Integrated Transmission Assessment Surveys (iTAS) of Lymphatic Filariasis and Onchocerciasis in Cross River, Taraba and Yobe States Nigeria.

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Abstract

Background: Integrated Transmission Assessment Surveys (iTAS) has been recommended for evaluation of transmission of both lymphatic filariasis and onchocerciasis, as the prevalence of both diseases move toward their respective elimination targets in Nigeria. Therefore, iTAS was conducted between May and December 2017 in five local government areas also known as implementing units (IU) in Cross River, Taraba and Yobe States of Nigeria.

Methods: TAS comprises of two phases: The Pre-iTAS and the iTAS. Three states (Cross-Rivers, Taraba and Yobe) comprising of 5 LGAs and 20 communities that have completed 5 rounds of combined treatment with ivermectin and albendazole for LF and 12 rounds of ivermectin were selected for the study. For the Pre-iTAS, Filariasis Test Strip (FTS) and Biplex rapid diagnostic test (Ov16/Wb123 RDT) were used to test 2000 children from age 5-9 for onchocerciasis and 300 persons aged 10 years and above for LF. For the iTAS, only LGAs where all sampled communities during the Pre-iTAS were with less than 2% antigenemia prevalence for LF was selected.

Results: Four out of the five LGAs passed the pre-iTAS except Ikom LGA which had an antigenemia prevalence of more than 2%. A total of 11531 school-aged children were tested for LF and onchocerciasis across the four LGAs. Bade tested 2,873, Bekwara 2,622, Gashaka 3,026 and Karim Lamido 3,010 from 148 schools. For LF prevalence, zero prevalence was recorded for Bade and Karim Lamido while Bekwara and Gashaka recorded 0.19% and 0.23% respectively using FTS. The same was not recorded using Ov16/Wb123 biplex as Bade, Bekwara, Gashaka and Karim Lamido recorded 0.03%, 0.53%, 0.43% and 0.03% respectively. For onchocerciasis prevalence, Bade and Karim Lamido recorded zero prevalence while Bekwara, Gashaka recorded 3.09% and 1.75% respectively.

Conclusion: This study has provided additional information on the current burden of onchocerciasis and lymphatic filariasis (LF) in the 4 IUs sampled where MAM for both infections has been ongoing for years. The study identifies that LF-MAM can be safely stopped in all 4 of the studied IUs. However, MAM for onchocerciasis needs to continue, although this may pose a challenge for LF surveillance. Based on the preliminary results from all four sites, this study has fulfilled the primary objective of determining the programmatic feasibility of an integrated transmission assessment survey (iTAS), to be used to simultaneously assess onchocerciasis and LF prevalence in areas co-endemic for the two infections that have completed the recommended treatment for one or both infections, and to make decisions on how to proceed.

Background

Lymphatic filariasis (LF) and onchocerciasis are infections caused by microscopic nematodes *Wuchereria bancrofti* and *Onchocerca volvulus* transmitted respectively by mosquitoes and black flies of the genus *Simulium* (1). LF is found to be endemic in 73 countries with a projected 1.1 billion individuals at risk while, at least, 169 million people are estimated to be at risk of infection with onchocerciasis in 31 countries in Africa require mass administration of medicine (MAM) (2).

Infection with LF leads to blockages of the lymphatic system, which result in swellings of limbs and genitals (lymphedema, elephantiasis, and hydrocele in men), and painful recurrent bacterial infections. The control approach in Africa is MAM (or mass drug administration - MDA) of single-dose combination therapy with albendazole and ivermectin or diethylcarbamazine (3). When given for an estimated period of five to six years with an annual minimum therapeutic coverage of 65%, MAM can interrupt transmission of *W. bancrofti* in a population. A total of 583 local government areas (LGAs) are endemic for LF in Nigeria, with 567 LGAs conducting at least one MAM round and 30 LGAs in post-MAM surveillance. However, there are 16 LGAs yet to start MAM due to funding challenges (4).

Onchocerciasis, on the other hand, causes intense skin disease and may eventually result in blindness. Control and elimination efforts focus on MAM using ivermectin, with sporadic vector control where conditions are favourable (4, 5). Nigeria has the highest burden of onchocerciasis globally with about 50 million persons in over 40,000 communities at risk of infection, accounting for about 40% of the global population at risk. In Nigeria, a total of 480 LGAs are targeted for the elimination of onchocerciasis transmission with over 85% geographic coverage currently being achieved (6).

The African Programme for Onchocerciasis Control (APOC), which replaced the Onchocerciasis Control Programme (OCP), supported the control of onchocerciasis through annual or six-monthly ivermectin-based MAM as well as vector control in selected foci (7). When treatment occurs at least once a year for about 15 years or more, it is possible to interrupt transmission (8). APOC goals transitioned from control to elimination of onchocerciasis after a study, which took place in Mali and Senegal, and published in 2009 provided the first evidence that the elimination of onchocerciasis was feasible in Africa with ivermectin distribution alone (9).

National LF programs focus on a series of critical steps following standardized WHO protocols: i) mapping to determine endemicity, ii) implementation of MAM with a minimum of 65% treatment coverage once yearly for at least five years in endemic areas, iii) a survey to determine whether prevalence is low enough for MAM to stop, iv) post-MAM surveillance, and v) validation of elimination of LF as a public health problem (10).

