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Original Article

Clinical Profile of Diabetic Foot Infections

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Abstract

Background: Diabetic foot infections (DFIs) are associated with substantial morbidity and mortality. Patients with a DFI should be evaluated comprehensively, and employing multidisciplinary foot teams improve outcomes.

Aims and Objectives: To study the clinical profile and microbial flora of diabetic wound infections along with antibiotic therapy.

Methods: This study included 253 patients admitted in the department of general medicine between March 2015 and August 2016. A thorough clinical examination was done. Peripheral neuropathy was evaluated by monofilament and vibration sense. Wound ulcer was graded according to Wagner grading. A basic laboratory workup along with fundus examination was done to rule out microvascular and macrovascular complication of diabetes. ECG and 2D ECHO were done for patients with CAD. Wound swab from the ulcer edge was taken after removing the necrotic material and sent for culture. Pus swab was also sent for culture. Antibiotic therapy and duration was calculated.

Results: The study included 253 patients, 169 males and 84 females. 65 patients presented with Grade I ulcer, 175 with Grade II ulcer, and 13 had Grade III ulcer. 12 patients required ICU care and 241 patients were managed in the ward. The mean age was 57.57. Mean fasting and post-prandial sugars were 157.48 and 244.21, respectively. The mean HbA1c was 9.49 with a mean duration of hospital stay of 12.44 days. 40 patients grew *Staphylococcus aureus*, 40 patients grew coagulase-negative *Staphylococcus* (CONS), 28 *Escherichia coli*, 20 *Streptococcus* species, 20 *Enterococcus* species, 10 *Proteus* species, 12 *Klebsiella* species, 25 *Pseudomonas* species, and 6 *Candida* species. Polymicrobial growth was seen in 26 patients. 25 patients had no growth in cultures. A majority of *S. aureus* was sensitive to penicillin and cloxacillin (MRSA was found in two patients), *Streptococcus* to penicillin and clindamycin, CONS to clindamycin and linezolid, and *Enterococcus* was sensitive to linezolid and ampicillin.

Conclusion: The present study revealed the increased incidence of diabetic foot ulcers and is more common above the fifth decade of life with male preponderance. Our study has showed that 90% and 9.6% of DFIs were monomicrobial and polymicrobial, respectively. CONS and *S. aureus* were the most commonly identified Gram-positive microorganisms, respectively. *E. coli* and *Pseudomonas aeruginosa* were the most commonly identified Gram-negative organisms.

Key words: Coagulase-negative *Staphylococcus*, Diabetic foot, Penicillin, *Staphylococcus aureus*, Wagner grading

INTRODUCTION

Diabetic foot infections (DFIs) are associated with substantial morbidity and mortality. Risk factors for the development of DFIs include neuropathy, peripheral vascular disease, and poor glycemic control. In sensory neuropathy, there is diminished perception of pain and temperature. Autonomic neuropathy can cause diminished sweat secretion resulting in dry, cracked skin that facilitates the entry of microorganisms to the deeper skin structures. In addition, motor neuropathy can lead to foot deformities, which lead to pressure-induced soft tissue damage. Peripheral artery disease can impair blood flow necessary for healing of ulcers and infections. Hyperglycemia impairs neutrophil function and reduces host defenses. Trauma in patients with one or more of these risk factors precipitates the development of wounds that can be slow to heal and predispose to secondary infection.

DFIs are a frequent clinical problem. Infection in foot wounds should be defined clinically by the presence of inflammation or purulence, and then classified by severity.

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Many organisms, alone or in combinations, can cause DFI, but Gram-positive cocci, especially staphylococci, are the most common. Definitive therapy should be based on cultures of infected tissue. Imaging is especially helpful when seeking evidence of underlying osteomyelitis, surgical interventions of various types are often needed and proper wound care is important. Patients with a DFI should be evaluated for an ischemic foot, and employing multidisciplinary foot team improves outcomes.[1,2]

The present study was aimed at analyzing the clinical presentation, diagnosis, microbiology, and management of DFIs. We also observed the correlation between various parameters with the outcome.

