Original Research Article

A study on prescribing patterns of antimicrobials in diabetic foot ulcer in a tertiary care hospital

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Abstract

Background: Diabetic foot ulcers (DFUs) are one of the most feared complications of Diabetes Mellitus (DM), which often become infected leading to complications like osteomyelitis, amputations and septicemia. There are scanty reports of data regarding the patterns and the cost analysis of antibacterial therapy to treat DFUs.**Objectives**: To study the prescribing pattern, approval status, inclusion in World Health Organization (WHO) essential medicines list/National List of Essential Medicines (NLEM) and rationality of antibacterials prescribed in the management of DFUs.**Methods**: Data was collected from records of 52 inpatients with a diagnosis of DFU from Saraswati Medical College, Unnao, U.P., India. The prescribing patterns, approval status, cost and listing of antibacterials in WHO essential medicines list/ NLEM were analysed. The data was presented as percentages, mean and standard deviations.**Results**: Among the 13 positive culture data, 10(77%) were gram negative in nature. Of the 155 antibacterial prescriptions analysed, single drug formulations were most commonly prescribed [109 (70.32%)]; 144 (92.90%) were approved by Drug Controller General of India (DCGI) and 135 (87.10%) by United States Food and Drug Administration (USFDA); 101 (65.16%) antibacterials were included in both WHO and NLEM; parenteral formulations were the commonly used dosage forms [97 (62.58%)]. The most common class of antibacterials prescribed were beta-lactams [Anatomical Therapeutic Chemical (ATC) class: J01C and J01D], both before and after culture and sensitivity (C/S) testing [79(63.2%) and 15(50%) respectively]. Only 16 (10.32%) drugs were prescribed by their generic names. The average cost per dose and the total cost during hospital stay for quinolones were Rs. 7.24, Rs. 92.95 and Rs. 416.97, Rs. 5539.06 for β-Lactams respectively.**Conclusion**: Gram negative organisms were most commonly isolated. Parenteral formulations were preferred over oral formulations and single drug formulations over fixed dose combinations (FDCS) in the management of DFUs. Beta-lactams comprised the major class of antibacterials prescribed before and after C/S testing. More than 80% of the antibacterials prescribed were approved by DCGI and USFDA and almost 60% were included in the WHO essential medicines list and NLEM. The average cost per dose and the total cost during hospital stay were highest for β-lactam antibacterials and least for quinolones.

Key words: Prescribing patterns; Antibacterials; Diabetic foot ulcer

Introduction

Diabetes mellitus (DM) represents a group of metabolic diseases characterized by hyperglycemia resulting either from defects in insulin secretion, insulin action, or both[1].Around 347 million people worldwide have diabetes. Type 2 DM accounts for around 90% of all diabetics worldwide[2]. India has around 50.8 million diabetic patients at present and the figures may double by 2025[3]. DM is predicted to become the seventh leading cause of death in the world by the year 2030. Deaths from diabetes related complications are projected to rise by more than 50% in the next 10 years. In developed countries most

