Original Article

Infective agents in diabetic foot ulcers and their sensitivity patterns

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Abstract

Objective: The present study aims to determine the culture & sensitivity pattern of bacteria in a stated cohort of patients at a Surgical Unit.

Materials and Methods: This prospective cohort study was conducted over a period of 1-year duration at a tertiary-care-Hospital. All patients presenting with diabetic foot who had not been subjected to empiric antibiotic therapy were enrolled. Demographic & lesion-based variables were studied and the Culture & Sensitivity pattern was evaluated and statistically analyzed.

Results: 100 patients were included in the study, of which 80 were male (mean-age 60.8±12.7 years) & the rest female (mean-age 58.4 ± 11.3 years). 35% of cultures yielded no growth. The remaining cases showed the following pathogens in descending order of incidence. Maximal sensitivity was also reported as mentioned. 1) Staphylococcus aureus & Klebsiella-Pneumoenae– Piperacillin/Tazobactam, 2) Pseudomonas-Aerugionas-Cefotaxime, 3)E-coli–Amikacin& Sulbactam, 4) Proteus -Gentamicin, 5) Streptococci– Amikacin and 6) Bacteroides – Cefoperazone & Aztreonam. Of 71 cases, 70 had aerobic-organisms isolates & only 1 had anaerobic-isolate.

Conclusion: Six pathogens were identified in the present study of which Staphylococcus-Aureus was the most prevalent as well as the most resistant. Streptococci & Gram-negative Organisms were observed in the remaining cases. While the formulation of an adequate antibiotic regime is rendered difficult by resistance & mixed infections, targeted antibiotic administration is decisively crucial to achieving optimal & timely outcomes in the diabetic foot.

Keywords: Diabetic Foot, Microbial Resistance, Diabetes Mellitus.

Introduction

Diabetes mellitus is a disorder of sugar metabolism which is characterized by chronic hyperglycemia either due to insufficient insulin secretion (Type I), insulin insensitivity (Type II), or both.[1] Side effect of diabetes can be devastating if not controlled. It has been postulated that hyperglycemia hinders proper wound healing. This is a result of advanced glycation end-products (AGEs) which amplify the production of inflammatory molecules like tumor necrosis factor and interleukin-1. These mediators interfere with the formation of collagen. Diabetic foot syndrome is a catastrophic condition in patients suffering from diabetes mellitus. It has a cumulative lifetime incidence that can be up to 25 percent.[2] In diabetics, foot abnormalities result from peripheral neuropathy, macroangiopathy, and other aftermaths of metabolic disturbances. Patients usually present with foot ulcers and Charcot foot deformity, with many ending up with amputation of parts of the foot or part of the leg.[3] In diabetic patients, neuropathy predisposes them to an increased incidence of foot infections while angiopathy has a strong influence on their outcome. Other factors for infections and subsequent amputations are foot ulcer that remains unhealed, advancing age, male gender, and smoking. The timely detection and control of infections can avert this potentially dangerous situation and save many patients from impending amputations.[4,5]

A variety of bacteria can infect the diabetic foot. The most frequently isolated organisms involved in diabetic foot ulcers include Staphylococcus aureus, Streptococcus pyogenes, Enterococci, and Pseudomonas aeruginosa. Many of these microorganisms have developed resistance to commonly used antibiotics.[6] In one study conducted in Nigeria, bacterial cultures that were isolated from the ulcer base were all sensitive to quinolone antibiotics.[7] A similar study done in India found imipenem to be effective against the isolates.[6] It is also suggested that contrary to the West, gram-negative bacteria dominated wound infections in the patients with diabetic foot infections in India. Polymicrobial multidrug-resistant gram-negative bacillus infections were also found commonly.[8] Empirical broad-spectrum antibiotic treatment is widely practiced to ameliorate diabetic foot infections and the selection of an appropriate antibiotic regimen is guided by the severity of the infection.[9] In an era where microorganisms are getting increasingly resistant, targeted antimicrobial therapy for the treatment of ulcers in patients suffering from diabetes has become crucial.[10] The present study was undertaken to determine the microbiology and the current antimicrobial sensitivity pattern of the bacteria isolated from the patients with infected diabetic foot ulcers presenting to our hospital.