In most communities in Nigeria, there is substantial overlap between LF and onchocerciasis. Both diseases overlap in 366 LGAs in Nigeria. In those co-endemic LGAs, ivermectin is commonly distributed with albendazole during mass administration of medicines campaigns. Filariasis programs in countries have typically functioned vertically and, until a few years ago in Nigeria, the decision to start MAM was often made for each disease independently without taking into account the endemicity of the other disease.

As the country begins to reach a sufficient number of effective rounds of MAM, a decision needs to be made on whether the implementation unit (IU) can safely stop MAM for one infection without compromising the success of both elimination programs. The IU in the country context is the local government areas LGAs. An integrated assessment for both filariasis could therefore be a cost-effective tool to make joint stop decisions for lymphatic filariasis and onchocerciasis. One integrated survey would assess the serological prevalence of both diseases by targeting young children as indicators of recent exposure to the two parasites.

Based on this background, the study set out to determine the programmatic feasibility of an integrated LF transmission assessment survey (iTAS) and onchocerciasis epidemiological evaluation for simultaneous assessment of both diseases in co-endemic areas, which have completed the recommended period of treatment.

Methods

Study design, selection of study sites and sampling strategies

The study was divided into two phases: The Pre-iTAS and the main iTAS. The initial phase (Pre-iTAS) was subjected to the WHO's eligibility criteria for conducting LF Transmission Assessment Surveys (TAS) which qualifies an implementing unit with less than 2% antigenemia prevalence to pass TAS (11, 3).

Pre-iTAS

A total of 5 LGAs (Implementation Units –IUs) in 3 States were selected for the Pre-iTAS, namely Ikom and Bekwara LGAs in Cross River State, Gashaka and Karim-Lamido LGAs in Taraba State, and Bade LGA in Yobe State. The selected LGAs had successfully conducted a minimum of 5 effective rounds of ivermectin and albendazole combined treatment for LF, as well as more than 12 effective rounds of ivermectin treatment alone for onchocerciasis. In each IU, two sites were selected for Pre-iTAS which focused on LF. The two sites comprised of one LF sentinel site with a high baseline prevalence for LF and one onchocerciasis sentinel site founded on a high risk of onchocerciasis infection at baseline REMO. Each of the onchocerciasis sentinel sites served as a spot-check site for either infection.

To assess interruption for LF, a total of 300 persons aged 10 years and above were selected by convenience sampling in the 2 sentinel sites selected in the IUs (one LF sentinel site and one spot-check site). They were tested for both LF and onchocerciasis using FTS and Biplex RDT (Ov16/Wb123).

For the onchocerciasis assessment, 4 communities were selected in each IU which included the LF sentinel site and spot-check site as above, as well as 2 additional first-line villages. A total of 100 children aged 5 – 9 years were sampled in each of the 4 communities through convenience sampling and tested for both LF and onchocerciasis using FTS and Biplex RDT (Ov16/Wb123).

Table 1: Communities selected for Pre-iTAS in the IUs/LGAs

State	LGA (IU)	Communities
Cross River	Bekwara	Afrike
		Itekpa
		Atibulum
		NyanaOlim
	Ikom	Agbaragba
		Balep
		Etikpe
		Ukpochi
Taraba	Gashaka	Gashaka
		Mayo Selbe
		Nybar
		Shinbon
	Karim Lamido	Bandawa
		Gwomu
		Kodei
		Panya
Yobe	Bade	Dagona
		Gafiwa
		Gwio Kura
		Tagali

iTAS

The qualification for TAS was that all the selected sites in an IU achieve less than 2% antigenemia prevalence for LF in each of the five LGAs. Using random cluster sampling, a minimum of 30 schools were selected from each LGA from a sampling frame of all the primary schools in the LGA. A total of 2,500 to 2,700 participants aged 5 - 9 years were included in each LGA. Target grades chose to represent the majority of pupils aged 5-9 were Grades 1 - 3 for public schools and 1 - 4 for private schools Table 2.

Table 2: Schools selected for iTAS in the IUs/LGAs

State	LGA (IU)	Total number of schools	Number of persons planned to be tested
Cross River	Bekwarra	34	2,590
Taraba	Gashaka	30	2,500
	Karim Lamido	52	2,700
Yobe	Bade	30	2,700

Figures 1 – 4 show the location of the selected schools in the three States.

Inclusion Criteria

From the records, communities with 12-24 treatment rounds for onchocerciasis and 5–7 treatment rounds for LF were selected to participate in the study in Cross River, Taraba and Yobe State, Nigeria. All pupils in the target grades in the selected schools were enrolled for the survey using simple random selection.

Diagnostic testing

Participants were tested using SD BIOLINE Oncho/LF IgG4 Biplex RDT (Ov16 and Wb123) and the Filariasis Test Strip (FTS). The Biplex is a rapid test that detects antibodies against both the *O. volvulus* Ov16 and the *W. bancrofti* Wb123 antigens. The FTS is an antigen test currently recommended by WHO for use for LF tests.

Data Analysis

Frequencies and 95% confidence interval (CI) for LF antigenemia, Wb123 and Ov16 positivity were determined using SPSS 21 (IBM Corp, Armonk, NY, USA). The 95% CI of the prevalence or frequencies was calculated by using a binomial confidence interval exact test calculator.

