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Epidemiology of the clinical manifestations of lymphatic filariasis in five endemic local government of Ogun State, South Western Nigeria

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Abstract

Lymphatic filariasis is a tropical disease that affects the lower extremities. The parasite Wuchereria bancrofti affects 90% of the Nigerian population which is the third affected globally. About 60 million people are affected with the clinical manifestations which is leg elephantiasis, hydrocele and breast elephantiasis. This leaves its victim highly stigmatized with poor per capital income. The clinical manifestation of lymphatic filariasis (LF) has been one of the diagnostic tools in assessing endemic communities. There is a need to assess the clinical manifestation of those living in this endemic in Ogun State, to assess their readiness to the elimination goal of the Global Programme to Eliminate Lymphatic Filariasis. Overall, 1714 voluntary participants were gathered through a clinical study using cluster survey, in five Local Government health center in Ogun State. They were observed for clinical manifestations and graded according the World Health Organization Standard. Limbs elephantiasis, breast elephantiasis and hydrocele were observed in the studied population. Ifo LGA (5.3%) showed the highest manifestation in males and Yewa LGA (4.5%) among the females. Within the communities, Igbesa in Ado-Odo/ Ota LGA had the highest (12.5%) among the females while Abeloju in Ifo LGA had the highest among the males. Ifo LGA (1.6%) alone indicated the presence of breast elephantiasis among the LGAs. The distribution of hydrocele across the LGAs indicated that Ifo LGA (25%) showed the highest manifestation followed by Ado-Odo/LGA (7.8%) and then Yewa South (5.6%). The distribution of limb elephantiasis were greater in females than in males. Males with hydocele more than those with limb elephantiasis in the studied population. Grading of both hydrocele and limb elephantiasis were observed in the advanced stages in the studied population. Some of the participants with clinical signs did not show infection with microfilaria. Ifo LGA showed greater distribution of the clinical signs. There is a need for a parasitological survey, mass drug administration and health education.

Introduction

Background of study

Lymphatic filariasis is a disease that is caused by a nematode parasite of filarial origin whose vector is female mosquitoes of Anopheles, Culex and Mansona species. About 200 people are affected globally. The clinical manifestation of lymphatic filariasis (LF) has been one of the diagnostic tools in assessing endemic communities with Wuchereria bancrofti in Nigeria (Omudu, 2011). Nigeria is the third endemic population globally and 90% of infection are caused by Wuchereria bancrofti (WHO, 2020).

The signs and symptoms of LF varies depending on the clinical expressions (Gyapong, 2014). In Bancroftian filariasis, the legs and the genitals are the areas that are often affected. Repeated episodes of inflammation leads to blockages of the lymphatic system especially in the genitals and the legs. This causes the affected area to become grossly enlarged with thickened coarse

skin leading to a condition called elephantiasis (Thomson, 2006). The disease exhibit symptoms such as enlargement of the arms, legs, breast and swelling of the scrotum. The long, threadlike worms blocks the body's lymphatic system which is a network of channels of lymph nodes, and organs that helps maintain proper fluid levels in the body by draining lymph from tissues, into the blood stream (Carter centre, 2018).

Other clinical manifestations of the disease ranges from periodic reoccurring incidences of localized inflammation, fever, pain, chyluria and haematuria, while the visible signs are lymphoedema and hydrocele, causing social stigma and low per capital income (Gyapong, Owusu, da-Costa Vroom, Mensah & Gyapong, 2018).

