

## Clinical Study

# Profile, Bacteriology, and Risk Factors for Foot Ulcers among Diabetics in a Tertiary Hospital in Calabar, Nigeria

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Diabetic foot disease is a major medical, social, and economic problem. This retrospective study assessed the profile of diabetes mellitus patients with foot ulcers in the University of Calabar Teaching Hospital (UCTH), Nigeria. Admission records of all patients admitted unto the medical wards of UCTH over a 5 year period were analysed. The records of diabetic patients were retrieved. Data on patient characteristics and possible risk factors for diabetes mellitus foot ulcers was extracted. Of the 3,882 patients admitted, 297 (7%) were on account of complications of diabetes mellitus. Foot ulcers accounted for 63 (21.2%) of all diabetic admissions. The elderly constituted the majority of patients admitted with foot ulcers. The average duration of stay of diabetics with foot ulcers was 38.5 days. Diabetics admitted for other conditions had average duration of admission of 15.8 days. *Staphylococcus aureus* was the commonest organism isolated from swabs of foot ulcers. Most of the organisms identified from ulcer swab cultures were sensitive to quinolones and resistant to penicillins. These diabetic foot ulcers were significantly associated with peripheral sensory neuropathy, peripheral vascular disease, intermittent claudication, and walking barefoot. An effective diabetes foot programme is required to address these risk factors and reverse the current trend.

## 1. Introduction

Diabetes mellitus (DM) remains a very common endocrine disorder with major public health consequences arising from severe damage to numerous end organs [1]. DM affects all populations worldwide and the prevalence of this disease is increasing at a very alarming rate [2, 3]. The International Diabetes Federation (IDF) currently estimates that about 366 million persons in the world have DM, with projections that this will increase to 552 million by 2030 [4]. The IDF estimated that there were 12.1 million people living with diabetes in Africa in 2010 with a projected rise to 23.9 million by 2030 [5]. In Nigeria, DM remains the most common chronic endocrine-metabolic disorder similar to what is found in other parts of the world [6, 7].

As the incidence of DM is rising dramatically worldwide, so is the incidence of diabetic foot disease [8]. Diabetic foot

disease is a major medical, social, and economic problem, that is, seen in every continent and constitutes a major burden to the patient and the health care system [8]. The lifetime risk of a person with diabetes developing diabetes mellitus foot ulcers (DMFU) is reported to be as high as 25% [9]. In Nigeria, around 10% of people with diabetes suffer lower limb complications and the incidence is rising [10]. In 2005, people with diabetes related foot ulceration made up almost 12% of total hospital admissions in a tertiary hospital in Nigeria [11]. Presently, DMFU account for the majority of nontraumatic amputations performed in two Nigerian tertiary hospitals [12, 13]. Therefore, it is pertinent to research further into DMFU in a bid to ameliorate the growing disease burden.

This study was to assess the profile, bacteriology, and risk factors for foot ulcers in patients with DM in the University of Calabar Teaching Hospital (UCTH), Nigeria, over a 5 year period from January 2008 to December 2012.

## 2. Materials and Methods

The UCTH is the only tertiary health care centre in Calabar, Nigeria. Calabar is the capital of Cross River State and lies between latitude  $8^{\circ} 15^1$  E and  $8^{\circ} 27^1$  E and longitude  $5^{\circ} 07^1$  N and  $4^{\circ} 53^1$  N and has an area of 161.44 Sq Km [14].

This retrospective study included Type 1 and Type 2 diabetes patients (>18 years of age) admitted unto the medical wards in UCTH over a 5 year period from January 2008 to December 2012. These patients were receiving insulin, oral hypoglycaemic agents, or a combination of both.

The admission records of all patients (both male and female) admitted unto the medical wards of UCTH during the study period were analysed. Patients admitted on account of complications of DM were identified. The case records of these patients were then retrieved from the central records section of UCTH. Information relevant to this research was extracted from the standardized case report sheets which are routinely completed for all diabetics on the medical wards of UCTH. This information was recorded unto a predesigned proforma. Information retrieved included sociodemographic data such as age and sex. Other information included type of diabetic complication, packed cell volume (PCV), and duration of hospital admission.

