Original Article

Lymphatic Filariasis in a Tertiary Hospital in South-East Nigeria: A Tale of Neglect, Low Social Class and Disability

Iroezindu MO[1], Unigwe US[1], Udoette S[2], Umenzekwe CC[3], Nna E[4], Onyeaghala CA[1,5], Chika-Igwenyi NM[1,6], Mmerem JI[1,7], Onodugo OD[1]*

1. *Department of Medicine, University of Nigeria Teaching Hospital, Ituku/Ozalla, Enugu, Nigeria*
2. *Department of Internal Medicine, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria*
3. *Department of Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria*
4. *Safety Molecular Pathology Laboratory, Enugu, Nigeria.*
5. *Department of Internal Medicine, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria*
6. *Department of Internal Medicine, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi State, Nigeria*
7. *Department of Internal Medicine, Federal Medical Centre, Owerri, Imo State, Nigeria*

**Corresponding author: mikezindu@yahoo.com*

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ABSTRACT

Background: Lymphatic filariasis (LF) is a neglected tropical disease affecting over 40 million people globally. It is associated with profound disfigurement /disability, pain, and social stigma partly due to late presentation. We described the socio-demographic, clinical and laboratory characteristics of patients with confirmed LF in order to improve the case detection/management in resource-constrained settings.

Methods: A retrospective cohort study of patients referred /presenting to the Infectious /Tropical Diseases unit of the University of Nigeria Teaching Hospital with a provisional diagnosis of LF from October 2012 to September 2017. Data was extracted from medical records. Laboratory confirmation of LF was based on Giemsa -stained blood film for microfilaria.

Results: Of 50 patients with a provisional diagnosis of LF, 18 (36%) had microfilaria confirmation. The mean age among the confirmed cases was 48.3 ± 9.5 years, women were in the majority 12 (66.7%), 7 (38.9%) had primary or no formal education, and 5 (27.8%) were widowed. They were predominantly rural dwellers 12 (66.7%), farmers 8 (44.4%), and of low social class13 (72.2%). The mean duration of lymphoedema was 6.5 ± 2.3 years. Wuchereria bancrofti was identified in 17 (94.4%) cases. Limitation of movement and secondary skin/soft tissue infections were evident in 14 (77.8%) and 15 (83.3%) patients, respectively. Anaemia 4 (22.2%) and depression 2 (11.1%) were co-morbidities. A combination of filaricidal therapy/supportive care led to noticeable reduction in lymphoedema and resolution of skin infections in 10/17 (58.8%) and 13/14 (92.9%) patients, respectively.

Conclusions: LF remains a tale of neglect, low social class and disability. Surveillance and active case search in endemic regions is needed for prompt diagnosis and improved outcomes.

Key words: lymphatic filariasis, lymphoedema, microfilaria, disability, poverty

INTRODUCTION

Lymphatic filariasis (LF) is a mosquitoe-borne, chronic infection caused mainly by three parasitic nematodes - *Wuchereria banccrofti*, *Brugia malayi*, and *Brugia timori* [1]. The parasites can live for several years in human lymphatics causing lymphatic damage and destruction, leading to recurrent swelling / disfigurement of the limbs, genitalia and breasts [2,3]. Although, most infections are asymptomatic, late stages of the disease are characterized by chronic lymphoedema, hydrocoele, elephantiasis, increased susceptibility to bacterial / fungal limb infections, disfigurement, disability, social stigmatization and economic losses [2]. It is one of the neglected tropical diseases (NTD), and a leading causes of disability globally[1,2].

In 2000, the World Health Organization (WHO) estimated that LF was endemic in 83 countries and that about 1.3 billion people worldwide were at risk, 120 million people were infected (40 million in Africa) and 40 million people (comprising 25 million males and 15 million females) had long-term sequelae of the infection [4]. The disease is endemic in some countries in Africa, South East Asia and Latin America. In Africa, the disease is endemic in 34 countries [5]. Nigeria has the highest burden of LF in Africa with an estimated 120 million people at risk of the infection [6,7]. In 1997, the World Health Assembly passed a resolution encouraging member states to eliminate LF and three years later, the WHO launched Global Programme to Eliminate Lymphatic Filariasis aimed at stopping the spread of the disease and controlling its morbidity [1]. This mandate is yet to be achieved in Nigeria.

