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Buruli Ulcer Disability in Ghana: The Problems and Solutions

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Author's contribution

This work is a sole-authorship one. The author designed the review, wrote the draft of the manuscript and managed the literature searches; diligently read and approved the final manuscript.

Review Article

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ABSTRACT

Buruli ulcer (BU) is a tropical disease caused by Mycobacterium ulcerans (M. ulcerans) but with "unknown" means of transmission. In order to help reduce this disease, many preventive and treatment measures have been recommended and used in the past years around the globe. This aims to review BU disability problems, prevention and treatment procedures used in Ghana. The review was done by soliciting information from literatures, published articles, news reports and presentations on Buruli ulcer disability prevention and treatment in Ghana. BU disease results in disabilities such as contractures, amputation of the arms and legs, loss of eyes and eyelids and loss of nose among others. Antimicrobial therapies, prevention of deformities and surgical interventions have been the main treatment options for BU in Ghana. Prevention of disabilities caused by BU can be achieved by early detection, treatment of the disease supported by intensive health education programs within the prone areas and empowerment of patients through small-scale welfare grants.

Keywords: Buruli ulcer; disability; prevention; health education; intervention.

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1. INTRODUCTION

Buruli ulcer (BU) is an infectious disease that affects the skin, subcutaneous tissue and sometimes the bone but the natural reservoir of the bacillus and the mode of transmission of the disease are unclear [1,2]. Globally, BU is the third most common mycobacterial disease after tuberculosis and leprosy [3]. In Ghana, BU is currently the second mycobacterial infection after tuberculosis [4]. BU may affect all parts of the body but most frequently the lower extremities [5,6] and the infection is usually restricted to relatively small geographical areas and patchy in its distribution [7,8]. This review identifies the problems of BU disabilities and the various methods used in their prevention and treatment in Ghana. It was done by soliciting information from published articles, news reports and presentations on Buruli ulcer disability prevention and treatment in Ghana.

2. EPIDEMIOLOGY

M. ulcerans infection was first described in Australia in 1948 [9]. The disease was named after Buruli County in Uganda (now called Nakasongola District), because of the many cases that occurred there in the 1960s [10,11]. Africa tops the list of the most affected regions and according to WHO's statistics, Cote d'Ivoire recorded 24,000 cases, Ghana recorded 11,000, and Benin has 7,000 confirmed cases [12]. Thus currently, Ghana is the second most endemic country (recording about 10,048 cases) of BU after Cote d'Ivoire [13]. It is a severe disabling and disfiguring disease caused by *M. ulcerans* [14,15]. BU was first brought to the public's attention in Ghana in 1993 when several cases were reported from the Amansie West District of Ashanti Region [16] although earlier cases have been reported from the Densu and Afram plains [14,17]. In Ghana, a national survey conducted in 1999 found 6000 cases and showed that BU is in all 10 regions [16]. Since then, cases have been reported from many districts and about 2800 new cases have been recorded [18]. The overall national prevalence rate of active BU is 20.7 per 100,000 of the population, but as high as 150.8 per 100,000 has also been reported [16]. The worst affected regions are Ashanti, Central, Brong Ahafo, Greater-Accra and Eastern including some areas in the Volta Region [16,18,19]. The disease is prevalent mainly in poor rural communities where the indigenes depend on soil tilling for their survival [16,19]. Even though cases are reported in all age groups worldwide, it affects primarily children less than 15 years of age [14,15]; a study in Amasaman in the Greater Accra Region of Ghana reported similarly [20].

3. PATHOGENESIS

M. ulcerans, the causative organism, has been identified by molecular tools from the environment and recently cultured [21]. BU is generally believed to be an infection by an environmental microorganism [21]. BU is apparently associated with aquatic habitat especially in many tropical and subtropical countries [22-24]. Aquatic insects, notably Naucoris and Dyplonychus may serve as a vector of *M. ulcerans* [25,26] even though a typical vector has not been convincingly identified [27,28]. There is a striking association with stagnant and slowly flowing water bodies [23,29-31] and Case control studies among people living in endemic areas have identified risk factors to contract the disease [32].