Materials and Methods

The study was conducted at Surgical Unit I of Benazir Bhutto Hospital, Rawalpindi from April 2017 to September 2018. Patients presenting with a diabetic foot ulcer in the emergency or the out-patient departments, who were not on any empirical antibiotic therapy before the onset of symptoms, were included in the study. Patients with a prior history of surgery for diabetic foot and patients with foot ulcers, infection, and gangrene due to causes other than diabetes-like varicose veins, peripheral vascular disease, and lymphatic obstruction were excluded from the study.

Patients were included in the study according to the non-probability consecutive sampling technique. Their demographic details and the site and the type of the lesion were documented. An appropriate sample for culture and sensitivity was collected by first removing any overlying necrotic debris from the ulcer site. This was accomplished by vigorously scrubbing the wound with saline-moistened sterile gauze. The sample was then collected, preferably, from the expressed pus. Both aerobic and anaerobic organisms were identified. Data were analyzed using the statistical package for social sciences (SPSS version 23). Mean and standard deviation was calculated for the continuous variables. For the categorical variables, the frequency was calculated.

Results

One hundred patients were included in the study, out of which 80 (80%) were men (mean age 60.8 ± 12.7 years) and 20 (20%) were women (mean age 58.4 ± 11.3 years). Diabetic foot predominantly affected right foot in our cohort (76% vs. 22%). Most patients with diabetic foot did not have proper control of their diabetes and this was statistically significant (p=0.03). Other diabetic complications (neuropathy or angiopathy) coexisted in 36% of the patients (Table 1).

In our study, the severity of diabetic foot was normally distributed with patients in grade II and III in abundance, cumulatively accounting for over 60% of

the patients whereas patients in grade IV and V accounted for only 32% and 6% of the patients. However, the incidence of coexisting diabetic complications like neuropathy, angiopathy, or both was significantly greater in patients with grade IV or V disease (p=0.018) (Table 2). The graphical representation in figure 1 shows the skewed incidence of diabetic complications in patients with severe disease (Figure 1).

Staphylococcus aureus was the most resistant organism among all the isolates. However, 35% of cultures yielded no growth. Staphylococcus aureus & Klebsiella-Pneumoenae was resistant to Piperacillin/Tazobactam whereas Pseudomonas-Aerugionas was resistant to Cefotaxime. E-coli demonstrated significant resistance to Amikacin& Sulbactam, and Proteus was not sensitive to Gentamicin. In Streptococci, Amikacin showed reduced efficacy. Similarly, Bacteroides was resistant to Cefoperazone & Aztreonam. Of 71 cases, 70 had aerobic-organisms isolates & only 1 had anaerobic-isolate (Table 2).

Table 1: Characteristics of the population with diabetic foot

Parameters		*P-value*
Gender	Male (n=80) Female (n=20)	0.35
Age	65.6 ± 10.3	-
Affected Feet	Right foot (n=76) Left foot (n=22) Both feet (n=2)	0.018
Surgical Procedure	Wound debridement (n=62) Minor amputation (toe or ray) (n= 38)	0.6
Diabetic control	Controlled Diabetes (n=24) Uncontrolled Diabetes (n=76)	0.03
Presence of other diabetic complications	None (n= 64) Neuropathy (n=24) Angiopathy + Neuropathy (n= 12)	0.23

Table 2: Comparison of severity of diabetic foot with other diabetic complications

Grade	*Presence of other diabetic complications*	*No other diabetic complications*
I (n=2)	**-**	**2**
II (n=46)	**2**	**44**
III (n=14)	**1**	**13**
IV (n=32)	**28**	**4**
V (n=6)	**5**	**1**

