectin treatment. Two communities (Amuro and Umulolo) were purposively selected based on previous onchocerciasis research works while Amano, Ihube and Aku were selected at random. Altogether five communities were studied. The study communities were rural and most of the people were subsistence farmers residing near the vector breeding sites.

Ethical Clearance

Ethical clearance for the study was obtained from the Imo State Ministry of Health and Okigwe Local Government Health Unit and heads of study communities for the conduct of the research activities. Black flycatchers were informed about the risks and benefits of participation.

Epidemiological Studies

Clinical Diagnosis

This was based on the rapid assessment method (RAM). The method relies on the presence of nodules and leopard skin on the chin from a random sampling of adult males aged ≥20 years or 50 men and women of all ages in each community who consented to be assessed. Prior to the assessment, demographic details of the subjects were obtained before being subjected to clinical examination for signs and symptoms of onchocerciasis.

Parasitological Examination

A total of 540 individuals aged 5 years and above who consented to participate were skin snipped for the presence of dermal microfilariae (mf) using the standard skin snip technique. Adults served as proxy for children consent determination. Two bloodless skin snips were taken from the iliac crest of the participants and placed in microtone plates containing normal saline and allowed to stay overnight at ambient temperature for emergence of mf. After this the snips were removed to each well for the purpose of fixation of any mf therein. The mf observed was enumerated under inverted microscope for positive cases.

Entomological Studies

Adult Black fly Collection

Biting adult females were caught by human bait along the bank of ‘Lolo’ River from Amuro and ‘Ibii’ River from Umulolo respectively. Each station was sampled four times a month and fly caught was between 7:00 am to 6:00 pm by two fly collectors working alternatively (Walsh et al 1978). Each fly collector was dressed in short-sleeved shirt, knickers and no shoes and was seated in shade. Any fly perching on the exposed body parts was caught before the probe by inverting a small glass tube over it. All tubes containing black flies were then labeled to indicate time, date and place of capture. All captured black flies were packed in a cold box filled with ice packs to prevent subsequent microfilariae development in the flies before they were taken to the laboratory.

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Morphological Identification

The morphological identification was done according to Nwoke (2019) criteria. Adults were identified as either Savannah or Forest species on the basis of colour of some parts viz the wing tuft, arculus, fore coxa and basal segment of the antenna as either pale for Savannah or dark for Forest species.

Dissection, Parity, Infection / Infectivity Assessment

Standard protocol for dissection was adopted (Mokry 1980). Black flies were inactivated individually with chloroform and then placed on a grease free slide containing a drop of saline. Parous or Nulliparous black flies were noted if they had not completed at least one gonotrophic cycle. Parous flies were further dissected to determine if they had stages of mf in different body parts (head, thorax and abdomen). The number of sausage-shaped larvae (L_1), pre-infective stage (L_2) and infective stage (L_3) of *Onchocerca volvulus* implicated were counted and recorded.

Calculation of Biting and Transmission Indices

The density and level of transmission of onchocerciasis were quantified by entomologic indices (the monthly biting rate and Transmission Potentials). The monthly biting rate (MBR) were measured as the theoretical black flies bite received by a person stationed at a catching site during the 11 hours (7:00 am to 6:00 pm) of the day light for one month in a given area. The monthly transmission potentials (MTP) was estimated as a total number of L_3 that would be received in one month by an individual stationed at a point for 11 hours of the daylight. These indices were evaluated by established methods (Walsh et al 1978).

Socio-Economic Studies

The questionnaires instruments used were; ivermectin household coverage record forms applied to 100 randomly selected participants from each community and structured questionnaires issued to health staff (3-supervising ivermectin distributors at Umulolo and Amuro), village heads (5) and community Directed Distributors of Ivermectin (CDDs-5, one from each community). For the ivermectin household coverage questionnaire, a total of 500 individuals from these households were selected randomly and all individuals therein interviewed as to receiving and swallowing ivermectin in the last treatment round. Parents / Guardians stood in for their under aged children. Participatory / focus group discussion were also held in each village. The research team also reviewed available community treatment registers. The questionnaire focused on the level of awareness, attitude and perception (KAP) on onchocerciasis, its vector, treatment, drug compliance and control activities, benefits derived from taking ivermectin and other aspects of socio-economy.

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RESULTS

Epidemiological Studies

Of the 540 individuals skin snipped in the evaluation studies, 69 were positive for mf giving an overall prevalence of 12.8% (Table 1). Prevalence rates varied according to communities ($P<0.05$).

Entomological studies

Of the 889 black flies dissected, 6 (0.7%) had larval stages of O. *volvulus* (Table 2). The highest infection rate (2.8%) was recorded in March followed by November (2.2%) and May (1.0%) while other months had no infection. Status of the black flies (Table 3) showed that 51.4% and 48.6% of the flies' populations came from Lolo and Ibii rivers respectively. The entomologic details from Lolo river showed that a total of 22.1% were parous with 3 0.6%) infected. None were infective.

