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ABSTRACT... Objective: The objective of this study is to know the frequency of methicillin resistant *Staphylococcus aureus* and its antibiotic sensitivity in diabetic foot infections in our setup. **Design:** Cross sectional descriptive study. **Setting:** Surgical Department, Khyber Teaching Hospital, Peshawar. **Period:** January 2008 to January 2010. **Materials and Methods:** A total of 84 patients, including 64 males and 20 females. Patient's identity, age, gender and the bacterial isolate on culture and sensitivity report were noted on a standardized proforma and analyzed on SPSS version 16.0. Patients of 18 years and both gender with type I & II Diabetes mellitus, diabetic foot ulcers of Wagner Classification System Grade 1 to 5 of 3 weeks duration, with infection and with no evidence of healing were enrolled in the study. **Results:** The overall mean age of patients was 60.8 years \pm 6.5SD with 9.2 \pm 0.5% HbA1c level. Frequency of methicillin resistant *Staphylococcus aureus* was 28.57%. Methicillin sensitive *Staphylococcal aureus* (51.19%), *Pseudomonas aeruginosa* (48.80%) and *Escherichia coli* (46.42%) were the common organism cultured. Methicillin resistant *Staphylococcus aureus* showed 100% sensitivity to Vancomycin, Linezolid, Meropenem, Imepenem and Piperacillin/tazobactam. **Conclusions:** There is an alarming trend of increase in methicillin resistant *Staphylococcus aureus* because of indiscriminate use of antibiotics in our set up which should be discouraged and a detailed knowledge of bacterial susceptibility to antimicrobial agents is necessary.

Key words: Diabetic foot infection, Methicillin resistant *Staphylococcus aureus*.

INTRODUCTION

The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 111 million in 2000 to 366 million in 2030¹. Foot ulcers are among the leading causes of morbidity in diabetics and are the most common indication for admission in this population². Foot ulceration is the precursor to approximately 85% of all diabetic amputations, and it is estimated that 14%–20% of patients with foot ulcers will have to undergo amputation. Infection of the ulcer increases the risk of amputation³. Infection and ischemias are especially important and the common reasons for ulcer failure to heal⁴ leading to amputation⁵. The most common organisms involved in diabetic foot infections (DFI) are *pseudomonas aeruginosa*, *staphylococcus aureus*, *Escherichia coli*, *Staphylococcus epidermidis* and *Proteus*⁶. Anaerobes are suspected in cases of ischemic necrosis or deep tissue infections^{7,8} and the common anaerobes are gram negative⁹. The most widely used therapies for treating foot ulcers are operative procedures and systemic

antibiotics, highlighting the importance of infection control^{10,11}. Currently patients with diabetic foot ulcers are treated with systemic antibiotics only on evidence of infection⁷ and the duration of antibiotic treatment is adjusted to severity of infection⁹. Antibiotic therapy is continued till the infection is controlled, not up to healing of wound⁸.

The main resistant microorganism in diabetic foot infections requiring hospitalization is methicillin-resistant *Staphylococcus aureus* (MRSA), which accounts for up to 42.86 % of *Staphylococcal aureus* isolates from diabetic foot infections¹². The increasing prevalence of MRSA is now a major cause of hospital acquired infections posing a growing threat to public health¹³. The emergence of MRSA was reported just one year after the launch of methicillin¹⁴. The main factor for high prevalence of MRSA infection in diabetic foot wounds is the overuse of antibiotics and selection of broad, rather than narrow spectrum agents¹². Many of these MRSA isolates are becoming multidrug resistant, and are susceptible only to glycopeptides antibiotics such as

Vancomycin. Low-level resistance to Vancomycin is emerging at present¹⁵.

Despite increasing vigilance, the prevalence of MRSA continues to increase; a recent study from Manchester has reported MRSA isolation in 30.2% of patients attending a diabetic foot clinic, a 100% increase compared to three years earlier¹⁶. Our study is aimed to find out MRSA in diabetic foot infections and its antibiotic susceptibility pattern.