Results

Pre-iTAS:

Demographic characteristics of study participants during Pre-ITAS

A total of 5,312 participants from 20 communities were enrolled on the study. Of the total enrolled, (98% 5,244) persons were tested across the 5 LGAs (Table 3). The study demographics showed that 2,829 (53.95%) of the study participants were female and 2,415 (46.05%) were male. Of the number tested, 2,101 (40.06%) were children aged 5 - 9 years.

Table 3: Distribution of study participants by age and sex

S/N	State	LGA	Name of Community	No. sampled (5 yrs <10yrs)			No. Sampled (≥10 yrs)			Total sampled
				M	F	Total	M	F	Total	
1	Yobe	Bade	Dagona	54	46	100	99	211	310	410
2			Gafiwa	58	58	116	0	0	0	116
3			Tagali	54	51	105	153	158	311	416
4			Gwio Kura	47	58	105	0	0	0	105
Sub Total				*213*	*213*	*426*	*252*	*369*	*621*	*1047*
5	Cross River	Ikom	Ukpochi	47	55	102	0	0	0	102
6			Agbaragba	63	38	101	0	0	0	101
7			Etikpe	57	53	110	144	154	298	408
8			Balep	56	60	116	166	139	305	421
Sub Total				*223*	*206*	*429*	*310*	*293*	*603*	*1032*
9	Cross River	Bekwara	Nyanya-Ulim	49	52	101	0	0	0	101
10			Atibulum	49	51	100	0	0	0	100
11			Itekpa	46	55	101	73	215	288	389
12			Afrike-Okpeche	49	51	100	86	218	304	404
Sub Total				*193*	*209*	*402*	*159*	*433*	*592*	*994*
13	Taraba	Gashaka	Shinbon	29	32	61	0	0	0	61
14			Gashaka	47	46	93	0	0	0	93
15			Mayo-Selbe	115	81	196	249	102	351	547
16			Nyabar	38	32	70	160	221	381	451
Sub Total				*229*	*191*	*420*	*409*	*323*	*732*	*1152*
17	Taraba	K/Lamido	Bandawa	53	58	111	103	207	310	421
18			Panya O	51	52	103	130	165	295	398
19			Gwomu O	52	52	104	0	0	0	104
20			Kodei O	38	68	106	0	0	0	106
Sub Total				*194*	*230*	*424*	*233*	*372*	*605*	*1029*
TOTAL				1052	1049	2101	1363	1780	3,143	5,244

LF antigenemia prevalence during Pre-iTAS

A total of 5,191 valid tests was conducted using FTS. From the valid tests, an overall antigenemia prevalence of 0.5% was recorded across all the study areas. Among the LGAs, the highest antigenemia prevalence of 1% (10/1,026) was recorded in Ikom LGA in Cross River State, followed by Gashaka LGA (7/1,152) in Taraba State and Bekwarra LGA (5/1,011) in Cross River State both recording 0.6% prevalence respectively (Table 4). Among the communities surveyed, Agbaragba in Ikom LGA had the highest prevalence of 5.9% (6/101). Karim Lamido LGA recorded no positive case for LF using the FTS. In total, fourteen communities across all study areas recorded zero antigenemia positive cases for LF using the FTS.

Table 4: LF prevalence with FTS by age group

State	LGA	Name of Community	Total sampled	Total valid FTS	FTS +ve 5 - <10 yrs	FTS +ve 10 Yrs& above	Total FTS +ve
Yobe	Bade	Dagona	410	400	0	0	0
		Gafiwa	116	116	0	0	0
		Tagali	416	380	1(0.3)	2(0.5)	3(0.8)
		Gwio Kura	105	105	0	0	0
Sub Total			**1047**	**1001**	**1(0.1)**	**2(0.2)**	**3(0.3)**
Cross River	Ikom	Ukpochi	102	102	0	0	0
		Agbaragba	101	101	6(5.9)	0	6(5.9)
		Etikpe	408	405	0	0	0
		Balep	421	418	0	4(1.0)	4(1.0)
Sub Total			**1032**	**1026**	**6(0.6)**	**4(0.4)**	**10(1.0)**
Cross River	Bekwara	Nyanya-Ulim	101	101	0	0	0
		Atibulum	100	100	0	0	0
		Itekpa	407	407	2(0.5)	4(1.0)	6(1.5)
		Afrike-Okpeche	404	403	0	0	0
Sub Total			**1012**	**1011**	**2(0.2)**	**4(0.4)**	**6(0.6)**
Taraba	Gashaka	Shinbon	61	61	0	0	0
		Gashaka	93	93	0	0	0
		Mayo-Selbe	547	547	1(2.1)	2(0.4)	3(0.6)
		Nyabar	451	451	0	4(0.9)	4(0.9)
Sub Total			**1152**	**1152**	**1(0.1)**	**6(0.5)**	**7(0.6)**
Taraba	K/Lamido	Bandawa	421	395	0	0	0
		Panya O	398	396	0	0	0
		Gwomu O	104	104	0	0	0
		Kodei O	106	106	0	0	0
Sub Total			**1029**	**1001**	**0**	**0**	**0**

