ORIGINAL ARTICLE

DIABETIC FOOT INFECTIONS AND THEIR MANAGEMENT IN A TERTIARY CARE HOSPITAL

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Background: Diabetic foot is a common complication of diabetes world over. We conducted this study to determine common microbiological pathogens in Diabetic Foot Infections (DFI) at a tertiary care hospital and their management. **Methods**: In this observational study deep wound swabs of all admitted diabetic patients were taken, pathogens isolated, antibiotic used and its response depending on complete resolution of symptoms and biochemical markers were recorded. Data were analysed on SPSS-11. **Results**: A total of 114 cases were recorded. Sixty-eight (59%) cases had ulcers on forefoot, 28 (25%) mid-foot and 18 (16%) hind-foot. One hundred and four pathogens were isolated from wound swabs after debridement. Commonest pathogen isolated was *Staphylococcus aureus* (52, 46%) followed by *E. coli* (11, 10%), MRSA was found in 10 (9%) cases, streptococcus in 6 (5%) and pseudomonas in 5 (4%) cases. Polymicrobial infection was also seen in a few cases. Surgical intervention included superficial debridement in 88 (77%) cases, toe amputation/forefoot amputation in 19 (17%) cases, and below/above knee (major) amputation in 7 (6%) cases. Commonest antibiotic used was Cefoperazone/Sulbactam in 43 (38%) cases, alone or in combination, followed by Ceftraixone 36 (33%) cases. Linezolid was used for MRSA. Ninety-four (82%) patients responded to treatment and were recorded as 'cured'. **Conclusion**: Diabetic Foot ulcers often present with serious foot infections. Commonest pathogens are *Staph. aureus*, *E. coli*, Pseudomonas spp. and MRSA. Treatment was effective with Cefoperazone/Sulbactam and Ceftraixone. MRSA was treated successfully with Linezolid.
Keywords: Diabetic foot, Diabetic foot infections (DFI), Staph. Aureus, E. coli, MRSA, antibiotics

INTRODUCTION

Foot ulcers remain one of the most distressing complications of a diabetic patient.[1,2] With high prevalence of diabetes in Pakistan[3], chronic complications like foot ulcerations are high and also because of poor infrastructure at primary level and late referral of the leg ulcer cases to tertiary care hospitals contribute to higher numbers. Apart from common causes of foot ulcer[4] (neuropathy, deformity and injury to the foot) infection leads to devastating complications including sepsis, osteomyelitis, amputations and death in severe cases. It is estimated that approximately 85% of amputations precede a foot ulcer.[5–7] Thus outcomes of foot ulcers depend at what stage of the disease patients presents. In Pakistan amputation rate has been shown to be as high as 21–48%.[8–10] Most of the cases if identified early and treated appropriately initially in the community can be treated effectively with antibiotics at an early stage and in an out patient setting.[11] But unfortunately because of the late referrals primarily and also alternate medicines, herbal medicines, and poor medical facilities in the far flung and tribal areas, less knowledge regarding diabetes in general and foot ulcers in particular leads to loss of limbs and loss of life in some cases even when they reach a tertiary care hospital.

We aimed to conduct this observational study to obtain a real picture from large number of cases which were being seen at a tertiary care teaching hospital one of the three largest hospitals in the province. Because of the close proximity to Afghanistan border which is only 50 kilometres from Peshawar city centre large number of referrals were from neighbouring country Afghanistan. Because of recent unrest in tribal areas and neighbouring Afghanistan medical facilities are either nonexistent or very primitive in these areas.

We planned to study the type of microbiological infections commonly seen and antibiotics used to treat them in a diabetic foot referred to foot clinic of Department of Diabetes, Endocrine and Metabolic Diseases at Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar, Pakistan.

METHODS

This observational study was carried out between September 2005 and December 2006. The study was approved by hospital ethical committee. All patients attending the outpatients department and later requiring admission to the hospital with diabetic foot were included in the study. Patients who were seen in the outpatients and were not admitted were excluded from the study. Data was collected on a performa and transferred to computer.