Several studies highlighting the incidence and impact of LF have been conducted in many countries including Nigeria [1-4]. So far, most studies carried out in Nigeria did not explicitly highlight diagnostic challenges occasioned by diverse clinical presentations, spectrum of co-morbidities and possible treatment response of patients with LF [5,8]. The tendency to miss the diagnosis of LF during evaluation for unilateral or bilateral leg swelling especially in the early stages of the disease continues to be a challenge even among specialist physicians.

The aim of this study was to highlight the burden of confirmed LF among patients with clinical suspicion of LF and to describe the socio-demographic, clinical / laboratory characteristics, complications and treatment response of confirmed LF cases in order to improve case detection and management in resource-constrained settings where LF is endemic.

METHODS

Study design: This was a retrospective cohort study.

Study setting /Population: The University of Nigeria Teaching Hospital (UNTH) is a tertiary care health facility with about 500 bed capacity. It is located in Ituku/Ozalla, Enugu, South-East Nigeria. The UNTH is the largest referral hospital in the region. Lymphatic filariasis is endemic in parts of South-East Nigeria. The study population comprised adult patients aged 18 years or more presenting or referred to the Infectious / Tropical Diseases unit of the UNTH with a clinical suspicion of LF from October 1, 2012 to September 30, 2017. Patients without blood film confirmation of microfilaria were excluded from the final analysis.

Ethical considerations: Ethical approval was obtained from the Health Research Ethics Committee of the UNTH. As part of the procedure of the managing physicians, photographs of affected parts of the body were taken after obtaining an informed consent from the patients. Confidentiality was ensured.

Data collection: Data was extracted from the medical records of the patients. A proforma was used to obtain socio-demographic data (age, sex, level of education, marital status, location of residence, occupation and social class), clinical characteristics (duration of symptoms, presence /absence of lymphedema, limitation of movement, secondary skin infections and complications). Laboratory results (blood film for microfilaria, complete blood count, and Erythrocyte Sedimentation Rate [ESR]) were also obtained.

Blood Film Microscopy : Five (5) ml of venous blood was collected from each patient into ethylene diamine tetraacetic acid (EDTA) tube for complete blood count , ESR and blood film microcopy for microfilaria . Circulating microfilariae were identified by microscopic examination of Giemsa - stained thick smear (20 -60 µ L) of finger -prick blood obtained at 12 midnight, 2 a.m. and 12 noon.

Treatment : supportive care (including twice daily washing of limbs with soap and water , intermittent crepe bandage application , leg raising at nights) was provided to all patients . Patients were treated with a combination of filaricidal drugs (either combination of diethylcarbamazine /albendazole / doxycycline or ivermection /albendazole / doxycycline), other antimicrobials as indicated (for treatment of secondary bacterial or fungal skin infections). Nutritional support , haematinics and psychotherapy were offered as appropriate . Monitoring of lymphoedema was carried out by measurement of limb circumference using a tape . The measurement was performed every 72 hours for in-patients and during each out-patient visit for out- patients.

Statistical analysis : The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23 (Chicago , IL , USA). Categorical variables were reported as percentages while quantitative variables were reported as mean ± standard deviation (SD).

The clinical characteristics of the patients with confirmed LF are shown in Table 2 while photographs of two (2) of the patients are shown in Figures 1 and 2. The mean duration of illness prior to presentation was 6.5 ± 2.3 years . Lymphoedema was bilateral in slightly over half of the patients 10 (55.5%). There was an incidental finding of blood film microfilaria in one (1) patient without lymphoedema who was being investigated for parasitic infestation . Limitation of movement was observed in 14 (77.8%) patients while 13 (72 .2%) patients had either a secondary bacterial or fungal skin/ soft tissue infection at presentation . Various co - morbidities were found in the patients notably Diabetes mellitus [DM] 5 (27.8%), hypertension 4 (22 .2%), anaemia 4 (22 .2) and depression 2 (11.1%).

