Onchocercal Skin Disease Profiles Following Ivermectin Treatment in the middle Imo River Baisn, Nigeria.

Abstract

In Nigeria infection with onchocerciasis has been under control with the introduction of ivermectin in most affected communities for a decade. To assist 'stop mass drug administration (MDA)' decision, a cross-sectional survey evaluated the impact of ivermectin on onchocercal Skin Diseasesb (manifestations) from 540 participants in 5 endemic communities. The rapid epidemiological assessment (REA) method with palpable nodules and skin depigmentation (leopard skin, LS) as diagnostic indices were used. The prevalence profiles of palpable nodules and leopard skin was 5.9% and 12.2% respectively. Males had significantly higher prevalence of these indices (palpable nodules 6.8(%; LS 13.3%) than females (palpable nodules 4.6%; LS 11.1%). Although, Onchocercal Skin Diseaes (clinical manifestations) were observed in all age groups, it occurred most in older groups. These groups with nodules could portend as reservoir for transmission. The implications of the results were discussed in the context of the on-going prediction of possible elimination of onchocerciasis in Africa and 'stop MDA' decision.

Keywords: Ivermectin treatment, Diagnostic indices, Onchocercal skin disease.

Introduction

Onchocerciasis is a leading cause of visual impairment and blindness in many developing countries. The main complications are severe eye disease characterized by popular or hypopigmented lesions and intense itching. The disease is caused by the filarial nematode *Onchocerca volvulus* that is transmitted by *Simulium damnosum* species of black flies (WHO 1995). According to WHO(1997), the disease affected about 17 to 18 million people in 37 countries of the world with approximately 123 million being at risk of infection. The disease is widespread in Nigeria and causes blindness in most rural communities. Of all the countries of the

world, Nigeria has the largest number of persons with onchocerciasis accounting for about a third of the global prevalence with about 40 million at risk of infection (Nwoke 1990).

Onchocerciasis in Nigeria is solely transmitted by members of *S. damnosum* complex which is widespread in the Savannah forest, Savannah mosaic and rainforest areas. They are known to be common in the rocky sections of the River Niger and its tributaries (Eneanya and Nwogu 2001). In Imo State rapid epidemiological mapping of onchocerciasis (REMO) study in sentinel villages (Ezinachi, Umulolo, Umuele, Ndioji and Isiokwe) recorded a palpable nodule range of 40-56% and 24-48% of leopard skin (LS). This lead to Imo State being classified as an endemic State and necessitating community- wide ivermectin treatment (Nwoke et al 1994). Dozie et al (2003) study showed that blindness associated with onchocerciasis is fewer in the rainforest zone compared to the Savannah zone. The pattern is less clear in central Africa with severe blinding as well as less blinding onchocerciasis presents in both Savannah and rainforest belts. Onchocercal skin diseases (OSD) is found in East Africa where blindness is rare (WHO 1995). Skin disease and severe pruriries (troublesome itching) has recently been recognized to be affecting more than 50% of the populations in some rural communities in the rainforest belt with relative low blindness prevalence (Kale 1998).

The clinical presentation of the disease is varied from changes in the skin (dermatitis), lymphatic system and ocular (eye) changes leading to blindness. The symptoms include skeletal pain, prurities, skin lesions, impaired vision (patial or total blindness) and premature death. The infective microfilariae is introduced by the bite of black flies which latter form swellings called nodules. These nodules vary in sizes as they contain adult worms. In patients in Africa, nodules tend to be located on the lower tonso, pelvis and lower extremities as against patients in Central and South America (Aapredbook Publications 2009). The relationship between the sites of biting by the vector and the localization of the nodules showed that many nodules were found on the lower parts of the body whereas in Central America as many as 70% were found on the head (Adetokumbo and Herbert 2003). The localization of the nodules has been related to the area of bitten by different vector species (Ubachukwu 2004). In an effort to know whether onchocerciasis transmission had been halted / interrupted since on-going treatment characterized by varied compliance, this study evaluated nodules and dermatitis as signs of onchocerciasis in the study area.