LF and onchocerciasis seroprevalence using SD Bioline Biplex RDT during Pre-iTAS

Using the Biplex, a total of 31 LF seropositive cases (0.01%) were detected from the valid tests in all the 20 communities visited for all ages. The highest number (19) was recorded in Bekwarra LGA in Cross River State while Bade LGA in Yobe State had zero seropositive cases. Only 2 communities had LF seropositive cases (3 each) for children less than 10 years - Agbaragba community in Ikom LGA (3.0%) and Gashaka in Taraba State (3.2%). A total of 317 onchocerciasis seropositive cases (6.02%) were detected from the valid tests using the Biplex in all the 20 communities visited for all ages. The highest number (142) was recorded in Ikom LGA, followed closely by Bekwarra LGA (126) both in Cross River State (Table 5). Bade LGA in Yobe State and Karim Lamido in Taraba State had no seropositive cases. Seven (7) communities had onchocerciasis seropositive cases by Biplex for children less than 10 years, with the highest seroprevalence of 8.2% being recorded in Shibon community in Gashaka LGA of Taraba State.

Figures 5 and 6 show Ov16 prevalence in Bekwerra (Cross River) and Gashaka (Taraba)

Table 5: Seroprevalence of onchocerciasis and LF with Biplex by age group

State	LGA	Name of community	Total sampled	Total valid Biplex	Biplex +ve 5-<10		Biplex +ve 10 yrs& above		Total Biplex +ve	
					Oncho	LF	Oncho	LF	Oncho	LF
Yobe	Bade	Dagona	410	410	0	0	0	0	0	0
		Gafiwa	116	116	0	0	0	0	0	0
		Tagali	416	415	0	0	0	0	0	0
		Gwio Kura	105	105	0	0	0	0	0	0
		Total	**1047**	**1046**	**0**	**0**	**0**	**0**	**0**	**0**
Cross River	Ikom	Ukpochi	102	102	0	0	0	0	0	0
		Agbaragba	101	101	1(1.0)	3 (3.0)	0	0	1(1.0)	3(3.0)
		Etikpe	408	408	2(0.5)	0	70(17.2)	1(0.3)	72(17.7)	1(0.3)
		Balep	421	421	1(0.24)	0	68(16.2)	0	69(16.4)	0
		Total	**1032**	**1032**	**4(0.4)**	**3(0.3)**	**138(13.4)**	**1(0.0.1)**	**142(13.8)**	**4(0.4)**
Cross River	Bekwara	Nyanya-Ulim	101	100	4(4)	0	0	0	4(4)	0
		Atibulum	100	100	0	0	0	0	0	0
		Itekpa	407	407	0	0	27(6.6)	4(1.0)	27(6.6)	4(1.0)
		AfrikeOkpeche	404	404	0	0	95(23.5)	15(3.7)	95(23.5)	15(3.7)
		Total	**1012**	**1011**	**4(0.4)**	**0**	**122(12.1)**	**19(1.9)**	**126(12.5)**	**19(1.9)**
Taraba	Gashaka	Shinbon	61	61	5(8.2)	0	0	0	5(8.2)	0
		Gashaka	93	93	0	3(3.2)	0	0	0	3(3.2)
		Mayo-Selbe	547	547	4(0.7)	0	10(1.8)	0	10(1.8)	0
		Nyabar	451	451	3(0.7)	0	31(6.9)	3(0.7)	34(7.5)	3(0.7)
		Total	**1152**	**1152**	**12(1.0)**	**3(0.3)**	**41(3.6)**	**3(0.3)**	**49(4.3)**	**6(0.5)**
Taraba	Karim Lamido	Bandawa	421	421	0	0	0	2	0	2
		Panya O	398	398	0	0	0	0	0	0
		Gwomu O	104	104	0	0	0	0	0	0
		Kodei O	106	106	0	0	0	0	0	0
		Total	**1029**	**1029**	**0**	**0**	**0**	**2(0.2)**	**0**	**2(0.2)**

iTAS:

The results of the Pre-FTAS in the studied LGAs indicated that most of the communities had an antigenemia prevalence of less than 2%. However, Ikom LGA could not proceed to iTAS due to the 5.9% prevalence recorded among children who are considered serological markers of new infection in the Agbaragba community. The (iTAS) phase employed random sampling to select a total of 148 schools to give an equal chance of selection for each school and eliminate bias.

Demographic characteristics of study participants during iTAS

A total of 148 schools were visited and sampled across 4 LGAs. Of these, 131 (88.51 %) were classified as rural while 17 (11.49 %) were urban. All (100 %) communities where these schools were located had conducted onchocerciasis MAM for 17 - 21 years and LF MAM for 5 – 7 years. Total enrolments in the sampled schools within the targeted grades were 17,707. Bade LGA had the highest (48.53%) number of enrolments (Table 6). 11,564 pupils were registered for the study with the highest number being recorded in Gashaka LGA (Table 7). Both genders were equally represented with females being 5,805 (50.20%) and males 5,759 (49.80%) (Table 7). The grade with the highest number of registered pupils was Grade 1 with 4,816 (41.75%), followed by Grade 2 with 3,344 (28.99%), and then Grade 3 with 3,254 (28.21%). Expectedly, Grade 4 had the lowest number registered with 120 (1.04%). Age group <10 years were 9,656 (83.50%) and the age group ≥10 years were 1,908 (16.50%).