All patients with diabetes mellitus according to WHO definition 1999[12] and foot ulcer were included in the study. Diabetic foot infection was

defined clinically and bio chemically on the basis of foot ulcer with purulent discharge and with three or more of the following including fever(>38c) or whit cell count >10000mm^3, localized oedema, signs of inflammation like erythema, tenderness, pain, warmth or induration.[13] Patients with suspected osteomyelitis were referred for radiological examination including plain X-ray and Magnetic Resonance Imaging and were also included in this study.

Deep tissue swabs were collected from the patient's wounds and were tested in local hospital microbiological laboratory. As patients were coming from far flung tribal areas and also from Afghanistan and those who were even on antibiotics but clinically unwell as described above were swabbed after necessary debridement.

All the demographic data was collected and included general information as well as duration of diabetes, diabetic control as assessed by HbA$_1$c other diabetic complications specially neuropathy, deformity, peripheral vascular disease and other co-morbid conditions. Retinopathy was diagnosed after doing fundoscopy. Peripheral neuropathy was assessed using the modified neuropathy disability score system.[14]

A six-point foot deformity score assessed small muscle wasting, hammer or claw toes, bony prominences, prominent metatarsal heads, charcot arthropathy, and limited joint mobility; an overall score of <3 indicated significant foot deformity.[1] Femoral, popliteal, dorsalis pedis and posterior tibial pulses on both sides were palpated to assess peripheral arterial status, which was further assessed by Ankle-Brachial Index and values <1.0 were considered peripheral vascular disease. We also recorded history of trauma, type and site of ulcers on the basis of Wagner's classification[15] and whether any surgical intervention was done. Pathogens isolated along with its sensitivity pattern, antibiotic used and its response depending on complete resolution of symptoms of infection and biochemical markers but not the healing of the wound were recorded. Standard off-loading technique was used as required and included locally designed footwear or total contact cast.

Clinical outcomes were categorised as follows: 'Cure' resolution of all clinical signs and symptoms of infection after 5 days of therapy; 'improvement', resolution of ≤2 but not all clinical signs or symptoms of infection after 5 days of therapy and 'failure,' persistence or progression of baseline clinical signs and symptoms of infection after 2 days of therapy. Data was analysed on SPSS-11.

RESULTS

A total of 114 cases were recorded during this period. Sixty nine patients were referred from Afghanistan.

Fifty nine (52%) were males. Mean age for both sex patients was 52.4 years with SD ±9.99. One hundred and five (92%) patients had type 2 diabetes mellitus. Mean duration of diabetes was 10.6 years with SD± 5.2. Seventy (61%) patients had neuropathy, 67 (58%) had nephropathy, 63 (55%) had retinopathy, peripheral vascular disease was present in 12 (10%) cases and two patients had stroke in the past.

Ninety-three (82%) patients had HbA$_1$C more than 8%, 17 (15%) between 7and 8% and only 4 (3%) less than or equal to 7%. Apart from diabetes 38 (33%) patients had hypertension, 31 (27%) patients had high lipid profiles and 32 (28%) had ischaemic heart disease while 13(11%) didn't have any other co morbid conditions apart from diabetes. Sixty-eight (59%) patients presented ulcers on forefoot, 28 (25%) with midfoot ulcers and 18 (16%) with hind foot lesion. Only 32 (28%) had history of trauma or remembered some injury to the feet prior to development of foot ulcer. Seventy-six (66%) patients presented with Wagner's grade 2 ulcers, 19 (17%) with grade 3 ulcers and 16 (14%) with grade 4 ulcers and 3 (2%) grade 5. Osteomyelitis was recorded in 27 (24%) cases.

One-hundred-four 104 pathogens were isolated from deep wound and tissue swabs after debridement. Commonest pathogen isolated was Staphylococcus Aureus 52 (46%) followed by E. coli 11 (10%), and MRSA was found in 10 (9%) cases, Streptococcus in 6 (5%) and Pseudomonas in 5 (4%) cases. Polymicrobial infection was also seen. Sixteen (14 %) cases didn't show any growth after 48 hours of incubation and was thought to be due to use of antibiotics prior to hospital admission.

Surgical intervention included superficial debridement in 88 (77%) cases, toe amputation/forefoot amputation in 19 (17%) cases, and below/above knee (major) amputation in 7 (6%) cases. All 7 patients requiring major amputation were grade 4–5 ulcers.