Materials and Methods

Study Area and Population

The study area is Okigwe Local Government Area of Imo State Nigeria. Okigwe is located in the Northern part and is one of the 27 LGAs of the State. There are 115 villages in Okigwe, all has been receiving mectizan/ ivermectin since 1995 (Global 2000/River Blindness). The communities where the study was carried out were all in the Imo River Basin of Nigeria located between Lat. $5^{0}40^{1}$-$5^{0}57^{1}$N and Long. $7^{0}10^{1}$-$7^{0}26^{1}$E. They are drained by several fast flowing streams and rivulets which empty into the main river in the area, the Imo River (Atlas of Imo State, 1984). The seasons are well defined: a wet season from October to March and a dry season from April to September. The range of annual rainfall is between 1700 and 2000 mm with average relative humidity of about 80% and mean annual temperature of 29^{0}C (Dozie et al 2006).The vegetation is forest. Subsistence farming, fishing, hunting, wine tapping and petty trading are the main occupation of the people who are Ibo ethnic group.

Ethical Clearance and Mobilization

The State Ministry of Health, Local Government Area Health Unit and the village heads were notified before the study commenced through a letter of intent from the Research Team under the approval of the Head of Department of Zoology, Imo State University, Owerri Nigeria. The purpose of the study was explained in each village to the village heads and the elders, and their consent was obtained for the mobilization by the respective communities.

Subject Examination

Five farming communities; Amano, Amuro, Ihube, Umulolo and Aku along the fast flowing rivers were selected for the study.They population census with the help of field assistants was conducted in each communities. Out of a combined population ,540 subjects male and females aged 5 years and above were chosen based on household records. 150 from Amuro and Umulolo and 80 respectively from Aku, Amano and Ihube endemic communities. Subjects were asked to gather at the health center in the communities. A health talk was made to them for enlightment on the existing health problem. Their verbal consent were obtained thereafter before they were

physically examined; leopard skin, palpation for presence of onchocercal dermatitis and nodules, scrotal and clitoral enlargements, hanging groin, itching and virtual acuity by the optometrist in the team. Subjects' records on history and use of ivermectin as well as demographic data (age, sex, occupation and marital status) were taken.

Data Analysis

Simple percentages were used to estimate the prevalence rate of various parameters by the subjects. Chi-Square was used to ascertain significance in sex and age on the prevalence of clinical manifestations among subjects at 0.05 level of probability.

Results

A total of 5 farming communities were surveyed between May and November, 2019. The highest infection rate was found in Umulolo (15.4%) followed by Amuro (13.1%), Aku, Ihube and Amano had 9.3%, 8.5% and 8.3% respectively. The overall prevalence was 54.6% (Table 1). Results of onchocerciasis manifestations revealed that leopard skin was the commonest (12.2%) feature. Lizard skin (11.3%), onchocercal nodules (5.9%), itching (8.0%), musculoskeletal pains (10.0%) and poor vision (3.5%) were also reported. Leopard skin was highest in Amuro (21.3%) and Ihube (18.8%) and lowest in Amano (7.3%). The prevalence of onchocercal nodules was highest in Amuro (8.7%) and lowest in Ihube (2.5%). Onchodermatitis was highest in Ihube (5.0%) and lowest in Aku, Amano and Amuro (0.0%). Poor vision was highest in Aku (7.3%) and lowest in Amuro (0.0%). No scrotal and clitoral enlargements were recorded. Prevalence of infections increases with age group (Table 2). Males had significantly higher prevalence than females ($p<0.05$; Figure 1). Leopard skin, lizard skin, onchodermatitis, poor vision, itching and musculoskeletal pains were noted from 21-30 years old. Hanging groin was found in 31 years and above (Table 3).

In occupation prevalence, farmers (19.5%) had the highest prevalence followed by others (teachers and applicants) 12.2%, Traders and school children had 10.8% and 4.1% respectively (Figure 2). Plates 1 and 2 showed subjects with onchocercal nodules and leopard skin.