MATERIALS AND METHODS

The study was a prospective study done at Sri Ramachandra University from March 2015 to August 2016. All patients with diabetes mellitus presenting with wound infection above 18 years are included in the study. Post-operative patients developing wound infection and patients with multiple septic foci are excluded from the study. Patient demographics and clinical data were recorded from oral questionnaires and hospital records. A thorough clinical examination was done. Peripheral neuropathy was evaluated by monofilament and vibration sense. Wound ulcer was graded according to Wagner grading. Peripheral vascularity was assessed by ankle-brachial index measurement. A basic laboratory workup along with fundus examination was done in all patients. ECG and 2D ECHO were done for patients with coronary artery disease. Wound swab from the ulcer edge was taken and sent for culture. Antibiotic therapy and duration was calculated. The results of the study were analyzed and statistical data were summarized using SPSS 21 software. Chi-square test and Pearson's correlation were done for specific variables.

RESULTS

The study included 253 patients, 169 males and 84 females. Most of the patients were in the age group of 51–70 years. 14 patients below 40 years, 51 patients between 41 and 50 years, 85 patients between 51 and 60 years, 82 patients between 61 and 70 years, 18 patients between 71 and 80 years, and 3 patients above 80 years. The study characteristics and profile of patients are summarized in Table 1.

About 108 patients (42.7%) had coronary artery disease, 152 had hypertension (60.1%), and 154 patients (60.9%) were on oral hypoglycemic agents while 128 patients (49.8%) were on insulin. 65 patients (25.7%) presented with Grade I ulcer, 175 (69.2%) with Grade II ulcer, and 13 (5.1%) had Grade III ulcer as per Wagner grading [Table 2].

About 12 patients required ICU care and 241 patients were managed in the ward. The mean age was 57.57. Mean fasting and post-prandial sugars were 157.48 and 244.21, respectively. The mean HbA1c was 9.49 with a mean duration of hospital stay of 12.44 days. 40 patients (15.8) grew *Staphylococcus aureus*, 41 (16.2%) patients grew coagulase-negative *Staphylococcus* (CONS), 28 patients (11.2%) had *Escherichia coli*, 20 (7.9%) patients had *Streptococcus* species, 20 (7.9 %) patients had *Enterococcus* species, 10 (4%) patients had *Proteus* species, 12 (4.7%) patients grew *Klebsiella* species, 25 (9.9%) patients had *Pseudomonas* species, and 6 patients (2.4%) had *Candida* species. Polymicrobial growth was seen in 26 (10.3%) patients. 25 (9.9%) patients had no growth in cultures. Gram-positive organisms were responsible for more than 30% of infections. Among Gram-positive organisms, a majority of *S. aureus* was sensitive to penicillin and cloxacillin (MRSA was found in two patients), *Streptococcus* to penicillin and clindamycin, CONS to clindamycin and linezolid, and *Enterococcus* was sensitive to linezolid and ampicillin. Among Gram-negative organisms, a majority of *E. coli* was sensitive to amikacin, cefoperazone, and gentamicin, *Pseudomonas* to ciprofloxacin and gentamicin, *Proteus* to imipenem, and *Klebsiella* was sensitive to imipenem and ciprofloxacin. 238 recovered, 2 patients died and 13 were discharged against medical advice. There was no significant correlation between age and outcome. Significant vascular occlusion had no correlation with outcome. All patients who died had a HbA1c of more than 8.5. Two patients in the study group who expired had a Wagner Grade III. In our study, we found that one patient with *Klebsiella* growth and one with Streptococcus growth expired. Even patients with polymicrobial growth had a favorable outcome. There was high association of

Table 1: The study profile

Descriptive statistics

Parameter	N	Minimum	Maximum	Mean	SD
Age	253	22	90	57.57	10.560
FBS	253	70	362	157.48	56.395
PPBS	253	103	698	244.21	90.652
HbA1C	253	5	18	9.49	2.431
RFT	253	0.6	6.8	1.353	0.8010
Hospital stay in days	253	1	78	12.44	12.071
Total counts	253	600	26000	11338.74	4331.181
Valid N (listwise)	253				