Commonest antibiotic used was Cefoperazone/ Sulbactam in 43 (38%) cases alone or in combination followed by ceftraixone 36 (33%) cases. Linezolid was the antibiotic of choice for MRSA cases. Other antibiotics used were Ciprofloxacillin, Clindamycin, Vancomycin and Piperacillin/Tazobactum in different cases.

Ninety-four (82%) patients responded to treatment and were recorded as 'cured', 12 (10%) patients showed 'improvement' in response to antibiotics and appropriate antibiotic was changed/ added to the treatment according to microbiological report. Eight (7%) patients were recorded as 'failure' to the treatment. Thirty-two (28%) patients used combination of antibiotics. The mean duration of treatment was 52 days.

Surgical interventions like major amputations (above knee and below knee) were more in grade 4 and

5 ulcers and were statistically significant (Table-1). Also there were more amputations in patients with longer duration of diabetes (Table-2).

Table-1: Surgical interventions by grades of foot ulcers

Type of Surgical Interventions	Wagners Grading, n (%)				Total n (%)
	Grade 2	Grade 3	Grade 4	Grade 5	
Superficial debridement	71 (93.4)	16 (84.2)	1 (6.3)	0 (0)	88 (77.2)
Toe/fore foot amputation	5 (6.6)	3 (15.8)	11 (68.8)	0 (0)	19 (16.7)
Above/below knee Amputation	0 (0)	0 (0)	4 (24.))	3 (100)	7 (6.1)
Total	76	19	16	3	114

Table-2: Surgical interventions by duration of diabetes

Type of Surgical Interventions	Duration of diabetes, n (%)			Total
	≤5 yrs	>5–10 yrs	>10 yrs	
Superficial debridement	16 (88.9)	37 (75.5)	35 (74.5)	88 (77.2)
Toe amputation	1 (5.6)	11 (22.4)	7 (14.9)	19 (16.7)
Major Amputations	1 (5.6)	1 (2.0)	5 (10.6)	7 (6.1)
Total	18	49	47	114

DISCUSSION

This study shows a clinical and microbiological survey of infected diabetic foot ulcers in hospitalized patients in our part of the world. This is the first study from North-West Province of Pakistan looking at common pathogens involved and their response to treatment in clinical setting. Previous data from Pakistan is mostly on the clinical outcome of diabetic foot ulcers[8–10,16,17] and most of the microbiological data is from other countries.

Duration of diabetes and poor control are known risk factors for diabetic foot ulcers[18] as shown by Lipsky and Sheehan[19]. In our study most of the patients were poorly controlled. Many other studies from developing countries have reported similarly.[8–10,17]

Only 28% of our patients had history of trauma prior to developing ulcer while the other majority of patients that is 72% didn't remember any trauma which correlates with peripheral neuropathy present in 61% of our patients. As peripheral neuropathy is considered to be a major contributor for developing diabetic foot ulcer[21], it need to be stressed to the treating physicians especially in primary care settings to confirm the presence or absence of neuropathy in order to identify foot at risk.

Our results confirmed that most of the ulcers were in the forefoot. Lipsky[21] showed that around 50% of infections involved the toes, and similar results were seen by Kaufman.[22]

We used Wagner's classification for ulcers because of its simplicity and in our report most of the cases were of grade 2–5. This signifies the fact that ulcers are not well managed in the community in our setting because of poor infrastructure and health system in developing world.[23]

In our survey microbiological studies were done in all patients including those who were on antibiotics prior to admission to the hospital. This yielded 104 pathogens. Many organisms may cause infections in diabetic foot ulcer patients, but gram-positive cocci are the most frequent and virulent pathogens giving systemic symptoms. The commonest organism was *Staph. aureus* like other studies reported earliar.[24,25] This is also in line with some of the local studies from southern part of the country where again *Staph. aureus* was the main isolated pathogen.[8,9] Pseudomonas which is also considered to be a pathogen responsible for severe tissue damage in diabetic patients, should never be considered as insignificant in foot ulcers unless its role as a pathogen has been excluded.[26,27] Abdul Razak *et al* showed in 86 consecutive diabetic patients that *Staph. Aureus* (38.4%) was the most common isolate being recovered from the cases. Other organisms were *Pseudomonas aurigenosa* (17.5%), *P. mirabilis* and anaerobic gram-negative organisms. This is in contrast to our study where although *Staph. aureus* was the main isolated organism (46%), followed by *E. coli* 10%, and Pseudomonas was isolated in only 4% of cases.

