



### EVALUATION OF THE IMPACT OF IVERMECTIN ON THE PREVALENCE OF MICROFILARIA AFTER 20 YEARS IVERMECTIN DISTRIBUTION IN SOME LOCAL GOVERNMENT AREAS OF ADAMAWA STATE NIGERIA

## \*Pukuma M. S., Lucky D., Qadeer M.A.

Department of Zoology, Modibbo Adama University, Yola, Adamawa State, Nigeria

\*Corresponding authors' email: pukumam2000@mau.edu.ng

### ABSTRACT

The attempt to control Onchocerciasis through the distribution of Ivermectin in Adamawa state has been ongoing for the past 20 years The current study assessed the impact of Ivermectin drugs on the prevalence of microfilaria. Eight (8) communities were selected in Four LGAs, Tongo, Song, Yola South and Hong for the study. The prevalence of microfilaria was determined using skin snip. Out of 396 Participants whose skin snip was collected only 6(2%) tested positive. The results obtained showed prevalence of microfilarial as follows; Kwapre (2%), Kukta (4%), Bolki (3%) and Ganzamanu (3%). Whereas Shashau, Dalasum, Bando and Bantaje communities had zero (0%) prevalence. Microfilaria prevalence in relation to gender was significant (P>0.05). Males had higher infection (2.0%) compared to female (1.0%). The microfilaria prevalence in these communities in 1989 was between 40-61%, compared to the current 2% in 2019 in the same selected communities. In addition, clinical signs in 1989 showed nodules 3%, Skin Disfiguration 3%, Blindness 2% while result obtained in 2019 showed Nodule 0.4%, Skin disfiguration 1% and blindness none (0.0%). In 1989 Bolki (8%) and Ganzamanu (4%) had the highest prevalence of microfilaria, but much lower in the current study 3% and 1% respectively. The results showed very low endemicity of the disease as a result of over 2 decades of Mass Drug Administration of Ivermectin in the LGAs. This implies the continuous distribution of the drug was achieved.

Keywords: Microfilaria, Prevalence, Transmission, Ivermectin, Onchocerciasis

### INTRODUCTION

Human infection with the filarial parasite Onchocerca volvulus which is the causative agent of Onchocerciasis, also known as 'river blindness, one of the Neglected Tropical Diseases (NTDs) of public health significance in Nigeria (Crump, 2012). About 40% of the global population are at risk of infection. It is the world's second-leading infectious cause of blindness after glacoma (CDC,2020, WHO, 1995). Over 99% of all cases of Onchocerciasis and Onchocercalrelated blindness are found in Africa; with Nigeria having the greatest burden of the disease. Nigeria has about 50 million persons in over 40,000 communities at risk. The disease occurs in 35 countries: 31 in Africa, 3 in Latin America and Yemen (WHO, 2016). The transmission from person to person is due to the bite of infected female black flies. Adult filarial worms reproduce and live in skin nodules of the human body for a long period, even for more than fifteen years (Mitra and Mawson, 2017). Black flies of Simulium species, especially, Simulium damnosum, is the vector and reservoir for onchocercal microfilaria (WHO, 2016). Infection with microfilarial worm leads to skin disease and anatomical impairment, which includes, dermatitis, pruritus or itching, depigmentation of the skin or leopard skin, onchocercomata, hanging groin, and temporary vision loss leading to blindness (Ranganathan, 2012). Evidence showed that more than 120 million people are at risk of Onchocerciasis infection in the Africa region, of which 26 million people are infected and over 265,000 people are blind. People who live near river banks were more vulnerable to Onchocerciasis infection (Lagatie et al., 2016). As a preventive measures against the diseases the then Gongola State (now Adamawa State) lunched the Community Directed Treatment with Ivermectin (CDTI) in 1992 which was an initiative of the African Programme on Onchocerciasis Control. Residents in various communities were administered Ivermectin drugs as prophylactic to prevent the transmission

of the parasite. Onchocerciasis control and elimination through community-directed treatment with Ivermectin have been on going in the study area for the past twenty years and it has recorded treatment coverage of 65% and above in the endemic Local Government Areas (LGAs). Hence the objective of this study was to assess and compare the microfilaria prevalence after 20 years of mass drug administration with Ivermectin in the selected LGAs of Adamawa State and the current status of microfilaria among inhabitants of these communities.

