
Clinical Profile of Buruli Ulcer Patients in a Referral Hospital in Anambra State, Nigeria

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ABSTRACT: Background: Buruli ulcer is a chronic, debilitating, necrotizing disease of the skin and soft tissue caused by *Mycobacterium ulcerans*. Early detection and appropriate treatment of the patients are currently the most important measures for preventing the debilitating consequences of the disease.

Objective: To assess the clinical profile of Buruli ulcer patients presenting in a referral hospital in Anambra state, Nigeria.

Methods: A cross-sectional descriptive study was carried out among a cohort of 39 Buruli ulcer disease patients referred to a referral hospital in Anambra State between July and December 2021. A semi-structured, interviewer-administered questionnaire was used to collect data on the socio-demographic characteristics and the clinical presentation of the patients. Data were analyzed using SPSS version 22; with alpha set at $p\text{-value} \leq 0.05$.

Results: Twenty one (53.8%) of the study participants were males while 18 (46.2%) were females. Their mean age was 28.41 ± 18.668 . Active lesions in the form of ulcers were seen in 38 (97.4%) of the participants while lesions were seen in the lower limbs in 35 (87.2%) of them. Statistically significant association existed between the clinical presentation of Buruli ulcer disease and the occupation of the respondents ($p \leq 0.05$).

Conclusions: Buruli ulcer still exists in the Nigeria and presents majorly with ulcers on the lower limbs. Public health efforts aimed at patient education and to assist with early detection of the disease to minimize associated morbidity should be instituted.

KEYWORDS: Buruli ulcer, clinical profile, hospital, Anambra State, Nigeria

1. INTRODUCTION

Buruli ulcer is a chronic, debilitating, necrotizing disease of the skin and soft tissue caused by *Mycobacterium ulcerans* (*M. ulcerans*) (1,2). It has been variously called Bairnsdale ulcer, Daintree ulcer, Mossman ulcer, and Searl ulcer depending on the geographic area where they are found (3). It was first described by Sir Albert Cook in 1897 at Mengo hospital in patients from the Buruli County of Uganda, while its causative organism, *Mycobacterium ulcerans*, was first isolated in 1948 by MacCallum in the Bairnsdale region of Victoria, Australia (4).

Buruli ulcer has been reported in many regions of the world especially in the tropical regions of West and Central Africa, Australia, and Japan (2,5-9). The exact burden of the disease at the global and national levels is not entirely known. However, approximately 6000 cases of the disease are reported annually globally, especially from rural Africa (10). Buruli ulcer is also endemic in Nigeria though its current distribution is unclear (11-18). The disease most commonly affects impoverished inhabitants in remote rural areas with limited access to health care. It often occurs in close proximity to slow-flowing or stagnant bodies of water. There are no specific racial or sexual predilections for the disease. All ages may be affected though most cases occur in children aged 5-15 years, except in Australia, where it is more prevalent in adults older than 50 years (19,20). Buruli ulcer has a low mortality rate. However, it is a significant source of morbidity and socioeconomic burden. The skin and soft-tissue necrosis it causes can be extensive, involving as much as 15% of the patient's skin surface and may extend deep, exposing fascia, muscle, and bone (10,21). It heals slowly and may result in cosmetically disfiguring scars and functional disabilities if treatment is delayed. Half of these patients develop crippling sequelae (22). Long-standing Buruli ulcers may also transform into squamous cell carcinomas (22,23). Affected individuals and their households live through trauma arising out of societal prejudice about the cause of the disease, and the accompanying stigma and social seclusion associated with the disease could prevent some household members from working and affected women in particular, may consequently suffer divorce and other forms of indignity (24-27).

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The exact mode of transmission of the disease is unknown, however it has been postulated that *Mycobacterium ulcerans* most likely causes infection through contamination of traumatic wounds. Cases occur in areas around bodies of water that are stagnant or slow moving, with many cases occurring during the rainy season. In areas of endemicity, reservoirs of the mycobacterium appear to be in biofilms in water sources, aquatic insects, mollusks, and fish (9). The incubation period of the disease ranges from 1-9 months, with a mean of 4.5 months. Consequently, most patients do not recall an inciting event before its onset (28). Lesions usually begin as a single, painless and occasionally pruritic, dermal papule or subcutaneous nodule; and suppuration and necrotic ulceration occur within 1-2 months. Apart from these, the patients are generally healthy. Systemic symptoms such as fever or lymphadenopathy are rare owing to the immunosuppressive effects of mycolactone, elaborated by *M. ulcerans* (29).