Table 1: Results of Onchocercal clinical features of the subjects.

Clinical features	Amano	Amuro	Umulolo	Aku	Ihube	Total
Musclo-skeletal pain	09(11.3)	11(7.3)	13(8.7)	13(8.7)	08(10.0)	54(10.0)
Poor vision	01(1.3)	00(0.0)	07(2.0)	06(7.5)	05(6.3)	19(3.5)
Onchocercal nodules	04(5.0)	13(8.7)	08(5.3)	05(6.3)	02(2.5)	32(5.9)
Leopard skin	17(21.3)	11(7.3)	14(9.3)	09(11.3)	15(18.8)	66(12,2)
Lizard skin	07(8.8)	17(11.3)	23(15.3)	11(13.8)	03(3.8)	61(11.3)
Itching	07(8.8)	16(10.7)	13(8.7)	03(3.8)	04(5.0)	43(8.0)
Hanging groin	00(0.0)	03(2.0)	00(0.0)	03(3.8)	05(6.3)	11(2.0)
Scrotal/Clitoral Elanrgement	00(0.0)	00(0.0)	00(0.0)	00(0.0)	00(0.0)	00(0.0)
Rashes and Onchodermatitis	00(0.0)	00(0.0)	05(3.3)	00(0.0)	04(5.0)	09(1.7)
Total	**45(8.3)**	**71(13.1)**	**83(15.4)**	**50(9.3)**	**46(8.5)**	**295(54.6)**

Table 2: Age-related Distribution of Onchocerciasis among the subjects

Communities	5-10		11-20		21-30		31-40		41-50		51+	
	No Exam	No(%)+ve	No Exam	No(%)+ve	No Exam	No(%)+ve	No Exam	No(%)+ve	No Exam	No(%)+ve	No Exam	No(%)+ve
Amano	7	1(5.9)	7	0(0.0)	17	4(23.5)	15	3(20.0)	18	3(17.7)	13	3(23.1)
Amuro	33	1(3.0)	13	2(15.4)	25	3(12.0)	23	3(13.0)	31	2(6.5)	25	3(12.0)
Umulolo	26	1(3.8)	17	2(11.8)	31	3(9.7)	24	2(8.3)	23	3(13.0)	29	5(17.2)
Aku	13	0(0.0)	4	1(25.0)	13	3(23.1)	19	2(10.5)	16	2(12.5)	15	2(13.3)
Ihube	15	0(0.0)	3	1(33.0)	13	4(30.8)	19	3(15.8)	23	5(21.7)	10	2(20.0)
Total	**94**	**3(3.2)**	**44**	**6(13.6)**	**99**	**17(17.2)**	**100**	**13(13.0)**	**111**	**15(13.5)**	**92**	**15(16.3)**

Table 3: Results of Onchocercal clinical features by Age and Gender

Age groups (Years)	Sex	No Exam	Musclo-skeletal pain	Poor vision	Nodules	Leopard skin	Lizard skin	Hanging groin	Rashes and Onchodermatitis	Itching	Scrotal/Clitoral enlargement	Total
05-10	M	61	0	0	0	0	0	0	0	0	0	0
	F	43	0	0	0	0	0	0	0	0	0	0
11-20	M	21	0	0	0	0	0	0	0	0	0	0
	F	13	0	0	0	0	0	0	0	0	0	0
21-30	M	51	3	2	0	4	3	0	2	0	0	14
	F	48	2	0	0	5	0	0	1	4	0	12
31-40	M	47	7	4	3	7	5	1	1	7	0	35
	F	53	3	2	3	3	7	0	0	5	0	23
41-50	M	52	11	3	5	13	7	4	1	3	0	47
	F	59	5	1	3	7	12	1	1	7	0	37
51+	M	47	14	3	11	13	8	3	2	10	0	64
	F	45	9	4	7	14	19	2	1	7	0	63
Total	M	279	35(12.5)	12(4.3)	19(6.8)	37(13.3)	29(10.4)	8(2.9)	6(2.2)	20(7.0)	0(0.0)	160(29.6)
	F	261	19(7.3)	7(2.7)	13(4.6)	29(11.1)	32(12.3)	3(1.1)	3(1.1)	23(8.8)	0(0.0)	135(25.0)
Grand total		**540**	**54(10.0)**	**19(3.5)**	**32(5.9)**	**66(12.2)**	**61(11.3)**	**11(2.0)**	**9(1.7)**	**43(8.0)**	**0(0.0)**	**295(54.6)**