RESULTS

Fifty patients comprising 33 females and 17 males with clinical suspicion (provisional diagnosis) of LF were seen . Of the 50 patients , LF was confirmed by presence of blood film microfilaria in 18 (36 %) patients (12 females and 6 males). The remaining 32 patients were diagnosed with cellulitis (9), deep vein thrombosis (5), thrombophlebitis (2), chronic liver disease (2), and heart failure (2), while 12 had lymphoedema without a confirmatory /definitive diagnosis . The mean age of the patients with confirmed LF was 48 .3 ± 9.5 years . Seven (38 .9%) of the patients had only primary education or no formal education while 8 (44 .4%) were either single or widowed . They were predominantly rural dwellers 12 (66.7%), farmers 8 (44.4%) and of low social class 13 (72 .2 %). Table 1 shows the socio -demographic characteristics of the patients.

Table 1: Socio-demographic characteristics of patients with confirmed lymphatic filariasis in Enugu, Nigeria

Characteristics	**Frequency** (%), N=18
Age (years), mean ± SD	48.3 ± 9.5 years
Age (years)	
< 40 years	2 (11.1)
≥ 40 years	16 (88.9)
Sex	
Male	6 (33.3)
Female	12 (66.7)
Level of education	
None	2 (11.1)
Primary	5 (27.8)
Seconday	7 (38.9)
Tertiary	4 (22.2)
Marital status	
Married	10 (55.5)
Single	3 (16.7)
Widowed	5 (27.8)
Location of residence	
Rural	12 (66.7)
Urban	6 (33.3)
Occupation	
Farmer	8 (44.4)
Trader	6 (33.3)
Student	1 (5.6)
Unemployed	2 (11.1)
Civil servant	1 (5.6)
Social class	
High (I-III)	5 (27.8)
Low (IV-V)	13 (72.2)

SD: standard deviation

Table 2: Clinical characteristics of patients with confirmed lymphatic filariasis in Enugu, Nigeria

Variable	N=18
Mean duration of symptoms (years)	6.5 ± 2.3
Lymphoedema	
None	1 (5.6)
Unilateral	7 (38.9)
Bilateral	10 (55.5)
Limitation of movement	
Yes	14 (77.8)
No	4 (22.2)
Seconary skin/soft tissue infections	
None	4(22.2)
Fungal infection	4 (22.2)
Cellulitis/bacterial infection	9 (50)
Pyomyositis	1 (5.6)
Co-morbidities	
None	2(11.1)
Anaemia	4 (22.2)
Hypertesion	4 (22.2)
Diabetes Mellitus	5 (27.8)
Depression	2 (11.1)
Mitral Valve Prolapse	1 (5.6)

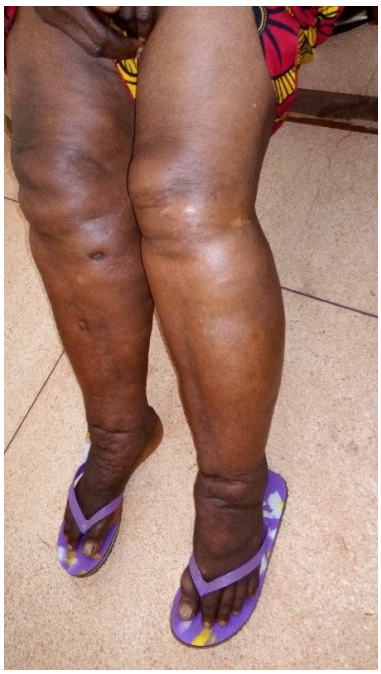

Fig. 1: An 80-year-old farmer with bilateral lymphoedema of 15 years secondary to lymphatic filariasis

Fig. 2: A 22-year-old seamstress with unilateral lymphoedema of four years secondary to lymphatic filariasis. She developed pyomyositis following scarification by traditional healers.

Wuchereria bancrofti was identified in nearly all the cases 17 (94.4%) while 1 (5.6%) case of Brugia malayi was seen. The combination of samples that most frequently yielded blood film microfilaria was 12midnight/2a.m samples, 8 (44.4%). The mean haemoglobin level, percentage eosinophic and ESR of the patients were 9.7 ± 1.5 g/dL, 11.1 ± 3.3%, and 43 ± 7 mm/1st hour, respectively. The laboratory results of the patients with confirmed LF are shown in Table 3.