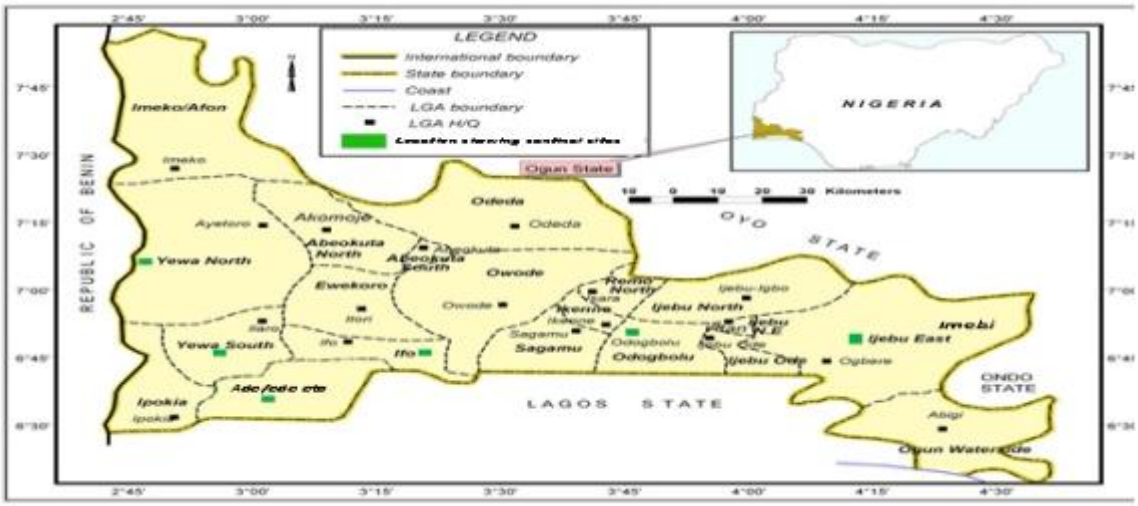
Sometimes, mf density in the peripheral blood shows periodicity of parasite and as such venous blood samples should be collected at night to match the peak in mf density. Periodicity means that the density of mf per ml of peripheral blood varies with time of day. Different patterns of mf periodicity occur in different regions of the world ((Turkington , 2006 & WHO, 2017). Not all patients infected with LF have mf in the blood. Several reasons had been reported for this occurrence: infection may not be patent because the parasites are immature, worms of only one sex are present, females are etete, which means they have stopped producing mf, or the host immune response has cleared the mf Weil and Ramzy 2007). It has also been reported that antigen tests detect antigens associated with female worms capable of producing microfilaria (Weil and Ramzy 2007) In some cases, the morphology of mf detected in the blood can be used to identify the species of parasite (Orihel et al., 1997).

As Nigeria seeks to meet the target of the Global Programme to Eliminate Lymphatic filariasis (GPELF) mandate on elimination programme (WHO, 2020). There arises a need to assess individuals living in endemic communities with clinical expressions. Those with clinical expressions with circulating microfilaria who can transmit the disease in the community and will be needing Mass Drug Administration, while also, assessing those without circulating microfilaria who will be needing morbidity management (WHO, 2019). This research seeks to categorise individuals in certain endemic communities in Ogun state with clinical manifestation of lymphatic filariasis so as suggest appropriate treatment, prevention and control measures in lieu of elimination goal of GPELF

MATERIALS AND METHODS

Description of the Study Area

Ogun State is in South-Western Nigeria. It covers a land mass of 16,472 km^2 and lies between longitude 2^o 45$^{'}$E and 3^o 55$^{'}$ E and latitude 7^o 01 N and 7^o 13$^{'}$N 2008). The State is bordered to the west by the Republic of Benin, to the east by Ondo State, to the north by Osun State and Oyo States and to the south by Lagos State and the Atlantic Ocean Agriculture is the major occupation of the people, and their products are ofada rice ,cassava and cocoa among others (Britannica.com, 2023)



Ethical Permission and Informed Consent
The ethical permission was obtained from Health Research Ethics Committee of the College of Medicine, University of Lagos (CMUL/HREC/12/19/784). Informed consent form was administered to each participant after the purpose of the research was read out and explained in the local dialects.

Study Population
The study comprised all participants that consented to be recruited in the study between the ages of 5 years of age to 70years of age. Sample size determination was according to WHO criteria: at least 300 blood samples must be collected from within each endemic region (WHO, 2017). The **s**tudy design was a clinically based study. Cluster survey was used to gather 1,714 consenting participants in the Health Centres of the five LGAs distributed across the three senatorial district of Ogun State. The purpose of the research was explained to the health workers, community heads, ward heads, Community Development Administrators, who in turn explained it to the participants in English and their native language. Consenting participants were made up of 341 persons from Ado-Odo/Ota, 458 from Yewa South, 310 from Ifo, 300 from Ijebu East and 305 from Odogbolu LGAs.

Clinical Survey
In each LGA, a section of the Health Centre was designated for clinical examination for the symptoms and signs of LF. The same consenting participants for parasitological study were ushered individually into this place, behind closed doors for physical examination by trained health workers. Females' examination included the legs, arms and breast while that of males included the genitals, legs and arms. The presence of leg elephantiasis, breast elephantiasis and hydrocele, were identified and recorded.