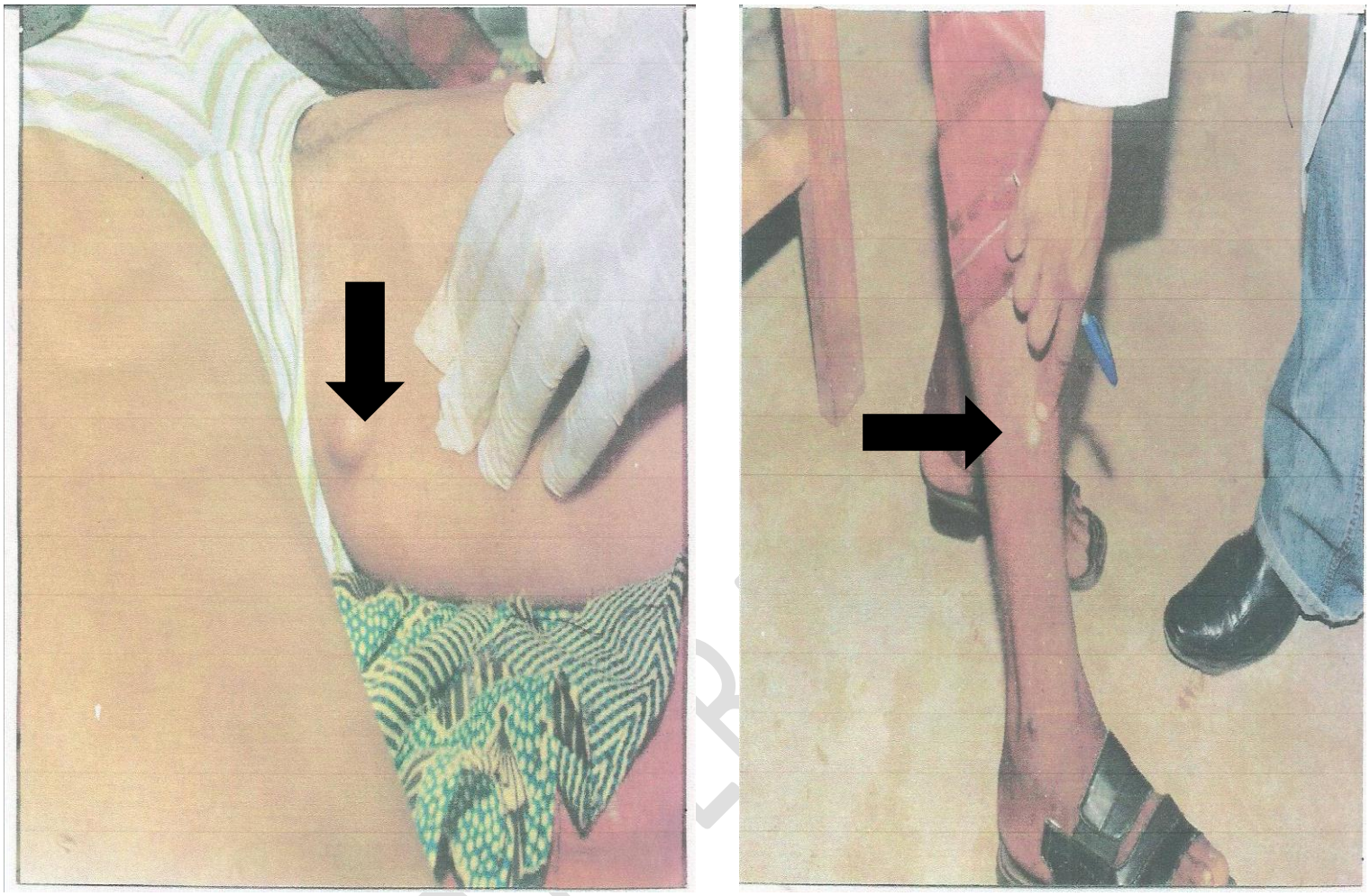

Plate 1: showing subjects with Onchocercal nodules

