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Research Article

PRESCRIBING PATTERNS OF ANTIMICROBIALS IN DIABETIC FOOT ULCER IN A TERTIARY CARE TEACHING RURAL HOSPITAL

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Abstract

Background: Diabetic foot ulcers (DFUs) are one of the most feared complications ofDiabetes Mellitus (DM), which often become infected leading to complications likeosteomyelitis, amputations and septicaemia. 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. So this study was planned with the objectives to study the prescribing pattern and rationality of antibacterials prescribed in the management of DFUs. **Methods**: Data was collected from records of 27 in patients with a diagnosis of DFU fromIndex Medical College and Research Centre, Indore. The prescribing patterns, approval status andlisting of antibacterials in WHO essential medicines list/ NLEM were analysed. **Results**: From among the 27 patients record the data for culture and sensitivity were available for 10 patients. Among them 7 showed positive culture data, 5(71.42%) were gram negative in nature and 2(28.57%) gram negative. Ofthe 88 antibacterial prescriptions analysed, single drug formulations were mostcommonly prescribed [65 (73.86%)]; 62 (95.38%) wereapproved by Drug ControllerGeneral of India (DCGI) and 64 (98.46%) by United States Food and DrugAdministration (USFDA); the most common class of antibacterialsprescribed were beta-lactams [51(57.95%)]. **Conclusion**: Gram negative organisms were most commonly isolated. Parenteralformulations were preferred over oral formulations and single drug formulations overfixed dose combinations (FDCS) in the management of DFUs. 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.

Key words: Antibacterials; Diabetic foot ulcer; Prescribing patterns

INTRODUCTION

Diabetes mellitus (DM) represents a group of metabolic diseases characterized by hyperglycaemia resulting either from defects in insulin secretion, insulin action, or both.[1]Around 347 million people worldwide have diabetes. Type 2 DM accounts for around90% 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.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 diabeticulcers.[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% ofDM 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 relatedcomplications. Around 85% of diabetic foot amputations are due to inadequate and latetreatment of diabetic foot ulcers and infections. The lifetime incidence of foot ulcers maybe as high as 25%.[3] Peripheral neuropathy, peripheral vascular disease and infectionwhich are among the long term complications of DM contribute to the multifactorialpathogenesis of DFUs.[5] These ulcers frequently become infected, cause great morbidity,give rise to considerable financial burden and may end up in lower extremityamputations.[7] Recognizing and treating foot problems early can help diabetic patientsavoid serious complications.[3]

Foot infections in diabetic patients are initially treated empirically. Hence, whileselecting antibacterial, one should consider severity of infection, route of drugadministration, co-morbidities and spectrum of organisms to be covered. Therapydirected at known causative organisms can significantly improve the outcome and reduceinfection related morbidity and mortality. The increasing association of multi-drug resistant (MDR)pathogens with DFUs further challenges the physician or the surgeon in treating diabeticulcers without resorting to amputation.[6]

Drug utilization study is component medical audit that does monitoring and evaluation of drug prescribing patterns and suggests necessary modifications in prescribing practices to achieve rational therapeutic practice as well cost effective health care.[8]

Keeping the above things in mind, the present study was taken up to evaluate theprescribing patterns of antibacterial used in the management of DFUs.

MATERIALS AND METHODS

This was a prospective, cross sectional study and was observational in nature that was conducted at a tertiary care teaching hospital, attached to Index Medical College Hospital & Research Centre (IMCHRC), Indore. Prior approval for carrying out the study was obtained from the Institutional Ethics Committee (IEC).

All the participants were examined on the day of admission and relevant details were noted in the structured format. To evaluate the drug prescribing pattern, proforma containing relevant details such as demographics, duration of hospital stay, clinical data(clinical diagnosis and associated co-morbid condition), laboratory parameter (Hb%,FBS, PPBS,RBS, HbA1C%, blood urea, serum creatinine, urine routine, culture and sensitivity) were recorded. Antibacterials prescribed with respect to dosage, route, frequency and duration administration, before and after culture sensitivity were recorded as per proforma.

