

NEGLECTED TROPICAL SKIN DISEASES IN A NIGERIAN TERTIARY HOSPITAL.

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ABSTRACT

Background: Neglected tropical diseases (NTD) are a subset of chronic infectious diseases commonly found among the less privileged in developing countries. The World Health Organization (WHO) seeks to reduce and eventually eradicate these chronic disabling diseases which propagate poverty and under-development. The cutaneous manifestation of NTD is the major cause of morbidity and stigmatization. Thus the dermatologist has a key role to play in the abovementioned WHO goal. This study aims to identify skin NTD in a dermatologic practice in Nigeria and to mention some challenges to effective control of some.

Materials and Methods: This is a descriptive retrospective study in which the records of all patients presenting with skin NTD were extracted from the general dermatology out-patient records and analyzed.

Results: Two thousand seven hundred and fifty (2750) records of patients in the dermatology out-patient clinic were assessed, out of which 154 had skin NTD, accounting for 5.6% of the total population. The vast majority were males (63.6%), with a male to female ratio of 1.8:1; and a mean age of 28.4 ± 17.4 . Six NTD were identified, and the predominant type was scabies (66.9%), which was more common in males and students. Onchodermatitis (14.3%) on the other hand had a female preponderance.

Conclusion: Neglected tropical skin diseases (NTSD) are common in the urban dermatology clinic. The most prevalent (scabies) is a highly contagious disease, whose diagnosis remains sub-optimal among healthcare practitioners. Dermatologists are best positioned to ensure early diagnosis of a good number of NTD and stem their progression before the morbidity, disfigurement, stigmatization, and attendant short, and long-term complications develop.

Keyword: Neglected Tropical Skin Diseases, Nigeria, Scabies, Leprosy, Cutaneous Leishmaniasis, Lymphatic filariasis, Cutaneous larva migrans.

Running title: Neglected Tropical Skin Diseases in Nigeria

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INTRODUCTION

Neglected tropical diseases (NTD) include an assortment of communicable diseases prevalent in low-income countries in the tropics and sub-tropics. They are regarded as diseases of abject poverty, affecting the 'bottom billion' of the world's population, and due to their chronic, disabling, and stigmatizing characteristics promote the vicious cycle of poverty in regions where they occur.^{1,2} The stigmatization associated with many of these diseases arises from the observed skin manifestations. The term NTD was birthed when the global health community was alerted to the neglect of certain infectious

diseases by the pharmaceutical industry and public-private partnerships. These diseases were often devoid of effective, affordable and easy to use drugs.³ The reason for this neglect was obvious – profit making drives the development of new drugs, thus pharmaceutical companies were less likely to invest in the production of drugs for diseases that thrive among the poorest of the earth.

There are currently twenty entities listed in the NTD portfolio by the WHO⁴ [See Table 1], over 90% of which have dermatologic manifestations, while a good number can be diagnosed based on their appearance on the skin e.g., leprosy, onchodermatitis or scabies. The cutaneous manifestations of NTD often are the major reasons for morbidity and disfigurement, which foster stigmatization and discrimination. The role of dermatologists in diagnosis and management of NTD cannot be

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overemphasized; Hotez et al.⁵ state that dermatologists will be at the forefront of reducing the burden of NTD through accurate diagnosis and specific drug management. Hitherto, NTD have been described as diseases confined to rural areas and urban slums of the developing world, and it is true that they are preponderant in these areas; however the quest for treatment by rural dwellers, wars and displacement of persons, and the progressive rural-urban migration of people for economic advancement, invariably lead to the transmigration of NTD to urban areas.

The continued neglect of NTD locally and indeed globally is not an option, as this will be at the expense of public health, particularly when viewed against the backdrop of indices used in determining population health, such as disability-adjusted life years (DALYs), which is a summary measure of the burden of disease in a population. This measure ascertains the general health of a given population by incorporating two requisite health defining terms: Years of life lost from premature mortality (YLL); and years lived with disability (YLD) – the goal of which is the attainment of the standard life expectancy in sound health.⁶

This study thus seeks to document the spectrum of NTD seen in a Nigerian urban dermatology clinic, outlining the frequency, and some challenges encountered in the effective management of these conditions. This may help prevent the neglect of urban 'sanctuary sites' of NTD, which could form a nidus for continuous dissemination of infections.