Table 2: Wagner grading

Wagner grade	Frequency (%)
Valid	
Grade I	65 (25.7)
Grade II	175 (69.2)
Grade III	13 (5.1)
Total	253 (100.0)

Gram-positive organism growth with Grade I ulcer and Klebsiella growth was common in Grade III ulcer. No specific bacterial growth association was seen with Grade II ulcer. Empirical antibiotic therapy was started for all patients, 186 patients received monotherapy and 77 patients were given dual antibiotics. Amoxicillin-clavulanate was the preferred antibiotic (108 patients), followed by clindamycin in 98 patients, other antibiotics given were cefoperazone-sulbactam (96), piperacillin-tazobactam (58), linezolid (36), and ciprofloxacin (32). The duration of antibiotic therapy ranged from 7 to 14 days.

DISCUSSION

The study included 253 patients with diabetes mellitus presenting with wound infection, 169 males and 84 females. Most of the patients were in the age group of 51–70 years. The present study depicts the mean age of the study population was 57.57 years with more than 70% cases were above the age of 50 years and as age increases the chance of getting a foot ulcer also increases. Similar findings have also been reported by Mohite *et al*.,[3] Bansal,[4] and Kahn *et al*.[5] The proportions of male patients with diabetic foot ulcer have been higher (66.8%) than females. Similar findings have also been reported by Mohite *et al*.,[3] Bansal,[4] and Banashankari.[6]

65 patients presented with Grade I ulcer, 175 with Grade II ulcer, and 13 had Grade III ulcer. No patients had Grade IV and Grade V ulcer. 66% of the patients had an ulcer on the right side. In a study by Mohite *et al*.,[3] 53.80% of the cases had ulcers of Grade III and IV, whereas 12 patients had extensive gangrene (i.e., Grade V). 67.9% with majority of lesions located over sole area. A similar finding has also been observed by Banashankari *et al*.[6] The peripheral neuropathy, a major associated complication (56.45%) was observed in this study. A similar finding has also been observed by Shailesh *et al*.[7] However, Paul *et al*.[8] observed neuropathy in 33.3% of cases, whereas Banashankari *et al*.[6] reported in 76% of cases. The feet were the target of peripheral neuropathy leading chiefly to sensory deficit and autonomic dysfunction could be the cause for high proportion.

Bacterial etiology could be identified among 228 cases out of 253 (90%); single organism was isolated in 206 (90.3%) among which CONS (41 cases) and *S. aureus* being the most common (in 40 cases), followed by *E. coli* (28 cases) and *Pseudomonas* (in 25 cases). Polymicrobial association was found in 22 cases. Zubair *et al*.,[9] Anandi *et al*.,[10] Ramakant *et al*.,[11] Pappu *et al*.,[12] and Citron *et al*.[13] have reported 56.6%, 19%, 23%, 92%, and 16.2% monomicrobial infections and 33%, 67%, 66%, 7.7%, and 83% of polymicrobial infections, respectively. In our study, we had monomicrobial infection in 90.3%. The findings of this study correlate with findings of Pappu *et al*.[12] and Dhansekaran *et al*.[14] Gram-positive cocci were more prevalent (121 out of 238, i.e., 50.84%) than Gram-negative bacilli (111 out of 238, i.e., 46.63%). In our study, CONS (41 cases) and *Staphylococcus* (in 40 cases), followed by *E. coli* (28 cases) and *Pseudomonas* (in 25 cases) were observed. CONS, *S. aureus*, *E. coli*, and *Pseudomonas aeruginosa* were predominant among the monobacterial isolates. The interesting observation made was that there was a near equal distribution of Gram-positive and Gram-negative growth. Similar observations were reported by Citron *et al*.,[13] Zubair *et al*.,[9] and Alavi *et al*.[15] with *S. aureus* as the predominant pathogen, which comprised 57.2%, 28%, and 26.2% of their isolates, respectively. In contrast, Pappu *et al*.[12] reported that 76% of the organisms which were isolated were Gram-negative bacilli, *Pseudomonas* being the predominant pathogen (23%), followed by *S. aureus* (21%). Zubair *et al*.[9] reported *E. coli* (26.6%) and *P. aeruginosa* (10.6 %) as the predominant Gram-negative isolates. In the study of Benwan *et al*.[16] which was done in Kuwait, they reported that more Gram-negative pathogens (51.2%) were isolated than Gram-positive pathogens (32.3%) or anaerobes (15.3%). The increased prevalence of CONS could indicate the changing microbiological profile of DFIs. Tables 1 and 2 summarize the pathogens isolated in various other studies.