Patients of either sex with age in-between 20-80 years with diagnosis of diabetic foot ulcer and those willing to sign informed consent form were included in study. Pregnant and lactating mother, diabetic patients with HIV and tuberculosis, diabetic patients with cancer chemotherapy, long term steroid use and other immunosuppressant drug were excluded from study.

RESULT

A total of 27 patients admitted with diagnosis of DFU, during 1stJanuary 2014 to 31st may 2014 were enrolled in the study. Out of 27 patients, 19 (70.37%) were male patients and

8(29.62%) were female patients. The mean age of males was 57.02 ± 10.98 years and that of females 60.6 ± 14.15years.

Majority of the patients [11 (40.74%)] were in the age group between 51-60years. The least affected were between 30-40years [3 (11.11%)], followed by 71-80 years [5(18.51%)].

Out of 27 patients, 10(37.03%) had hypertension (HTN), 2(7.4%) diabeticnephropathy, 1(3.70%) cerebrovascular accidents (CVA), 1(3.70%) ischemic heart disease(IHD) and 1(3.70%) osteomyelitis. The remaining 13(48.14%) did not have any co morbidillnesses.

Among 27 inpatient records, culture sensitivity data was available only for10(37.03%) patients as[Fig.1 and Table 1].Of the 10 inpatient records having culture sensitivity data, 7(70%) showed positive cultures [Fig.2].Out of 7 positive culture data, 2(28.57%) organisms were gram positive and5(71.42%) were gram negative in nature [Fig.3].Klebsiella 3(42.85%) and Pseudomonas 2(28.57%) were the most commonorganisms isolated [Table.3].

Table 1.Culture/sensitivity data

Sr. no	Data	Number	Percentage (%)
1	C/S Available	10/27	37.03
2	Growth	7/10	70
3	No growth	3/10	30

Figure 1. Culture and sensitivity data available

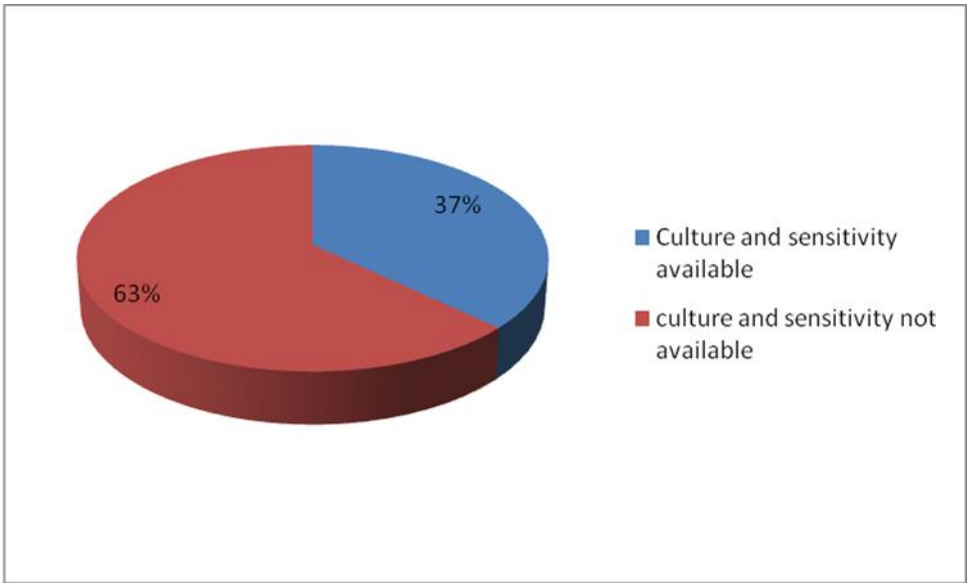

Figure 2.Culture characteristic (%)