### MATERIALS AND METHODS

#### **Study Area**

The study was conducted in Adamawa State, North-Eastern Nigeria, with its capital in Yola. It lies between Latitude 9°19'60.00"N and Longitude 12°29'59.99"E. It has a landmass of about 36,917 square kilometres and a projected population of 4.260.744 (Adebavo et al., 2020). It is bordered by the states of Borno to the Northwest, Gombe State to the west and Taraba State to the Southwest. Its eastern border form the national eastern border with Cameroon. It is made up of 21 Local Government Areas (LGAs) of which 17 LGAs had recorded cases of Onchocerciasis. The state has a tropical climate, marked by dry and rainy seasons. The rainy season commences from May and ends in the middle or late October. While the dry season starts in late October and ends in late April. Maximum temperature in Yola can reach 40°C, around April, while minimum temperature could be as low as 18 -.30 °C between December and early January. The major occupation of the people is farming, crops grown include cotton, groundnuts, maize, yam, cassava, guinea corn, millet and rice. Communities living on the banks of the rivers engage in fishing and irrigation. While others rear animals. (Adebayo and Tukur, 1999). The distribution of Ivermectin commenced in 1992 as a pilot project with the assistance of AFRICARE an American NGO, in nine (9) LGAs, and was later expanded to 17 LGAs. In 1999 a new approach called Community Directed Treatment with Ivermectin was developed making the community a major partner in implementing the CDTI. This later metamorphose into the Mass Drug Administration (MDA). The Onchocerciasis control unit under the Ministry of Health is saddled with the responsibility of implementing and supervising the distribution of the drug Ivermectin in the state.

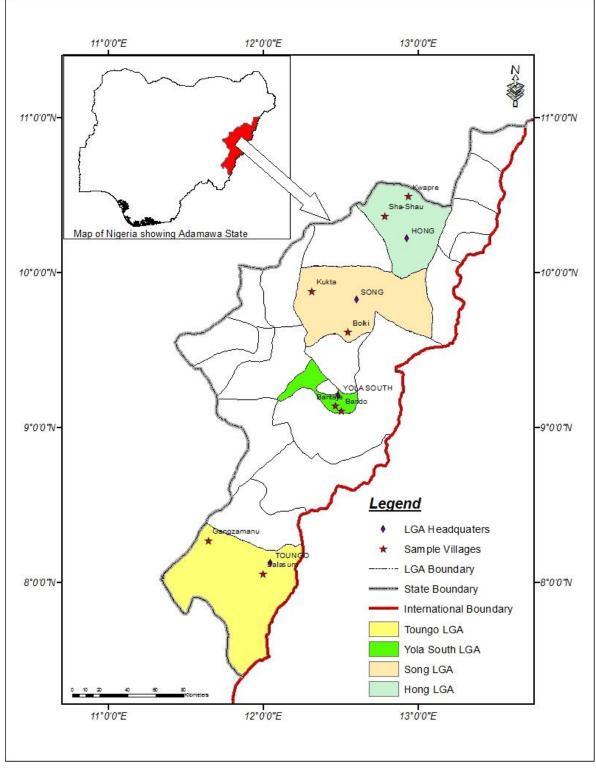


Figure 1: Map of Adamawa State Showing the Local Government Area and Sampling Communities

#### **Research Design**

A purposive study was conducted between December 2018 to December 2019 in four (4) Local Government Areas of Adamawa State. The election criteria of the LGAs and communities requires that the distribution of Ivermectin has been on going and there was records of previous baseline survey conducted in 1989. Only LGAs where treatment with Ivermectin has being on going for the past years were selected for the study. In addition only persons that are resident in the selected communities five years and above were used for the study. The LGAs selected were Toungo, Yola South, Song and Hong. In each of the LGAs, two (2) communities were selected as the sentinel sites giving a total of Eight (8) Communities. The methods employed for the study was the use of skin snip and OV16 RDT. A total of one thousand three hundred and eleven (1,311) persons were tested using Ov16 RDT. While three hundred and ninety-six (396) were tested using the skin Snip test. All study subject were first examined for Onchocerciasis signs and symptoms which include, skin nodules, prurities, hanging groin etc.