As gram-positives are the most isolated organisms in most studies, we used intravenous Cefoperazone/Sulbactam and/or Ceftraixone empirically to treat infection per policy of the unit. It yielded almost 92% success depending on cure or improvement in clinical condition as per protocol. But where other organisms or multiple organisms were isolated antibiotics were switched depending on the microbiological and sensitivity results. Other antibiotics used were Ciprofloxacillin, clindamycin, vancomycin and Piperacillin/Tazobactum. Their use in percentile is shown in graph below.

There is increasing prevalence of MRSA species worldwide[28–30] which requires aggressive therapy as infection with this organism may have a worse outcome and leaves treating physician with smaller choice in terms of use of antibiotics. We noticed higher number (9%) of MRSA infection in our cases which is generally not recognised serious at primary care level in our setup. As we recruited all the patients including those who were receiving antibiotics in the community prior to admission to our tertiary care unit and may be one reason leading to selective survival advantage of pathogen. Recently two cases of even Vancomycin resistant *Staph. aureus* have been reported.[31] Traditionally, diabetic foot infections have been treated by intravenous antibiotics to assure adequate antibiotic concentrations, especially in patients with severe infection. Newer agents with therapeutically equivalent intravenous and oral formulations allow initial treatment to be oral for persons who are clinically stable and allow an early switch from intravenous to

oral antibiotics for those who are responding to therapy. In our study we used Linezolid orally, as this was the only formulation available and was used after the report of sensitivity was confirmed.

Linezolid is effective for treatment of infections due to gram-positive bacteria, including methicillin-, cephalosporin-, and vancomycin-resistant strains[32,33], but it has minimal activity against gram-negative bacteria. A highly bio-available oral formulation, is administered twice per day, and achieves therapeutic concentrations in soft tissue and bone.[34,35] However, as Linezolid is expensive, we preferred to reserve it for treatment of documented antibiotic-resistant organisms. In our study 28% of patients used combination therapy, which was utilised for more severe foot ulcers at presentation in comparison with moderate ones.

For the empirical treatment of severe infections, Infectious Diseases Society of America (IDSA) suggests use of combination antibiotic therapy or broad spectrum antibiotics.[13] IDSA also suggest use of oral antibiotics for most mild to moderate infections. In our study we only used mostly intravenous antibiotics because of moderate to severe infections and also as it was an inpatient setting.

Finally, we observed that median duration of antibiotic therapy was 52 days (range 21–130) days. IDSA guidelines suggest that the duration of antibiotic treatment should be 1–2 weeks for mild infections, 2–4 weeks for moderate infections and ≥6 weeks for residual osteomyelitis and severe deep tissue infections. This was rather long duration of treatment but that again can be expected in our inpatient setting where patients admitted were usually very ill and required long term antibiotic therapy particularly infections involving deep tissues and bone.

To our knowledge this is the first study from Northern Pakistan highlighting the potential microbiological data and use of appropriate antibiotics. In some respects choice of antibiotics may have been different considering gram-negative load in chronic wounds but another study to compare different antibiotics may give an answer to this, though it is well established that while treating DFI gram positive should be first consideration pending the results of culture and sensitivity.

University of Texas grading may have been appropriate to highlight the grading in more detail. This system, which combines grade and stage, is more descriptive and shows a greater association with increased risk of amputation and prediction of ulcer healing when compared with the Wagner system.[36] In our study we didn't include healing time as the outcome predictor in which case University of Texas classification may have been a better way to determine the outcome.

CONCLUSION

DFIs are common in diabetics and pose serious health problems for developing countries. Common aetiology is *Staph. aureus*, *E. coli*, and Pseudomonas which can be treated effectively with cephaperazone/β-lactamase inhibitors, ceftraixone and flouroquinolones. MRSA is also seen in diabetic foot ulcers and can be effectively treated with Linezolid orally.

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