Table 6: Schools visited and the respective grade enrolments

LGA (IU)	No of Schools Sampled	Number Enrolled in Targeted Grades				
		Grade 1	*Grade 2*	*Grade 3*	*Grade 4*	Total
Bade	30	2,655	3,042	2,803	93	8,593
Bekwara	34	1,109	900	992	77	3,078
Gashaka	30	1,325	855	846	0	3,026
Karim Lamido	52	1,321	777	912	0	3,010
Total	**148**	**6,410**	**5,574**	**5,553**	**170**	**17,707**

Table 7: Number of pupils tested by gender, grade and age group

LGA (IUs)	Number Tested by Gender			Number Tested by Age Group			
	Male	*Female*	*Total*	*< 5 years*	*5 - 9 years*	*> 9 years*	*Total*
Bade	1,387	1,488	2,875	0	2,388	487	2,875
Bekwara	1,343	1,279	2,622	0	2,222	400	2,622
Gashaka	1,561	1,465	3,026	0	2,551	475	3,026
Karim Lamido	1,438	1,572	3,010	253	2241	516	3010
Total	**5,729**	**5,804**	**11,533**	**253**	**9,402**	**1,878**	**11,533**

LF antigenemia prevalence during iTAS

Twelve (12) LF antigenemia positive cases (0.10%) were recorded in all the 4 LGAs using the FTS. Six (50%) of these cases were pupils in Grade 1, one case (8.33%) in Grade 2, and 5 cases (41.67%) in Grade 3. No case was recorded in Grade 4. Both sexes had about the same proportions. Gashaka and Bekwerra LGAs had antigenemia prevalence of 0.23% and 0.19 % respectively while zero prevalence was observed in both Bade and Karim Lamido LGAs. Of the total 12 positive cases, 11 (91.67%) were children <10 years old while 1 (8.33%) fell in the ≥10years age group.

LF and onchocerciasis seroprevalence using SD Bioline Biplex RDT during iTAS

A total of 29 LF seropositive cases (0.25%) were recorded from the valid tests using the Biplex in all the 148 schools visited. Of these cases, 12 (41.38%) were in Grade 1, 7 (24.14%) in Grade 2, and 10 (34.48%) in Grade 3. No case was recorded in Grade 4. The majority (19 - 65.52%) of the positive cases were male. Bekwerra and Gashaka LGAs had almost the same seroprevalence - 0.53% and 0.43% with 14 and 13 cases respectively. Bade and Karim Lamido both had one case each with a seroprevalence of 0.03%. Among the 148 schools sampled, 19 (12.84%) had positive cases (>0%) with the highest site-specific prevalence (7.9%) observed in Bekwerra LGA. A total of 135 onchocerciasis seropositive cases (1.17%) were recorded from the valid tests using the Biplex in the 4 sites (Table 10). Of these, 77 (57.04%) were male and 58 (42.96%) female. A total of 99 (73.33%) seropositive cases were recorded among children <10 years and 36 (26.67%) among children ≥10 years. Children in Grade 3 had the highest number of positive

cases (53 - 39.26%) followed by those in Grade 2 with 45 (33.33%) cases, and then children in Grade 1 with 37 cases (27.41%). Children in Grade 4 recorded zero seropositive cases. Of the four sites, the highest seroprevalence of 3.09% (81 cases) was recorded in Bekwerra LGA. Bade LGA had zero sero-prevalence. Only 1 positive case (0.003%) was observed in Karim Lamido while Gashaka recorded a 1.75% seroprevalence with 53 cases. Sero-prevalence among those aged <10 years was 1.05% with Bekwerra having 3.02% seroprevalence and Gashaka 1.22%. Of the 148 schools sampled, 46 (31.08%) recorded onchocerciasis positive cases and seroprevalence >0.1% with the highest site-specific prevalence (22.86%) recorded in Gashaka LGA. Twenty-four (24) of those schools were in Bekwerra LGA and 20 schools in Gashaka LGA Five schools (3 in Gashaka LGA and 2 in Bekwerra LGA) had onchocerciasis seroprevalence >10%.

Table 8: LF antigenemia prevalence with FTS by gender, grade and age group

SN	LGA	Total Tested	Total Valid Tests	FTS Positive									Total Positive	Prevalence (%)
				Gender			Grades				Age Group (Yrs)			
				M	F	Total	1	2	3	4	<10	10-14		
1	Bade	2,875	2,873	0	0	0	0	0	0	0	0	0	0	0.00
2	Bekwara	2,622	2,622	3	2	5	3	0	2	0	5	0	5	0.19
3	Gashaka	3,026	3,026	4	3	7	3	1	3	0	6	1	7	0.23
4	Karim Lamido	3,010	3,010	0	0	0	0	0	0	0	0	0	0	0.00
	Total	**11,533**	**11,531**	**7**	**5**	**12**	**6**	**1**	**5**	**0**	**11**	**1**	**12**	**0.10**