In the case of male genital involvement, swelling of the spermatic cord was graded as hydrocele stage I, and true hydroceles were graded as stage II (6–10 cm in length), stage III (11–15 cm), or stage IV (>15 cm). Leg elephantiasis was graded as stage I (early pitting oedema), stage II (non-pitting oedema with thickened skin and loss of elasticity), or stage III (evident elephantiasis with skin folds and/or warty lesions) (Cheesbrough, 2005).

Parasitology Survey
Blood samples were taken from all consenting participants with clinical representation by qualified health workers between the hours of 10 pm- 2 am, which coincides with the nocturnal periodicity of the parasite (Cheesbrough, 2005). A cotton wool swap containing 70% methylated spirit was used to sterilize the area below the wrist from where the needle used to take the blood was inserted. The tourniquet was used to tie the lower arm to prevent excess blood loss and expose the vein. Two mls of venous blood was then collected from participants with 2mls syringe and needle. The blood was stored in an EDTA sample bottle and taken to the laboratory for analysis

Microscopy
Blood sample in EDTA bottles were drawn with heparinized capillary tube. This was used to draw three vertical lines of thick blood films of approximately 20μL of blood each on a clean-labelled glass slide (Weil and Ramzy, 2007). These slides were air-dried, dehaemoglobinized under running water, air dried again and stained with Giemsa solution. The stained air-dried smears were viewed under microscope at X10 and X40 objective lens. .

Results

Clinical manifestation of leg elephantiasis as observed in the communities in the studied Area

Table 1 showed that three out of the five Local Government Areas sampled showed the clinical manifestation of leg elephantiasis. These were Ado-Odo/ Ota, Yewa South and Ifo. Leg elephantiasis were observed in all the communities in the LGA. Within the LGA, Ifo (5.3%) showed the highest manifestation of leg elephantiasis in males and Yewa LGA (4.5%) among the females. However, within the communities, Igbesa in Ado-Odo/ Ota LGA had the highest (12.5%) among the females while Abeloju in Ifo LGA had the highest among the male.

Table 19: Clinical manifestation of leg elephantiasis as observed in the communities in the studied Area

Local Government Area	Communities	Female examined	Female with Leg Elephantiasis (%)	Male examined	Male with leg Elephantiasis (%)
Ado- Odo/Ota	Igbesa	8	1(12.5)	55	1 (1.8)
	Ketu Adiowe	60	4(6.1)	48	2 (4.2)
	Alapoti	45	2 (4.4)	50	0 (0.0)
	Total	**188**	**7 (3.7)**	**153**	**3 (1.9)**
Ijebu East	Fetedo Imobi	26	0 (0.0)	23	0 (0.0)
	Fowosoje	28	0 (0.0)	09	0(0.0)
	Itapanpa	20	0 (0.0)	09	0 (0.0)
	1ba	13	0 (0.0)	10	0(0.0)
	Terelu	22	0 (0.0)	4	0(0.0)
	Ebute Imobi	13	0 (0.0)	6	0(0.0)
	Tioluwo	13	0 (0.0)	08	0(0.0)
	Okemakun	24	0 (0.0)	13	0(0.0)
	Okigbode	27	0 (0.0)	13	0(0.0)
	Denurin	8	0 (0.0)	11	0(0.0)
	Total	**106**	**0 (0.0)**	**194**	**0(0.0)**
Yewa South	Eredo	86	2 (2.3)	69	4(5.8)
	Oke – Ella	66	3(4.5)	51	3(5.9)
	Ajilete	108	6 (5.6)	78	2(2.6)
	Total	**260**	**11(4.6)**	**198**	**9 (4.5)**
Ifo	Agbado	52	2 (3.8)	35	0 (0.0)
	Lerin	20	1 (5.0)	40	2(5.0)
	Abeloju	40	3(7.5)	32	2(6.3)
	Jagunna	58	3(5.2)	33	2(6.1)
	Total	**170**	**9 (5.3)**	**140**	**6(4.3)**
Odogbolu	Hemerin	30	0 (0.0)	30	0 (0.0)
	Moloko	75	0 (0.0)	80	0 (0.0)
	Okunowa	50	0 (0.0)	40	0 (0.0)
	Total	**155**	**0(0.0)**	**150**	**0 (0.0)**

Clinical manifestation of leg and breast elephantiasis in relation to infection as observed in the endemic LGAs.

Table 2 showed that only Ifo LGA was observed with the clinical manifestation of breast elephantiasis 1.6%. The sampled LGAs also indicated that not all participants with clinical manifestation of breast elephantiasis were infected microfilaria. The clinical manifestation of leg elephantiasis and breast elephantiasis were not significantly related to infection of LF in the studied area.