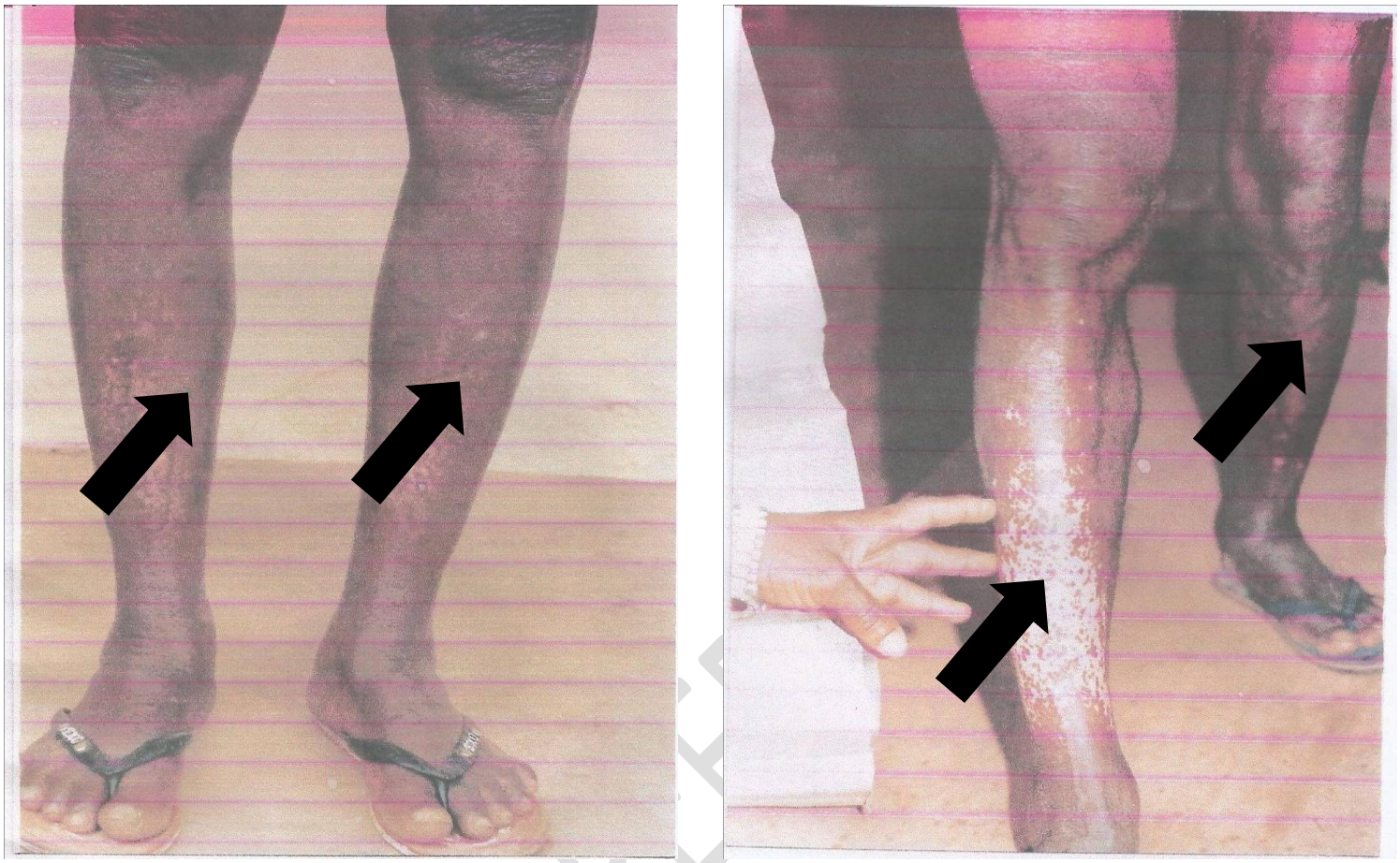

Plate 2: showing subjects with Leopard skin

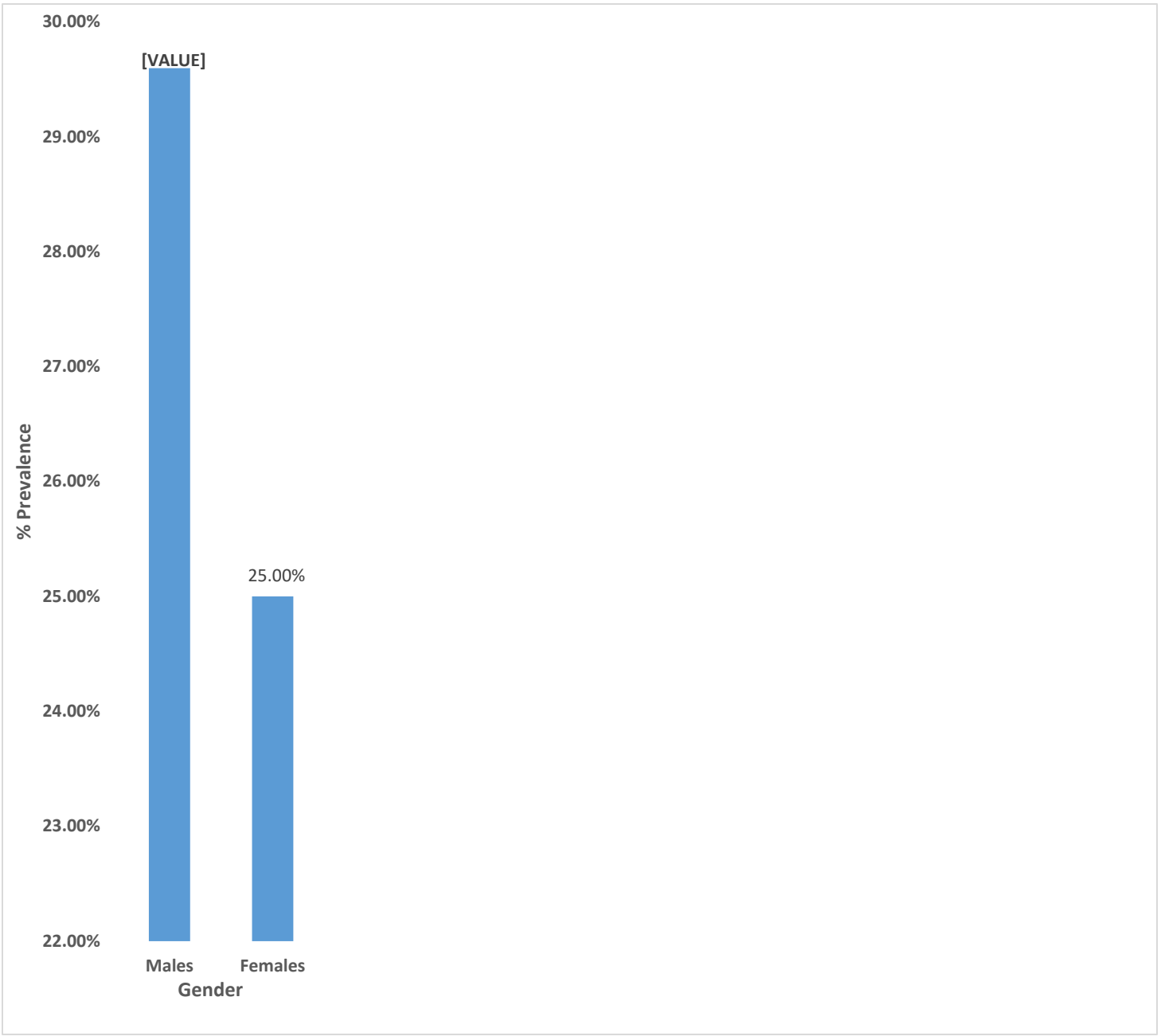