4. DIAGNOSIS

Factors such as the patient's age, location of lesions, pain and geographic area should be considered when diagnosing BU. There is no diagnostic test that can be used to diagnose

BU but some authors recommend IS*2404* polymerase chain reaction (PCR) because it has the highest sensitivity and results can be available within 48 hours [3,15] and is sufficiently specific in patient samples [3]. Acid fast bacilli (AFB) for Ziehl-Neelsen (ZN) test, histopathology and culture and sensitivity may help in the diagnosis; however, AFB smear for ZN test is most suitable and could be used in rural areas where the disease occurs more frequently [33,34]. In Ghana, Agbenorku et al. (2012) detected BU for both ulcerated and nonulcerated cases based on clinical findings and confirmed by any two positives of ZN test for AFB, PCR and histopathology [33]. At Tepa District Hospital in the Brong Ahafo Region of Ghana, confirmation of the diagnosis was done with swabs and punch bi-opsies for PCR, direct smear examination, culture and histopathology [35]. Other Diagnostic specimens were processed by dry reagent-based IS2404 PCR, microscopic examination, and culture with use of standardized procedures [36-38].

5. PROBLEMS

The disease usually starts as a painless nodule, a plaque or oedema and seldomly as a papule, in the skin. If this is not excised, necrosis of the skin and subcutaneous tissue may result [29,39,40]. Few patients may visit the hospital with this stage of the disease. In the ulcerative stage, skin ulcers with typically undermined edges can be clinically diagnosed from other skin disorders. A granulomatous (an inflammation found in many diseases) healing response often occurs, fibrosis, scarring, calcification and contractures with permanent disabilities may result [41]. The infection leads to destruction of skin and soft tissue with large ulcers usually on the legs or arms. Patients who are not treated early suffer long-term functional disability such as restricted joint movements and noticeable cosmetic problems [34]. Sometimes it may cause tendinous or bone exposure when it involves a joint or close to it and a contracture may result [40,41]. Healing of ulcers with fibrosis may lead to significant deformity, with secondary lymphedema, scarring and contractures of the lower limbs [42]. Deformity results from secondary intention after sloughing of epidermis and subcutaneous fat with re-epithelialisation. On the extremities scarring leads to contractures, subluxation of joints, disuse atrophy and distal lymphedema [43].

BU disease in the head and neck region, especially the face, may lead to serious sequelae such as ulcerative destruction of the eyelids, loss of the nose, or deformity of the face [33,44-46]. BU is mostly coupled with complications such as secondary bacterial infections, extensive scarring, contractures, deformities to the limbs, amputation of the leg and arms, and destruction of other parts of the body such as the eye, breast and genitalia [29,31,47]. These complications are affected by factors such as the location and extent of the lesion, individual healing factors and wound management techniques. The techniques used for the removal of necrotic tissues and subsequent skin grafting or local skin flaps would influence the type and extent of scar formation. Patients with BU disability are also faced with economic, social and psychological problems which make them more vulnerable and dependent [47]. Patients become anti-sociable because they are faced with emotional problems such as shyness, anxiety, inferiority complex and fear of been shunned by people and these make them lonely and timid [33,48]. With these psychological problems they are reluctant to engage in economic activities. Most of the patients affected by this disease are from poor households and this coupled with long hospitalization makes them poorer since they cannot engage in any economic activities. They therefore spend the little resources at their disposal [49].

6. TREATMENT

Even though there is no standard definition for acceptable treatment delay, public health programmes encourage BU-affected persons to seek treatment as early as possible during the pre-ulcer stage of infection which is often characterized by a nodule, plaque or oedema [50]. Early treatment can prevent progression of the disease and the severe long term functional disability [51].