Table 2: Clinical manifestation of leg and breast elephantiasis in relation to infection as observed in the studied area.

LGA	No examined	No with leg Elephantiasis (%)	Prevalence of Infection (%)	Pvalue	Breast Elephantiasis (%)	Prevalence of infection %	P value
Ado/ Odo Ota	341	10 (2.9)	7 (2.1)		0 (0.0)	0(0.0)	
Yewa South	458	20 (4.4)	15 (3.3)	0.13	0(0.0)	0(0.0)	
Ifo	310	15 (4.8)	9 (2.9)		5 (1.6)	5(100)	0.18
Ijebu North east	300	0 (0.0)	0 (0.0)		0(0.0)	0(0.0)	
Odog bolu	305	0 (0.0)	0 (0.0)		0(0.0)	0(0.0)	
Total	**1714**	**45 (2.6)**	**31(1.8)**		**5 (0.3)**	**5 (0.3)**	

Clinical manifestation of hydrocele as observed in the studied communities

Table 3 showed the clinical manifestation of hydrocele across the LGAs. The highest manifestation of hydrocele was observed in Ifo LGA (25%), followed by Ado-Odo/Ota LGA (7.8%) and then Yewa South (5.6%). Apart from Ifo having the highest manifestation of hydrocele among the LGAs, the communities in Ifo showed higher manifestations of hydrocele than other communities in the LGA.

Table 3: Clinical manifestation of hydrocele as observed in the studied communities

Local Government Area	Communities	Male sampled	Participants with Hydrocele (%)
Ado Odo/Ota	Igbesa	55	3 (5.5)
	Ketu Adiowe	48	6 (12.5)
	Alapoti	50	3(6.0)
	Total	**153**	**12 (7.8)**
Ijebu East	Fetedo Imobi	23	0 (0.0)
	Fowosoje	09	0 (0.0)
	Itapanpa	09	0 (0.0)
	1ba	10	0 (0.0)
	Terelu	4	0 (0.0)
	Ebute Imobi	6	0 (0.0)
	Tioluwo	08	0 (0.0)
	Okemakun	13	0 (0.0)
	Okigbode	13	0 (0.0)
	Denurin	11	0 (0.0)
	Total	**194**	**0 (0.0)**
Yewa South	Eredo	69	4 (5.8)
	Oke – Ella	51	3 (5.9)
	Ajilete	78	4 (5.1)
	Total	**198**	**11(5.6)**
Ifo	Agbado	35	11(31.4)
	Lerin	40	6 (15)
	Abeloju	32	8 (25)
	Jagunna	33	10 (30.3)
	Total	**140**	**35 (25.0)**
Odogbolu	Hemerin	30	0 (0.0)
	Moloko	80	0 (0.0)
	Okunowa	40	0 (0.0)
	Total	**150**	**0 (0.0)**

Clinical manifestation of hydrocele in relation to infection among participants in the studied LGAs

Table 4 showed that not all participants with clinical manifestation of hydrocele were infected with microfilaria. There was also no significant difference between clinical manifestation of hydrocele and infection in the studied LGAs ($p \geq 0.5$)

Table 4: Clinical manifestation of hydrocele in relation to infection among participants in the studied LGAs

Local Government Area	No sampled	No with Hydrocele (%)	Prevalence of infection (%)	P value
Ado-Odo/Ota	341	12 (3.5)	11 (3.2)	
Yewa South	458	11(2.4)	9 (1.9)	0.15
Ifo	310	35 (11.3)	31(10.0)	
Ijebu Northeast	300	0(0.0)	0(0.0)	
Odogbolu	305	0 (0.0)	0(0.0)	
Total	**1714**	**58(3.4)**	**51(2.9)**	

Grading of hydrocele and leg elephantiasis.
Tables 5 and 6 showed the grading of hydrocele and leg elephantiasis. Type III-IV (1.9%) hydrocele (Advanced stage of hydrocele) were observed as the most distributed in the LGAs followed by Type II hydrocele (0.9%) and then by type I hydrocele as seen in Table 5 below:

Table 5: Grading of hydrocele as observed in the studied communities

Local Government Area	No sampled	No with Hydrocele (%)	Type I (funiculitis) (%)	Type II (%)	Type III-IV (%)
Ado-Odo /Ota	341	12 (3.5)	3(0.9)	2 (0.6)	7 (2.1)
Yewa South	458	11(2.4)	2(0.4)	1(0.2)	8(1.7)
Ifo	310	35 (11.3)	7 (2.3)	10 (3.2)	18(5.8)
Ijebu Northeast	300	0(0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Odogbolu	305	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	**1714**	**58(3.4)**	**12 (0.7)**	**13 (0.8)**	**33 (1.9)**

Grading of elephantiasis as observed in the studied communities
Table 6 showed that the various stages of hydrocele: Stage I, Stage II and Stage III was observed in the endemic LGAs. The last stage of elephantiasis was most predominant observed in the LGAs.