Possible risk factors for diabetes mellitus such as walking barefoot, intermittent claudication, sensory neuropathy, and glycaemic control were extracted. In line with hospital protocol, all the wound swabs from DMFU had been subjected to Gram staining and microscopic examination. Blood, MacConkey, and chocolate agar were used as primary isolation media for gram-positive and negative bacteria, respectively. The wound specimens were inoculated on these media and incubated appropriately at  $35\text{--}37^{\circ}\text{C}$ . All isolates were subjected to antibiotic sensitivity testing using the disc diffusion technique.

Peripheral vascular disease was identified from the record of clinical assessment of the intensity of dorsalis pedis and posterior tibialis pulsations. Poor glycaemic control was defined as fasting plasma glucose levels of  $>7$  mmol/L from the most current blood glucose record. Peripheral sensory neuropathy was identified by the absence of perception of the Semmes Weinstein monofilament at 2 of 10 standardized plantar sites on either foot which is the standard for admitted diabetics in UCTH.

Data generated were entered and analysed using the Statistical Package for Social Sciences (SPSS) IBM version 20.0. Categorical variables were presented as percentages and Chi-Square test. Univariate analysis was carried out to identify possible temporal associations of DMFU. Statistical significance was established as  $P < 0.05$ .

## 3. Results and Discussion

**3.1. Profile of Diabetes Mellitus Patients.** A total of 3,882 patients were admitted unto the medical wards (male and female) of UCTH during the period under review. Of this number, 297 (7%) were admitted on account of DM complications with 166 (55.9%) being males and 131 (44.1%) being

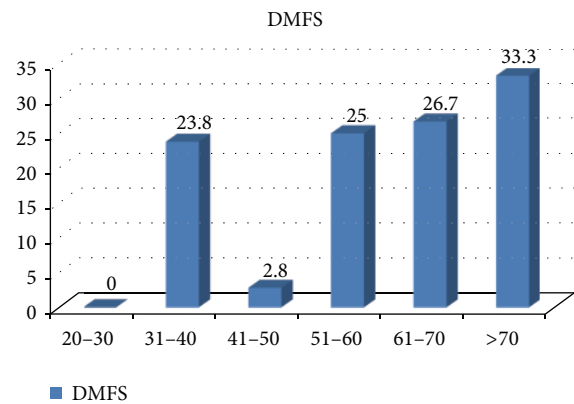


FIGURE 1: Age distribution of DMFU patients.

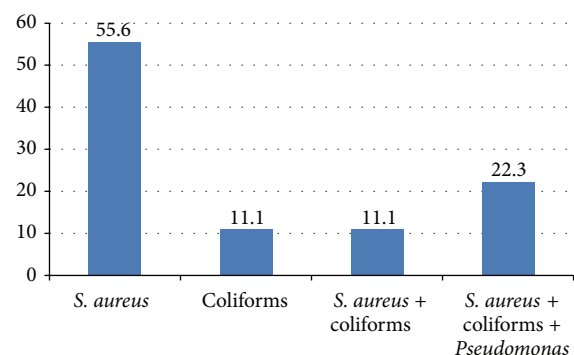


FIGURE 2: Organisms implicated in DMFU.

females. Out of these 297 patients, foot ulcers accounted for 63 (21.2%) admissions.

The elderly (>70 years of age) constituted the majority of patients admitted with DMFU as shown in Figure 1.

The average duration of stay of DMFU patients was 38.5 days. Diabetics admitted for other conditions had average duration of admission of 15.8 days. This finding was statistically significant (testing with Chi Square) at a  $P$  value of 0.01.

**3.2. Laboratory Parameters.** A wide range of organisms were identified from the ulcer swabs of patients admitted with DMFU as shown in Figure 2.

Most of the organisms identified from ulcer swab cultures were sensitive to quinolone antibiotics as shown in Figure 3.

Most of the organisms identified from ulcer swab cultures were resistant to penicillin antibiotics. Only a few isolates showed resistance to cephalosporins (mainly ceftriaxone) as shown in Figure 4.

The average PCV of those with DMFU was 31.5% as compared with the average PCV of 47.3% among other diabetics. However, this finding of lower PCV values among diabetics with DMFU was not statistically significant.