Public health programmes recommend early medical treatment for BU infection so as to prevent pre-ulcer conditions from progressing to ulcers and minimize osteomyelitis for surgical intervention so as to prevent disability and improve treatment outcomes [52-54]. In most cases BU would start as a nodule in the skin, if it is excised, the extensive ulceration can be prevented [29,32]. However, affected persons may delay medical treatment due to various social, economic, cultural and health system factors [3,55-57]. The health seeking behavior of patients have made it difficult due to certain beliefs such as attributing the cause of the disease to curse, ancestral punishment and other spiritual reasons. Fear of surgery and amputation of affected areas and other anticipated effects of surgery discourage early reporting of patients to the hospital thereby making them rely on traditional and herbal medicine [19,54]. In Ghana, patients with advanced BU are usually hospitalized for a long time resulting in huge loss in productivity for adult patients and family caregivers and loss of educational opportunities for children victims [58]. Some patients use traditional medicine as sources of healing as opposed to any other available method [18] but herbal medications could serve as additional sources of secondary micro-organic infections in some cases [29]. But patients give various reasons for their choice of treatment, such as no health facility in their community, long distance between place of residence and the nearest health facility, inadequate funds and many others [18].

6.1 Antibiotics

Antibiotic treatment of patients with early *M. ulcerans* disease can render the diseased tissue culture negative. This was reported in a study conducted in Ghana which revealed effectiveness of Rifampicin and Streptomycin within 4 weeks duration of administration [59]. Although antimycobacterial drugs are relatively effective during the pre-ulcerative stage of the disease, antibiotic treatment requires optimization [60]. Antibiotics such as Rifampicin in combination with Streptomycin or Amikacin have been reported to be active against BU lesions in humans; this is because the antibiotics can penetrate the necrotic subcutaneous fatty tissue in which *M. ulcerans* organisms are seen on tissue sections of patients [59,19]. However, the 3 to 6 month incubation period of the pathogen and its strong ability to confer resistance has limited the effectiveness of drugs [61]. Currently it is known that only early (less than six months old) and smaller (less than 10cm diameter) lesions can be cured by antibiotics alone without surgery [62]. A category three ulcer may heal by antibiotic treatment alone; however since healing is by secondary intention, wound contraction would be excessive and a contracture may result [63]. There might also be recurrence of the ulcer due to insufficient antibiotic treatment before and after surgery [47,59]. Recurrence rates after surgical treatment are variable and depend upon the experience of the surgeon in defining the disease-free margins of the lesion and on the severity of the disease [59]. Therefore antibiotics treatment should precede surgery by a minimum of four weeks in cases which may require a combination of surgery and antibiotics [64,65]. Several case reports have documented the successful replacement of the aminoglycoside with other antibiotics in combination with Rifampicin for Buruli ulcer treatment to prevent disability [66]. Rifampicin

and Clarithromycin can achieve a successful treatment of BU in pregnant women and children [66,67]. The use of fluoroquinolone like Rifampicin-Moxifloxacin for antibiotic combinations is also effective [68]. The combination of Rifampicin and Ciprofloxacin has 100% treatment success and tolerability [69]. Moxifloxacinclarithromycin, a nonrifampicin based regimen, has also been studied in the laboratory and shown to have limited activity [69]. Other antibiotics that can be used to treat Buruli ulcer to prevent disability include: Rifapentine, Rifabutin, Dapsone, Epiroprim and Diarylquinoline TMC207 [69].