P=0.018

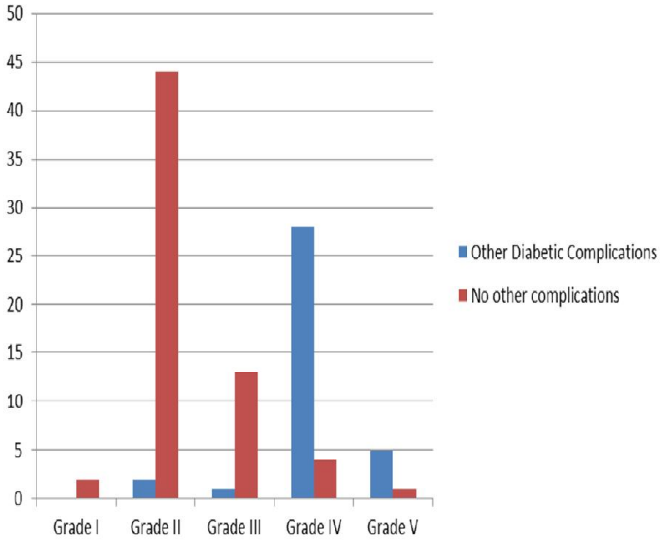

Figure: 1 Comparison of diabetic foot severity with other diabetic complications

Table 3: Resistance profile of the cultured bacteria

Sr No.	*Antibiotic*	*Percentage* Staphalococcus Aureus	*Percentage* Klebsiella Pneumonia	*Percentage* Pseudomonas Aurogenosa	*Percentage* E. Coli	*Percentage* Proteus	*Percentage* Streptococci	*Percentage* Bacteroides	*P-Value*
1	Amikacin	24.3%	27.2%	71.4%	83.3%	33.3%	50%	0	0.02
2	Salbactam	12.1%	9%	0	83.3%	0	0	0	0.01
3	Gentamicin	19.5%	45.5%	42.8%	50%	66.6%	0	0	0.9
4	Pipercillin/ Tazobactam	95.1%	54.5%	71.4%	50%	0	0	0	0.001
5	Aztreonam	63.4%	18.1%	28.5%	50%	0	0	100%	0.02
6	Amoxicillin/ Clavulanate	78%	9%	0	33.3%	0	0	0	0.4

7	Cefoperazone	31.7%	9%	57.1%	33.3%	0	0	100%	0.2
8	Cefotaxime	24.3%	9%	85.7%	33.3%	0	0	0	0.1
9	Ceftriaxone	21.9%	45.5%	57.1%	33.3%	66.6%	0	0	0.4

Discussion

In a study conducted in Postgraduate Medical Institute, Peshawar, in 2011, one hundred and four disease-causing microbes were cultured from ulcer bases. These cultures were isolated after wound debridement. The commonest pathogens that were cultured in the lab were Staphylococcus aureus (52, 46%). E. coli (11,10%) was the second most common microorganism in the culture. MRSA (10 cases 9%) was also isolated. Streptococcus (65%) and Pseudomonas (54%) cultures were also seen in this study. A few specimens contained polymicrobial infection as well. The commonest antibiotics against these microbes were cefoperazone/sulbactam in (n=43) 38% of the cases. This was used alone or in combination with other antibiotics. This was followed by ceftriaxone in (n=36) 33% of the case. MRSA was treated by Linezolid in the case study. 82% (n=94) of the patients responded to antibiotic therapy. These patients were labeled as cured in the study.[11]

In our study, culture reports for 35% of the patients showed no growth although only those patients were included in the study who had not received any antibiotics for 48 hours, before taking specimen for culture from deep abscesses and shifting it to the laboratory immediately. This could be related to a high incidence of self-medication with empirical antibiotics among the general population, laboratory error, or fungal infections.[12]

