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Original Article

PROFILE, BACTERIOLOGY AND ANTIBIOTIC SUSCEPTIBILITY PATTERN OF DIABETIC FOOT ULCERS AT FEDERAL MEDICAL CENTRE, MAKURDI

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Abstract

The reported increase in the prevalence of diabetes mellitus is expected to be accompanied by a corresponding increase in associated complications. Foot problems are important public health complications of diabetes mellitus. A major obstacle in the management of foot ulcers in diabetes is the colonisation of wounds by virulent pathogens, increasing morbidity and mortality. This was a review of the profile, bacteriology and antibiotic susceptibility pattern of foot ulcers in type 2 diabetes mellitus to aid planning of services and provides a sensible approach to empirical antibiotic therapy while awaiting culture and sensitivity report. It was a hospital based retrospective study in individuals with type 2 diabetes mellitus admitted for foot ulcer(s) over a 3 year period (2012 - 2014) at the Federal Medical Centre. Approval for the study was obtained from the Ethics Committee of the institution. Relevant data (gender, age, residence, occupation, diabetes mellitus duration, ulcer duration, glycoslated haemoglobin status) were extracted from the files. One hundred and nine type 2 diabetes mellitus case files made up of 44 females and 65 males (1:1.5) with a mean age of 53.5 ± 11.4 years were extracted. They were mostly farmers in their fifties with poor glycaemic control who had type 2 diabetes mellitus for more than a decade and foot ulcers for more than 6 months. Late presentation, poor glycaemic control, high rate of wound infection with Staphylococcus aureus, resistance to Penicillins and sensitivity to Quinolones were noted.

Keywords: Diabetes Mellitus, Ulcer, Bacteriology, Antibiotic Susceptibility

Introduction

Reliable estimates projected an astronomic increase in the prevalence of diabetes mellitus¹. The rise in prevalence will be associated with a corresponding increment in associated complications. Foot problems are increasingly important complications of Diabetes Mellitus (DM). These range from mild discomfort through debilitating paraesthesia to fungating ulcers. They are known to be leading cause of admission to hospitals and prolong stay on

admission; straining man-power, draining resources and often associated with unnecessary and untimely death.^{2,3} Diabetes associated foot conditions constitute different percentages of diabetes admissions from different reports even in the same country.^{2,3,4,5} A major obstacle in the management of diabetes related foot ulcer is the colonisation of wounds by virulent bacterial pathogens⁵, increasing cost, morbidity and mortality.

In this paper, we present a review of the profile, bacteriology and antibiotic susceptibility pattern of foot ulcers in type 2DM patients (T2DM) hospitalized at Federal Medical Centre (FMC), Makurdi. This will engender better understanding of these patients that present with bacteriological and antimicrobial susceptibility patterns of foot ulcer. It will also provide a sensible approach to empirical antibiotic therapy while awaiting results of wound swab microscopy, culture and sensitivity.

Materials and Methods

Folders of individuals with T2DM admitted at FMC, Makurdi from January 2012 to December 2014 were assessed to determine the profile, bacteriology and antibiotic susceptibility of their foot ulcer(s). Federal Medical Centre is a 400-bed tertiary referral centre in Makurdi, Benue state, Nigeria. Benue state is located in the North-Central region of Nigeria on geographical co-ordinates of latitude $7^{0}42$ ' and $10^{0}0$ ' East, longitude $6^0 25'$ and $6^0 8'$ North. Approval for the study was obtained from the Ethics Committee of the institution. Relevant data (gender, age, residence, occupation, duration of diabetes, ulcer duration, glycaemic control at presentation using HbA1c, comorbid conditions) were extracted from the case files. Individuals with other types of diabetes were excluded (e.g. type 1 DM, Latent Autoimmune diabetes in Adults, drugs and endocrinopathies acting as the cause of diabetes). All foot ulcers were swabbed using sterile swab sticks and taken to the laboratory within one hour of sample collection. All swabs were subjected to Gram staining, microscopic examination and culture. Blood, MacConkey and

chocolate agar were used as primary isolation media for gram-positive and negative bacteria. The wound specimens were inoculated on these media and incubated appropriately at 35–37°C. All isolates were subjected to antibiotic sensitivity testing using the disc diffusion technique. The data generated was subjected to simple descriptive statistical analysis using frequencies and percentages.