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people with DM are above the age of retirement, whereas in developing countries those most frequently affected are aged between 35 and 64[2]. DM is the leading cause of end-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness[2,4].The increasing incidence of DM has given rise to problem of chronic diabetic ulcers[5]. Diabetic foot ulcer (DFU) is one of the dreadful complications of DM and is the leading cause of hospitalization among diabetic patients[6]. Approximately 15 to 20% of DM patients have foot problems and 10 to 15% of all hospital admissions are due to major foot infections. 50% of all non-traumatic major amputations are due to DM related complications. Around 85% of diabetic foot amputations are due to inadequate and late treatment of diabetic foot ulcers and infections. The lifetime incidence of foot ulcers may be as high as 25%.[3] Peripheral neuropathy, peripheral vascular disease and infection which are among the long term complications of DM contribute to the multifactorial pathogenesis of DFUs[5]. These ulcers frequently become infected, cause great morbidity, give rise to considerable financial burden and may end up in lower extremity amputations[7].Recognizing and treating foot problems early can help diabetic patients avoid serious complications[3].Foot infections in diabetic patients are initially treated empirically. Hence, while selecting antibacterials, one should consider severity of infection, route of drug administration, co-morbidities and spectrum of organisms to be covered. Therapy directed at known causative organisms can significantly improve the outcome and reduce infection related morbidity and mortality. In India, the choice of empirical antibacterials is extrapolated from data available from western countries, which may or may not be appropriate for Indian patients[8]. The increasing association of multi-drug resistant (MDR) pathogens with DFUs further challenges the physician or the surgeon in treating diabetic ulcers without resorting to amputation[6].The principal aim of drug utilization research is to facilitate the rational use of drugs in populations i.e., the prescription of a well documented drug at an optimal dose, together with the correct information, at an affordable price. Information on the past performance of prescribers is vital for any auditing system. A precise knowledge of how drugs are being prescribed and used is essential to initiate a discussion on rational drug use or to suggest measures to improve prescribing habits. Drug utilization research in itself does not necessarily provide answers, but it contributes to rational drug use in important ways[9].Keeping the above things in mind, the present study was taken up to evaluate the prescribing patterns of antibacterials used in the management of DFUs.

Materials and methods

Study location: Saraswati Medical College, Unnao, U.P., India

Study design: Cross-sectional study

Data collection: The relevant data was collected from records of 52 inpatients with a diagnosis of diabetic foot ulcer admitted during Saraswati Medical College, Unnao, U.P., India. The study was initiated after approval from the institutional human ethics committee.

To evaluate the drug prescribing pattern, a proforma containing relevant details such as demographics (age, sex), inpatient number, admission and discharge dates, duration of hospital stay, clinical data (Clinical diagnosis and associated co-morbid conditions), surgical data (debridement, amputation, skin grafting), laboratory parameters (hemoglobin %, FBS, PPBS, RBS, A1C%, blood urea, serum creatinine, urine routine, culture and sensitivity) were recorded. Antibacterials prescribed (generic/brand name) with respect to dosage, route, frequency and duration of administration, before and after culture sensitivity were recorded as per proforma. Drugs prescribed apart from antibacterials were also recorded in the same proforma.

Inclusion criteria

Age: 20-80 years

Sex: Either sex

Patients with a diagnosis of diabetic foot ulcer

Exclusion criteria

Pregnant and lactating women

Ulcers in sites other than foot

Diabetic patients with HIV and tuberculosis

Diabetic patients on cancer chemotherapy, long term steroid use and other immunosuppressant drugs

Analysis of data

The data was subjected to descriptive analysis using Microsoft Excel version 2007.

Utilization of different classes of drugs as well as individual drugs were analyzed and presented as percentage.Approval status of the drugs was checked in the official website for Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services, India[10] and Drugs@FDA: FDA Approved Drug Products [11].Whether the

prescribed antibacterials were listed in the WHO essential medicines list and National List of Essential Medicines was found out from the WHO Model List of essential medicines 2011 and NLEM India 2011[12,13].

Drugs were classified into different groups based on WHO/ATC classification.

ATC/DDD of each antibacterial prescribed was adopted from official website of WHO[14].

Daily defined dose (DDD) of each drug type was calculated as the total quantity of drug administered divided by the number of patient-days the drug was given[15].

Cost of individual drugs was calculated by taking into consideration the average cost of leading brands of drugs available.

Results

Demographic data

52 patients admitted with a diagnosis of DFU were included in the study. Out of 52 patients, 47(90%) were males and 5(10%) females (fig.4), with male to female ratio of 9.4:1.The mean age of males was 56.02 ± 11.95 years and that of females 65.6 ± 15.19 years.Majority of the patients [16 (30.77%)] were in the age group between 51-60 years. The least affected were between 71-80 years [7 (13.46%)], followed by 30-40 years [8 (15.38%)].