There are basically two clinical presentations of *Mycobacterium ulcerans* disease. These are the non-ulcerative and the ulcerative forms (30). In the pre-ulcerative stage, Buruli ulcer manifests initially as a firm, non-tender, subcutaneous nodule measuring 1-2 cm in diameter. Less common presentations include a dermal papule or indurated plaque. A more aggressive edematous variant is frequently seen in Australia. The edematous variant causes a rapid onset of diffuse swelling, which can involve an entire extremity and evolves into an extensive ulcer. This is frequently misdiagnosed as cellulitis (20). The ulcerative stage occurs days to weeks later and may reach up to a year (31). The skin covering the plaque or nodule slowly sloughs, leaving an extensive necrotic ulcer with undermined edges. The ulcers may also be very deep and may expose tendons and bone with an attendant osteomyelitis. The surrounding skin may be edematous and show changes in pigmentation. The subcutaneous necrosis may extend several centimeters beyond the edge of the ulcer thus the lesion may appear smaller than its actual size. Characteristic lesions have a scalloped border and a sloughing, necrotic base. The ulcers may appear yellow or green and have a characteristic smell. Pain and local lymphadenopathy suggest secondary infection (32).

Classically, Buruli ulcers are considered an expanding ulceration of the lower extremity, even though they can occur on any part of the body. Approximately 90% of the lesions occur on the limbs, with 60% occurring on the lower extremities. Patients present with non-ulcerative lesions in 0-30% of cases and with ulcerative lesions in 70-100% of cases (33). Buruli ulcers may also destroy nerves, appendages, and blood vessels and may invade bones. Metastatic lesions may occur on the skin, soft tissue, or bone via spread through the vasculature or lymphatics. Approximately 33% of patients present with underlying osteitis, osteomyelitis, or joint involvement (10). However, one fourth of the patients with *M. ulcerans* osteomyelitis have no apparent history of cutaneous Buruli ulcer (22).

Effective treatment of Buruli ulcers relies on timely and accurate diagnosis. The differential diagnosis of the disease is varied and may depend on the frequency of other diseases with similar manifestations in different geographical locations (4,6). However, in a known endemic area, its diagnosis can be made based on clinical observation that considers clinico-epidemiological features which indicate that most cases are in children under 15 years of age, about 85% of lesions are on the limbs and lower limb lesions are twice as common as upper limb lesions. When Buruli ulcer is treated early, antibiotics therapy alone is adequate. If treatment is delayed, surgical debridement, skin grafts, extensive wound care, and physical therapy may be needed to attenuate debilitating sequelae.

This study was aimed to assess the clinical profile of Buruli ulcer cases presenting in a referral hospital in Anambra state, Nigeria. The findings from this study are expected to provide the information that will bring to the fore the issue of advocacy for enhancing awareness, diagnosis and early case detection at the community level as well as to guide the policy makers in strengthening and improving the existing Buruli ulcer control programme in Anambra State and in other parts of Nigeria.

2. MATERIALS AND METHODS

2.1. Study Area: This study was carried out at St Joseph's Hospital, Adazi Nnukwu, Anambra State Nigeria. St Joseph's Hospital, Adazi Nnukwu is a missionary hospital run by the Catholic Church Archdiocese, Awka. The hospital provides general health care services to its patients who generally come from Anambra State and its environs. The hospital also serves as a referral centre for the detection and treatment of Buruli ulcer disease in Anambra State and other parts of Nigeria under the auspices of the Buruli Ulcer Control Programme. This programme is supported and fully funded by the German Leprosy and Tuberculosis Relief Association, Nigeria and the services (including accommodation, drugs, surgery and dressing materials) are rendered at no cost to the patients. The Buruli ulcer patients are recruited in cohorts from endemic areas and referred to the hospital within treatment periods stipulated by the sponsors. The recruitment is facilitated through active surveillance by a network of community-based Buruli ulcer focal persons living in the endemic areas or through outreach programmes organized on ad-hoc basis to create awareness on Buruli ulcers.