Results

A total of 604 T2DM individuals were admitted within the 3 years reviewed with 127 (21%) of them having foot ulcer(s). Eighteen (14.2%) had incomplete records (and were subsequently not included in the analysis), while a hundred and nine (85.8%) had complete results. There were 44 females and 65 males (1:1.5) with a mean age of 53.5 ± 11.4 years. Other aspects of socio-demographic data were as depicted in table I. Relevant clinical data in table 2 shows that majority had DM for more than a decade, had foot ulcer for more than 6 months and also had poor glycaemic control on presentation. The age group 50 - 59 had the highest number of patients on admission as depicted in Table 3 while Table 4 showed the observed microbes and their relative frequencies. Repeated swabs from three ulcers did not grow any organism on bacterial culture. One of these swabs eventually became positive for fungi, two remained negative on standard preparation for organisms with very strict handling and for non bacterial pathogens. Figure.I is a graphical presentation of antibiotic sensitivity and resistance pattern showing a high sensitivity to Quinolones and high resistance to Penicillins.

Table I: Socio-demographic characteristics of participants.

Parameter	Frequency	Percentage	
Age		- or or or of the second se	
Mean	53.5+11.4 years		
Range	38-92 years		
Distribution: 30 – 39	3	2.8	
40 - 49	17	15.6	
50 - 59	38	34.8	
60 - 69	28	25.7	
70 - 79	15	13.8	
80 - 89	7	6.4	
≥90	1	0.9	
Total	109	100	
Residence			
Rural	49	44.9	
Urban	60 55.1		
Total	109	100	
Educational Level			
Primary	65	59.7	
Secondary	30	27.5	
Tertiary	14	12.8	
Total	109	100	
Occupation			
Farmers	58	53.2	
Civil / public service	34	31.2	
Self employed	5	4.6	
Unemployed (including retired)	12	11.0	
Total	109	100	

Table 2: Clinical characteristics of participants

Parameter	Frequency	Percentage	
DM duration			
- <5 years	24	22.0	
- 5 -10 years	33	30.3	
- ≥ 11 years	52	47.7	
- Total	109	100	
Ulcer duration			
- < 3months	30	27.5	
- 3 – 6months	31	28.4	
- > 6months	48	44.1	
- Total	109	100	
HbA1c at presentation			
- good (<6.5)	24	22.0	
- poor (6.5 - 8)	35	32.1	
- very poor (>8)	50	45.9	
- Total	109	100	

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Age range/ Year	30-39	40 - 49	50 - 59	60 - 69	70 - 79	80 - 89	≥90	Total
2012	1	4	12	11	3	2	0	33
2013	0	7	16	10	9	3	1	46
2014	2	6	10	7	3	2	0	30
Total	3	17	38	28	15	7	1	109

Table 3: Admission pattern in each age range

Table 4: Implicated microorganisms and their relative frequencies

Organism	Frequency	percentage
Staphylococcus aureus	34	31.2
Escherichia coli	28	25.7
Pseudomonas	20	18.4
Streptococcus	12	11.0
Kliebsiella	8	7.3
Candida albican	1	0.9
Staphylococci + Coliforms	4	3.7
No growth	2	1.8
Total	109	100



Figure I: Antibiotic Sensitivity and Resistance Pattern

Discussion

In this study, most patients with T2DM presenting with leg ulcers were in the prime of their lives as evidenced by a mean age of 53.5 years. The peak age of DM complications are thought to be highest in individuals less than 60 years of age.^{6,7} Majority of the patients (58%) were still under this age. The relatively young age of people developing limb ulcer(s) may have economic implications in any economy. Also, complications generally ascribed to older age groups are frequently being encountered in younger patients with diabetes, contributing to early mortality.⁶