MATERIALS AND METHODS

This prospective descriptive cross sectional study was carried out at surgical department, Khyber Teaching Hospital, Peshawar during December 2007 to December 2009. Total of 84 patients were included in the study comprising of 64 males and 20 females. After detailed clinical history, all diabetic foot wounds were examined and graded according to Wagner Classification System (WCS)²⁷. Each patient was enrolled only once in this study. The inclusion criteria for this study was; Patients of 18 years and above, both gender with type I & II Diabetes mellitus, foot ulcers for more than 3 weeks duration with no evidence of healing, the wounds of Grade 1 to 5 according to WCS and those who were using antibiotics for more than 72 hours with no response to treatment. Grade 0 wounds according to WCS were excluded from the study. The investigations included Full Blood Count, HbA1c level, fasting blood sugar, random blood sugar, blood urea, serum creatinine, serum electrolytes and plain X-rays of the involved limb. Informed written consent was taken from patients and the purpose of study, use of data for research and publication was explained to them.

Wound samples were collected from patients under direct vision with proper illumination. The wound specimens included tissue from skin or deep wound, curettage of the base of the ulcer, needle aspiration of the abscess/bullae without unroofing and the bone in case of osteomyelitis and deep wound swab. Two samples were obtained from each patient before starting antibiotics. Initially, intravenous amoxicillin/ clavulanic acid in dose of 1.2g every 8 hourly and Metronidazole intravenous 500mg every 8 hourly were used empirically until the availability of culture and sensitivity results and

thereafter, the antibiotics were changed accordingly. In case of swab samples, commercially available pre-packed sterilized cotton swabs were used. One specimen in universal sterile bottle and the other in anaerobic media (Thioglycollate broth) was sent within 30 minutes after collection to microbiological laboratory of Pathology department, Khyber Medical College, Peshawar for culture of aerobic and anaerobic bacterial pathogens respectively. All the relevant information was recorded in the proforma for each patient.

RESULTS

The total number of patients in this study was 84 comprising of 64 (76.19%) males and 20 (23.89%) females. The mean age of males and females were 61.6 years + 5.8SD and 59.5 years + 7.4SD respectively. The HbA1c was 9.2% ± 0.6SD in males and 9.0% ± 0.5SD in females respectively. Type II Diabetes mellitus was in 82 (97.61%) patients. Recurrence of diabetic foot ulcer and history of previous hospitalization was noted in 43 (51.19%) patients and 60 (71.42%) patients respectively. The patients who were using antibiotics with proper culture and sensitivity tests and presented with uncontrolled infections were only 4 (4.76%). The other clinical features of all patients are summarized in Table-I.

There were 49 (58.34%) patients who were taking self prescribed antibiotics and 28 (33.34%) patients were taking their treatment for DFIs from local dispensers. The detail is shown in Table-II.

Frequency of methicillin resistant *Staphylococcus aureus* was 28.57%. The most common organism cultured was methicillin sensitive *Staphylococcus aureus* (51.19%) followed by *Pseudomonas aeruginosa* (48.80%) and *Escherichia coli* (46.42%). The detail of all the microorganisms is given in Table No. III.

Methicillin resistant *Staphylococcus aureus* showed 100% sensitivity to Vancomycin, Meropenem, Imepenem and Piperacillin/tazobactam, while the sensitivity of MRSA to Ciprofloxacin, Ofloxacin and Levofloxacin was 58.33%, 62.50% and 62.50% respectively. The sensitivity and resistance of MRSA are noted in Table no. IV.

Table-I. Clinical features of 84 patients with Diabetic foot infections.

Clinical feature	Overall	Mean ± SD or n (%)	Male	Mean ± SD or n (%)	Female	Mean ± SD or n (%)
Age (Years)		60.8±6.5		61.6±5.8		59.5±7.4
Sex		84 (100%)		64 (76.19%)		20 (23.89%)
Type of diabetes mellitus						
Type I		2 (2.38%)		2 (2.38%)		-
Type II		82 (97.61%)		72 (87.80%)		10 (11.90%)
Diabetic medication						
Insulin		30 (35.71%)		22 (26.19%)		8 (9.52%)
Oral anti diabetic		44 (52.38%)		36 (42.86%)		8 (9.52%)
Oral antidiabetic + insulin		10 (11.90%)		8 (9.52%)		2 (2.38%)
Duration of foot infection						
> 1 month		75 (89.29%)		58 (69.04%)		17 (20.24%)
< 1 month		9 (10.71%)		7 (8.33%)		2 (2.38%)
Duration of diabetes mellitus						
> 10 years		72 (85.71%)		51 (60.71%)		21 (25%)
< 10 years		12 (14.28%)		7 (8.33%)		5 (5.95%)
HbA1c (mean ± SD%)		9.1±0.7		9.2±0.6		9.0±0.5
Previous hospitalization		60 (71.42%)		49 (58.33%)		11 (13.09%)
Recurrent ulcer		43 (51.19%)		33 (39.28%)		10 (11.90%)
Site of ulcer						
Planter		33 (39.28%)		24 (28.57%)		9 (10.71%)
Margin		11 (13.09%)		7 (8.33%)		4 (4.76%)
Heel		9 (10.71%)		7 (8.33%)		2 (2.38%)
Interdigital		27 (32.14%)		15 (17.86%)		12 (14.28%)
Malleoli		2 (2.38%)		1 (1.19%)		-
Leg		1 (1.19%)		-		1 (1.19%)
Multiple areas		1 (1.19%)		-		1 (1.19%)
Culture and sensitivity test for DFIs						
Yes		11 (13.10%)		7 (8.34%)		4 (4.76%)
No		69 (82.14%)		56 (66.67%)		13 (15.48%)
<i>n=number of isolates, %=Percentage, SD=Standard deviation</i>						

