Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 8, Issue 1, 2016

Original Article

IS BACTERIOLOGY A CONTRIBUTING FACTOR IN UNSALVAGEABLE NATURE OF DIABETIC FOOT INFECTIONS?–A STUDY IN A DISTRICT HOSPITAL IN MALAYSIA

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Received: 08 Aug 2015 Revised and Accepted: 25 Nov 2015

ABSTRACT

Objective: The objective is to study bacterial pathogens isolated in diabetic foot infection (DFI) and their sensitivity pattern to antibiotics commonly used in the management of DFI in the salvageable and unsalvageable groups of patients in a district hospital.

Methods: 122 patients with diabetic limb infections treated at the Orthopedic Department of Hospital Sultan Abdul Halim, Sungai Petani, Kedah State in Malaysia. Clinically, limb infections were classified as salvageable and unsalvageable infections. Salvageable-mild, superficial/deep, localized ulcer with no systemic derangements necessitating conservative treatment or surgical procedures with minor amputations of limb (toe/ray amputation). Unsalvageable-deep seated extensive or spreading ulcers threatening the integrity of limb with or without toxic symptoms or metabolic derangement and could result in major limb amputation. A standard questionnaire was used to collect demographic, clinical and microbiological details of patients in both groups. Co-morbid illnesses, type/severity of limb infection during presentation and results of routine blood investigations were recorded. Details of nature of each specimen, species of isolate pathogen and sensitivity pattern to antibiotic of each clinical isolates were recorded.

Results: 62 and 60 patients respectively belonged to the salvageable and unsalvageable groups. Only 11.66% presented with evidence of toxemia in the unsalvageable group. ESBL was the commonest nosocomial organisms. Percentage of organism sensitivity was most to vancomycin, ceftazidime, and gentamicin.

Conclusion: All severe infections do not present with toxemia in diabetic patients. Gram-negative organisms were predominant in both groups although Staphylococcal organisms were the single largest group in the unsalvageable group. 3rd generation antibiotics are more useful in its control.

Keywords: Diabetic foot infections, Diabetic foot microbiology, Salvageable diabetic foot infection, Bacterial profile, Antimicrobial susceptibility.

INTRODUCTION

There is a growing incidence of diabetes in the world. Presently the prevalence of diabetes mellitus in Malaysia is estimated to be 22.9% of the population [1]. Foot infections are a frequent complication in patients with diabetes mellitus, accounting for up to 20% of diabetes-related hospital admissions [2]. Many studies have reported on the bacteriology of diabetic foot infections.

Lipsky *et al.* proposed that Gram-positive bacteria are predominant in acute diabetic foot infections and that chronic infections may involve Gram-negative bacteria and anaerobes. Although infection is rarely an important cause in the pathway leading to ulceration, it is a significant risk factor for lower limb amputation [2].

Management of DFI remains a challenge to practicing physicians and surgeons. Diabetic limb complications are a major cause of hospitalization with a source of huge economic and personal burden. Diabetic foot infections (DFI) if not treated promptly and timely may develop to sepsis and gangrene. When all the common surgical procedures and attempts to salvage the limb fail, amputation is the likely option to save the life of the patient. The risk of amputation is in fact 15 to 40 times higher in diabetic patients than in non-diabetic population, and 40-45% of patients undergoing non-traumatic amputation are diabetic. Many patients needlessly undergo amputations because of improper diagnostic and therapeutic approaches [3]. A comparative study of bacteriology of DFI among the unsalvageable group and the salvageable (control) group is lacking. This study reports the possible nature of the bacterial infections that contribute to the unsalvageable condition of the foot and thereby may help in the effective management of DFI.

MATERIALS AND METHODS

This was a cross-sectional study where data was collated and complied retrospectively from case reports of the 122 diabetic patients who attended the Orthopedic Department, Hospital Sultan Abdul Halim, Sungai Petani, Kedah State in Malaysia over a period of 2 y. The data was segregated to make two groups of diabetic patients. Patients who required to undergo amputations in the treatment of their diabetic foot infection were grouped as a unsalvageable group (60 patients), where there is a limb threatening condition after failed conservative management (some of such cases were due to an extremely late presentation or after failed traditional treatment). The level of amputation is usually determined after demarcation or intraoperatively after removing all infected & devitalized tissues. In such cases, tissues from the amputated limb were sent for culture and sensitivity. The culture for anaerobic microorganisms was not routinely performed.