**3.3. Risk Factors for DMFU.** Explorations into temporal associations of DMFU revealed significant results. DMFU was significantly associated with peripheral sensory neuropathy,

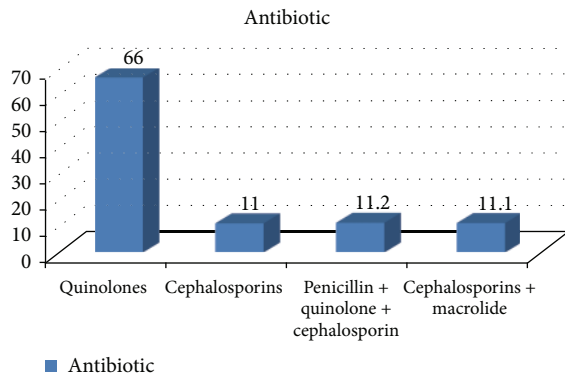


FIGURE 3: Antibiotic sensitivity pattern.

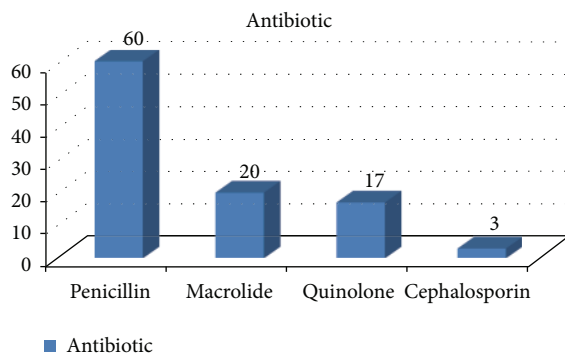


FIGURE 4: Antibiotic resistance pattern.

peripheral vascular disease, intermittent claudication, and walking barefoot as shown in Table 1.

DM remains a significant cause of morbidity and mortality especially in Nigeria where healthcare services and accessibility are poor [10, 15]. The 7% contribution of DM to the overall medical burden in the present study is in keeping with findings by other authors. Ogbera et al. had shown in earlier studies that DM accounted for 10%, 12%, and 15% of medical admissions [10, 15]. These high figures appear to be a reflection of the high prevalence rates of DM in our environment. A 2012 survey of DM in Cross River State Nigeria put the prevalence rate for DM at 7.9% [16]. Similarly high DM prevalence rates were reported in Calabar of 6.5% [17] and 10.5% in nearby Uyo metropolis (Akwa Ibom State Nigeria) [3]. This is in sharp contrast to the report of a DM survey in Ibadan in 1971 that put the DM prevalence at 0.4% and a similar survey in 1989 in Lagos metropolis that reported a DM prevalence of 1.6% [3]. This suggests a steady upward trend in DM prevalence in Nigeria which may be associated with potentially modifiable factors such as lifestyle changes, overweight and obesity, physical inactivity, alcohol consumption, poor dietary habits, and cigarette smoking. DMFU also accounted for 21.2% of all diabetic admissions which confirms the significance of this complication among diabetics. This supports a much earlier report by Ogbera et al. that stated that about 10% of diabetics in Nigeria suffer lower-limb complications and the incidence would rise [10].

The same report also estimated that about a quarter of people in Nigeria with newly diagnosed DM already suffer foot ulceration [10]. DMFU is arguably a reflection of failure or poor outpatient care of DM patients.

The elderly (>70 years of age) constituted the majority of patients admitted with DMFU. This may be explained by the fact that the elderly are likely to have lived with DM for a longer duration than the younger patients thereby making them more prone to the complications that predispose to foot ulceration. Such complications include peripheral neuropathy and peripheral vascular disease. This assertion is supported by Shashi and colleagues who identified DMFU to be associated with age >50 years (OR = 6.97,  $P = 0.00$ ), duration of diabetes 4 to 8 years (OR = 2.47,  $P = 0.00$ ) and >8 years (OR = 3.03,  $P = 0.00$ ) among 678 diabetic patients in North India [18]. Kumar et al. also reported that a substantial proportion of Type 2 diabetic patients, often elderly patients who do not attend hospitals, suffered from peripheral neuropathy and peripheral vascular disease. These patients were at greater risk of foot ulceration [19].