The calculated MBR, MPBR and MTP for Lolo River were 3,291.75, 770 and 0 respectively. The indices for Ibii River were 19.9% parous and 0.7% infection profiles. While as the MBR, MPBR and MTP were 3,507.75, 657.25 and 0 respectively.

Socio-economic Studies

Majority of the respondents (96.2%) knew onchocerciasis in the areas and attributed it to black fly bites (71.6%). They were also well educated on the manifestations of the disease (90.8%). One hundred and fifty (30%) of the participants preferred complaining to CDDs while 44.2% patronized chemist stores and other methods as health care preferences (Table 4). Among the Healthcare providers and village heads, all knew onchocerciasis and mode of transmission as well as control programmes which is on-going. Knowledge on ivermectin and its distribution was highly appreciated (Table 5). The respondents reported benefits, dislikes and challenges are presented on Table 6.

Table 1: Skin Snip Assessment for microfilariae of *O. volvulus* in the study area.

Villages	Estimated population	No Examined	No +ve	% +ve
Amano	1,800	80	12	18.3
Amuro	1,805	150	14	9.3
Aku	4,990	80	10	12.5
Umulolo	8,081	150	17	11.3
Ihube	6,703	80	16	20.0
Total		**540**	**69**	**12.8**

Table 2: Monthly distribution of *O.volvulus* in black flies from the study area

Months	No Caught/Dissected	No (%) infected	Relative Abundance (%)
March	107	3(2.8)	50.0
February	37	0(0.0)	0.0
May	98	1(1.0)	16.7
June	105	0(0.0)	0.0

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July	90	0(0.0)	0.0
August	57	0(0.0)	0.0
September	133	0(0.0)	0.0
October	116	0(0.0)	0.0
November	93	2(2.2)	33.3
January	53	0(0.0)	0.0
Total	**889**	**6(0.7)**	**100.0**

Table 3: Status of blackflies and transmission indicies

Classification of Data	Lolo River	Ibii River	Total
Person per day	4	4	8
Total (%) flies caught	457(51.4)	432(48.6)	889
Average daily catch per person	114	108	222
(%) flies dissected	457(51.4)	432(48.6)	889
No (%) parous flies	101(22.1)	86(19.9)	187
No (%) Nulliparous flies	356(77.9)	346(80.1)	702
Total (%) of infected flies	3(0.6)	3(0.7)	6
No (%) flies with L1 and L2	3(0.6)	3(0.7)	6
No (%) flies with L3	0(0.0)	0(0.0)	0
Monthly bitting rate (MBR)	3,291.75	3,507.75	6,779.25
Maximum monthly biting rate	585 (Sept)	487.5 (June)	997.5
Minimum monthly biting rate	112 (February)	147 (February)	289.0
Monthly parous bitting rate (MPBR)	770.0	657.25	1,427.25
Monthly transmission potential (MTP)	0	0	0

Table 4: Respondents awareness on Onchocerciasis

Villages	Description		Causes/Transmission		HCP			OSD	
	Correct	Incorrect	Correct	Incorrect	PHC	CDDs	Others	Correct	Incorrect
Amano	93(18.6)	07(1.4)	71(14.2)	29(5.8)	31(6.2)	20(4.0)	49(9.8)	91(18.2)	09(1.8)
Amuro	97(19.4)	03(0.6)	68(13.6)	32(6.4)	33(6.6)	25(5.0)	42(8.4)	79(15.8)	21(4.2)
Umulolo	98(19.6)	02(0.4)	77(15.4)	23(4.6)	32(6.4)	27(5.4)	41(8.2)	96(19.2)	04(0.8)
Aku	95(19.0)	05(1.0)	73(14.6)	27(5.4)	29(5.8)	31(6.2)	40(8.0)	95(19.0)	05(1.0)
Ihube	98(19.6)	02(0.4)	69(13.8)	31(6.2)	25(5.0)	26(5.2)	49(9.8)	93(18.6)	07(1.4)
Total	481(96.2)	19(3.8)	358(71.6)	142(28.4)	150(30.0)	129(25.8)	221(44.2)	454(90.8)	46(9.2)

Key:

HCP: Health care preferences
PHC: Primary health care

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CDDs: Community directed distributors
OSD: Onchocerca skin disease