2.2. Study Design: This was a cross-sectional prospective study of a cohort of Buruli ulcer patients recruited and referred to the hospital between July and December 2021.

2.3. Study Population: Patients with suspected Buruli ulcer recruited and referred to the hospital between July and December 2021.

Inclusion Criteria: Patients with Buruli ulcer who gave informed consent to participate in the study

Exclusion Criteria: Patients with Buruli ulcer who did not give informed consent or were not present on the days of data collection.

2.4. Study Instruments: A semi-structured interviewer-administered questionnaire adapted from the manual for health care providers for the management of *Mycobacterium ulcerans* disease (30) was used for this study. The questionnaires were used to

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collect information on the socio-demographic characteristics of the respondents as well as their clinical presentations and care-seeking behaviours.

2.5. Data Collection Methods: The semi-structured questionnaires were administered to the thirty nine (39) eligible respondents presenting at the referral hospital using face-to-face interviews conducted by the principal researcher and the trained research assistants. Prior to the administration of the questionnaires, each respondent gave verbal informed consent. Each questionnaire took about 20 minutes to administer. Data collection lasted for a period of six months corresponding to the duration for recruiting and referring the patients to the hospital.

2.6. Data Processing and Analysis: The clinical presentations of the Buruli ulcer patients were classified as active and inactive cases. Active cases included papules, nodules, plaques, edematous forms, ulcers and osteomyelitis while inactive cases included amputations, scars and scar deformities (30). Statistical data analysis was carried out with the aid of the International Business Machines-Statistical Package for Social Sciences (IBM-SPSS) version 22 (34). Frequency distribution of all relevant variables was developed. Their means and proportions were calculated. The association between the clinical presentation of Buruli ulcers as active or inactive cases and the socio-demographic characteristics of the respondents were tested using Fishers exact test. Level of statistical significance was set at $p\text{-value} \leq 0.05$.

3. RESULTS

A total of 39 questionnaires were administered to all the clinically diagnosed Buruli ulcer patients referred to the hospital between July and December 2021. All the questionnaires were retrieved, giving a response rate of 100%.

Table 1. Socio-Demographic Characteristics of the Respondents

Variable	Frequency (n = 39)	Percentage (%)
Age at last birthday (Years)		
<=15	13	33.3
16-32	10	25.6
33-49	9	23.1
>=50	7	17.9
Mean ± SD	28.41±18.668	
Minimum, Maximum	2,68	
Gender		
Male	21	53.8
Female	18	46.2
Religion		
Christianity	39	100
Islam	0	0
Traditional religion	0	0
Others	0	0
Educational status		
No formal education	2	5.1
Primary	19	48.7
Secondary	15	38.5
Tertiary	3	7.7
Occupation		
Student	14	35.9
Trader	6	15.4
Farmer	4	10.3
Artisan	9	23.1
Unemployed	1	2.6
*Others	5	12.8
Parent's occupation (n = 19)		
Civil servant	2	10.5
Trader	10	52.6
Farmer	5	26.3
Artisan	2	10.5

*Others = Driver, Pastor, Retired teacher

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Table 1 summarizes the socio-demographic characteristics of the respondents. Their ages ranged from 2 to 68 years while their mean age was 28.41 ± 18.668 . Majority of the respondents (33.3%) were in the age range of ≤ 15 years. However, a significant proportion of the respondents were in the age range of 16 – 49 years and when combined, this age range contains the highest proportion (48.7%) of the respondents. All the respondents were Christians and most of them attained some level of formal education. Only 5.1% of them did not attain any level of formal education. Majority of the respondents were students (35.9%) and artisans (23.1%).