Table 9: LF seroprevalence with Biplex by gender, grade and age group

SN	LGA	Total Tested	Total Valid Tests	Biplex Positive									Total Positive	Sero-Prevalence (%)
				Gender			Grades				Age Group (Yrs)			
				M	F	Total	1	2	3	4	<10	10-14		
1	Bade	2,875	2,873	1	0	1	1	0	0	0	1	0	1	0.03
2	Bekwarra	2,622	2,622	10	4	14	6	3	5	0	12	2	14	0.53
3	Gashaka	3,026	3,026	8	5	13	5	4	4	0	8	5	13	0.43
4	Karim Lamido	3,010	3,010	0	1	1	0	0	1	0	1	0	1	0.03
	Total	**11,533**	**11,531**	**19**	**10**	**29**	**12**	**7**	**10**	**0**	**22**	**7**	**29**	**0.25**

Table 10: Onchocerciasis seroprevalence with Biplex by gender, grade and age group

SN	LGA	Total Tested	Total Valid Tests	Biplex Positive									Total Positive	Sero-Prevalence (%)
				Gender			Grades				Age Group (Yrs)			
				M	F	Total	1	2	3	4	<10	10-14		
1	Bade	2,875	2,873	0	0	0	0	0	0	0	0	0	0	0.00
2	Bekwarra	2,622	2,622	35	46	81	28	26	27	0	67	14	81	3.09
3	Gashaka	3,026	3,026	42	11	53	8	19	26	0	31	22	53	1.75
4	Karim Lamido	3,010	3,010	0	1	1	1	0	0	0	1	0	1	0.00
	Total	**11,533**	**11,531**	**77**	**58**	**135**	**37**	**45**	**53**	**0**	**99**	**36**	**135**	**1.17**

Discussion

Effective monitoring and evaluation are important throughout the lifespan of the MAM programmes. This is needed to effectively assess whether the infection has been reduced to levels where transmission may be assumed to be no longer sustainable, and recrudescence is unlikely to occur even in the absence of drug intervention (12). Surveillance should target the entire population in an evaluation area or implementation unit. However, due to limited resources and time constraints, a careful selection of sites to be monitored is needed. The preliminary results from the integrated transmission assessment survey (iTAS) conducted with FTS indicate an overall LF antigenemia prevalence of 0.10% with slight variations among the LGAs (Bade – 0.0%; Bekwerra – 0.19%; Gashaka – 0.23%; and Karim Lamido – 0.0%). The seroprevalence was not significantly different among the LGAs. Only two schools (both in Gashaka LGA) had antigenemia prevalence > 2%. Zero onchocerciasis sero-prevalence was recorded for Bade and Karim Lamido.

These results are consistent with what was obtained from the Pre-iTAS (except for the onchocerciasis seroprevalence from Bekwerra and Gashaka). Interestingly, the Pre-iTAS LF results from Bekwerra LGA which was close to the 2.0% seroprevalence criteria to qualify for iTAS had come out better with a 0.19% seroprevalence in the subsequent iTAS, thus justifying the decision to include the LGA for iTAS. This suggests that for LF, Pre-TAS LGAs that have results hovering below or above the 2% antigenemia prevalence should be considered for iTAS.

Based on the WHO guidelines (3), 4 LGAs were deemed to have passed TAS for LF. There are, however, indications of 'hotspots' - schools with prevalence > 2% - in Bekwerra and Gashaka, although the small sample size may have accounted for the relatively high seroprevalence recorded in those schools. It is understood that MAM will still be carried out in the LGAs during the year of study irrespective of the outcomes of the iTAS. Subject to availability of resources, however, it will be suitable to conduct additional treatment campaigns targeted at the ‘hotspot’ schools and to further conduct tests following the second round of treatment to determine whether there is transmission is ongoing.

The Wb123/Ov16 Biplex results suggest that transmission of onchocerciasis infection may have been interrupted in Bade and Karim Lamido LGAs, given the zero seroprevalence recorded during iTAS. This is further corroborated to a large extent by similar results from the Pre-ITAS. Nevertheless, these results are not sufficient to recommend a stop/halt for onchocerciasis MAM in any of these LGAs. The Biplex serological test as a whole is not approved yet as a tool for surveillance. The Ov16 RDT serological test, which has been approved for surveillance, is not to be solely utilized in deciding to stop onchocerciasis MAM. In Nigeria, the State is regarded as the transmission zone and the evaluation unit, and the decision to stop onchocerciasis MAM will require a state-wide assessment followed by entomological evaluation of adult black flies to determine < 1/2000 infectivity rate before pronouncing stoppage of MAM (4).

The current status of LF recorded in the studied LGAs is expected given the treatment coverage of over 85% achieved annually which had initially qualified them for Pre-iTAS, the low pre-intervention antigenemia prevalence of < 10% in 3 out of the 5 LGAs

studied having ≤ 2.0%, and the long history of treatment with ivermectin ranging between 17–21 years. There exists a possibility of the indirect microfilaricidal effect of ivermectin treatment for onchocerciasis interrupting transmission of LF (13).

The relatively high level of transmission of onchocerciasis observed in Gashaka raises concern. Although the pre-intervention endemicity and outcomes of previous epidemiological assessments using skin snips had been high (14), the impact of mass treatment over the years ought to have been observed in the pattern of endemicity. Similarly, the relatively high transmission of onchocerciasis in Bekwerra LGA is unexpected due to the low pre-intervention endemicity and the long history of annual treatments in the LGA. It is noticeable that transmission remains ongoing in both Bekwerra and Gashaka due to seroprevalence recorded among children population, who are serological markers of a new infection. These may be due to inadequate compliance to (attrition, fatigue) annual treatment by the target populations in those areas. Consequently, the strengthening of MDA interventions and the supervision process is of critical importance.