Comorbid illness

Out of 52 patients, 20(38%) had hypertension (HTN), 3(6%) diabetic nephropathy, 2(4%) cerebrovascular accidents (CVA), 1(2%) ischemic heart disease (IHD) and 1(2%) osteomyelitis. The remaining 25(48%) did not have any co morbid illnesses. The mean duration of hospital stay was 22.81 ± 18.57 days.(Fig.1)

Table 1: Surgical interventions

Sl no	Surgical interventions	Numbers(n=52)	Percentage
1	Debridement as one of the surgical interventions	33	63.46
2	Skin grafting as one of the surgical interventions	9	17.31
3	Amputation as one of the surgical interventions	5	9.62
4	Debridement as the only surgical intervention	22	42.31
5	Skin grafting as the only surgical intervention	0	0
6	Amputation as the only surgical intervention	2	3.85
7	Debridement + skin grafting	9	17.31
8	Debridement + amputation	2	3.85
9	More than one surgical intervention	11	21.15

Out of 52 patients, 33(63%) had undergone debridement, 9(17%) skin grafting and 5(9.6%) amputation; 11(21.15%) had undergone more than one surgical intervention. (Table 1).

Microbiological Data

Table 2: Culture/sensitivity data

Sl no	Data	Number	Percentage
1	C/S available	16/52	30.77
2	Growth	13/16	81.25
3	No growth	3/16	18.75

Among 52 inpatient records, culture sensitivity data was available only for 16(30.77%) patients as shown in table 2.

Of the 16 inpatient records having culture sensitivity data, 13(81.25%) showed positive cultures.Of the 13 positive culture data, 3(23%) organisms were gram positive and 10(77%) were gram negative in nature as shown in Fig.2

Table 3: Organisms isolated

S.no	Organism	Number among positive cultures (n=13)	Percentage
1	Staphylococcus aureus	1	7.69
2	Klebsiella	5	38.46
3	Pseudomonas	5	38.46
4	Coagulase negative staphylococcus aureus	1	7.69
5	Diphtheroids	1	7.69

Klebsiella 5(38.46%) and Pseudomonas 5(38.46%) were the most common organisms isolated (Table 3).

Table 4: Drug prescription characteristics

S. no	Particulars	Mean ± S.D.
1	Average number of drugs prescribed per patient (including antibacterials)	10.25 ± 3.94
2	Average number of drugs other than antibacterials prescribed per patient	7.1 ± 3.0
3	Average number of antibacterials prescribed per patient	3.06 ± 1.67

Table 5: Drugs other than antibacterials prescribed

S. no	Drug class	Number of patients (n=52)	Percentage
1	Insulin	41	78.85
2	Oral antidiabetic drugs	31	59.62
3	Antiplatelets	12	23.08
4	Statins	7	13.46
5	Analgesics	40	76.92
6	Drugs for treatment of peptic ulcer	43	82.69

Anti-peptic ulcer agents [43(82.69%)], Insulin [41(78.85%)] and analgesics [40(76.92%)] were the most common drugs prescribed other than antibacterials. (Table V)

Table 6: Agents prescribed for the management of diabetes mellitus

S no	Drug class	Number(n=52)	Percentage
1	Insulin as one of the agents	41	78.85
2	Oral antidiabetic drugs as one of the agents	31	59.62
3	Both Insulin and Oral antidiabetic agents	20	38.46
4	Insulin as the only agent	21	40.38
5	Oral antidiabetic drugs as the only agent	11	21.15

Insulin [41(78.85%)] was the most common antidiabetic agent used in the management of diabetes mellitus (Table 6).

Antimicrobial data

A total of 155 antibacterial agents were prescribed in 52 patients. Mean number of antibacterials prescribed per patient: 3.06 ± 1.67 Mean duration of antibacterial usage: 5.89 ± 3.48 days

Table 7: Antibacterial prescription characteristics

S.no	Particulars	Numbers(n=155)	Percentage
1	Single drug formulations	109	70.32
2	Fixed dose combinations	46	29.68
3	Drugs approved by DCGI	144	92.90
4	Drugs approved by FDA	135	87.10
5	Drugs prescribed listed in WHO essential drug list	101	65.16
6	Drugs prescribed listed in national essential drug list	101	65.16
7	Parenteral dosage forms prescribed (injectable)	97	62.58
8	Tablet dosage forms prescribed	50	32.26
9	Capsule dosage forms prescribed	8	5.16
10	Oral route administered	58	37.42