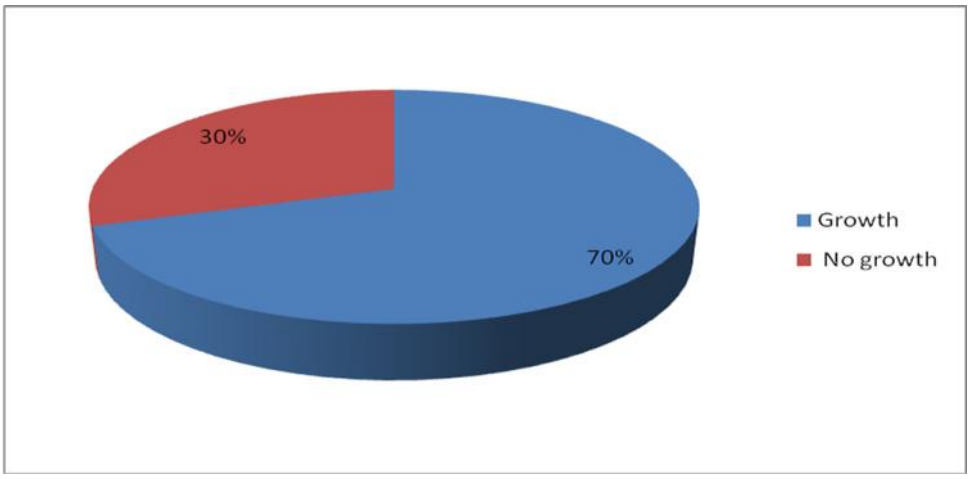

Fig.3 Gram +ve& Gram -ve organismsisolated(%)

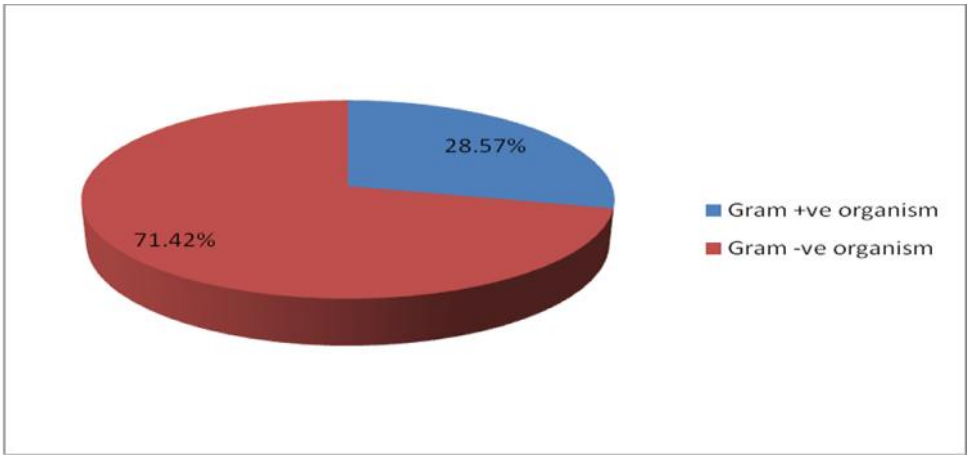

Table 3. Organisms isolated

Sr. no	Organism	Number among positivecultures (n=7)	Percentage(%)
1	Klebsiella	3	42.85
2	Pseudomonas	2	28.57
3	Coagulase negative staphylococcus Aureus	1	14.28
4	Staphylococcus aureus	1	14.28

Antimicrobial data

A total of 88 antibacterial agents were prescribed in 27 patients.Mean number of antibacterials prescribed per patient: **3.18 ± 1.8**

Out of the 88antibacterials, single drug formulations were the most commonlyprescribed [65 (73.86%)], out of which 62 (95.38%) drugs were approved by DCGI and 64 (98.46%)by FDA. 55 (84.61%) drugs were included in both WHO and NLEM. Out of 88 antibacterials Parenteralformulations were the commonly used dosage forms [61 (69.31%)]. Only 10 (11.36%)drugs were prescribed by their generic names. 62 (70.45%) antibacterials wereprescribed before and 26 (29.54%) after culture sensitivity testing was done [Table.4, Fig.1].