Table-II. Prescription of Commonly Used Antibiotics to 84 Patients with Diabetic Foot Infections

Prescribed by	Type of antibiotics				Total
	Penicillin n (%)	Cephalosporin n (%)	Quinolones n (%)	Aminoglycosides n (%)	
Self	22 (26.19%)	12 (14.28%)	12 (14.28%)	3 (3.57%)	49 (58.34%)
Local Dispenser	13 (15.48%)	7 (8.34%)	6 (7.14%)	2 (2.38%)	28 (33.34%)
General practitioner	2 (2.38%)	-	-	-	2 (2.38%)
Consultant (Medical Specialist / General Surgeon)	2 (2.38%)	-	2 (2.38%)	-	4 (4.76%)
Total	39 (46.43%)	19 (22.62%)	20 (23.81%)	5 (5.92%)	-

Table-III. Frequency of bacterial isolates in 84 patients with diabetic foot infections

Name of organisms	Male n (%)	Female n (%)	Total n (%)
Methicillin sensitivity <i>Staphylococcus aureus</i>	38 (88.37%)	5 (11.62%)	43 (51.19%)
Methicillin resistant <i>Staph. Aureus</i> (MRSA)	21 (87.5%)	3 (12.5%)	24 (28.57%)
<i>Staphylococcus epidermidis</i>	6 (46.15%)	7 (53.85%)	13 (15.48%)
<i>Streptococcus viridians</i>	6 (50%)	6 (50%)	12 (14.28%)
<i>Escherichia coli</i>	27 (69.23%)	12 (30.77%)	39 (46.42%)
<i>Proteus mirabilis</i>	4 (80%)	1 (20%)	5 (5.95%)
<i>Proteus vulgaris</i>	5 (71.43%)	2 (28.57%)	7 (8.33%)
<i>Pseudomonas aeruginosa</i>	26 (63.41%)	15 (36.59%)	41 (48.80%)
<i>Peptostreptococcus sp.</i>	3 (100%)	-	3 (3.57%)
<i>Clostridium sp.</i>	5 (83.33%)	1 (16.69%)	6 (7.14%)

Staph. Aureus = Staphylococcus aureus

DISCUSSION

WHO has included diabetes in classification of immunodeficiency diseases. Infection occurs with a greater frequency and severity in diabetics than in non-diabetics²⁸. Male sex preponderance (76.19% vs 23.89%) was obvious from our study showing M to F ratio 4:1.25 and this predominance of male sex has also been shown by other local studies^{6,17,18}. In addition, mean age

of presentation in our study was 60.8years + 6.5SD which is about similar to a local study (59years + 3.7SD)¹⁷. Most of our patients were type 2 diabetics (97.61%) having poor glycemic control (HbA1c%=9.1 + 0.7), this observation is in accordance to other local studies^{6,17}.

In the present study, a total of 193 organisms were

Table-IV. Sensitivity and resistance of cultured MRSA to various Antibiotics in 84 patients with Diabetic foot infections

Antibiotic drug	Methicillin resistant <i>Staphylococcus aureus</i> (MRSA)	
	Sensitivity n (%)	Resistance n (%)
Ampicillin	-	24 (100%)
Cefazolin	11 (13.09%)	13 (54.16%)
Vancomycin	24 (100%)	-
Ciprofloxacin	14 (58.33%)	10 (41.67%)
Ofloxacin	15 (62.50%)	9 (37.50%)
Cefaparazone + Sulbactam	22 (91.67%)	2 (8.33%)
Methicillin	-	24 (100%)
Ceftriaxone	15 (62.5%)	9 (37.50%)
Cefotaxime	13 (54.16%)	11 (13.09%)
Levofloxacin	15 (62.5%)	9 (37.50%)
Amikacin	17 (70.83%)	7 (29.16%)
Meropenem	24 (100%)	-
Pipracillin / tazobactam	24 (100%)	-
Imepenem	24 (100%)	-
Linezolid	24 (100%)	-

isolated from 84 patients which represent an average of 2.29 organisms per patient. This is quite high from the local studies (1.27)⁶ and 1.21¹⁹ but such high yield of isolates in diabetic foot infection has been reported in the literature²⁰.