The longer duration of stay for diabetics with foot ulcers in the present study when compared with other diabetics is likely to be due to the long duration required for ulcer healing. Similar results were documented by Kerr in the United Kingdom in 2012. Kerr estimated that in 34,836 admissions coded to nonfoot-ulcer related diabetics, there were 417,804 excess bed days for patients with foot ulceration [20]. The economic implications of providing qualitative care for DMFU cannot be overlooked as this may influence the duration of stay. The inability to promptly pay for the required services in a country like Nigeria without an effective health insurance scheme may promote longer hospital stay for DMFU patients. This is against the backdrop of high economic cost of managing DMFU. This high cost of caring for DMFU was mirrored by findings of Ogbera et al. in a study done well over a decade ago in Lagos that put the mean costs for successfully treating a patient with DMFS at Nigerian Naira (NGN) 180,581.60 [21]. The National Bureau of Statistics of Nigeria had in February 2012 released figures that showed that about 112 million Nigerians (or 67.1 percent of the country's total population of 167million) lived below poverty level—that is living below US\$1.00–US\$1.25 per day [22]. This would place the cost of caring for DMFU beyond the reach of the average Nigerian. The huge economic cost of DM care is not peculiar to Nigeria as the total cost of direct patient care in the United Kingdom in 2010/11 was estimated at £9.8 billion which was approximately 10% of the National Health Service (NHS) budget. DMFU and amputation costs for 2010/11 were the most expensive complication to treat in terms of hospital costs, followed by kidney failure and other renal costs [23].

The present study identified *Staphylococcus aureus*, coliforms, and *Pseudomonas* as infective agents in DMFU. The exact same pattern of *Staphylococcus aureus*, coliforms, and *Pseudomonas aeruginosa* was reported by Edo and Eregie in Benin, Nigeria, as common isolates from nongangrenous diabetic ulcers [24]. The finding of *Staphylococcus aureus* to be the commonest organism to be isolated in the present study is in agreement with Okunola et al. who

TABLE 1: Characteristics of persons in relation to DMFU.

Characteristics	DFMU	No DMFU	Total	Pearson Chi Square	Significance (two sided)
Peripheral sensory neuropathy	32 (29.9%)	75 (70.1%)	107	5.857	0.016*
Peripheral vascular disease					
Diminished dorsalis pedis pulsation	37 (88.1%)	5 (11.9%)	42	66.396	0.001*
Diminished posterior tibialis pulsation	22 (91.7%)	2 (8.3%)	24	40.860	0.001*
Intermittent claudication	19 (39.6%)	29 (60.4%)	48	16.032	0.001*
Poor glycaemic control using FBS	42 (16.7%)	210 (83.3%)	252	0.885	0.347
Walking barefoot	23 (65.7%)	12 (34.3%)	35	17.904	0.001*

\*Statistically significant.

reported *Staphylococcus aureus* to be the most commonly isolated organism on wound swabs of DMFU patients in Oshogbo, Nigeria [25]. Edo and Eregie in Benin, Nigeria, also reported similar results with *Staphylococcus aureus* accounting for 38% of nongangrenous DMFU [24]. Zubair et al. in a study in India also reported that *Staphylococcus aureus* was the most common isolate, accounting for 28%, followed by *Escherichia coli* 26.6%, *Pseudomonas aeruginosa* 10.6%, and beta haemolytic *Streptococcus* spp. 6.6% [26]. This was at variance with findings of a study in Enugu, Nigeria, that reported *Clostridium* species (50%), *Escherichia coli* (20.4%), *Staphylococcus aureus* (16.3%), and *Klebsiella aerogenes* (12.3%) as the most common causes of diabetic foot infections.

In the present study, polymicrobial infection constituted 22.3% of the DMFU infections, and this consisted of *Staphylococcus aureus*, coliform organisms, and *Pseudomonas*. The polymicrobial nature of DMFU has been well documented in the literature [26]. Orji et al. reported a prevalence of polymicrobial pathogens of 36.6% of DMFU patients in Enugu, Nigeria [27]. Edo and Eregie in Benin, Nigeria, found in 20 nongangrenous ulcers of the foot, single organisms were isolated in 15 (75%) swabs, mixed organisms in 5 (25%) swabs, and no organisms in 2 swabs in the initial specimen analysed. Zubair et al. in India found polymicrobial aetiology in 13.3% and monomicrobial in 30% of patients [26]. Also in the United Arab Emirates (UAE), the polymicrobial nature of diabetic foot ulcers has been documented [28].