Figure 1: Prevalence by gender across all study subjects

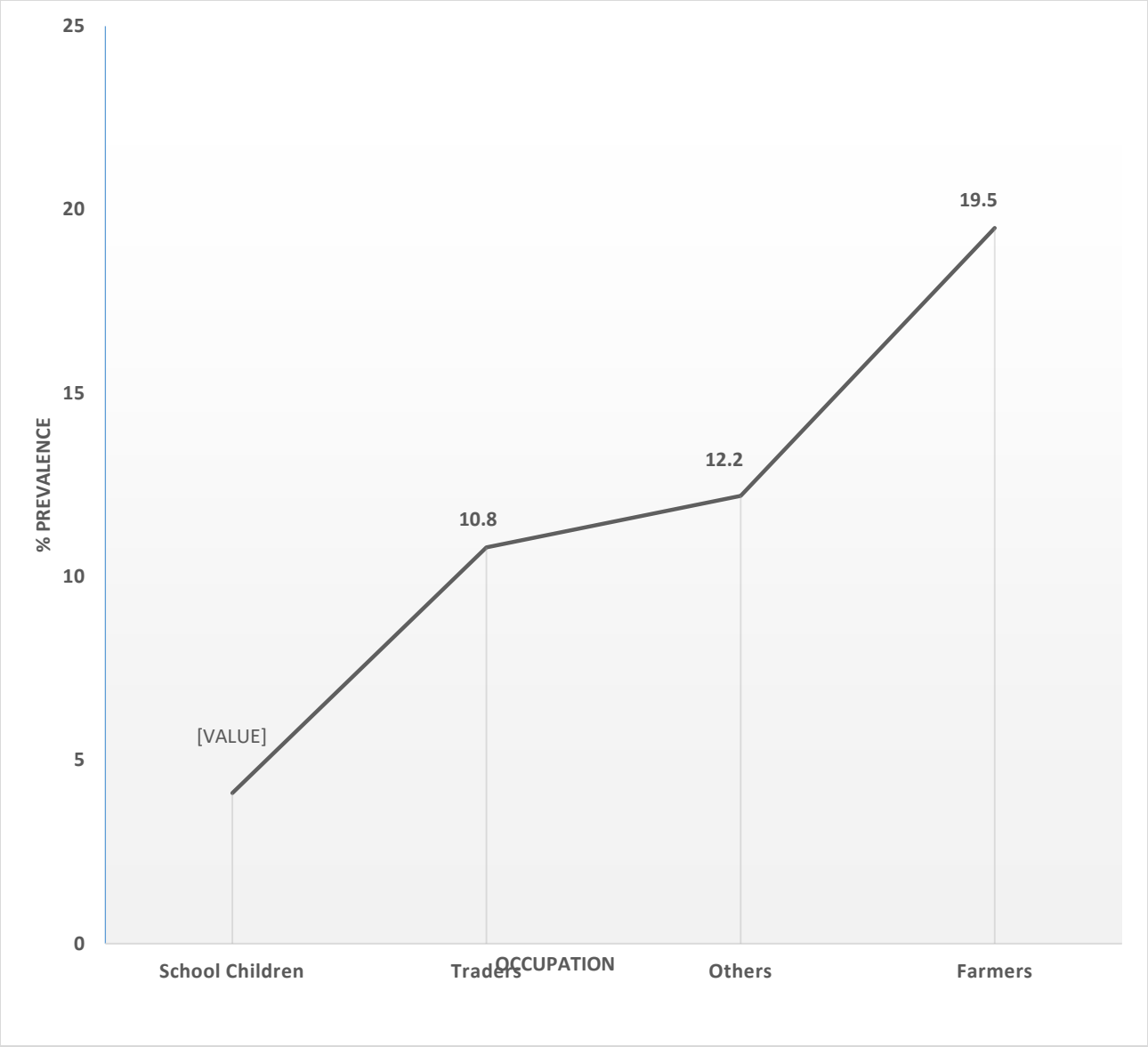

Figure 2: Prevalence of Onchocerciasis with relation to occupation in the study area.