MATERIAL AND METHODS

This was a retrospective survey in which the records of all consecutive first-time attendees to the dermatology outpatient clinic spanning a twelve year period - April 2006 to March 2018 were accessed. The records of persons with any form of NTD as specified by

the World Health Organization were extracted and analyzed. Diagnoses were predominantly clinical, however, in certain cases, confirmatory investigations included light microscopy for scabetic scrapings, skin biopsies, slit skin smear, skin snips, and blood tests. Data was captured in an excel sheet and analyzed via Statistical Package for Social Sciences version 20 (SPSS Inc, IL, Chicago, USA) in which the mean, frequencies and percentages were calculated. Results were presented using tables and figures.

RESULT

A total of 2750 new patients were seen at the dermatology outpatient clinic during the specified survey period, of which 160 had NTD accounting for 5.82% of the patient population. Due to incomplete entries in the data of some selected patients, only 154 cases were analysed. Six specific skin NTDs were encountered, with an age range of one to 89 years, and a mean age of 28.4 ± 17.4 ; patients in the third decade formed the predominant group in the survey, and there was an overall male preponderance with a male to female ratio of 1.8:1. (see Figure 1) This pattern was almost uniform to varying proportions across the various dermatoses except for onchodermatitis where females predominated as depicted in Table 2. Nearly half the survey population were students, while farmers formed the least represented group (Figure 2). Scabies was the most common dermatosis and was responsible for close to 70% of the entire diseases. Although there was a higher proportion of males with scabies, particularly among those aged 20 – 29 years as shown in Table 3, a chi-square test performed found no significant relationship between sex and scabies infestation. $\chi^2(1, N=154)=1.87, p=0.17$; however, there was a significant relationship between age/occupation and scabies infestation, $\chi^2(1, N=154)=20.14, p=.005$. Persons aged between 20 – 29 years were more likely to have scabies than others.

Table 1: List of Neglected tropical diseases

S/No	NEGLECTED TROPICAL DISEASES
1	Buruli Ulcer
2	Chagas disease
3	Dengue and Chikungunya
4	Dracunculiasis (guinea-worm disease)
5	Echinococcosis
6	Foodborne trematodiasis
7	Human African trypanosomiasis (sleeping sickness)
8	Leishmaniasis
9	Leprosy (Hansen's disease)
10	Lymphatic filariasis
11	Mycetoma, chromoblastomycosis and other deep mycoses
12	Onchocerciasis (river blindness)
13	Rabies
14	Scabies and other ectoparasites
15	Schistosomiasis
16	Soil-transmitted helminthiasis
17	Snakebite envenoming
18	Taeniasis/Cysticercosis
19	Trachoma
20	Yaws (Endemic treponematoses)

Figure 1: Age and sex distribution of the study

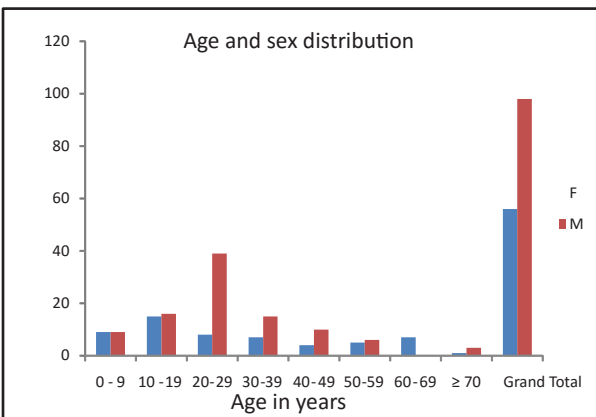


Table 2: Sex distribution of specific skin NTDs

Diseases	F	M	Grand Total
Cutaneous larva migrans	1 (0.6)	3 (1.9)	4 (2.6)
Cutaneous leishmaniasis	2 (1.3)	2 (1.3)	4 (2.6)
Leprosy	2 (1.3)	8 (5.2)	10 (6.5)
Lymphoedema	5 (3.2)	6 (3.9)	11 (7.1)
Onchodermatitis	13 (8.4)	9 (5.8)	22 (14.3)
Scabies	33 (21.4)	70 (45.5)	103 (66.9)
Grand Total	56 (36.4)	98 (63.6)	154 (100.0)

p = 0.19

Figure 2. Pie chart showing distribution of occupation.