Table 4. Single drug formulation antibacterials characteristics

Sr no.	Drug	No (%) of prescriptions (n=65)	DDD WHO	DDD Calculated	Mean duration of antibacterials (days) prescribed ± S.D.
Drug class: Aminoglycoside antibacterials					
1	InjAmikacin	2(3.07)	1	1	4.33±1.15
2	Inj Gentamicin	1(1.53)	0.24	0.18	5
Drug class: Other beta – lactam antibacterials					
3	InjCefepime	1(1.53)	2	2	6
4	Tab Cefixime	10(15.38)	0.4	0.4	8.67±5.69
5	InjCefotaxime	6(9.23)	4	2	5.97±2.51
6	Inj Ceftriaxone	11(16.92)	2	2	5
7	Tab cefuroxime	3(4.61)	0.5	0.5	4.80±1.70
8	InjMeropenem	1(1.53)	2	2	5
Drug class: Quinolone antibacterials					
9	Tab Ciprofloxacin	2(3.07)	1	1	6±4.58
10	Tab Gatifloxacin	1(1.53)	0.4	0.4	5±1.41
11	Tab Ofloxacin	2(3.07)	0.5	0.5	7.5±2.38
Drug class: Macrolides, lincosamides&streptogramins					
12	Tab Clindamycin	4(6.15)	1.2	0.7	4.22±2.54
13	Cap Clindamycin	4(6.15)	1.2	0.9	6.13±3.09
14	Inj Clindamycin	2(3.07)	1.8	0.6	6.25±2.50
Other antibacterials					
15	Inj linezolid	4(6.15)	1.2	0.9	4.63±1.41
16	Tab linezolid	2(3.07)	1.2	0.6	8
17	Inj metronidazole	9(13.84)	1.5	1.5	6.13±3.91

Table 5. Fixed dose combination antibacterials characteristics

Sr no.	Drug	No (%) of prescriptions (n=23)	DDD WHO (gm)	DDD Calculated (gm)	Mean duration of antibacterials (days) prescribed ± S.D.
Drug class: Beta-lactam antibacterials, Penicillins					
1	Tab Amoxicillin + Clavulanic acid	2(8.69)	1	1	6±1.41
2	Inj Amoxicillin + Clavulanic acid	4(17.39)	3	2.5	4.44±2.51
3	InjPiperacillin + Tazobactam	2(8.69)	14	10	5.15±2.38
Other beta-lactam antibacterials					
4	InjCefoperazone + Sulbactam	3(13.04)	4	3.5	3.86±2.41
5	Inj Ceftriaxone + Sulbactam	7(30.43)	NA	3	4.67±2.73
6	InjCeftriaxone + Tazobactam	1(4.34)	NA	2.5	5
7	Tab Cefixime + Clavulanic acid	2(8.69)	NA	NA	5
8	InjCefotaxime + Sulbactam	2(8.69)	NA	3	5

Table 6.Most common antibacterials prescribed

Sr no	Drug	Number (n=88)	Percentage (%)
1	Inj Ceftriaxone	11	(12.5)
2	Inj/Tab/Cap Clindamycin	10	(11.36)
3	Tab Cefixime	10	(11.36)
4	Inj Metronidazole	9	(10.22)

Of the 88antibacterials,Inj Ceftriaxone 11 (12.50%), Inj/Tab/Cap Clindamycin 10(11.36%), Tab cefixime 10(11.36%),and Inj Metronidazole were most commonly prescribed 9 (10.22%) [Table 6].

Table 7.Most common single drug formulation antibacterial prescribed

Sr no	Drug	Number (n=65)	Percentage (%)
1	Inj Ceftriaxone	11	16.92
2	Inj/Tab/Cap Clindamycin	10	15.38
3	Tab Cefixime	10	15.38
4	Inj Metronidazole	9	13.84

Of the 88 antibacterials, Inj Ceftriaxone 11 (16.92%), Inj/Tab/Cap Clindamycin 10(15.38%), Tab cefixime 10(15.38%),and Inj Metronidazole were most commonly prescribed 9 (13.84%)[Table 7].