# Collection, Handling and Processing of Skin Snip Specimen

A total of three hundred and ninety-six (396) skin snip were collected with the aid of 2mm corneoscleral punch and examined for microfilariae. The skin snips were taken from the shoulder and iliac crest using the standard method as described by (Chesbrough, 2006). Each snip was placed in a microtitre plate (Flat bottom, 96 wells) containing saline solution. The specimens were placed in warm normal saline in the well of a microtitre plate and allowed to stand for 30 minutes or longer and were examined for microfilariae that migrate from the tissue into the saline water. If no microfilariae were seen, the preparation was left overnight and re-examined for microfilariae. Microfilariae were observed by direct microscopy at x40 magnification after staining with Giemsa stain as described by (Arora and Arora, 2010). The presence of microfilaria in any of the skin snips confirmed the diagnosis for onchocerciasis.

### Blood Samples Collection for Onchocerciasis Rapid Diagnostic Test (Ov16)

Blood samples was collected through the use of one use disposable lancet as described by Chesbrough (2006). The finger of each participant was swabbed with alcohol and allowed to dry. The fingertip was squeezed and pricked with disposable sterile lancet. Using a capillary pipette 10 µL of blood specimen was collected and dispensed into the buffer well. The subjects were arranged in serial order corresponding with the number written on each SD Bioline IgG4 Onchocerciasis Monoplex (REF. 61FK10) (Manufactured by Standard Diagnostic, INC, South Korea Republic) cassette using a permanent marker. The kit was used according to the manufacturer's instructions.

Four (4) drops of assay diluent was immediately added vertically into the square assay diluent/buffer well on the test cassette and the time recorded. The test result was interpreted after 30 minutes. The area marked 'C' indicates the control line, while the area marked 'T' designates the test line. Result was recorded negative when one purple line appear on the control region 'C' on the result window or cassette, Two purple lines on the 'C' and 'T' in the result window indicated positive result for microfilaria. While test was considered invalid when no control 'C' in the result window or only 'T' line appeared. All invalid results were re-tested as recommended by (Chesbrough, 2006).

### **Research Ethics**

The research ethical clearance was granted by Adamawa State Ministry of Health ethical committee before the conduct of the research. Community and individual consent was obtained during the research in all the communities and individual subjects were at liberty to decline or discontinue with the study. Absolute confidentiality of the identity of study participant was observed.

#### **Data Analysis**

The data obtained was analysed using SPSS Version 22.0 and associations were determined by the use of chi-square ( $\chi^2$ ) at a confidence level of P=0.05 and t-test. Results analysed are presented in tables and discussed as appropriate. The outcome of the present study was compared to previous base line survey conducted in the same community.

### **RESULTS AND DISCUSSION**

# Microfilarial Prevalence of *O. volvulus* in the selected sentinile Communities.

Out of the 396 persons that were tested using skin snip for microfilaria only 6(2%) tested positive for the presence of microfilaria. Kwapere in Hong LGA and Kukta in Song LGA each had 2 persons that tested positive for the presence of microfilaria. This was followed by Bolki and Gangzamanu each with one (1) person infected. However, the remaining communities tested negative for microfilaria (Table1).

## Microfilarial prevalence in Relation to Gender

Table 2 showed microfilaria prevalence in relation to gender in sentinel sites, males were more infected than female.Chi  $\chi^2$  analysis showed significant association between infection and gender P <0.05. Out of 230(58%) males examined for microfilaria 4(2%) tested positive for microfilarial, whereas of the 166(42%) females that were tested for microfilaria, 2(1%) tested positive for microfilaria. Giving a total prevalence in both males and females as 6(2%).

# Microfilaria prevalence in Relation to Age in the communities using skin snip.

The study showed that 2 persons tested positive for microfilaria among those in 21-40 years of age. While 3 persons tested positive for microfilaria among those in ages 41-60 years, and only one person among those above 60 years tested positive for microfilaria.(Table 3).

# Changes in Microfilaria Prevalence between 1989 and 2019 in Sentinel Communities

A review of previous prevalence records in 1989 showed that in the same selected sentinel communities the prevalence of microfilaria was between 40- 61% compared to the study in 2019 which showed a prevalence of 2% (Table 4). In all the communities in 1989 prevalence of microfilaria was above 40% .Compared to the present study where in the same communities prevalence is between 1% and 2% .While some had zero prevalence (Table 4).

### Changes in Clinical Signs of Onchocerciasis in Sentinel Communities between 1989 and 2019 in the Selected LGAs.

In all the Eight (8) sentinel communities' previous baseline survey in 1989 revealed that the common clinical signs of Onchocerciasis were, nodule on the body (3%), skin disfiguration (30%), and blindness (2%). Whereas the clinical signs in the current study conducted in 2019 showed, 0.4% nodule, 1% Skin disfiguration and 0% blindness (Table 5).