Ov16 results from both the pre-iTAS and iTAS brought out a few important issues. Results for Ov16 during the iTAS indicated that prevalence increased with age. Given this outcome, a sampling strategy that includes children ages 5–9 compared to ages 6–7 as in traditional LF TAS resulted in a more conservative pre-stop assessment. WHO may therefore wish to look for more evidence for the inclusion of this age bracket in future assessments. The pre-iTAS results indicated that purposeful selection of first-line villages was insufficient at identifying the sites with the highest Ov16 prevalence by RDT in 5-9year olds, suggesting that random sampling may be necessary to identify sites with the potential transmission.

Conclusion

This study has provided additional information on the current burden of Onchocerciasis and Lymphatic Filariasis (LF) in the 4 IUs sampled where MAM for both infections has been ongoing for years. The study identifies that LF-MAM can be safely stopped in all 4 of the studied IUs. However, MAM for onchocerciasis needs to continue, although this may pose a challenge for LF surveillance. Based on the preliminary results from all four sites, this study has fulfilled the primary objective of determining the programmatic feasibility of an integrated transmission assessment survey (iTAS), to be used to simultaneously assess onchocerciasis and LF prevalence in areas co-endemic for the two infections that have completed the recommended treatment for one or both infections, and to make decisions on how to proceed. Given the preliminary results, LF MAM can be stopped in Bade, Bekwerra, Gashaka and Karim Lamido LGAs. Subject to availability of resources, an additional round of MAM in schools where antigenemia prevalence is > 2% is recommended. A further test, following the second round of treatment after the survey, can be undertaken to assess ongoing localized transmission. The State and National authorities should institute adequate surveillance to detect recrudescence. Xeno-monitoring of blackflies in LGAs where the threshold for onchocerciasis elimination by serological assessment has been met in the context of the OR study sites is recommended, followed by strengthening of onchocerciasis MAM and improved supportive supervision particularly in Bekwerra and Gashaka LGAs. Improved synergy with the States and supporting partners on program implementation timelines are recommended to avoid a situation where treatments for schistosomiasis commenced while pupils were being subjected to tests for TAS.

Declarations

Ethics approval and consent to participate

Ethical clearance for the study was obtained from the Federal Ministry of Health's Bioethics Committee in the Department of Planning and Research. Details of the procedure were explained to all participants and heads of the schools during social mobilization. Verbal assent of the Head Teachers as well as informed consent from parents and legal guardian of all children that participated were sought. Participation was voluntary.

Consent for publication

All authors consent to the publication of this research work

Availability of data and material

All data will be made available to the journal

Competing interests

The authors declare no competing interest

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Authors' contributions

Conceived and initiated the article: OC, SOA, AIN, SYA, DE

Prepared tables: OC, SOA, OP, SJ, NG, UZ, IM

Prepared figures: BK, EUF

Wrote the paper: AIN, SYA, SOA, OC, DE, OP, IM, NA, EUF, AUA, BK, SJ, NG, UZ

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Figures

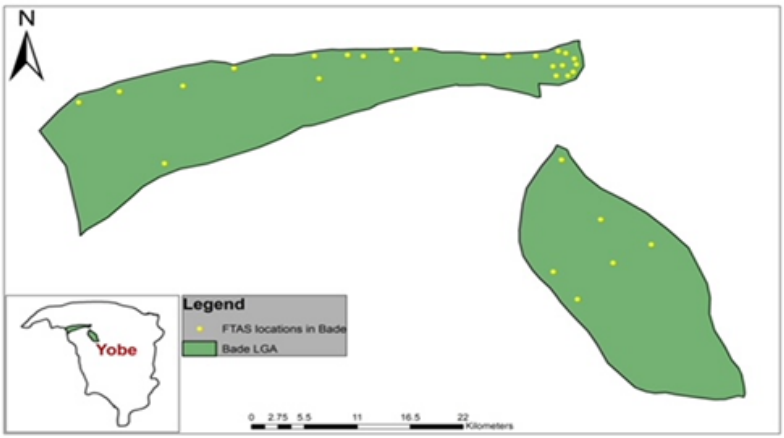

Figure 1

Maps of study sites in Bade LGA (Yobe state).

Figure 2

Maps of study sites in Bekwerra LGA (Cross Rivers state).

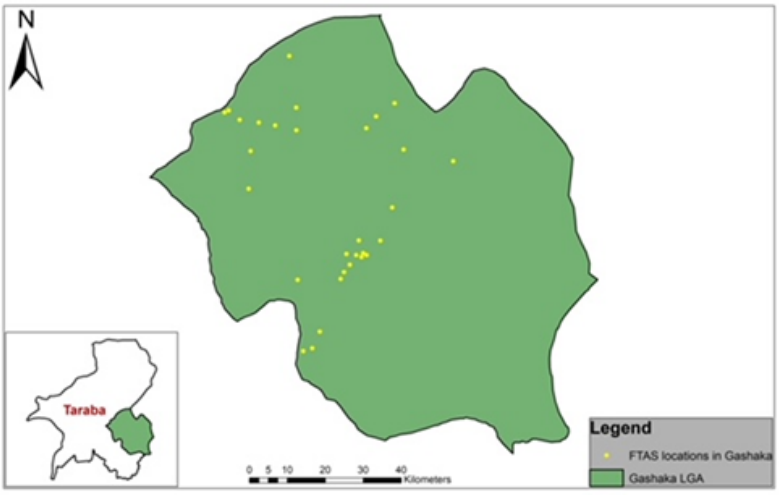

Figure 3

Maps of study sites in Gashaka LGA (Taraba State).