Recent studies have reported a predominance of gram negative infections^{6,17,21} but *Staphylococcus aureus* (51.19%) was the most frequent pathogen followed by *Pseudomonas aeruginosa* (48.81%) in our study.

In our study the isolation of MRSA was 28.57% which showed uniform sensitivity to Vancomycin, Meropenem, Pipracillin/tazobactam, Imepenem, and Linezolid. Some

studies has shown isolation rate of MRSA as 5%²² and 15%²⁸ and as high as 57.1%²³. The high rate of MRSA in our study was attributed to the previous hospitalization, indiscriminate use of antibiotics, recurrent ulcers, use of antibiotics without proper culture and sensitivity tests. High isolation rate of MRSA due to previous hospitalization and indiscriminate use of antibiotics has been observed by others as well^{6,17,25}. Recurrent hospitalization, prolong hospital stay and wide spread use of broad spectrum antibiotics has led to the selective survival and emergence of resistant organism and it has been reported by the results of other study^{17,25,26}.

This study was conducted as pilot study; further data collection is under process in the concerned unit of surgical department.

CONCLUSIONS

In conclusion, a detailed knowledge of the bacterial susceptibility to antimicrobial agents is necessary to control the alarming increase in the resistance of MRSA. Prior to starting empirical antibiotic therapy in all cases of diabetic foot infections, appropriate specimens must be obtained for culture and sensitivity testing. By following the strict protocols for control of bacterial infection, some centers have reported a decrease in MRSA rate from 48.15% to 30%²⁴. The antibiotic therapy must be continued until there is evidence that the infection has resolved. For uninfected diabetic foot ulcerations, prescription of antibiotics either to enhance wound healing or as prophylaxis against infection must be avoided. The available published evidence does not support the use of antibiotics for the management of clinically uninfected ulcerations. In some circumstances, when it is difficult to decide whether a chronic wound is infected, a brief, culture-directed course of antibiotic therapy may be appropriate.

In this study we lacked the facility of modern diagnostic tests like polymerase chain reaction with the help of which we can detect most species of the main pathogens of diabetic foot infections within hours and can be helpful to optimize antibiotic therapy for diabetic foot infections.