### Prevalence of Onchocerciasis among Community Members using OV16 RDT

Out of 1,311 samples examined for Onchocerciasis using OV16RDT 81(6%) tested positive for microfilaria. Prevalence in relation to sentinel communities showed Shashau 10(6%), Kwapre 13(8%), Bolki 15(9%), Kukta 9(5%), In Dalasum 11(7%), Gangzamanu 6(4%), Bantaje 9(5%) and Bando 8(5%).Prevalence was highest in Bolki 9% and lowest in Gangzamanu 4% (Table 6)

#### Discussion

Population-based treatment with Ivermectin known as mass drug administration is the current core strategy to eliminate onchocerciasis, with a minimum requirement of 80% therapeutic coverage. At least 12-15 years of annual treatment are required in hyper and meso endemic areas to eliminate transmission, corresponding to the lifespan of the adult Onchocerca volvulus (WHO 2016). The study showed decline in prevalence of microfilaria over the years to the present 2% prevalence of microfilaria. This demonstrates a transition from hyper endemic to hypo-endemicity following years of continuous treatment with Ivermectin in these sentinel communities. The level of endemicity has fallen below 7%, the threshold recommended APOC (2006). The low prevalence of onchocercal microfilaredermia in the study area despite the presence of abundant fast-flowing rivers, streams which serve as the breeding sites for the black flies, could be attributed to the continuous use of Mass drug administration with ivermectin leading to the disruption in the transmission. A review of records of Adamawa State Onchocerciasis control units showed that all the selected LGAs have been reporting >65% therapeutic coverage and 100% geographical coverage for over 15 years with Ivermectin distribution. Hence the 2% prevalence of infection observed could be attributed to disruption of transmission This is an indication that the sustained administration of Ivermectin has interrupted the transmission of the microfilaria within these communities. Hence the low prevalence of microfilaria recorded compared to what was recorded in the past. This findings was similar to that of Henri et al.(2011) who recorded 3% in Cameroun but differs from that of Bedili et al. (2019) and Keneth et al.( 2019). Who recorded in Ghana (13.2%), Ethiopia (6.3%) respectively.

Microfilaria prevalence in relation to gender in the selected area was not statistically significant (P>0.05). Microfilaria prevalence rate was slightly higher among the male subjects than the females. The microfilaria (skin snip) showed that 4% of males were positive for microfilaria while 1% of females were positive for microfilaria. This implies that Males were more likely to be infected with the microfilaria parasite compared to the females. The males engaged more in socioeconomic activities such as fishing and farming which is the predominant occupation in the selected communities. This predisposes them more to the likelihood of being bitten by the female infected blackfly. Unlike the females that were mostly indoors and even when they had to go out they do cover their body which is a requirement and part of the clothing required of women when they go out. Hence they are less exposed to being bitten by blackflies. The high prevalence of microfilaria infection in men could also be attributed the travelling habits which puts the male at an increased risk of being bitten by infected black flies. This findings was in tandem with the reports of Dana et al.(2015); Mu, (2015); Hermandez-Gonzalex et al. (2016) and Kanga et al. (2016).. That males are frequently involved in outdoor activities and have `more probability to be exposed to black fly bites than females. This finding was similar to that of Adeyeba and Adegoke, (2002); Wogu and Okaka, (2008); Afolabi *et al.*(2014)

Microfilaria (mf) prevalence in relation to age of the subject was statistically not significant. However, the age groups 21–40 and 41–60 years had significantly higher mf prevalence. Those within age groups 5-20 years fall within the period that marks the commencement of the distribution of Ivermectin distribution. Hence over time the transmission has being interrupted through the continuous distribution of Ivermectin. This explains why microfilaria was not observed among this age groups.

Individuals in the age groups of 41-60 and >60 years were more likely to develop the infection due to prolonged period of exposure. Compared to subjects in the age group of 5-20 years. The findings agrees with the studies conducted in the Jimma zone, West Welega zone, Nigeria, Equatorial Guinea, and Senegal where age was independently associated with onchocerciasis infection (Kamalu and Uwakpe, 2014; Dana et al., 2015). The result of this study however differs from the report of Umeh et al. (2010) who reported a prevalence of 18.6%, 18.6% and 20.7 % prevalence of microfilaria among age group 15-24 years in Cross River, Taraba and Kogi respectively. These differences might be a result of climatic differences between the forest and the savannah zones. In the northern part of Nigeria which is characterized by savannah vegetation, the younger age groups are engaged more in farming activities than their older age groups counterparts while in the southern part of the country the case is reverse.