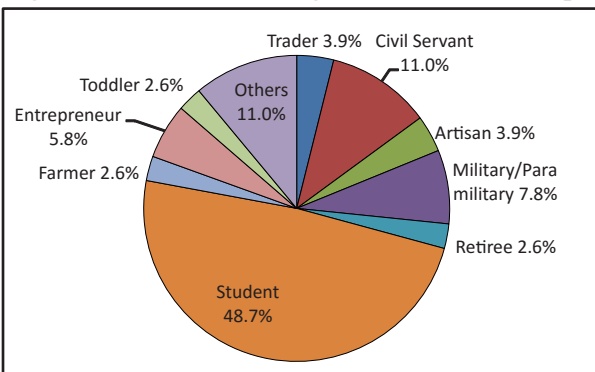


Table 3: Sociodemographic characteristics of persons with and without scabies

Variable	Present n (%)	Absent n (%)	p-value
Sex			
Female	34 (32.7)	22 (44.0)	X ² = 1.87 P=0.17
Male	70 (67.3)	28 (56.0)	
Age range			
0 – 9	16 (15.4)	2 (4.0)	P=0.005
10 – 19	20 (19.2)	11 (22.0)	
20 – 29	37 (35.6)	10 (20.0)	
30 – 39	15 (14.4)	7 (14.0)	
40 – 49	6 (5.8)	8 (16.0)	
50 – 59	7 (6.7)	4 (8.0)	
60 – 69	1 (1.0)	6 (12.0)	
≥ 70	2 (1.9)	2 (4.0)	
Occupation			
Trader	2 (1.9)	4 (8.0)	P=0.001
Civil Servant	7 (6.8)	10 (20.0)	
Artisan	3 (2.9)	3 (6.0)	
Military/Paramilitary	9 (8.7)	3 (6.0)	
Retiree	0 (0)	4 (8.0)	
Student	60 (58.3)	15 (30.0)	
Farmer	0 (0)	4 (8.0)	
Entrepreneur	6 (5.8)	3 (6.0)	
Toddler	4 (3.9)	0 (0)	
Others	12 (11.7)	5 (10.0)	

DISCUSSION

Neglected tropical diseases, like skin diseases, are best known for their propensity to cause morbidities rather than mortalities. For a healthcare system that focuses more on mortality rates, this may probably account for why both entities are 'neglected' by governments and health organizations. As at 2012, Nigeria was said to be the African country with the highest number of NTD.⁷ The WHO global health observatory data for 2016, also places Nigeria as having the 4th highest burden of leprosy in Africa.⁸ These statistics portend an enormous public health crisis when the estimated population of Nigeria of 198 million⁹ is considered, and in view of her struggling healthcare system.

Among the six diseases identified in our survey, four including onchocerciasis, lymphatic filariasis, leprosy, and cutaneous leishmaniasis are endemic in Nigeria, with the region of this study having foci of onchocerciasis and lymphatic filariasis.^(8,10,12) Scabies and soil-transmitted helminthiasis have a worldwide distribution but are considered diseases of the poor. It is noteworthy that two-thirds of the study population fall between ages 20 – 59 in a

country with an average life expectancy of 53/56 (male/female).¹⁰ This implies that the most socioeconomically productive group are those at risk for the morbidities associated with NTD. Studies have shown the considerable impact of NTD in Nigeria and the potential for a public health crisis in the absence of requisite interventions.^{7,13,14} However, detailed epidemiological data are quite limited.

Specific Neglected Tropical Skin Diseases in the study

Scabies

Scabies is a ubiquitous highly communicable skin disease which was only recently included in the list of NTD.¹⁵ It is among the three most common NTD, with over 200 million people infested globally at any given time.^{16,17}

The marked proportion of scabies influenced variables such as age, sex, and occupation in the study. In spite of the huge burden of scabies in the society, especially among the rural poor and institutionalized persons^{18,19}, the epidemiology of scabies is little known in Nigeria. Prevalence values have ranged from 0.2 -16.2%, but these have involved children and adolescents.^{18,20,21} A systematic review of reports of skin diseases by dermatologists within this millennium showed scabies to be the 18th of 122 most common dermatoses seen in Nigerian skin clinics, with a relative frequency of 1.74%.²² Our study showed an increased frequency among males (not statistically significant), similar to that reported by Anderson et al.(23), and as seen in a welfare home in Malaysia(24), however, the influence of sex in one rural survey that involved different populations was varied(18). Children and adolescents are often more commonly affected.(25) However, the distribution in our study was highest among persons in the third decade of life, majority of whom were male undergraduates living in hostel facilities. University hostels

across Nigeria are known to be overcrowded, with close to 10 - 15 persons living in a space originally designated for two - four,^{26,27} it is therefore not surprising that the distribution was highest among this subset of persons, bearing in mind the contagiousness of scabies. Also, most of the diagnosis in children and young adolescents are made at the paediatric outpatient clinic, with the more challenging cases referred to our dermatology clinic. While data of patients' socio-economic status was not captured, a good number of the patients cannot in any way be classified as belonging to the 'bottom billion' or living under the poverty threshold as defined by The World Bank.^{28,29} In addition to students, there were wealthy businessmen and women, senior civil servants, university lecturers, military and paramilitary personnel who were diagnosed with scabies. All patients, irrespective of socioeconomic status were managed with 25% benzyl benzoate emulsion, as this was the only available stand-alone anti-scabicide (apart from oral ivermectin) in our area. A number of patients had also already used the agent for varying durations before presentation at our facility. The marked irritation of this medication was a strong deterrent to its correct application by patients and its use among the very young.