The number of patients from the urban areas was more than those from rural areas. Type 2 diabetes is closely associated with (rapid) urbanisation, westernization, sedentary lifestyle and obesity.^{1,6,7} These are common descriptive terms applicable to most urban locale with many rural areas threatening to catch up.^{1,8}

Both civil and public servants are known to farm extensively in Benue state where this health institution is located. In the peasant agrarian setting that most of these patients were drawn from, poverty, inadequate foot wear, increased risk of physical trauma, infection during farming activities and spontaneous blisters in bare-feet peasants and farmers were quite common.^{7,8} Farmers constitute more than half of those that presented with foot ulcers in this study. In addition, a situation where almost 60% of participants had primary or no western education, widespread ignorance about appropriate health promotive and preventive activities would be expected. The higher the educational level, the lower the incidence of foot ulcer.8 Other researchers had observed an even higher level of poor western literacy rate amongst their respondents. Akanji et al⁹ observed that up to 68% of their sample in a prospective study were without western education.

A number of research bodies on foot ulcers in people living with diabetes from the developing world feature late presentation to hospital as a common threat.^{8,10,11} Up to 27.5% of patients in this study sought medical attention after 3 months of home / alternative / unorthodox treatment as a result of many reasons, including ignorance, fear of orthodox medical practices and inadequate transport.¹¹ The challenges posed by late presentation to the hospital by individuals living with diabetes that developed foot ulcer is still begging for a solution.¹⁰ Sadly, many of the reasons were eminently solvable through education of individuals living with DM by their (primary) health care providers.^{12,13}

Generally, the patients in this study had poor glycaemic control as evidenced by HbA1c >6.5% which occurred in 78% of patients in this study. The Diabetes Control and Complications Trial (DCCT) Research Group were able to demonstrate a direct relationship between poor glycaemic control and microvascular complication¹⁴. Also, the United Kingdom Prospective Diabetes Study (UKPDS) clearly showed that each percentage point reduction in A1C was associated with a 35% reduction in microvascular complications (such as neuropathy, a cardinal cause of foot disease in people living with diabetes).¹⁵ Other researchers also noted varying degrees of poor glycaemic control in their subjects^{14,15,16,17} especially using casual and fasting plasma glucose estimation. Following from this, comparison would become rather difficult because of lack of uniformity: some researchers used HbAIc while others used random blood glucose or fasting plasma glucose assessment due to cost, convenience or unavailability of HbA1c.14,16,17

As a result prolonged exposure of tissue proteins to glycation processes, the duration of diabetes mellitus is thought to be a predisposing factor to diabetic complications in general, especially in poorly controlled patients.^{14,15} This is understandable in view of the variably long latency in the natural history of diabetes mellitus from the time of the initiating injury through clinical detection (as evidenced by the development of hyperglycaemia) up to the development of complications.¹⁶

Wound infection is a common occurrence in diabetes ulcer.^{5,18,19} This often lead to prolonged hospital admission^{18,19} and increased cost.¹⁹ On the whole, gram negative bacilli were the predominant organisms observed on Gram stain in this study, making up 50.9% of all the bacteria. However, the Gram positive cocci, Staphylococcus aureus constitute the majority of individual isolates at 31.2%. This is in agreement with the findings from other publications that demonstrated a preponderance of S. aureus.^{20,21,22,23} Staphylococcus aureus is a common skin commensal, harboured in the anterior nares by nearly half of the global population and

colonizing the armpits, perineum, and the respiratory tracts of countless others. Coupled with the relatively reduced immune activity of people living with diabetes mellitus, S. Aureus would become more ubiquitous, invasive and virulent. However, this is not a universal finding as studies equally exist, demonstrating the pre-eminence of a variety of other bacteriae.^{6,19}

Apart from monomicrobial pattern, other researchers have been able to culture more than one organism from an ulcer. Indeed, Polymicrobial culture is quite common.^{5,9,18,19,21} In this study, a combination of Staphylocci and Coliforms were cultured from only 4 ulcers out of the 109 studied.