6.2 Surgery

Initially surgical excision was the standard treatment of BU. When performed at the nodular stage it was curative and prevents disability [3].In most endemic areas patients present late with ulcerated lesions; for such cases wide surgical excision was the treatment of choice [43,70,71]. But studies have shown that surgery alone cannot completely remove all necrotic tissues and the possibility of recurrence is high [19,36,62] therefore there is the need for combined antibiotic and surgical treatment. Currently, surgical procedures used in Ghana include excision, skin grafting, excision and skin grafting, debridement, sequestrectomy, re-grafting and contracture release [35]. Surgery is technically difficult in some cases, resource intensive and often results in significant morbidity; it is also not easily accessible in terms of cost and availability [18]. The surgery is done mainly to remove necrotic tissue, cover skin defects and correct deformities [29,39,72]. Large ulcers are usually removed surgically and sometimes amputation is necessary [18]. Wound excision and grafting, if performed early in the course of the disease, can prevent or minimize the development of contractures [35] and this remains the only alternative for advanced lesions [60]. Patients with eyelid destruction may be reconstructed with an Indian forehead flap. Ulcerations that extend to the eyelid and base of the nose are treated usually by multiple surgical excisions, daily wound dressings and skin grafts and sometimes local skin flaps [40,47]. Patients with BU that have good healthy edges with hyper-granulation need only sharp debridement done. After meticulous hemostasis, the wounds are covered with split-thickness skin grafts or local transposition flaps. The grafts are dressed with Vaseline gauze and tie-over dressings. The recipient site dressings are changed on the 4th or 5th postoperative day while the donor sites (normally the thigh) are changed on the 14^{th} post- operative day [29,47]. Surgery is combined with antimycobacterial chemotherapy (Rifampin and Streptomycin) for 8 weeks and physiotherapy [29,59,72]. Patients with chronic BU ulcers have surgical excisions and are dressed over a long period with saline or 2% acetic acid lotions. Because of the difficulty in achieving good hemostasis, some of the excised ulcers are grafted secondarily after 24–72 hours [33,59].

6.3 Physiotherapy

Physiotherapy interventions of BU disability prevention include: Wound care, anti-deformity positioning, elevation, compression massage, early soft tissue and joint movement through exercise and participation in activities of daily living. Patients with deformed BU come for reviews after discharge from hospital whiles patients with minor BU heal 2 weeks after surgery and are discharged [29].

6.4 Other Interventional Measures

Ackumey et al. (2011) stated that intensifying health education and surveillance would create awareness and encourage early treatment [37]. However, it has been argued that “all over

the world those who do not comply are those least able to comply" [73]. So the main issues are the availability of care and the ability of the affected persons to overcome the barriers to assessing effective early diagnosis and treatment [54]. Other recommendations include collaboration with research laboratories for confirmation of cases, improving access to antibiotic treatment and wound care, integrating BU care with the management of similar diseases and disease mapping [74]. Also education must include the change in perception of many rural folks - that BU is a disease and not a curse, ancestral punishment or other spiritual reasons [17]. Wearing of trousers has also been reported to protect against BU even though it is not very effective because BU affects other parts of the body [73,75].

WHO has recommended the following strategies to be put in place: building capacity of nurses and other para-medical staff for effective case detection and management at designated health centers; training of community-based surveillance volunteers, school teachers, other health workers and traditional healers, to enhance BU knowledge for early detection; compiling a database on BU patients to ascertain the prevalence of the disease; providing surgical and antibiotic therapy for all BU patients [76,77].

7. CONCLUSION

Buruli ulcer disability can be prevented through community health education for early detection and treatment of the disease. Patients should be made aware of the disturbing conditions in their surroundings and the early detection of the major symptoms of the disease such as identification of any small lesions, nodules or plaques on one's body would help aid in early diagnosis and possible prevention of ulcers and disabilities since the mode of transmission of the disease is not known. Surgical excision and antibiotic therapy serve as the major treatment of BU disease. Patients should also undergo various physiotherapies to promote their physical and psychological wellbeing. They should also be empowered economically through the provision of small scale welfare grants at the end of hospitalization and treatment to enable them start life again after treatment.

CONSENT

Not applicable.

ETHICAL APPROVAL

The author hereby declares that the appropriate ethical approval was obtained from the Kwame Nkrumah University of Science and Technology School of Medical Sciences/Komfo Anokye Teaching Hospital Committee on Human Research, Publication and Ethics, Kumasi, Ghana and all procedures have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

The author has declared that no competing interests exist.

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