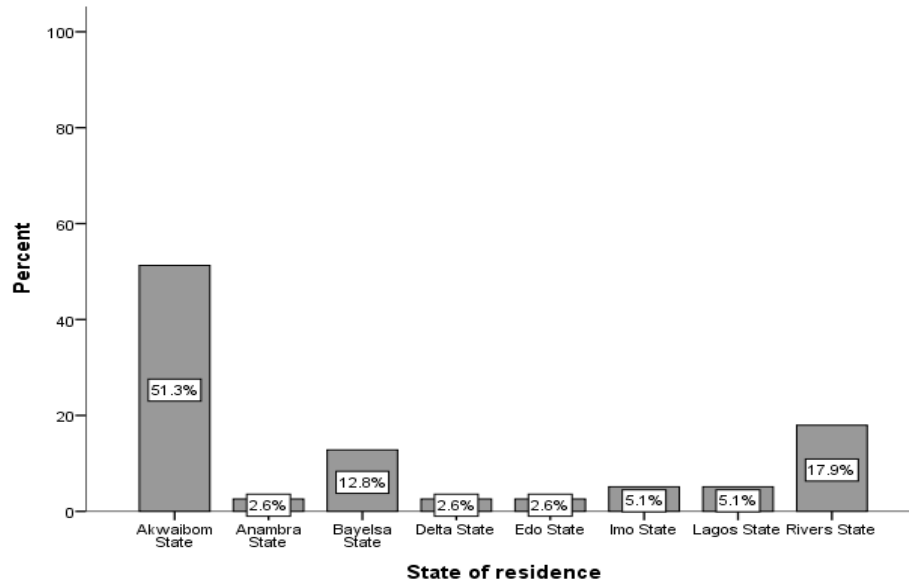


Figure 1. State of Residence of the Respondents

Figure 1 shows the state of residence of the respondents. More than half of all the respondents (51.3%) came from Akwaibom State while the least proportion of the respondents (2.6% each) came from Anambra, Delta and Edo States.

Table 2. Clinical Profile of the Respondents

Variable	Frequency (n = 39)	Percentage (%)
Classification of patient		
New case	20	51.3
Recurrent case	19	48.7
Type of lesion seen		
Active	38	97.4
Inactive	1	2.6
Clinical form of lesion seen (multiple answers)		
Papule	0	0.0
Nodule	2	5.1
Plaque	1	2.6
Oedema	2	5.1
Ulcer	38	97.4
Osteomyelitis	9	23.1
Amputation	1	2.6
Location of the lesion		
Left lower limb	17	43.6
Right lower limb	15	38.5
Left and right lower limbs	2	5.1
Left upper limb	2	5.1
Right upper limb	1	2.6
Left and right upper limbs	1	2.6
Right upper limb and right lower limb	1	2.6

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Table 2 shows the clinical profile of the respondents. The proportion of the new and recurrent cases was almost equal (51.3% versus 48.7%). Almost all the respondents (97.4%) presented with active lesions in the form of ulcers while 87.2% of the lesions were located in the lower limbs.

Table 3. Association between the clinical presentation of Buruli ulcer and the Socio-demographic Characteristics of the Respondents

Variable	Active clinical presentation (n = 38) (Number, %)	Inactive clinical presentation (n = 1) (Number, %)	Test statistic	P-Value
Age at last birthday (years)			F = 3.421	0.331
<=15	13 (100)	0 (0.0)		
16-32	10 (100)	0 (0.0)		
33-49	8 (88.9)	1 (11.1)		
>=50	7 (100)	0 (0.0)		
Gender			F = 0.880	0.348
Male	20 (95.2)	1 (4.8)		
Female	18 (100)	0 (0.0)		
Educational status			F = 1.642	0.650
No formal education	2 (100)	0 (0.0)		
Primary	19 (100)	0 (0.0)		
Secondary	14 (94.3)	1 (6.7)		
Tertiary	3 (100)	0 (0.0)		
Occupation			F = 39.000	0.000*
Student	14 (100)	0 (0.0)		
Trader	6 (100)	0 (0.0)		
Farmer	4 (100)	0 (0.0)		
Artisan	9 (100)	0 (0.0)		
Unemployed	1 (100)	0 (0.0)		
*Others	4 (80.0)	1 (20.0)		
State of residence			F = 0.975	0.995
Akwaibom State	19 (95.0)	1 (5.0)		
Anambra State	1 (100)	0 (0.0)		
Bayelsa State	5 (100)	0 (0.0)		
Delta State	1 (100)	0 (0.0)		
Edo State	1 (100)	0 (0.0)		
Imo State	2 (100)	0 (0.0)		
Lagos State	2 (100)	0 (0.0)		
Rivers State	7 (100)	0 (0.0)		

* = Statistically significant (≤ 0.05); F = Fishers exact test; Others = Driver, Pastor, Retired teacher

Table 3 shows the association between the clinical presentation of Buruli ulcers as active or inactive cases and the sociodemographic characteristics of the respondents. Statistically significant association existed between the clinical presentation of Buruli ulcer disease and the occupation of the respondents. The other variables were not statistically significantly associated with the clinical presentation of Buruli ulcers.