11	I.V. route administered	97	62.58
12	Drugs prescribed in generic name	16	10.32
13	Drugs prescribed before C/S testing	125	80.65
14	Drugs prescribed after C/S testing	30	19.35

Out of the 155 antibacterials, single drug formulations were the most commonly prescribed [109 (70.32%)], 144 (92.9%) drugs were approved by DCGI and 135 (87.1%) by FDA. 101 (65.16%) drugs were included in both WHO and NLEM. Parenteral formulations were the commonly used dosage forms [97 (62.58%)]. Only 16 (10.32%) drugs were prescribed by their generic names. 125 (80.65%) antibacterials were prescribed before and 30 (19.35%) after culture sensitivity testing was done (table 7).Out of 52 patients, a total of 35 (67.31%) received FDC antibacterial drug formulations, 17 (32.69%) received only single drug formulation antibacterials and 4(7.69%) received only FDCs; 41(78.85%) received both injectable and oral formulations, 11(21.15%) received injectables only and 1(1.92%) received oral formulations only.

Table 8: Single drug formulation antibacterials characteristics

[ATC class: J01: Antibacterials for systemic use]						
S no	**Drug**	**ATC code**	**No (%) of prescriptions (n=109)**	**DDD WHO**	**DDD Calcul-ated**	**Mean duration of antibacterials (days) prescribed ± S.D.**
ATC class: J01G; **Drug class:** Aminoglycoside antibacterials						
1	Inj Amikacin	J01GB06	3(2.75)	1g	1g	4.33±1.15
2	Inj Gentamicin	J01GB03	1(0.92)	0.24g	0.16g	5
ATC class: J01D; **Drug class:** Other beta – lactam antibacterials						
3	Inj Cefepime	J01DE01	1(0.92)	2g	2g	6
4	Tab Cefixime	J01DD08	15(13.76)	0.4g	0.4g	8.67±5.69
5	Inj Cefotaxime	J01DD01	11(10.09)	4g	2g	5.97±2.51
6	Tab Cefprozil	J01DC10	1(0.92)	1g	1g	5
7	Inj Ceftriaxone	J01DD04	15(10.09)	2g	2g	4.80±1.70
8	Tab cefuroxime	J01DC02	5(4.59)	0.5g	0.9g	5.60±2.07
9	Inj Meropenem	J01DH02	1(0.92)	2g	3g	5
ATC class: J01M**; Drug class:** Quinolone antibacterials						
10	Tab Ciprofloxacin	J01MA02	3(2.75)	1g	1g	6±4.58
11	Tab Gatifloxacin	J01MA16	2(1.84)	0.4g	0.4g	5±1.41
12	Tab Ofloxacin	J01MA01	4(3.67)	0.4g	0.5g	7.5±2.38
ATC class: J01F; **Drug class:** Macrolides, lincosamides & streptogramins						
13	Tab Clindamycin	J01FF01	9(8.26)	1.2g	0.7g	4.22±2.54
14	Cap Clindamycin	J01FF01	8(7.34)	1.2g	0.9g	6.13±3.09
15	Inj Clindamycin	J01FF01	4(3.67)	1.8g	0.6g	6.25±2.50
ATC class: J01X; **Drug class:** Other antibacterials						
16	Inj Linezolid	J01XX08	8(7.34)	1.2g	0.9g	4.63±1.41
17	Tab Linezolid	J01XX08	3(2.75)	1.2g	0.6g	8
18	Inj Metronidazole	J01XD01	15(10.09)	1.5g	1.5g	6.13±3.91