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REFERENCES

1. Wild S, Roglic G, Green A, Sicree R, King H. **Global prevalence of diabetes: estimates for the year 2000 and projections for 2030.** *Diabetes Care* 2004 May;27:1047-53.
2. Colayco CAS, Mendoza MT, Alejandria MM, Ang CF. **Microbiologic and clinical profile of anaerobic diabetic foot infections.** *Phil J Microbiol Infect Dis* 2002; 31(4):151-60.
3. Paola LD, Brocco E, Senesi A, Merico M, De Vido D, Assaloni R, et al. **Super oxidized solution therapy for infected diabetic foot ulcers.** *Wounds* 2006;18(9):262-70.
4. Frykberg RG, Zgonis T, Armstrong DG, Driver VR, Giurini JM, Kravitz SR, et al. **Diabetic foot disorders: a clinical practice guideline.** *J Foot Ankle Surg* 2006 Sept-Oct;45(Suppl 5):S1-66.
5. Farnsworth J, Paulman P. **Diabetic foot ulcer and poor compliance: how would you treat?** *J Fam Pract* 2005 Sept; 54(9):768-76.
6. Hayat AS, Khan AH, Masood N, Shaikh N. **Study for microbiological pattern and in vitro antibiotic susceptibility in patients having diabetic foot infections at tertiary care hospital in Abbottabad.** *World App Sci J* 2011;12(2):123-31.
7. Clayton W, Elasy TA. **A review of the pathophysiology, classification and treatment of foot ulcers in diabetic patients.** *Clin Diabetes* 2009;27(2):52-8.
8. Lipsky BA. **Medical treatment of diabetic foot infections.** *Clin Infect Dis* 2004; 39 Suppl 2:S104-14.
9. Leese G, Nathwani D, Young M, Seaton A, Kennon B, Hopkinson H, et al. **Use of antibiotics in people with diabetic foot disease: a consensus statement.** *Diabet Foot J* 2009;12(2):1-10.
10. Gibbons GW. **The diabetic foot: amputations and drainage of infection.** *J Vasc Surg* 1987;5(5):791-3.
11. Faglia E, Dalla Paola L, Clerici G, et al. **Peripheral angioplasty as the first choice revascularization procedure in diabetic patients with critical limb ischemia: prospective study of 993 consecutive patients hospitalized and followed between 1999 and 2003.** *Eur J Vasc Endovasc Surg* 2005;29(6):620-7.
12. Murugans S, Mani KR, Uma Devi P. **Prevalence of methicillin resistant Staphylococcus aureus among diabetes patients with foot ulcers and their antimicrobial susceptibility pattern.** *J Clin Diagn Res* 2008 August;2:979-84.
13. Duckworth G. **Controlling methicillin-resistant staphylococcus aureus: time to return to more stringent methods of control in the United Kingdom (editorial).** *BMJ* 2003;327:1177-8.
14. Rajaduraipandi K, Mani KR, Panneerselvam K, Mani M, Bhaskar M, Manikandan P. **Prevalence and antimicrobial susceptibility pattern of methicillin resistant Staphylococcus aureus: a multicentre study.** *Indian J Med Microbiol* 2006;24 (1):34-8.
15. Assadullah S, Kakru DK, Thoker MA, Bhat FA, Hussain N, Shah A. **Emergence of low level vancomycin resistance in MRSA.** *Indian J Med Microbiol* 2003; 21:1-3.
16. Turner JM, Hakeem LM, Lockman KA, Bhattacharyya DN, Campbell IW. **Diabetic MRSA foot infection – role of linezolid therapy.** *Br J Diabetes Vasc Dis* 2004 Jan/Feb;4(1):44-6.
17. Khoharo HK, Ansari S, Qureshi F. **Diabetic foot ulcers: common isolated pathogens and in vitro antimicrobial activity.** *Professional Med J* 2009 March;16(1):53-60.
18. Zubair M, Malik A, Ahmad J. **Clinico-bacteriology and risk factors for the diabetic foot infection with multidrug resistant microorganisms in north India.** *Biol Med* 2010; 2(4):22-34.
19. Vishwanathan V, Jasmine JJ, Snehalatha C, Ramachandran A. **Prevalence of pathogens in diabetic foot infection in South Indian type 2 diabetic patients.** *J Assoc Physicians India* 2002;50:1013-6.
20. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. **Diagnosis and Treatment of Diabetic Foot Infections.** *Clin Infect Dis* 2004 Oct;39 (1):885-910.
21. Goldstein EJC, Merrian CV, Lipsky BJ, Citron DM, Abramson MA. **Bacteriology of moderate to severe diabetic foot infection and in vitro activity of antimicrobial agent.** *J Clin Microbiol* 2007;45(9):2819-28.
22. Raja NS. **Microbiology of diabetic foot infections in a teaching hospital in Malaysia: a retrospective study of 194 cases.** *J Microbiol Immunol Infect* 2007;40:39-44.

23. Zubair M, Malik A, Ahmad J. **Clinico-bacteriology and risk factors for the diabetic foot infection with multidrug resistant microorganisms in north India.** Biol Med 2010;2(4):22-34.
24. Zia I, Vietahn vu, Hester M, Cheriya P, Marks J, Grossman AB. **Prevalence of MRSA in diabetic foot infections in a community teaching hospital.** Foot 2011;21:52-4.
25. Alavi SM, Khosravi AD, Sarami A, Dashtbozorg A, Montazeri EA. **Bacteriologic study of diabetic foot ulcer.** Pak J Med Sci 2007 Oct-Dec;23(5):681-84.
26. Bonomo RA. **Multiple antibiotic resistant bacteria in long term care facilities: an emerging problem in the practice of infectious diseases.** Clin Infect Dis 2000 Dec;31(6):1414-22.
27. Muqim RU, Griffin S, Ahmed M. **Evaluation and management of diabetic foot according to Wagner's classification. A study of 100 cases.** J Ayub Med Coll Abbottabad 2003 Jul-Sep;15(3):39-42.
28. Girish MB, Kumar TN, Srinivas R. **Pattern of antimicrobials used to treat infected diabetic foot in a tertiary care hospital in Kolar.** Int J Pharm Biomed Res 2010;1(2):48-52.

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