Candida growth was seen in 6 patients (2.5%). Manikandan *et al*.[17] observed 3.4% *Candida* growth in his study. MRSA was seen in 3 patients (1.2%). In contrast, Jayashree *et al*.[18] and Hefni *et al*.[19] observed the prevalence of MRSA to be 36.84% and 7.1%, respectively. In the present study, ESBL organisms were found to be 60.36%. Jayashree *et al*.[18] found the incidence of ESBL to be 46%. The increased incidence of ESBL is always expected as antibiotics are not judiciously used which have led to the emergence of resistant organisms. The incidence of Gram-positive organisms [Table 3] and Gram-negative organisms [Table 4] observed in various studies are summarized in Table 3.

With regard to the susceptibility patterns, amoxicillin-clavulanate and cefoperazone-sulbactam appeared to be the best antibiotics for therapy against Gram-positive and Gram-negative organisms, respectively. Vancomycin is usually only indicated for the treatment of MRSA. Superficial lesions were treated with amoxicillin-clavulanate, cefoperazone-sulbactam along with piperacillin-tazobactam were preferred for infections involving deeper tissue.

The strength of this study is that it included an adequate sample size and a detailed analysis was done. There are some limitations in this study. Like all the specimens evaluated here were collected from ulcer edge and pus

Table 3: Comparison of Gram-negative pathogens in various studies

Organism	Banashankari[83] (%)	Manikandan[97] (%)	Mama[98] (%)	Vimelin[99] (%)	Jayashree[100] (%)	Hefni[101] (%)	Mehta[102] (%)	Present study (%)
Proteus	18	6	16	6.3	3	6.1	7	18
E. coli	16	20	20	15.3	23.8	9.4	19	18
Pseudomonas	13	18	8	24.3	31.34	4.1	27	18
Acinetobacter	7	3	-	-	-	10.2	2	18
Klebsiella	7	10	10	9	3	15.3	22	18

Table 4: Comparison of Gram-positive pathogens in various studies

Organism	Banashankari[83] (%)	Manikandan[97] (%)	Mama[98] (%)	Vimelin[99] (%)	Jayashree[100] (%)	Hefni[101] (%)	Mehta[102] (%)	Present study (%)
S. aureus	19	17	32.4	42.3	22.4	10.2	17	15.8
Enterococcus	9	5	-	-	3	-	19	7.9
CONS	5	12	14.5	-	-	7.1	2	16.2
Streptococcus	-	6	-	-	-	-	-	7.9

swab. Sampling from deeper tissues and bone was not taken which could have given a different microbiological profile.

CONCLUSION

The present study revealed that as the grade of ulcer increased, the number of bacterial isolates also increased. Our study has showed that 90% and 9.6% of DFIs were monomicrobial and polymicrobial, respectively. CONS and *S. aureus* were the most commonly identified Gram-positive microorganisms, respectively. *E. coli* and *P. aeruginosa* were the most commonly identified Gram-negative organisms. Amoxicillin-clavulanate and cefoperazone-sulbactam appeared to be the best antibiotics for therapy against Gram-positive and Gram-negative organisms, respectively. Vancomycin is usually only indicated for the treatment of MRSA. Increased incidence of resistant organisms was observed in this study which is important, especially for patient management and the development of antibiotic treatment guidelines. Appropriate usage of antibiotics based on local antibiogram pattern can certainly help the clinician in reducing the burden of DFIs, which ultimately reduces the rate of amputations.

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