ATC class: NA **Drug class:** NA						
19	Tab Satronidazole	NA	1(0.92)	NA	0.6g	8

Table 9: Fixed dose combination antibacterials characteristics

Sl no	Drug	ATC code	No (%) of prescriptions (n=46)	DDD WHO	DDD Calcul-ated	Mean duration of antibacterials (days) prescribed ± S.D.
ATC class: J01C; **Drug class:** Beta-lactam antibacterials, Penicillins						
1	Tab Amoxicillin+ Clavulanic acid	J01CR02	4(8.70)	1g	1.56g	6±1.41
2	Inj Amoxicillin +Clavulanic acid	J01CR02	9(19.57)	3g	2.53g	4.44±2.51
3	Inj Piperacillin + Tazobactam	J01CR05	13(28.26)	14g	11.77g	5.15±2.38
ATC class: J01D; **Drug class:** Other beta-lactam antibacterials						
4	Inj Cefoperazone+ Sulbactam	J01DD62	7(15.21)	4g	3g	3.86±2.41
5	Inj Ceftriaxone +Sulbactam	J01DD54	6(13.04)	NA	3g	4.67±2.73
6	Inj Ceftriaxone + Tazobactam	J01DD54	2(4.35)	NA	2.25g	5
ATC class: NA; **Drug class:** NA						
7	Tab Ampicillin + Cloxacillin	NA	1(2.17)	NA	1.5g	6
8	Tab Cefixime + Clavulanic acid	NA	1(2.17)	NA	NA	5
9	Inj Cefotaxime +Sulbactam	NA	1(2.17)	NA	3g	5
10	Tab Cefpodoxime + Potassium Clavulanate	NA	1(2.17)	NA	0.65g	3

Table 10: Most common antibacterials prescribed

S no	Drug	Number(n=155)	Percentage
1	Inj/Tab/Cap Clindamycin	21	13.55
2	Tab Cefixime	15	9.68
3	Inj Ceftriaxone	15	9.68
4	Inj Metronidazole	15	9.68

Of the 155 antibacterials, Inj/Tab/Cap Clindamycin [21(13.55%)], Tab cefixime, Inj Ceftriaxone and Inj Metronidazole were most commonly prescribed [15 (9.68%)]; (Table X).

Table 11: Most common single drug formulation antibacterials prescribed

S no	Drug	Number(n=109)	Percentage
1	Inj/Tab/Cap Clindamycin	21	19.27
2	Tab Cefixime	15	13.76
3	Inj Ceftriaxone	15	13.76
4	Inj Metronidazole	15	13.76

Of the 109 single drug formulation antibacterials, Inj/Tab/Cap Clindamycin [21(19.27%)], Tab Cefixime, Inj Ceftriaxone and Inj Metronidazole were most commonly prescribed [15 (13.76%) each] (Table 11).

Table 12: Most Common FDC Antibacterials prescribed

Sr.no	Drug	Number(n=46)	Percentage
1	Inj Piperacillin + Tazobactam	13	28.26
2	Inj Amoxicillin + Clavulanic acid	9	19.57
3	Inj Cefoperazone + Sulbactam	7	15.22

Out of 46 FDC antibacterials prescribed, Inj Piperacillin + Tazobactam [13 (28.26%)] was the most common combination followed by Inj Amoxicillin + Clavulanic acid [9 (19.57%)] and Inj Cefoperazone + Sulbactam [7(15.22%)] {Table 12}.

Table 13: Most common antibacterials used as empiric agent

Sr. no	Drug	Number(n=125)	Percentage
1	Clindamycin	18	14.40
2	Ceftriaxone	14	11.20
3	Metronidazole	14	11.20
4	Cefixime	12	9.60
5	Piperacillin + Tazobactam	12	9.60
6	Amoxicillin + Clavulanic acid	11	8.80
7	Cefotaxime	10	8.00

Among 125 antibacterials prescribed as empiric agent i.e., before C/S testing, Clindamycin was the most preferred agent [18 (14.40%)] followed by both Ceftriaxone and Metronidazole [14 (11.20%)]. Beta-lactams comprised the major class of antibacterials prescribed before C/S testing [79(63.20%)].