4. DISCUSSIONS

This cross-sectional descriptive study was carried out to assess the clinical profile of Buruli ulcer cases presenting in a referral hospital in Anambra state, Nigeria. This study showed a nearly equal distribution of new and recurrent cases of Buruli ulcer disease among the respondents. However, almost all the lesions seen in this study were in the active phase while the most common clinical form of the lesion seen was ulcers. This finding is similar to findings from most studies of Buruli ulcer patients in rural, endemic areas of Africa where the clinical forms seen were mostly restricted to advanced ulcers. Here, patients present with non-ulcerative lesions in 0-30% of cases and with ulcerative lesions in 70-100% of cases (35-37). The finding that 23.1% of the respondents in this study had osteomyelitis is also similar to the findings elsewhere where approximately 33% of the patients presented with underlying osteitis, osteomyelitis, or joint involvement.³ This presentation has been thought to result from the necrotic process in an advanced

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lesion extending through deep fascia and exposing deeper structures like muscles or bones. These findings are however contrary to the findings from Australia where Buruli ulcer patient cohorts presented with early lesions (38). The presentation of most of the Buruli ulcer disease patients with ulcers in African settings has been attributed to cases typically reporting to health facilities at the late stages of the disease (35-37). However, the differences in the stages of presentation observed in different settings may also be explained by the results of molecular typing of *Mycobacterium ulcerans* from different parts of the world which showed that differences exist in the strains of the organism isolated as well as the different combinations of the mycolactones elaborated by these organisms in different settings (39). Strains of *Mycobacterium ulcerans* from Africa have been demonstrated to typically produce mycolactones A and B, which are more potent in causing necrosis whereas strains from Asia and Australia typically produce mycolactone C, with less amounts of mycolactones A and B. These strains are usually less virulent mycobacteria (40).

Statistically significant associations existed between the clinical presentation of Buruli ulcer disease and the occupation of the respondents in this study while the other variables did not achieve statistically significant associations. A further analysis of the occupation of these respondents showed that only the pastor presented with an inactive form of the disease while the others presented with the active form of the disease. It has been observed that treatment seeking behaviour could be related to the perception of the cause of the disease (18). In many developing countries and especially in sub-Saharan African countries, there is a widespread labeling of diseases as manifestations of satanic attack or 'bewitching' by wicked people (41-45). This observation presupposes that the religion of the patient will come to bear on the care-seeking practices he adopts. Thus many patients would have visited various spiritual houses with no visible improvement or cure before presenting for appropriate care. The finding in this study that only the pastor presented with an inactive form of the disease lends credence to this.

5. CONCLUSIONS/RECOMMENDATIONS

This study has shown a nearly equal distribution of new and recurrent cases of Buruli ulcer disease with almost all the lesions seen in the active phase. The most common clinical form of the lesion seen is ulcers occurring on the lower limbs. Therefore, in order to ensure the early confirmation of diagnosis and to facilitate the timely management of the disease, it is recommended that public health efforts aimed at patient education and to assist with early detection of the disease to minimize associated morbidity are necessary. Community-based volunteers should be trained in highly endemic areas by public health officials to assist in the surveillance and early detection of Buruli ulcers. Awareness campaigns and intensive appropriate health education on Buruli ulcer disease should also be given to community members by the organizers of Buruli ulcer control programmes and sustained by the appropriately trained community-based volunteers. This will lead to an increased capacity of community members to recognize Buruli ulcer disease symptoms and improve their attitude to the disease as well as their ability to refer suspected cases for appropriate medical treatment.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval (Ref: COOUTH/CMAC/ETH.C/VOL.1/FN:04/0098) for this study was obtained from the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Ethics Committee. Permission to conduct the study was obtained from the German Leprosy and Tuberculosis Control Programme, Enugu; Anambra State ministry of health and the management of St. Joseph's hospital, Adazi Nnukwu. In addition, verbal informed consents were obtained freely and without coercion from all the respondents and respect for confidentiality of the data obtained from them ensured.

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