With regards to sensitivity patterns, the present study revealed an outstanding sensitivity of the isolates to the quinolone antibiotics. There was no marked difference in sensitivity of the isolates to cephalosporins, penicillins, and macrolides. This finding is consistent with that of Orji et al. who reported a significant sensitivity to ciprofloxacin (78%) among DMFU isolates [27]. Resistance in this present study was highest for the penicillins (60%) and least for the cephalosporins (3%). This high resistance to the penicillins may be linked to the indiscriminate use of this older group of drugs in the Nigerian society.

In Nigeria, antibiotics are available without necessarily prescribed by a doctor at public places like motor parks and buses [27]. This gives rise to inadequate dosing, incomplete courses, and indiscriminate drug use that ultimately leads to the emergence and spread of antimicrobial resistance. This

assertion is corroborated by Onajole et al. who reported that 71% of the respondents in a Lagos Nigeria study admitted to drug misuse [29]. Omolase et al. reported even higher rates of self-medication (85%) among respondents in Owo, Nigeria [30]. The cephalosporins are relatively new in the Nigerian market and may not have been subjected to as much misuse as the penicillins which have been around for a much longer period.

The development of diabetic foot ulcerations is multifactorial in origin [31]. The independent predictors of DMFU in this study were peripheral neuropathy, intermittent claudication, diminished peripheral pulses, and walking barefoot as identified in previous studies. The history of intermittent claudication with diminished peripheral pulses is suggestive of a peripheral vascular disease which is a notable complication of diabetes mellitus. Peripheral neuropathy results from vascular disease occluding the vasa nervorum and chronic hyperosmolarity causing nerve trunk edema as a result of increased sorbitol and fructose [32]. Neuropathy causes loss of protective sensation and loss of coordination of muscle groups in the foot and leg, both of which increase mechanical stresses during ambulation. DM is associated with a 2-3fold increased risk of accelerated atherosclerosis [33]. Peripheral vascular disease due to underlying atherosclerosis affects the large- and medium-sized vessels, leading to limb ischemia and ulceration [32].

The practice of walking barefoot is common in low-middle income countries. Data from two clinical studies to examine whether there was a causal link between walking barefoot and DMFU in Sri Lanka suggest that walking barefoot is a risk factor for diabetic foot disease. This is consistent with the findings of the present study and makes a case for public health messages in countries with large rural populations who walk barefoot to strongly advise diabetics to use footwear [34].

#### 4. Conclusion

The prevalence of foot ulcers among diabetics presenting to UCTH is high. This is more common among the older age group (>70 years of age). DMFU causes prolonged hospitalization in the course of treatment. *Staphylococcus aureus*, coliforms, and *Pseudomonas* are common infective agents. Quinolones are useful in therapy. Risk factors for DMFU include: peripheral neuropathy, peripheral vascular

disease, and walking barefoot. This study has identified the burden and profile of DMFU among diabetics presenting to UCTH, Nigeria, and highlighted the magnitude of the problem.

An effective diabetes foot programme is required to address the identified risk factors for DMFU and reverse the current trend.

### Limitations

Being a retrospective study, the authors were unable to analyse some other risk factors of interest for DMFU. The authors were unable to provide more accurate assessments of glycaemic control and peripheral vascular disease such as HbA1c and doppler studies.

### Ethical Approval

All authors hereby declare that the protocol for this research was examined and approved by the Health Research and Ethics Committee of the University of Calabar Teaching Hospital, Nigeria. The research was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

### Conflict of Interests

The authors declare they have no conflict of interests.

### Authors' Contributions

Akaninyene Asuquo Otu, Victor Aniedi Umoh, Okon Ekwere Essien and Ofem Egbe Enang designed the study and wrote the protocol. Akaninyene Asuquo Otu, Patrick Ntui Mbu, Henry Ohem Okpa extracted the necessary information from the patients' records. Victor Aniedi Umoh performed the statistical analysis. Akaninyene Asuquo Otu wrote the first draft of the paper. All of the authors read and approved the final paper.

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