Table 14: Most common antibacterials prescribed after C/S reports

Sl no	Drug	Number(n=30)	Percentage
1	Linezolid	4	13.33
2	Clindamycin	3	10.00
3	Cefoperazone + Sulbactam	3	10.00
4	Cefixime	3	10.00
5	Ofloxacin	3	10.00
6	Amoxicillin + Clavulanic acid	2	6.67

Among 30 antibacterials prescribed after C/S testing, Linezolid was the highest [4 (13.33%)] followed by Clindamycin, Cefoperazone + Sulbactam, Cefixime and Ofloxacin [3 (10%) each] [Table XXXXIII]. Beta-lactams comprised the major class of antibacterials prescribed after C/S testing [15(50%)].

Table 15: Number of antibacterials approved and listed in WHO / National List of Essential Medicines

Drug formulation	Approved by		Listed in essential medicines list	
	DCGI	FDA	WHO	National
Single drug(n=109)	106 (97.25 %)	108 (99.08 %)	87 (79.82 %)	87 (79.82 %)
FDC (n=46)	38 (82.60 %)	27 (58.69 %)	14 (30.43 %)	14 (30.43 %)

Out of 46 FDCs, 38 (82.60%) and 27 (58.69%) drugs were approved by DCGI and FDA respectively and 14 (30.83%) drugs were listed in both WHO essential medicines list and NLEM (Table 15).

Table 16: Average cost of antibacterials prescribed

S no	Drug	Average cost of single dose of antibacterial in Rs. (Mean ±S.D.)	Average cost of antibacterials prescribed during hospital stay in Rs. (Mean ±S.D.)	Average Cost per calculated DDD in Rs. (Mean ±S.D.)
1	Inj Amikacin	69.92 ± 9.83	497.63 ± 76.27	139.85 ± 19.66
2	Inj Gentamicin	8.9	89	17.8
3	Inj Cefepime	190	2280	380
4	Tab Cefixime	19.16 ± 2.10	330.16 ± 210.68	38.32 ± 4.20
5	Inj Cefotaxime	30.99	366.25 ± 155.46	61.98
6	Tab Cefprozil	55	550	110
7	Inj Ceftriaxone	118.28 ± 19.98	1175.44 ± 464.11	236.56 ± 39.97
8	Tab Cefuroxime	76.28 ± 20.34	792.49 ± 147.54	152.56 ± 40.67
9	Inj Meropenem	2450	36750	7350
10	Tab Ciprofloxacin	8.3 ± 1.68	109.3 ± 88.14	16.6 ± 3.36
11	Tab Gatifloxacin	9.6 ± 3.39	45.6 ± 3.39	9.6 ± 3.39
12	Tab Ofloxacin	5.26 ± 1.27	104.37 ± 48.94	10.51 ± 2.55
13	Tab Clindamycin	37.78 ± 4.87	397.56 ± 293.30	93.07 ± 25.57
14	Cap Clindamycin	59.10 ± 21.06	704.28 ± 229.20	118.20 ± 42.12
15	Inj Clindamycin	84	1050 ± 420	168
16	Inj Linezolid	235.63 ± 75.04	1957.50 ± 952.41	435.00 ± 155.01
17	Tab Linezolid	49.38	790	98.75

Table 17: Average cost of injectable and oral formulations of antibacterials prescribed

Formulation	Mean duration prescribed (days)	Average cost of single dose of the formulation in Rs.	Average cost of the formulation prescribed during hospital stay in Rs.
Injectable	5.44 ± 3.13	215.28	2625.69
Oral	6.71 ± 3.95	33.92	431.33

Injectables were prescribed for a mean duration of 5.44 ± 3.13days and oral formulations for 6.71 ± 3.95 days. Average cost of single dose and that prescribed during hospital stay was Rs. 215.28 and Rs. 2625.69 for injectables and Rs. 33.92 and Rs.431.33 for oral formulations respectively.