The organisms most commonly causing foot infections are Staphylococcus aureus and Streptococcus pyogenes suggesting that these organisms are probably part of the patient's flora of the skin, while the anaerobes, the enterococci, and the coliforms are probably part of the patient's gut flora. Due to this, the issue of differentiating colonization from infection remains, even when the specimen is properly collected.[13] Also, similar studies performed in the past have always shown a complex polymicrobial microbiota in diabetic foot ulcers when compared to other wounds.[14] These results suggest that the patient's demographics and wound type are probably not linked to the microbiome of the chronic wound. Further research is needed to formulate a management plan according to a patient's microbiota to improve wound healing.[13]

In this study, about 90% of all staphylococcus organisms were resistant to penicillin antibiotics. These were treated with penicillinase-resistant penicillins such as flucloxacillin.

In a study published in 2010, MRSA was a significant pathogen that was present in infected foot ulcers due to diabetes. It was estimated to be prevalent in 15–30% of the cases. This is an alarming situation that could cripple the healthcare system in many countries. Multiple studies have been published that have recognized the growing resistance of MRSA to vancomycin.[15]

In our study, out of 71 positive culture reports, in 70 cases had aerobic organisms were isolated while only one had an anaerobic causative organism which is comparable to other studies.

Many disease-causing microbes cultured from diabetic foot infections are extremely resistant to regularly prescribed antibiotics. Hence, broad coverage of aerobic and anaerobic bacteria is necessary in these cases. Vascular impairment is a recognized complication in diabetes and it can affect the delivery of antibiotics to these tissues. This enhances the necessity and importance of drugs that can penetrate tissues extensively and even reach the bone.[16] Administration of ciprofloxacin or amoxicillin for two weeks demonstrated a remarkable result in treating diabetic foot infections in our study.

Treatment for infected ulcers due to diabetes needs specific goals. The main target in such a condition is to eradicate all clinical evidence of microbial invasion and also to avoid soft tissue loss and amputation. Overall the clinical response is satisfactory (i.e. infection resolves to imperceptible levels) when appropriate therapy is utilized. However, some factors like sepsis, osteomyelitis, necrosis, gangrene, the proximal invasion of infection, peripheral arterial disease (PAD), chronic renal insufficiency, and dialysis are associated with a poor response to therapy and consequently, poor outcomes are inevitable in these scenarios.[17] A study conducted in Pakistan linked male gender, age older than 50 years, residence in a rural area, and heel ulcers with poor outcomes in diabetic foot ulcers patients.[18]

The current scenario for foot care in diabetes revolves around prevention. These strategies combine many different interventions that can reduce the risk of

infection and ulcer formation. These include patient education, proper skin, and nail care, and footwear that protects against trauma. Individualized and patient-specific foot care remains the most important element in a comprehensive program for the eradication of diabetic foot. Low-risk patients must wear non-constrictive footwear.[19] The patient should be instructed to seek urgent medical attention once signs of deterioration appear. Increasing blood sugar and insulin requirement indicate early infection. An integrated approach to focus on the prevention of recurrence of foot ulcers in these patients must also be formulated. These strategies include strict and regular diabetes control, professional care of foot in diabetics at intervals of 1 to 3 months, proper footwear, and assessment of temperature of the foot to monitor inflammatory signs and intervention to ameliorate PAD. Early detection and treatment of new lesions (e.g. calluses) are also critical in avoiding complications.[20] Morbidity and mortality due to the diabetic foot can be lowered only if the utmost attention is given to the aforementioned strategies.

Conclusion

Gram-positive and gram-negative aerobes were the most commonly isolated organisms. The problem of widespread antibiotic resistance and polymicrobial infections makes the formulation of adequate antibiotic therapy for managing and caring for diabetic ulcers on the foot difficult. Therefore, proper administration of antibiotics according to the isolated organisms, prompt surgical treatment for extensive involvement of the foot, and an aggressive multidisciplinary approach is warranted to manage not only the foot problems in the diabetic patients but also to recognize and reduce mortality from other co-morbid conditions.

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