Untreated scabies can often get secondarily infected by group A streptococci (GAS) and staphylococci. The former has been associated with such sequelae as acute post-streptococcal glomerulonephritis, acute rheumatic fever and chronic rheumatic heart disease.^{30,34} This has the potential of causing chronic renal damage and valvular heart diseases which are also common among adults in developing nations.

While scabies might be regarded as a disease of the 'bottom billion', more than any other NTD, it possesses the capability to climb up the socioeconomic ladder rapidly, affect both rich and poor, and become a full-blown public health epidemic on account of its high

degree of contagiousness, and the impact of climate change which affords it the perfect milieu to thrive.^{35,36} These and the absence of the treatment of choice will make the goal of eradication of one of the most, if not the most contagious NTD a mirage.

Onchodermatitis

This is the skin manifestation of onchocerciasis, a condition which is sometimes referred to as 'river blindness'. The nickname follows its increased occurrence along flowing rivers, and its potential to cause blindness.^{37,38} However, the pathway to blindness is through the skin, and the early discovery of onchodermatitis can reduce the prevalence of blindness caused by onchocerciasis. The region where the data for this study was obtained is endemic for onchocerciasis and recorded the highest prevalence of site-specific blindness in a survey among three endemic states in the country.³⁸ Onchodermatitis was the second most common NTSD in our study, and there were more consultations by affected females, which was however not statistically significant. The most common form was chronic papular onchodermatitis (CPOD), others included leopard skin, depigmentation, and acute papular onchodermatitis. Pruritus was more marked in the former, which was also more common in adolescents and young people. A similar finding was reported by Bari³⁹, while Dozie et al.⁴⁰ found depigmentation to be the most common form, followed by CPOD. A few of the adolescents seen were students who had gone to boarding schools in endemic areas and returned with infections. Most affected persons had at one time or another been on yearly or six monthly doses of ivermectin, sometimes in addition to diethylcarbamazine – showing the impact of the African Programme on Onchocerciasis Control (APOC) with its Community-Directed Treatment with Ivermectin (CDTI). While this might in some way reflect the success of APOC, the corollary is the

observation that a significant proportion of patients presenting to the dermatologist for any form of pruritus or pruritic dermatoses are already on ivermectin without a definitive diagnosis.

The marked discomfort from the associated pruritus, the stigmatizing nature of chronic onchodermatitis, the disruption of social relationships^{41,42} and the marked risk of blindness with further social isolation makes it imperative that onchodermatitis be identified and treated early.

Lymphatic filariasis

Described as one of the world's leading cause of avoidable disability, Lymphatic filariasis (LF) is endemic in Nigeria, which currently holds the unenviable title of being the country with the second highest burden of LF in the world, after India.⁴³ Early infection which often occurs in childhood is characterized by the presence of adult worms in the lymphatics, and microfilariae in the blood, but is mostly asymptomatic.^{44,45} Hydrocoele, lymphoedema, and elephantiasis are the chronic sequelae of infections by any of the three species of mosquito-bearing parasites which cause damage to lymphatic vessels, including wuchereriabancrofti, brugiamalayi, and brugiatimori. Lymphoedema was the most common clinical presentation in our survey and mostly affected the lower limbs. About half of the affected persons also had recurrent interdigital tinea pedis, known to present a portal of entry for bacteria, leading to acute attacks of dermato-lymphangio-adenitis (ADLA) – frequent ADLA worsens lymphoedema and eventuates in elephantiasis.⁴⁴ Microfilariae were not demonstrable in the blood of any of the patients as is expected in the chronic stage of LF.⁴⁵ The findings in our study of patients with solely chronic sequelae of LF would presuppose that disease transmission might not be ongoing in the urban towns, this assertion is invalidated by studies which have proven the continued transmission of