Discussion

Antimicrobial agents are commonly employed in the management of diabetic foot ulcers, the most important and widely prescribed being antibacterial agents. All cases of diabetic foot ulcers with clinical evidence of infection must be treated with antibacterial agents. Empiric antibacterials are usually started based on previous experiences of clinicians and are narrowed down to definitive antibacterial therapy after culture and sensitivity reports have been obtained.[16] In the present study, the prescribing patterns of antibacterial agents and other drugs used concurrently in the management of DFUs have been studied. Also, an attempt has been made to analyse the cost of antibacterials used in the present study.The data of 52 patients admitted with a diagnosis of DFUs during the period XXXXX were analysed. In the present study, the prevalence of DFU was more in males [47 (90%)] than females [5(10%)] {fig.4}, which is similar to a study done by Bengalorkar GM et al[17]. The mean age of males

was 56.02 ± 11.95 years and that of females 65.6 ± 15.19 years. Patients aged between 51-60 years were the most affected [16 (30.77%)] .Hypertension [20(38%)] was the most common co-morbid illness followed by nephropathy [3(6%)] and cerebrovascular accidents [2(4%)] {fig.6}. The mean duration of hospital stay was 22.81 ± 18.57 days.The most common surgical intervention was debridement [33(63%)], followed by skin grafting [5(9.6%)] and only 11(21.15%) patients had undergone more than one surgical intervention.Unlike reports from western countries[18], the most common organisms isolated in the present study were gram negative in nature which included Klebsiella [5(38.46%)] and Pseudomonas species [5(38.46%)]. This is comparable to the results obtained by Bengalorkar GM et al.,.[6] The gram positive organisms isolated were Staphylococcus aureus, Coagulase negative staphylococcus aureus and Diphtheroids [1(7.69%) each] {Table XXXII, fig.10, 12}. The increased prevalence of gram negative bacilli in DFU patients could be attributed to unhygienic sanitary habits[8].The average number of overall drugs prescribed per patient was 10.25 ± 3.94.Excluding antibacterials, the average number of drugs prescribed was 7.1 ± 3.0.Excluding antibacterials, drugs for peptic ulcer [43(82.69%)] were the most commonly prescribed preparations, followed by insulin [41 (78.85%)] and analgesics [40 (76.92%)] . Insulin [41 (78.85%)] was the most common antidiabetic agent prescribed for the management of DM.The average number of antibacterials prescribed per patient was 3.06 ± 1.67. The mean duration for which antibacterials were prescribed was 5.89 ± 3.48 days. A total of 155 antibacterials were prescribed in 52 patients, of which 109(70.32%) were single drug antibacterial formulations, 46 (29.68%) were fixed dose combinations. 144 (92.90%) and 135 (87.10%) antibacterials were approved by DCGI and USFDA respectively. More than half of antibacterials [101 (65.16%)] used in the management of DFU were listed in both WHO essential medicines list and NLEM. Among the prescribed antibacterials, 2/3rd were injectables [97(62.58%)] and 1/3rd oral formulations 58(37.42%). Around 10% [16(10.32%)] of antibacterials were prescribed by their generic names. A total of 125(80.65%) and 30(19.35%) antibacterials were prescribed before and after C/S testing respectively.Out of 52 patients, a total of 35 (67.31%) received FDC antibacterial drug formulations, 17 (32.69%) received only single drug formulation antibacterials and 4(7.69%) received only FDCs; 41(78.85%) received both injectable and oral formulations, 11(21.15%) received injectables only and 1(1.92%) received oral formulations only. The most common antibacterials prescribed were Clindamycin [21(13.55%)], Cefixime 200mg BD, Ceftriaxone 1g BD and Metronidazole 500mg TID, [15(9.68%) each]. The most common injectables used were Inj. Ceftriaxone and Inj. Metronidazole [15(15.46%) each]; Tab/Cap Clindamycin [17(29.31%)] and Tab Cefixime [15(25.86%)] were the most common oral formulations used. The most common single drug formulations prescribed were Clindamycin [21(19.27%)], Cefixime 200mg BD, Ceftriaxone 1g BD and Metronidazole 500mg TID, [15(13.76%) each] {Table XXXX}. The most common FDC antibacterials prescribed were Inj. Piperacillin + Tazobactam 4.5g [13(28.26%)] followed by Inj. Amoxicillin + Clavulanic acid 1.2g [9(19.57%)] and Inj. Cefoperazone + Sulbactam 1.5g [7(15.22%.)].The most common class of antibacterials prescribed was beta-lactams (ATC class: J01D and J01C) [90(58.07%)]. Among the 155 antibacterials, 125(80.65%) were prescribed empirically and 30(19.35%) after C/S testing. Beta-lactams comprised the major class of antibacterials prescribed before and after C/S testing [79(63.2%) and 15(50%) respectively]. Beta-lactam antibacterials have wider gram negative coverage[19].Irrespective of C/S testing, majority of prescriptions in the present study were that of beta-lactam antibacterials. Since, C/S testing yielded more gram negative isolates, the prescription of above antibacterials is justified.The antibacterials which were not approved by DCGI include Gatifloxacin, Satronidazole, FDC of Ampicillin and Cloxacillin, Cefoperazone and Sulbactam; those not approved by FDA include Satronidazole, Ampicillin + Cloxacillin, Cefixime + Clavulanic acid, Cefoperazone + Sulbactam, Cefotaxime + Sulbactam, Cefpodoxime + Potassium Clavulanate, Ceftriaxone + Sulbactam and Ceftriaxone + Tazobactam. The antibacterials which were not approved by any of the regulatory bodies include Satronidazole, FDC of Ampicillin and Cloxacillin, Cefoperazone and Sulbactam.The antibacterials Cefepime, Cefprozil, Cefuroxime, Gatifloxacin, Linezolid, Meropenem, Satronidazole and all the FDCs except Amoxicillin + Clavulanic acid were not enlisted in the WHO essential medicines list and NLEM. Taking into consideration, the approval status, cost and the frequency in which