When the infection was treated without the need for amputation was grouped as the salvageable group (62 patients). These patients present with non-limb threatening conditions. All patients were managed either with sharp debridement or de sloughing followed by modern wound dressings in addition to the culture driven antibiotic choice. Tissue cultures were usually obtained during sharp debridement whereas swabs taken during wound dressing. All the materials were sent to the microbiology lab for culture and sensitivity testing. Septic work up and radiographs were ordered when clinically indicated. Other predisposing factors were not taken into consideration for the segregation of the groups.

Co-morbid illnesses and type or severity of the limb infection during presentation and results of routine blood investigations were also recorded. Details of nature of each specimen sent for microbiological study, species of isolated pathogen and sensitivity pattern to antibiotic of each clinical isolate were recorded. The profile and microbiological pattern of infection and sensitivity patterns in the two groups were studied.

RESULTS

Total study population

122 diabetic patients formed the cohort. There were 68 males (55.73%) and 54 females. 83 patients were Malays (68.03%), Indians (23%) and Chinese (14%).

35 patients (28.68%) were smokers. 40 patients (32.78%) had diabetes of 1-5 y duration, 39 patients (31.96%) for 6-10 y and 43 patients for more than 10 y (35.24%).

20 patients were on Insulin whereas most of them (95 patients–77.86%) were on oral anti-diabetics. Two patients were on both forms of medications and 5 were not on any medications for diabetes.

45.9% had no comorbidities (56 of 122 patients). Among the other 66 patients, 52 had associated hypertension (78.78%), 16 had ischemic heart disease (IHD), 6 patients had chronic renal failure, 2 had dyslipidemia and 20 patients had other comorbid illness like gout, congestive cardiac failure (CCF), gastritis, etc.

42 patients had a single comorbidity (63.63%), while 14 patients had two (21.21%) and the others had three or more comorbidities.

53% patients had no signs of infection or toxemia. Among the other 69 patients, 61 presented with fever (88.40%) at admission. 15 patients are presented with signs of toxemia (24.59%).

102 patients (83.60%) had an infection in the foot (with or without the involvement of the toes), 19.67% (24 of 122 patients) had infection affecting the toes, and 14 (%) patients had an infection at a site above the ankle. Only one patient had an infection at the level of the ankle.

105 of 157 infected lesions seen in 122 patients were ulcers (66.87%), 33 lesions (21.01%) were seen as gangrene of the affected region (24 with wet gangrene and 9 dry gangrene), 11 were soft tissue infections (7%) and 8 were seen with Osteomyelitis (5.09%). table 1, fig. 1.

Table 1: Patient profile

Profile	Groups	
	Salvageable	**Unsalvageable**
Age (average)	52.2	53
Gender		
Male	**42**	**26**
Female	**20**	**34**
Race		
Malay	43 (69.35%)	40 (66.66%)
Indian	10 (16.12%)	14 (23.33%)
Chinese	9 (14.51%)	6 (10%)
Duration of diabetes		
>5 y	71%	80%
<5 y	**29%**	**20%**
Comorbidity		
0	45%	48.50%
1	32%	37%
2	**18%**	**8%**
3	5%	6.50%
Patient admitted with uncontrolled diabetes	80%	85%

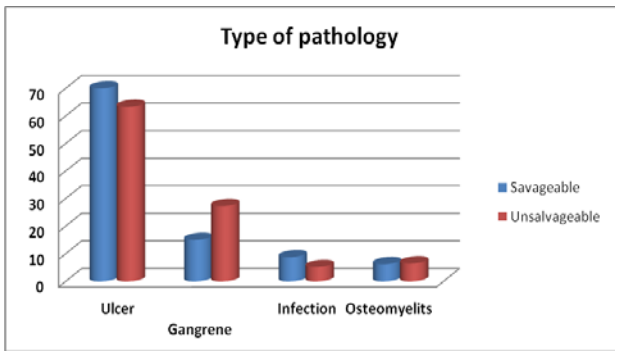

Fig. 1: Type of pathology

18 patients had bilateral lesions (14.75%). 38 feet in 122 patients had two or more lesions of infection on presentation (31.14%). fig. 2.