Changes in the prevalence of Microfilaria between the baseline surveys in 1989 with prevalence of (40-61%) compared to the current study conducted in 2019 with prevalence (2%) in all the selected communities. This is an indication that there is a shift in the prevalence status of microfilaria from being hyper endemic communities to hypo endemic status. (ADSMOH, 1989 Unpublished data). There was a drastic decrease in microfilarial prevalence between 1989 and 2019. This findings was similar to Ivermectin impact studies conducted elsewhere which showed a great reduction in microfilaria prevalence, and physical manifestation as well as parasitaemia (Tekle et al., 2012; Evans et al., 2014; Kamga et al., 2016). Microfilaria prevalence recorded in 1989 was 61% compared to the present 2% in 2019. The difference could be attributed to the introduction and sustained use of mass drug distribution with Ivermectin.

The prevalence 2% infection in 2019 in the selected communities suggests that the community is now hypoendemic. The low prevalence of onchocercal microfilaredermia despite the presence of black flies and an atmosphere that favours the interaction between humans and biting flies can be attributed to continuous annual distribution of Ivermectin among community members. Other reasons for low microfilaria prevalence could be attributed to the continuous use of agricultural pesticides and herbicides which has also impacted on the vector population. Thereby limiting human vector contact or destruction of the ecology of blackflies.in these communities. t-test showed that there was statistically significant difference in mf in 1989 and 2019 (P<0.005). Residential distance from breeding sites was also observed to be a risk factor for infection. Individuals who resides close to breeding sites are more likely to be infected compared to those who resided at greater distance from the breeding river. Njim and Aminde, (2017) reported that individuals who resides at less than 2Km from the breeding river may be more exposed to black fly bites as compared to their counterparts who farther away.

Changes in clinical signs between 1989 and 2019 of onchocerciasis were statistically significant (P<0.05). Based on the baseline data obtained in 1989 from Adamawa State Ministry of Health (ADSMOH, 1989 Unpublished data) in the selected communities, nodules were 3%, skin disfiguration i.e either lizard skin or leopard skin 30%, blindness 2% while in 2019 the clinical signs nodules 0.4%, skin disfiguration 1% and blindness 0%. The common skin manifestations, of onchocerciasis observed were, pruritis (itching), leopard skin or lizard skin, and nodules. Ivermectin administration has greatly reduced physical symptoms from 30% in 1989 to 1% in 2019. Several studies on the impact of Ivermectin had also recorded a reduction in skin manifestations after years of taking Ivermectin (Turner et al., 2013; Dunn et al., 2015). These cutaneous nodules were concentrated mainly around and below the waist which is typical of the African form of onchocerciasis. All individuals with nodules had a history of ivermectin treatment.

The majority of people with microfilaredermia, and nodules were aged above >60 years. This suggests that nodule formation is a characteristic of chronic infections and can be linked to intensity and level of exposure (Little et al., 2004). The study indicated that the overall prevalence of onchocerciasis infection in the eight (8) Sentinel Communities across the 4 LGAs after over 20 years of mass distribution of Ivermectin was 2%. The finding was similar to studies conducted in southwest Ethiopia, Cameroon, Senegal, and Equatorial Guinea (Hermandez-Gonzalex et al. (2016); Njim and Aminde (2017). The study however differ from the studies carried out in Jimma zone and West Welega zone and in Northern and Central Togo which showed a prevalence of 22.5% and 74.8%, 49% respectively (Dori et al., 2012; Dana et al., 2015). This difference might be attributed to the difference in coverage of community-with Ivermectin treatment. The World Health Organisation in collaboration with the African Program for Onchocerciasis Control (APOC) recommended repeated rounds of mass drug administration (MDA) with Ivermectin to interrupt transmission of the nematode worm that causes onchocerciasis (WHO, 2014)

The use of OV16 which is a rapid diagnostic test (RDT) with high sensitivity and specificity also showed a very low prevalence of 6%. This is further prove of interruption of transmission in these communities. Since both skin snip test and Ov16 RDT test indicate low prevalence of infection. Path (2016) reported that Ov16 RDT is a promising field friendly tool that could be applied to a large population for mapping and even post-MDA surveillance of Onchocerciasis.