the antibacterials were prescribed, the following drugs could be suggested to be included in the essential medicines list: Cefuroxime, Linezolid and Ceftriaxone + Sulbactam. Even though the cost of Piperacillin+ Tazobactam was very high (Rs. 681.91 ± 166.21), it was commonly prescribed. Hence, Piperacillin + Tazobactam preparations could be suggested for inclusion in the essential medicines list and as well be made available at reasonable rates.More than 97% of single drug formulations were approved by DCGI and FDA and 80% were enlisted in both WHO and NLEM. In comparison, the number of FDCs approved by DCGI and FDA were 38(82.60%) and 27(58.69%) respectively and only 30.43% were listed in both WHO and NLEM. These statistics suggest that most of the FDCs prescribed were not listed in Essential medicines list.Considering only the approved preparations, Inj. Meropenem (Rs. 2450) was the most expensive drug prescribed and Tab. Ofloxacin (Rs. 5.26) was the least. The total cost of antibacterial for the total duration of stay was least for Inj. Gentamicin (Rs. 89) followed by Tab. Ofloxacin (Rs.104.37) and it was the most expensive for Inj. Meropenem (Rs.36750) followed by Inj. Piperacillin + Tazobactam (Rs. 9591.15). The average cost per calculated DDD was least for Tab. Ofloxacin [Rs. 10.51 ± 2.55] and highest for Inj. Meropenem [Rs. 7350]. Taking the drug class into account, the cost per dose and the total cost during hospital stay was least for quinolones [Rs. 7.24 and Rs.92.95 respectively], and most expensive for β-Lactam antibacterials [Rs. 416.97 and Rs.5539.06 respectively].Quinolones have a wide range of coverage against organisms[19].These organisms include the ones isolated in the present study as well as other studies done in India by Umadevi S et al.[6]Ramakant P et al.[8] Bengalorkar GM et al.[17] and Gadepalli R et al[20]. As quinolones have wide antibiotic coverage and are cost effective, they could be preferred as an empiric agent in the management of DFUs keeping in mind their resistance patterns.

Conclusion

Gram negative organisms were the most common organisms isolated.Parenteral formulations were preferred over oral in the management of DFUs. Single drug formulations were preferred over FDCs in the management of DFUs. Beta-lactams comprised the major class of antibacterials prescribed before and after C/S testing. More than 80% of the antibacterials prescribed were approved by USFDA and DCGI. Almost 60% of the antibacterials prescribed were included in the WHO essential medicines list and National List of Essential Medicines. The average cost per dose and the total cost during hospital stay were highest for β- lactam antibacterials and least for quinolones.

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