Table 8.Most Common FDC Antibacterials prescribed

Sr. no	Drug	Number (n=23)	Percentage (%)
1	Inj Ceftriaxone + Sulbactam	7	30.43
2	Inj Amoxicillin + Clavulanic acid	4	17.39
3	InjCefoperazone + Sulbactam	3	13.04

Out of 23 FDC antibacterials prescribed, InjCeftriaxone +Sulbactam7 (30.43.26%) was the most common combination followed by Inj Amoxicillin + Clavulanic acid 4 (17.39%) andInjCefoperazone + Sulbactam 3(13.04%) [Table8].

Table 9.Most common antibacterials used as empiric agent

Sr. no	Drug	Number (n=62)	Percentage (%)
1	Ceftriaxone	10	16.12
2	Clindamycin	9	14.51
3	Cefixime	9	14.51
4	Metronidazole	8	12.90
5	Ceftriaxone+sulbactam	7	11.29
6	Amoxicillin + Clavulanic acid	4	6.45

Among 62antibacterials prescribed as empiric agent i.e., before C/S testing,Ceftriaxonewas the most preferred agent [10 (16.12%)] followed by both Clindamycin and cefixime 9 (14.51%)[Table 9]. Beta-lactams comprised the majorclass of antibacterials prescribed before C/S testing.

Table no 10. Most common antibacterials prescribed after C/S reports

Sr. no	Drug	Number (n=26)	Percentage (%)
1	Linezolid	4	15.38
2	Clindamycin	3	11.53
3	Ceftriaxone	2	7.69
4	Cefixime	2	7.69
5	Ofloxacin	2	7.69
6	Amoxicillin + Clavulanic acid	2	7.69

Among 26antibacterials prescribed after C/S testing, Linezolid was the highest 4(15.38%) followed by Clindamycin 3(11.53%), Ceftriaxone, Cefixime,Ofloxacinand Amoxicillin + Clavulanic acid 2 (7.69%) each [Table 10]. Beta-lactams comprised the major class ofantibacterials prescribed after C/S testing.

Table 11. 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=65)	62 (95.38 %)	64 (98.46 %)	55 (84.61 %)	55 (84.61 %)
FDC(n=23)	19 (82.60 %)	15 (65.21 %)	11 (47.82 %)	11 (47.82 %)

Out of 65 single drug formulations, 62 (95.38 %) and 64 (98.46 %) drugs wereapproved by DCGI and FDA respectively and 55 (84.61 %)drugs were listed in bothWHO essential medicines list and NLEM (Table.11).

Out of 46 FDCs, 19 (82.60 %) and 15 (65.21 %) drugs were approved by DCGIand FDA respectively and 11 (47.82 %) drugs were listed in both WHO essential medicines list and NLEM (Table.11).

DISCUSSION

Antimicrobial agents are commonly employed in the management of diabetic footulcers, the most important and widely prescribed being antibacterial agents. All cases ofdiabetic foot ulcers with clinical evidence of infection must be treated with antibacterialagents. Empiric antibacterials are usually started based on previous experiences ofclinicians and are arrowed down to definitive antibacterial therapy after culture andsensitivity reports have been obtained.[9]In present study, the prescribing patterns ofantibacterial agents in the management of DFUs havebeen studied.

The data of 27 patients admitted with a diagnosis of DFUs during the period Jan2014 to May 2014 were analysed. In the present study, the prevalence of DFU was morein males [19 (70.37%)] than females [8(29.62%)] The mean age of males was 57.02 ± 10.98 years and that

offemales 60.6 ± 14.15 years. Patients aged between 51-60 years were the most affected[11 (40.74%)].

Hypertension 10(37.03%) was the most common co-morbid illness followed bynephropathy 2(7.4%), cerebrovascular accidents, ischemic heart disease, osteomyelitis1(3.70%) each.