Table 6: Grading of elephantiasis as observed in the studied communities

LGA	No sampled	No with Elephantiasis	Stage I (%)	Stage II (%)	Stage III (%)
Ado-Odo/ Ota	341	10	0 (0.0)	4 (1.2)	6 (1.8)
Yewa South	458	20	0 (0.0)	7 (1.5)	13 (2.8)
Ifo	310	15	2 (0.6)	5 (1.6)	8 (2.5)
Ijebu Northeast	300	0	0 (0.0)	0 (0.0)	0. (0.0)
Odogbolu	305	0	0 (0.0)	0 (0.0)	0. (0.0)
Total	**1714**	**45(2.6)**	**2 (0.1)**	**16 (0.9)**	**27 (1.6)**

Plate 1: An adult man A and woman B in the studied population with limb elephantiasis. Stages II and III respectively

Plate 2: Breast elephantiasis in a participant in the studied area

Plate 3: A man in the studied area with hydrocele (Stage VI)

Discussion

The studied Local Government Areas showed all the clinical manifestations of LF ranging from leg elephantiasis, hydrocele and breast elephantiasis. Clinical manifestation of lymphatic filariasis (LF) has been one of the diagnostic tools in assessing endemic communities with Wuchereria bancrofti in Nigeria (Omudu, 2011).

Overall, the clinical manifestation of hydrocele were more than that of leg elephantiasis in the studied LGA. This is an indication that more males had the clinical manifestation than their female counterparts in the LGA. This has been the trend in most reported literatures both in and outside Nigeria. However, the clinical manifestation of leg elephantiasis was greater in females than that of males and these has been observed in other communities in Nigeria (Gypong et al., 2018 and Ramaiah et al., 2014)

The studied population also indicated that not all patients infected with LF have microfilaria in their blood. Previous studies had reported these occurrences to be found in individuals whose infection may not be patent because the parasites are immature. There also those who are infected with worms of only one sex,

females are etete, which means they have stopped producing microfilaria, or the host immune response has cleared the mf. It has been reported that antigen tests detect antigens associated with female worms capable of producing microfilaria. In some cases, the morphology of mf detected in the blood can be used to identify the species of parasite (Orihel et al., 1997). The absence of circulating filarial antigen in some endemic communities could also be attributed to acquired immunity after many years of exposure in those communities, death of adult worms in the body after living for 10-15 years, or it could also be because of established acquired immunity that prevents new infections to be established or MDA activities. This is in line with other previous findings (WHO, 2019).

The two communities that did not show any clinical sign had been undergoing active participation in Mass Drug Administration (MDA) in which anthelminthic drug is given to the entire community and this had been reported to enhance elimination (Hussain et al., 2014).

Ogun State has been undergoing mass drug administration; this could explain why some of the communities could not show any clinical manifestation. Previous reports had noted that wherever MDA had properly administered, notable clearance had been achieved (WHO, 2017).

Ifo LGA showed the various clinical manifestation of LF. Leg elephantiasis, hydrocele and breast elephantiasis. Clinical signs has been associated with endemicity of lymphatic filariasis (Gyapong, *et al.*, 2017). This is an indication that these communities in Ogun State are endemic for lymphatic filariasis and are still having active transmission.

Conclusions

There is a need to revisit these local governments with these clinical manifestations and do a parasitological survey to assess the level of threshold of antigenemia and microfilaria infectivity to assess their nearness to the elimination mandate.

There is a need to assess the knowledge of these studied areas to all the available treatment patterns, preventive and control measures.

There is a need to assess their Knowledge with ant anthelminthic drugs and their level of awareness and patronage of Mass Drug Administration

Ifo should be revisited to assess the reason for the distribution of manifestation of all the clinical signs and the appropriate attention given to the area. There is also a need to create awareness and health sensitization as regard LF in this area.

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