Many factors could explain the 'no growth' observed in 3 cultures. While it could be true that the ulcers were indeed sterile, poor swab technique, wrong storage conditions, long "wait" interval (between collection and inoculation in the lab), wrong growth media / conditions, strict aerobes and anaerobes, inappropriate antibiotics use, among other things should be borne in mind as possible factors in interpreting and taking decisions on this observation. It would be better to err on the side of caution, judging from the history, local findings around and on the ulcer and systemic examinations in evaluating this type of occurrence.

One of the "no growth" swab sample which was finally identified as a fungus was further characterised to be Yeast. Undiagnosed and with inappropriate anti-infective drugs, this ulcer may not heal. The time tested teaching emphasizing the need for further efforts in carrying out cultures of samples from refractory ulcers to ensure fungal colonization (especially Yeast) should be borne in mind.¹⁸

Two important observations stand out on antibiotic susceptibility testing: the high degree of resistance to Penicillins (especially Ampicillin) and the relatively high rate of sensitivity to Quinolones. The cephalosporins were seldom effective and unless suggested from antimicrobial susceptibility testing, these drugs should not be used as initial therapy for diabetic foot infections in our environment.¹⁹ The resistance to antibiotics of many of these microbesis not surprising because of drug misuse which is widespread in this environment. It is not uncommon to observe antibiotics being marketed in commercial vehicle parks, in the open markets and supermarkets by unlicensed vendors and being hawked in open

trays. Some of the strains of bacterial isolates that colonised the refractory diabetic ulcers in this study may have acquired genes for drug resistance through antibiotic misuse.⁵ Quinolones were therefore, recommended as the initial therapy for people living with diabetes in this environment with infected ulcers while awaiting culture results, which should be used to guide further antibiotic therapy.

Conclusion and Recommendation

There is a high degree of late presentation as well as poor glycaemic control and a high rate of wound infection due to colonisation by opportunistic pathogens especially bacteria. Staphylococcus aureus was the commonest organism isolated from swabs of foot ulcers in this study. Most of the organisms identified from swab cultures were sensitive to quinolones and resistant to penicillins. This is a major challenge in the management of foot ulcers in individuals living with diabetes where culture and sensitivity tests are not available or unreliable as the correct choice of antibiotics should only be made after antibiotic sensitivity testing. We therefore advocate the use of a Quinolone while awaiting sensitivity results.

Limitations

Bacterial culture result was a very important component of this study. The observed results may have been different if certain factors affecting the patient and or their investigations were different. For instance, where pathogen yield is a major determinant, wound biopsy is superior to wound swab. However, the centre where this study was undertaken lacked punch biopsy capability at the time these patients were documented.

The patients in tertiary hospitals in poor countries often attempt home management^{8,24} or unorthodox involvement^{8,11,24} before they finally seek attention or are referred to primary / secondary centres.^{8,11,24,25} Along this delivery chain of presentation to the tertiary centre, it has been observed that antibiotics use (and misuse) is very common in individuals living with DM nursing an ulcer⁵. Since this was a retrospective study, it was difficult to interrogate prior antibiotics use among the study population. It may be important in this context to know the type(s) of antibiotics used, the duration and the timing in relation to the onset of ulcer. Documented references to prior antibiotics use were scanty, with patients not knowing the types of drugs used before presentation. This may also affect the types of bacteria cultured while they were being managed in this facility.

Fastidious organisms, strict aerobes and anaerobes and the procedure with which swabs were taken, stored and handled were important determinants of the types of bacterial yield observed.

Conflicts Of Interest

None declared

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