Table 3: Laboratory findings in patients with confirmed lymphatic filariasis in Enugu, Nigeria

Parameter	N=18
Microfilaria type detected, *n (%)*	
W. bancrofti	17 (94.4)
B. malayi	1 (5.6)
Samples with positive microfilaria, *n (%)*	
2 am only	5 (27.8)
12 midnight only	4 (22.2)
12 midnight/2am	8 (44.4)
12 noon/2 a.m	1 (5.6)
Hb (g/dl)	9.7 ± 1.5
WBC (Total), x 10^9/L	5.1 ± 1.7
WBC (Differential), %	
Netrophils	48.1 ± 12.3
Lymphocytes	36.0 ± 14.5
Eosionophils	11.1 ± 3.3
Platelets, x 10^9/L	287 ± 45
ESR (mm/1st hour)	43 ± 7

Following treatment, reduction in lymphoedema was observed in 10 /17 (58 .8%) patients while resolution of secondary skin/soft tissue infection was seen in 13/ 14 (92.9%) patients . Of 6 patients who were able to have repeat blood film microscopy after filaricidal therapy , 5(83.3%) became afilaraemic . One patient required repeat filaricidal therapy before blood film became negative for microfilaria.

DISCUSSION

In this study, we found that one-third of patients with clinical suspicion of LF had blood film microfilaria confirmation . The patients were mostly women , middle aged , rural dwellers , farmers , poorly educated and of low social class . Late presentation with complications and disability was common . Improvement in lymphoedema was variable , while resolution of secondary skin infections and clearing of microfilaria (among patients with post -therapy blood film assessment) was the norm.

Unlike most parasitic infestations , the burden of LF and its debilitating sequelae is borne by adults at the peak of their productive years [2]. This was exemplified in our study as an overwhelming majority of our patients were over 40 years. Affected individuals are usually infected in childhood while the clinical features become apparent in adulthood [2]. A study conducted by Okorie et al in Ota, Ogun state, South - West Nigeria found that the prevalence of LF increases with age[5]. Unlike the global epidemiologic pattern , our patients were mostly females , a disparity that may be due to the better health-seeking behaviour of women considering that this was a hospital - based study.

Women are also more likely to seek health -care for cosmetic reasons when faced with a disfiguring illness . A community - based survey conducted at two sites in Ogun state, South -West Nigeria detected LF in more females than males at each site[8]. However , a survey conducted by Ladan et al, in Talata Mafara , Zamfara state , North -West Nigeria reported a significantly higher prevalence of microfilaraemia in men than in women [9]. Lymphatic filariasis is a disease of poverty and tends to affect people of low social class and those with low level of education.

This was the case in our study . Thus , the cycle of poverty, ignorance and disease is aptly captured in the narrative of LF and this is synchronous with other NTDs . Studies in Nigeria and India have shown that LF is common in patients with low socioeconomic status[9- 10]. Although patients with this disease are often abandoned by family members and stigmatized in communities , most of our patients were either married or widowed . Lymphatic filariasis is known to occur mostly in rural communities with poor housing and sanitation [2], as was evidenced in this study . However , both urban and rural dwellers can have LF[8,11].

The average duration of illness in this study was over six years . Bilateral lymphodema was more common than unilateral disease . There was however a single case of microfilaraemia without lymphoedema seen in a patient being evaluated for possible parasitic infestation . Lymphoedema was also the most frequent clinical feature of LF reported by Elkanah et al in Ardo Kola, Taraba state, North-East Nigeria [12]. Most of the other studies conducted in Nigeria did not highlight the pattern of clinical presentation of LF[5,8,9]. In this study , nearly 80% of patients had secondary skin /soft tissue infection , in keeping with the observation that chronic lymphoedema is often associated with recurrent episodes of secondary skin infections[2].

Limitation of movement was present in about three quarters of our patients. The disability imposed by this condition becomes more significant especially for those individuals whose livelihood depends on physical labour . Lymphoedema with accompanying limb infections leads to disfigurement resulting in physical disability [2]. A study in India revealed that patients with LF lose about one month of work per year due to the illness[13]. The contribution of LF to morbidity and premature deaths has been estimated using the Disability-Adjusted Life Years (DALY) with disability contributing more than mortality[14].

About 1% of the global DALYs is attributed to NTDs with LF accounting for 2.78 million DALY in the global burden o f diseases study[14]. Incidentally, disabilities caused by LF can be prevented by early diagnosis and appropriate treatment[1].