wuchereriabancrofti in urban areas including ours.^{46,47}

Leprosy

The highly disfiguring stigma of untreated leprosy makes it one of the most socially isolating diseases of all time. The number of new cases in the country dropped from 2892 in 2015 to 1362 in 2016, thus Nigeria now ranks 4th and 12th amongst countries with the highest burden of leprosy in Africa and globally respectively.⁸ All the cases we saw were newly diagnosed, and more than half were in their third decade of life. There was no sex or occupational predilection, and no child or adolescent was diagnosed. Most had the tuberculoid form, thus there was no marked disfigurement observed, notwithstanding, many of the patients had been to several healthcare facilities for prolonged periods prior to consultation with us without a diagnosis being made. This highlights the presence of delayed diagnosis, and the need for dermatologists to be involved in any programme that aims to eradicate diseases with skin manifestations, since dermatologists make more accurate dermatologic diagnoses compared to primary care physicians (PCP), in spite of the fact that PCP see more patients with skin diseases than dermatologists.^{48,49}

Cutaneous leishmaniasis

Cutaneous leishmaniasis is the most common, least fatal form of Leishmaniasis, with the other forms being visceral and mucocutaneous. It is both a zoonotic and anthroponotic infection caused by leishmania parasites, and spread by sandflies.⁵⁰ According to WHO, cutaneous leishmaniasis (CL) is endemic in Nigeria.¹² However, this endemicity have occurred in foci, which since the initial report by Dyce Sharp in Kaduna⁵¹, have been solely restricted to the Central and Northern parts of Nigeria.^{52,56} Thus the finding of four cases of CL in the Deep South, where to the best of our knowledge, no report of CL has emanated,

has important public health implications. All cases had recently returned from the Northern part of the country, where they had been resident, among whom was a military man who had just returned from Maiduguri, a city in North Eastern Nigeria, where he was deployed to fight against the Boko Haram (terrorist group) insurgency. His account which stated that the disease was common in the community, and was called 'Mallumfatori' by the locals, assisted dermatologists who had no previous exposure to such a condition to entertain a clinical suspicion of CL before the eventual histologic confirmation. Another had just returned from a one year mandatory national service (Youth Service) in the North, where she first noticed the rash which expanded rapidly within a short period. With the constant migration and displacement of people from one region to another, there lies a potential for rapid spread of CL to non-endemic areas, and a high probability of delayed or misdiagnosis due to the absence of the requisite diagnostic acumen required to identify the sometimes 'exotic' manifestation of the disease. Diagnosis of CL has sometimes been a challenge even in regions with high endemicity.⁵⁷

Cutaneous larva migrans

This is not in itself listed as a neglected tropical disease, however, as the larval form of a soil-transmitted helminth, (STH) it has been included among the group of NTSD. Cutaneous larva migrans (CLM) represents the clinical migration of animal hookworm larva through the skin. The infection is usually acquired through skin contact with larva-containing animal faeces in the soil. Common species of hookworm that cause CLM include *Ancylostomabraziliense*, *Ancylostomacanthinum*, and *Ancylostomaceylanicum*.⁵⁸ While most infections are self-limiting and do not progress beyond the creeping pruritic dermatitis in the skin, *A. ceylanicum* can establish infection in the human intestine.⁵⁹ Human hookworms such as *A. duodenale* and *Necatoramericanus* have also been known to cause CLM,

following the penetration of their larva into the skin.⁵⁹ About 1.5 billion people are infected with STH worldwide,⁶⁰ and as far back as eight years ago, close to 500 million people had hookworm infestation globally.⁶¹ Only a handful of persons presented with the disease, which is thought to be more common in tourists who visit the beaches in the tropics and sub-tropics where they come in contact with warm, moist contaminated sand.

Nigeria has a huge burden of STH, particularly hookworm infestation which accounts for over 3 million infected persons – the highest in Africa.⁶² With such an enormous burden of hookworm infestation and the chances of the human hookworms assessing the intestines via penetration and migration through the skin, the investigation of persons with CLM for intestinal hookworm infestation ceases to be an improbable option.

CONCLUSION

Neglected tropical skin diseases might have had their origin among the very poor in rural areas and urban slums; however, they are now evident in urban towns among the middle class, and in some cases the elite. The need for the integration of dermatologists at the forefront of the fight against NTD cannot be overemphasized. Dermatologists possess the knowledge and skill, and are strategically positioned to identify these infections/infestations early - before the development of disfigurement and stigmatizing features.

Limitations: This hospital-based study represents the group of persons with NTSD who sought intervention in an adult dermatology clinic of a tertiary health institution, and not the prevalence of NTSD in the general population. It, however, serves as a pointer to the existence of NTD in urban areas. It is of utmost importance that the findings in our study be interpreted in the context of the study design.

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