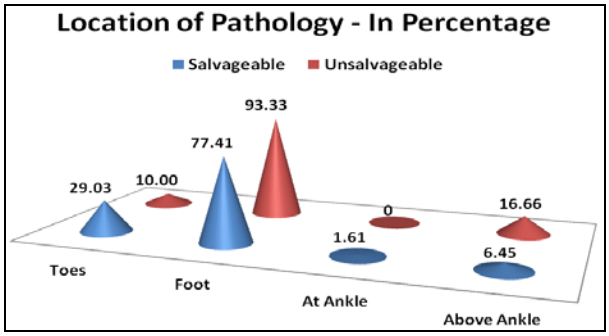

Fig. 2: Location of pathology in salvageable and unsalvageable groups

Microbiological and sensitivity pattern

273 specimens were examined in 122 patients. There was no growth seen in 49 specimens (17.95%). Gram-negative organisms were more commonly grown in the specimens (63%). Gram-positive organisms were grown in only in 17.21% of the specimens. The 5 common organisms grown were *Klebsiella* spp. (14.65%), *Pseudomonas* spp. (13.19%), *Staphylococcus* spp.(12.09%), the Bacter group (Citrobacter, Enterobacter, Acinetobacter, etc) of organisms (11.72%) and *E. coli* (11.36%). Mixed growth and contamination accounted for only (1.10%) of the specimens. There was one specimen showing fungal growth.

Most of the isolates were from swabs from the discharge of ulcers and wounds (53.47%). 80 isolates (29.30%) grew from tissues (including slough and bone). Isolated organisms were found to be more sensitive to antibiotics like vancomycin, ceftazidime, and gentamicin.

Salvageable group

62 patients belonged to this group. 42 were males (67.74%), and 20 were females. 43 were Malays (69.35%), 10 Indians and 9 Chinese in origin. 39 patients were non-smokers (62.90%). 19 patients had diabetes for 1-5 y (30.64%) on admission, 24 patients (38.70%) for 6-10 y and 19 patients (30.64%) for more than 10 y. 15 patients were on insulin (24.13%), and 43 patients were on oral anti-diabetic agents (69.35%). 3 patients received no treatment, and one patient was on both insulin and oral anti-diabetic agents for control of diabetes.

29 of 62 patients had no associated comorbidities (46.77%). Among the other 33 patients, 26 patients had hypertension (78.78%), 9 patients had IHD (27.27%), 7 patients had other comorbidities like chronic renal failure, dyslipidemia, CCF, gout, epilepsy, etc. 24 patients had one comorbidity (72.72%), 5 patients had 2 comorbidities (15.15%) while the others (4 patients) had three or more comorbidities.

37 patients of the 62 (58.67%) had no signs of infection or toxemia. Among 25 patients who presented with symptoms of infection, 22 patients had a fever (88%) on admission. 2 patients had features of toxemia.

There was infection found affecting the foot with or without the involvement of the toes in 48 patients (77.41%), the toes in 18 patients (29.03%), one patient had an infection at the level of the ankle, 4 patients had infection above the level of the ankle. There were 2 patients with bilateral involvement. 56 of 80 (70%) lesions were seen as ulcers, 12 were gangrene (15%), 7 lesions were soft tissue infections (8.75%) and 5 lesions were Osteomyelitis (6.25%). 8 patients had bilateral lesions and 15 feet in 62 (24.19%) patients had more than 2 infected lesions on presentation.

Microbiological pattern

125 specimens were examined in 62 patients. There was no growth seen in 18 specimens (14.40%). Gram-negative organisms were more commonly grown in the specimens (71.2%). Gram-positive organisms were grown in only 13.6% of the specimens. The 5 common organisms grown were *Klebsiella* spp. (16.8%), the Bacters (Citrobacter, Acinetobacter, Enterobacter-15.2%), *Escherichia coli*

and *Pseudomonas* spp.(12.8% each), *Proteus* spp. (12%) and *Staphylococcus* spp.(9.36%).

Most of the isolates were from swabs from the discharge of ulcers and wounds (60%). 36 isolates (28.8%) grew from tissues (including slough and bone). Isolated organisms were found to be more sensitive to antibiotics like ceftazidime, gentamycin, cefoperazone, rifampicin and vancomycin. fig. 3-5.

Unsalvageable group

60 patients belonged to this group. 26 were males (43.33%) and 34 were females (56.66%). 40 were Malays (66.66%), 14 Indians and 6 Chinese in origin.

Most of them, 48 patients were non smokers (80%). 21 patients had diabetes for 1-5 y (35%) on admission, 15 patients (25%) for 6-10 y and 24 patients (40%) for more than 10 y. 5 patients were on insulin (8.33%), and 52 patients were on oral anti-diabetic drugs (86.66%). 2 patients were on no antidiabetic treatment, and one patient was on both insulin and oral hypoglycemic agents for control of diabetes.