Table 5: Health care providers and village heads responds

Variables	Description		Transmission		Control		Ivermectin		Distribution	
	Correct	Incorrect	Correct	Incorrect	Correct	Incorrect	Yes	No	<10	>10
Health workers (2)	2(100.0)	0(0.0)	2(100.0)	0(0.0)	2(100.0)	0(0.0)	2(100.0)	0(0.0)	0(0.0)	2(100.0)
Village heads (5)	5(100.0)	0(0.0)	2(100.0)	0(0.0)	5(100.0)	0(0.0)	5(100.0)	0(0.0)	0(0.0)	5(100.0)
CDDs (5)	5(100.0)	0(0.0)	5(100.0)	0(0.0)	5(100.0)	0(0.0)	5(100.0)	0(0.0)	0(0.0)	5(100.0)

Table 6: Reported benefits, dislike and challenges

Variables	Villagers	Health providers
Benefits		
Productivity (farming)	+	+
Improved vision	+	+
Rashes reduction	+	+
Improved appetite	+	+
Feel strong and healthier	+	+
Worm expeller	+	+
Dislike		
Weakness	+	+
Irregular drug use	-	+
Challenges		
Drug shortage	+	+
Lack of government support	-	+

DISCUSSION

We have used a cross-sectional survey to measure the degree of transmission of O. *volvulus* in middle Imo River Basin, Nigeria by evaluating the parasitological and entomological indices after > 20 years post treatment. The epidemiological surveys showed very low potential for onchocerciasis transmission in the study communities. We found an overall mf prevalence of 12.8% and *Simulium* infection rate of 0.7%. These values contrasted with previous reports in the range of 23-68% for mf prevalence in South Eastern, Nigeria (Akujobi et al 2017,Nworie et al 2014, Okonkwo et al 2010, Uttah 2010, Dozie et al 2006, Okolo et al 2004, Ukpai and Ezeji 2003), other Southern states (Pijiah and Eneanya 2019,

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Wogu and Okaka 2008) and also 29.2-48.2% for infection rates for *Simulium* black flies reported previously (Nnadozie et al 2018, Maikaje et al 2015). One possible explanation for this study is effectiveness of annual ivermectin treatment in the study communities with over 75% ivermectin coverage based on quantitative household coverage evaluation and community registers (65-82%) coverage. Also the sinking of boreholes in selected places in these communities contributed to the drop in infection rates.

In the framework of elimination, the WHO (2016) stipulated that entomological results are satisfactory when the vector infectivity rate is <1 infective black fly/ 1000 parous flies representing a prevalence of 0.1%. Our results showed infectivity rate of 0.0 FLH/1000 parous flies which did not exceed WHO threshold. There were no infective larvae. All had ATP of zero but developing larvae indicative of residual infection. Also WHO (2016) stipulated an ATP of 20L3/ man/ year as a threshold in the framework of elimination of onchocerciasis and none of the sites exceeded this values. The parous and infection rates gave clues to the transmission potentials of the biting pattern of the black flies in the areas. The parous rate of 22.1% and 19.1% and the infection rates (0.6% and 0.7%) at the river sites were very low. The other entomologic indices; MBR (maximum 997.5 and minimum 289.0) bites/ person/ month when compared with the tolerable levels of 1,000 bites/ person/ year is lower for hyper endemic zone on treatment suggesting biting nuisance by the flies. Since infectivity rates was a standard for assessment of transmission, the remarkable low parity rates (when compared with nulliparity rates) and zero infective rates validates the testimony of ivermectin control of onchocerciasis. This was indeed evidence that the skin mf load had been drastically reduced by ivermectin annual post treatment. Joan et al (2007) made similar observations where an overall mf prevalence of 0.3% was found against earlier report of 27.9%. It is possible that the reservoir of skin mf available to the flies has continued to decrease and this progressive reduction may have led to a decrease in transmission. Elsewhere in Mali and Senegal, similar results were made (Barsboom et al 2003).

The socio-economic studies revealed high level of knowledge of onchocerciasis, its vector and ivermectin treatment by the participants. The 65% coverage obtained for Aku from the register may be due to drug shortage as notified by informants as well as absentees. Community census need to be regularly updated for proper drug supply. Also absentees should be educated on the need to avail themselves for treatment when they come back. These measures no doubt would help to scale treatment coverage above the minimum 65% treatment needed for effective coverage. Different health and productivity values were reported by the respondents over the years by the programme. The benefits of increased working days and productive life probably would culminated into huge farm yields and likely translate to more finance and improved quality of life for the inhabitants

Conclusively, this study showed remarkable evidence on the effectiveness of ivermectin in eliminating onchocerciasis and halting O. *volvulus*. The observations would complement on-going efforts in the assessment of long term ivermectin treatment for River Blindness control in Nigeria. Despite the promising results of ivermectin intervention and perceived benefits, plans towards implementation of vector control in the riverine vegetations especially in Rivers Lolo and Ibii should not be overlooked. The biting problems experienced by the residents will be reduced by this method. Furthermore, strengthening of education on the need to comply with ivermectin treatment by all eligible is advocated to eliminate what can be seen as pockets of infection.

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