## CONCLUSION

The findings suggest that the sustained administration of Ivermectin to inhabitants of the study communities has interrupted the transmission of microfilaria. This explains why the prevalence was very low and none of those under 20 years of age tested positive for the presence of microfilaria. Hence there is the need for adequate funding of the MDA with Ivermectin to enhance total coverage of the state. This will in the long run leads to the elimination of the disease in all the LGAs of the state where the disease is considered endemic. Therefore community drug administration with Ivermectin should be sustained for years in order to eliminate the parasite and risk of infection.

### ACKNOWLEDGEMENTS

The authors are grateful to Adamawa State Ministry of Health, Neglected Tropical Diseases Unit for their support in giving out previous baseline survey information for comparison with the current studies in the sentinel sites. We are also grateful to the Studied Primary Health Care Authorities for their support especially the Executive Secretaries and the Local Neglected Tropical Diseases Officers (LNTDs) who are the Neglected Tropical Diseases Coordinators of the LGAs.

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Age Group (Yea	ars)	No. Examined Using Skin Snip	No. +ve (%)	
5-20		39	(0.0)	
21-40		96	2(2.0)	
41-60		147	3(2.0)	
>60		105	1(1)	
Total		387	6(2)	
LGA	Community	No. tested		No. (%) Oncho
				+ve
Hong	Shashau	69		0 (0)
	Kwapre	49		2(4)
Song	Bolki	40		1(3)
-	Kukta	52		2(4)
Toungo	Dalasum	40		0(0)
	Gangzamanu	53		1(2)
Yola-South	Bantage	38		0(0)
	Bando	56		0(0)
Total		396 (100%)		6 (2%)

# Table 1: Prevalence of Microfilarial of *O. volvulus* in the selected LGAs based on Community and age

### Table 2: Microfilaria Prevalence in relation to Gender.

Gender	No. Examined by Skin Snip	No. Positive (%)
Male	223	4(2.0)
Female	164	2(1.0)
Total	387	6(2.0)

## Table 3: Prevalence of microfilaria in relation to age

Age Group (Years)	No. Examined Using Skin Snip	No. +ve(%)
5-20	39	(0.0)
21-40	96	2(2.0)
41-60	147	3(2.0)
>60	105	1(1)
Total	387	6(2)

## Table 4: Changes in the Prevalence of Microfilarial between 1989 and 2019

LGA	Community	No. examined in 1989	No. +ve (%)	No. examined in 2019	No. +ve (%)
Hong	Shashau	115	76(66)	69	0(0)
	Kwapre	127	98(77)	49	2(3)
Song	Bolki	85	43(50)	40	1(3)
-	Kukta	68	36(53)	52	2(4)
Toungo	Dalasum	50	30(60)	40	0(0)
-	Gangzamanu	153	91(59)	53	1(2)
Yola-South	Bantage	39	16(41)	38	0(0)
	Bando	78	44(56)	46	0(0)
Total		715	434(61)	387	6(2)

t=28.027 df=355 sig=0.00

# Table 5: Changes in Clinical Signs of Onchocerciasis between 1989 and 2019

Community	No examined in 1989	Nodule (%)	Skin Disfiguration (%)	Blind (%)	No. examined in 2019	Nodule (%)	Skin Dis. (%)	Blind
Shashau	32	1	8	0	166	0	1	0
Kwapre	90	23	31	0	162	2	1	0
Bolki	93	32	43	0	171	1	1	0
Kukta	62	18	21	0	165	0	1	0
Dalasum	15	8	6	5	155	1	1	0
Gangzamanu	57	21	10	2	164	0	2	0
Bantage	25	10	2	0	166	1	0	0
Bando	47	24	6	0	162	1	1	0
Total	421	137(3)	127(30)	7(2)	1311	6(0.4)	8(1)	0

LGA	Community	No. tested	No. (%) Oncho +ve
Hong	Shashau	166	10(6)
	Kwapre	162	13(8)
Song	Bolki	171	15(9)
	Kukta	165	9(5)
Toungo	Dalasum	155	11(7)
	Gangzamanu	164	6(4)
Yola-South	Bantage	166	9(5)
	Bando	162	8(5)
Total		1311	81(6)

Table 6: Seroprevalalence of Onchocerciasis in the Selected Communities Using OV16



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