Unlike reports from western countries[33], the most common organisms isolated inthe present study were gram negative in nature which included Klebsiella [3(42.85%)]and Pseudomonas species [2(28.57%)]. This is comparable to the results obtained byGadepalli R et al. and Umadevi S et al.[6,10]The gram positiveorganisms isolated were Staphylococcus aureus and Coagulase negative staphylococcusaureus[1(7.69%) each] (Table.3). The increasedprevalence of gram negative bacilli in DFU patients could be attributed to unhygienicsanitary habits.[11]

The average number of antibacterials prescribed per patient was 3.18 ± 1.8. Out of the 88 antibacterials, single drug formulations were the most commonly prescribed [65(73.86%)], 62 (95.38%) drugs were approved by DCGI and 64 (98.46%) by FDA. 55 (84.61%) drugs were included in both WHO and NLEM.Morethan half of antibacterials [101 (65.16%)] used in the management of DFU were listed inboth WHO essential medicines list and NLEM.

Out of the 88 antibacterials, single drug formulations were the most commonlyprescribed [65 (73.86%)], 62 (95.38%) drugs were approved by DCGI and 64 (98.46%)by FDA. 55 (84.61%) drugs were included in both WHO and NLEM. Parenteral formulations were the commonly used dosage forms [61 (69.31%)]. Only 10 (11.36%)drugs were prescribed by their generic names. 62 (70.45%) antibacterials werepreprescribed before and 26 (29.54%) after culture sensitivity testing was done (table 4, fig.1).

Out of 27 patients, a total of 18 (66.66%) received FDC antibacterial drugformulations, 9 (33.33%) received only single drug formulation antibacterials and4(14.81%) received only FDCs; 21(77.77%) received both injectable and oralformulations, 6(22.22%) received injectables only and 1(11.11%) received oralformulations only.

The most common antibacterials prescribed were Ceftriaxone[11(12.5%)], Clindamycin [10(11.36%)], Cefixime[10(11.36%)] and Metronidazole [9(10.20%)] (Table 6). 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 FDC antibacterials prescribed were Inj. Ceftriaxone + Sulbactam [7(30.43%)] followed by Inj. Amoxicillin + Clavulanic acid [4(17.39%)] and Inj. cefoperazone + Sulbactam [3(13.04%)] (Table 8).

The most common class of antibacterials prescribed was beta-lactams [51(57.95%)]. Among the 88antibacterials, 62(70.45%) werepreprescribed empirically and 26(29.55%) after C/S testing.

The antibacterials which were not approved by DCGI include Gatifloxacin, FDC of Ampicillin and Cloxacillin, Cefoperazone and Sulbactam; thosenot approved by FDA include Ampicillin + Cloxacillin, Cefixime +Clavulanic acid, Cefoperazone + Sulbactam, Cefotaxime + Sulbactam, Cefpodoxime +Potassium Clavulanate, Ceftriaxone + Sulbactam and Ceftriaxone + Tazobactam. Theantibacterials which were not approved by any of the regulatory bodies includeFDCs of Ampicillin and Cloxacillin, Cefoperazone and Sulbactam.

The antibacterialsCefepime, Cefprozil, Cefuroxime, Gatifloxacin, Linezolid,Meropenem and all the FDCs except Amoxicillin + Clavulanic acid werenot enlisted in the WHO essential medicines list and NLEM.

More than 97% of single drug formulations were approved by DCGI and FDAand 80% were enlisted in both WHO and NLEM. In comparison, the number of FDCsapproved by DCGI and FDA were 19(82.60%) and 15(65.21%) respectively and only11(47.82%) were listed in both WHO and NLEM. These statistics suggest that most of theFDCs prescribed were not listed in Essential medicines list.

Owing to the large incidence of DFUs, the studies have many limitations the sample size included is not sufficient to extrapolate the results to a larger population. Since, the culture and sensitivity data of many patients were not available; the actual incidence of the organisms colonizing DFUs could not be ascertained. Data on adverse drug reactions of the antibacterials prescribed was not available. Because of limitation of study protocol we were not able to assess outcome of DFUs after antibacterial therapy.

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