27 of 60 patients had no associated comorbidities (45%). Among the other 33 patients, 26 patients had hypertension (78.78%), 7 patients had IHD (21.21%), 17 patients had other comorbidities like chronic renal failure, dyslipidemia, CCF, valvular heart disease, anemia, etc. 19 patients had one comorbidity (72.72%), 10 patients had 2 comorbidities (30.30%) while the others (4 patients) had three or more comorbidities.

16 of the 60 patients (26.66%) had no signs of infection or toxemia. Among those who presented with symptoms of infection, i.e., 44 patients, 39 patients had a fever (88.63%) on admission. 13 patients (39.39%) had features of toxemia, and 9 patients had evidence of metabolic acidosis (27.27%).

There was infection found affecting the foot with or without the involvement of the toes in 56 patients (93.33%), the toes in 6 patients (10%), 10 patients (16.66%) had infection above the level of the ankle. There were 10 patients with bilateral involvement. 49 of 77 (63.63%) lesions were seen as ulcers, 21 were gangrene (27.27%), 4 lesions were soft tissue infections (5.19%) and 5 lesions were osteomyelitis (6.49%). 10 patients had bilateral lesions and 22 feet in 60 patients had more than 2 infected lesions on presentation.

Microbiological pattern

148 specimens were examined in 60 patients. There was no growth seen in 31 specimens (20.95%). Gram-negative organisms were more commonly grown in the specimens (56.08%). Gram-positive organisms were grown in only in 20.27% of the specimens. However among the more common organisms that were found in the isolates for this group, Staphylococci were the largest group (14.18%), followed by *Pseudomonas* spp. (13.51%), *Klebsiella* spp. (12.83%), *Proteus* spp. and *E. coli* (10.13%) and the Bacters (Citrobacter, Acinetobacter, Enterobacter–8.78%),

Most of the isolates were from swabs from the discharge of ulcers and wounds (47.97%). 44 isolates (29.72%) grew from tissues (including slough and bone). The isolated organisms were more sensitive to antibiotics like ceftazidime and vancomycin (fig. 3-5).