Discussion

The advent of ivermectin for the treatment of onchocerciasis and its sustainability for large scale application has been a major break-through against onchocercal skin diseases.. The results of this study have shown that the epidemiological profile has changed to hypo endemicity status. The five communities surveyed in the middle Imo River Basin had prevalence with one or two clinical features. Umulolo and Amuro communities located close to River Lolo and Ibii had highest manifestations (15.4% and 13.1%) while other farming communities (Ihube, Aku and Amano) which resides >5KM away had varied prevalences. These Rivers provide adequate breeding sites for black flies that have the capacity to bite 60-100 KM from these sites or windblown 300-500 KM away (Emuka et al 2004). Lolo and Ibii Rivers are tributaries of Imo River which serve these communities and may account for the prevalence (Akogun and Onwuliri 1991). The varied percentage reduction in these communities may be due to the difference in treatment coverage pattern in the River Basin. The relationship between ivermectin community coverage and community morbidity reduction was evidence in rapid epidemiological assessment (REA) results. Remarkable reduction on the common onchocerciasis symptoms were identified; nodules (5.9%), poor/ impaired vision (3.5%), itching (8.0%), leopard skin (12.2%) among others. Similar to previous studies (Ezigbo et al 2013) these indicators (nodule and leopard skin) showed that prevalence increased with age and males had higher prevalence than females. Nodular rates in the five communities ranged from 2.5% in Ihube to 8.7% in Amuro with overall rate of 5.9%. Leopard skin ranged from 7.3% in Amuro to 21.3% in Amano with overall rate of 12.2%. The nodule rate shows a decrease from the >20% nodules rate specified for definite CDTI area (Noma et al 2002) which indicated that annual ivermectin treatment is effective. The reported claim by a participant that his nodule size has reduced after several annual treatments provides support to the questionnaire and clinical studies elsewhere (Ukaga et al 2001; Emukah et al 2004). The observation on leopard skin among older age (>20 years) and the absence among younger age group (< 20 years) support the popular consensus that the symptom is a long standing manifestation induced by degenerating microfilariae, a very important diagnostic tool in the communities (Pajiah and Eneanya 2019).

The continued bulk of infection on the middle and elderly people remains significant and singled out these working groups (most active and productivity farming age) as the most at risk.

Occupational (farming, fishing, animal rearing /hunting etc) or residential exposure could be attributed to this observation. The infection reported among age group 5-10 (children) may be due to early contact with infective black flies bites by their visits to breeding sites or learning under trees inside school premises which is a common habit among the schools especially during hot weather. Three factors; length of time spent near river or work (women hardly exceed 3:00 pm while men stays till 6:00pm), culture which permit men to fend for their families while women give helping hands (men are full time farmers, fishermen, hunters etc while women combine farming with trading or other indoor activities) and dressing pattern (women are traditionally attired in dressing that cover them than men). These could explain the observed difference between males and females prevalence rates.

Winnen et al (2002) had posited that the efficacy of ivermectin in controlling onchocerciasis burden of any community depends on the consistency of the treatment regimen. Somewhere in Ghana (Osei-Atweneboawa et al 2007) demonstrated that skin microfilaria repopulation commenced in 12-90% of patients studied in various communities. The absence of complete clearance of onchocercal skin disease may be linked to intervals between treatment beyond 90 days which may allow the effective transmission of the parasite by the black fly vectors. These study areas also shared common boundaries with endemic areas of Abia State, Hence an obstacle to 'stop MDA' decision. We argue that associated operations research should be undertaken to allow data from the same samples and age groups to help stop MDA by technical committees

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