Lymphatic filariasis is often associated with co-morbidities that may compound the burden of disease. In our patients , the identified co - morbidities included DM, hypertension, anaemia and depression. It is possible that this is a reflection of the burden of these non - communicable diseases (NCDs) among adults attending health facilities in the study area, especially for hypertension and diabetes which are among the commonest NCDs in Enugu , South -East Nigeria [15]. There is a paucity of literature on the relationship between lymphatic filariasis and diabetes. An inverse relationship was reported by Aradvindhan et al [16], attributed to the lower levels of some pro-inflammatory cytokines in DM patients with coexisting LF[16].

Besides the physical disability , LF is usually associated with depression 4. Depression was present in one-tenth of our patients. A multi-centre study in Plateau state , Nigeria reported depression in 20% of patients with LF[17]. Depressive illness is a prevalent disability in LF possibly because of stigmatization and this has been estimated to be responsible for about 5 million DALY [18]. Anaemia was seen in about one -fifth of our patients. The aetiology of anaemia in patients with LF may be multifactorial . While our study design could not investigate this , possible causes of anaemia in patients with LF could include undernutrition and other co-morbidities. Inability to wear shoes also puts them at risk of hookworm infestation which is a well - recognised cause of anaemia in the tropics.

Laboratory confirmation of microfilaraemia was only achieved in 36% of patients who presented or were referred with provisional diagnosis of LF.

The average microfilaria prevalence rate across Nigeria is 8.2% with a range of 0 to 47 .4% [5]. Lymphatic filariasis is caused by *W. banccrofti , B. malayi , and B. timori*. About 90 % of all infestations globally and 100% of the infections in Africa are caused by W. Bancrofti [1]. In this study , over 90 % of infestations were caused by *W. Bancrofti*. It was unusual to find a single case of *Brugia malayi* in a Nigerian patient who has not lived outside Nigeria . The brugian parasites are usually confined to some areas in Asia notably India, Indonesia, Malaysia and Thailand [4]. Further studies in Africa are required to determine if this incidental finding is suggestive of changing epidemiology of *Brugian filariasis*.

One of the key lessons we learnt from this study is that LF continues to be a NTD whose tale is that of neglect , poverty and disability . With health education / community sensitization, improved training leading to high index of suspicion among clinicians and appropriate laboratory assessments , cases of LF could be identified earlier and treated with greater chances of good outcome . We also learnt that LF is commonly associated with multiple co -morbities including depression all of which might worsen the prognosis and increase the DALYs.

Our study had limitations that are worthy of note. Bearing in mind that this was a hospital -based study , the findings of this study is not generalizable to the communities in South -East Nigeria . No confirmatory diagnosis was ascertained in a quarter of patients despite evident lymphoedema and LF cannot be completely excluded in these patients . The non - availability of filarial antigen testing in our centre when the patients were managed is also a notable limitation . Giemsa -stained blood film has lower sensitivity than the filarial antigen testing [2,3], thus more cases could have been confirmed if filarial antigen testing was done. It is also possible that some of the patients had received anti-helminthic therapy as part of over-the-counter medications in the past which could reduce the chances of detecting peripheral blood microfilaria . Long -term use of antihelminthic drugs such as ivermectin has been shown to be capable of eliminating W. Bancrofti[18].

In conclusion , LF as seen in our practice is a tale of neglect (late presentation), low social class and disability . The enormosity of its physical and psychosocial complications is glaring. However, these complications can be ameliorated with early diagnosis and treatment. Poverty alleviation and improvement of living conditions of disadvantaged populations in endemic communities as well as intensified vector control are urgently needed for the control of LF.

DECLARATION

Competing interests: None.

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Author contributions : MOI and USU conceived the study . MOI , USU , SU and CCU designed the data collection tool and performed data collection. MOI, USU , SU and CCU managed the patients while EN conducted the laboratory diagnosis . MOI , SU , JIM , CAO , NMC and ODO conducted literature search . SU, CCU , JIM , and EN conducted data entry while MOI performed the data analysis . MOI and SU wrote the initial draft of the manuscript . All authors reviewed the manuscript and approved the final version.

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Ethical approval : Approval was obtained from the Health Research Ethics Committee of the UNTH.

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