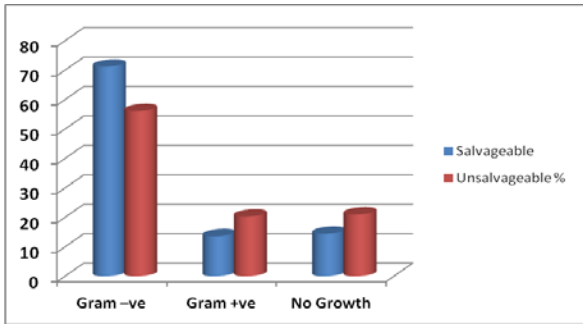

Fig. 3: Microbiology of in salvageable and unsalvageable groups

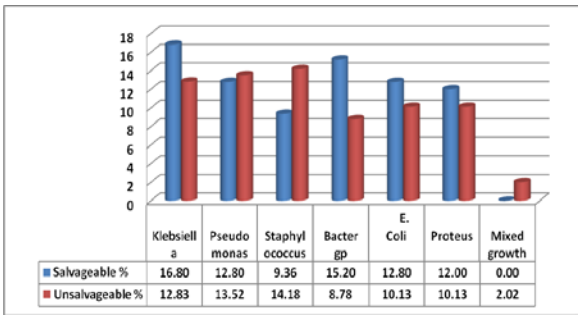

Fig. 4: Isolation of microorganisms in salvageable and unsalvageable groups

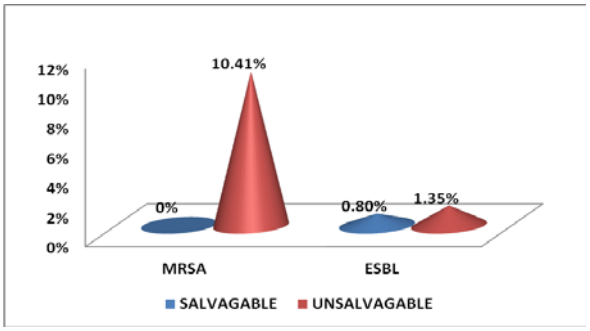

Fig. 5: Incidence of resistant groups in the study population

DISCUSSION

Most DFIs are polymicrobial, with aerobic Gram-positive cocci, and especially staphylococci, the most common causative organism. Aerobic Gram-negative bacilli are frequently co-pathogens in infections that are chronic or following antibiotic treatment, and obligate anaerobes may be co-pathogens in ischemic or necrotic wounds [3]. Calhoun *et al.* found that aerobic Gram-positive cocci were the most common organisms isolated from diabetic wounds in various studies, especially DFI that were categorized as mild to moderate [4]. Cultures of limb-threatening infections identified *Staphylococcus aureus*, group B streptococci, enterococcus, and facultative Gram-negative bacilli. *Pseudomonas aeruginosa* may be identified in macerated wounds, and obligate anaerobes may be present in necrotic or gangrenous infections [4]. In our study, Gram-negative organisms were most frequently isolated group in the cohort. This correlates with a study by Gadepalli et. al in 2006 where Gram-negative aerobes were most frequently isolated (51.4%), followed by Gram-positive aerobes and anaerobes (33.3 and 15.3%, respectively) [5].

Gadepalli et. al (5), also observed that majority of orthopedic wound infections were caused by resistant bacteria; 48.8% of Gram-negative bacteria were ESBL producers, and 30.0% of *S. aureus* were methicillin resistant. In our study, the involvement of bone (6.49%) and mixed growth (2.02%) was seen only in the unsalvageable group. Bacteremia with *Klebsiella* spp. and *Staphylococcus* spp. was observed in the unsalvageable group. Percentage of no growth was more in unsalvageable group & could be due to anaerobes.

Many studies have demonstrated the increasing role of MRSA in DFI [3]. Among hospitalized patients, the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in DFI is 15-30% depending on the geography [4]. Patients with recurrent ulcers were likely to have been previously hospitalized and treated with antibiotics, which were known risk factors for MRSA [7]. Combinations of anaerobic and facultative aerobic streptococci, enterococci, staphylococci, facultative Gram-negative bacilli, and obligate anaerobes, including *Bacteroides fragilis*, are often present concurrently, thus synergistically enhancing their pathogenicity [2].

In our study, the larger population of the cohort in the unsalvageable group were >50 y of age. The duration of diabetes mellitus, the incidence of infection and gangrene was also more in the unsalvageable group. Infection was widespread involving the foot in this group. The majority of the patients in this group were on oral anti-diabetic treatment.

There is variability of the prevalence of common bacterial pathogen as shown in different studies. Severe diabetic foot infection usually yields polymicrobial isolates albeit some study only report 43% incidence rate in such cases [7]. Mild infections are often mono-microbial. The antimicrobial therapy for infection depends on knowing the most common presumed pathogen. Multidrug-resistant infection is extremely common in hospitalized patients with diabetic foot ulcer and is associated with increased requirement for surgical treatment [5]. The selection of empiric antibiotic therapy depends on various factors such as infection severity, overall patient condition, medication allergies, previous antibiotic treatment, antibiotic activity, toxicity and excretion and glycemic control [7]. Several drugs are being used to treat non-limb threatening infection including beta-lactamase inhibitors, third generation cephalosporin, aminoglycosides, ampicillin, penicillin, quinolones, piperacillin-tazobactam, and linezolid. Vancomycin was found to be the most effective drug overall against Gram-positive organisms [7].

In our study, Gram-negative organisms were most frequently isolated group in the cohort and were sensitive to gentamicin & 3rd generation cephalosporin. Among Gram-positive organisms, S*taphylococcus* spp. was predominant & sensitive to vancomycin, oxacillin, rifampicin, and co-trimoxazole. Most of the Gram-positive and Gram-negative organisms in the unsalvageable group were resistant to the antibiotics used. Drug-resistant *S. aureus* was predominant in a unsalvageable group of our study.

CONCLUSION

Resistant Gram-positive and Gram-negative organisms contributed to the unsalvageable nature of the infection. The limitation of the present study is that the possible implication of other co-morbid parameters with relation to the salvageable and unsalvageable group has not been taken into consideration.

Further, the probable role of anaerobic organisms in the severity of the infection was not included in the study. Understanding the limitations of the retrospective study, the authors feel that a prospective study can throw more light on the findings. Nevertheless, this study is novel in the aspect that there are not many comparative studies of the microbiology of DFI among the salvageable and unsalvageable group available in the literature.

CONFLICT OF INTERESTS

Declared None

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