Figure 4

Maps of study sites in Karim Lamido LGA (Taraba State).

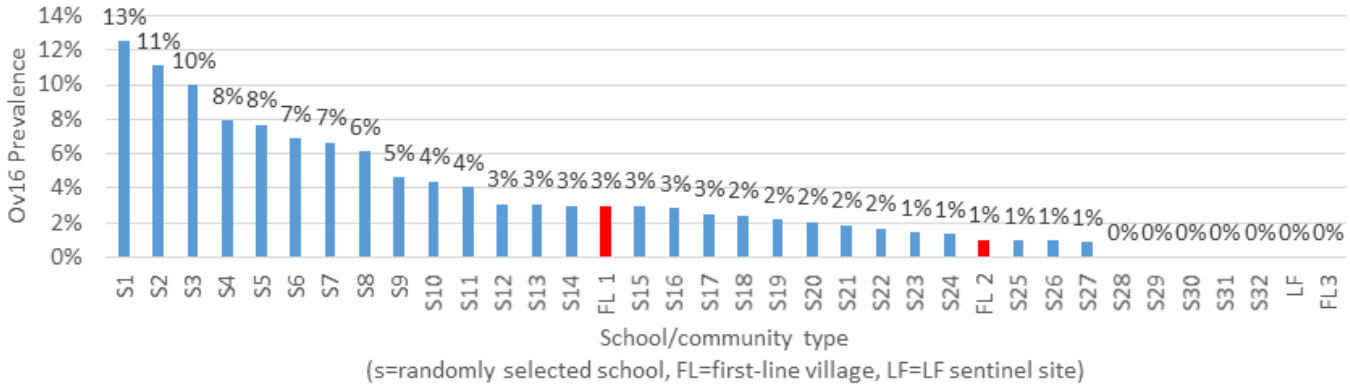

Figure 5

Ov16 prevalence by first-line village, LF sentinel site, or school-based cluster, among 2304 children ages 5-9 in Bekwara LGA, Nigeria, surveyed during pre-iTAS or iTAS in April 2017

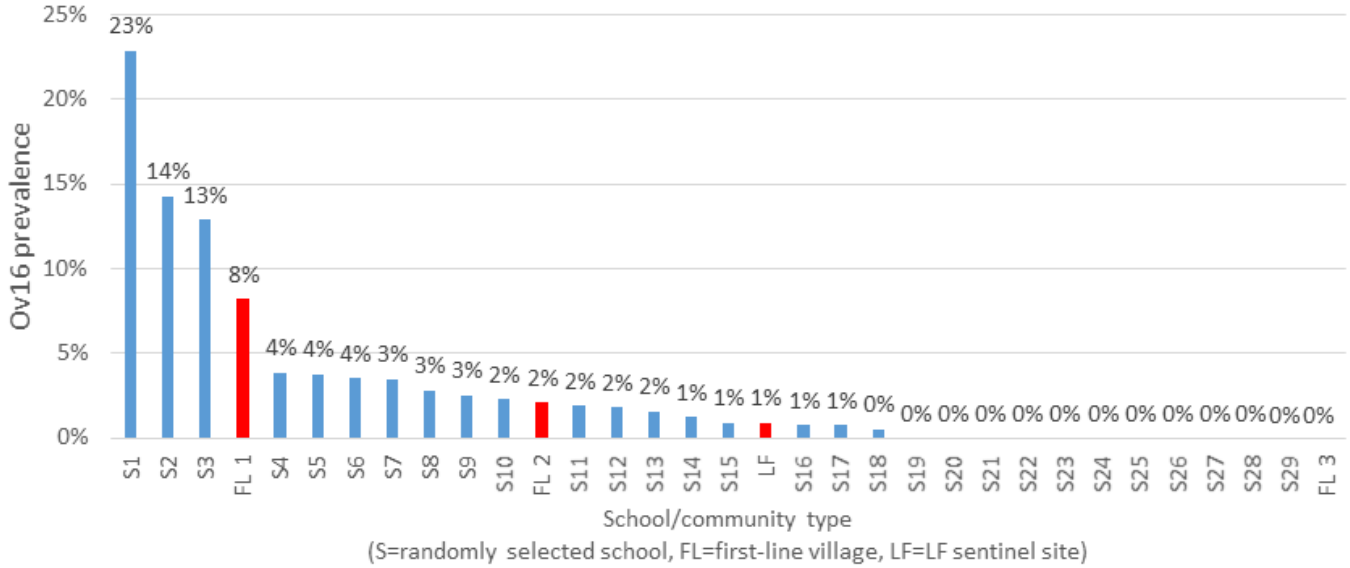

Figure 6

Ov16 prevalence by first-line village, LF sentinel site, or school-based cluster, among 2484 children ages 5-9 in Gashaka LGA, Nigeria, surveyed during pre-iTAS or iTAS in April 2017