

Prescription pattern of antibiotics in the skin and soft tissue infections in patients with diabetes mellitus: Experience from a tertiary care teaching hospital

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Abstract

Objectives: To report the clinical presentation of various skin and soft tissue infections, antimicrobial therapy and the outcome of diabetic patients. **Methods:** A retrospective descriptive study. **Results:** The prescriptions of 200 diabetic patients (Type 2=199) with a mean age of 58 years were analysed. There were more males than females (67:33). Retired personnel (35.0%) comprised a greater part of the study population, followed by homemakers (32%), and agriculturists (23%). Hypertension was the common comorbidity (13.5%). Diabetic ulcer (n=84, 42.0%), cellulitis (n=48, 24.0%) and gangrene of foot (n=31, 15.5%) were common presentations. Sensory, as well as motor neuropathy, was significant in 179 diabetic foot infections. None had peripheral autonomic neuropathy and vascular insufficiency. The most common isolated bacterial organism was *Staphylococcus aureus* and *Streptococcus* species. All received topical treatment and systemic medications. Iodine dressing for wounds (160, 80.0%) was done. Oral therapy (35%)(amoxicillin+ clavulanic acid 20%, metronidazole + cephadrine 12%, cefixime -3%) and parenteral (65%) administration of antibiotics were given; Of latter, combination of Ceftriaxone and metronidazole was preferred in 66 (33.0%), ceftriaxone alone in 55 (27.5%), combination of metronidazole with amoxicillin clavulunate (n=39, 19.5%), Cephadrine (n=24, 12.0%), cefotaxime (n=10, 5.0%) were prescribed. Infection was controlled with antibiotics in 119 (59.5%) patients without any further procedure. Wound debridement (16.0%), disarticulation of left interphalangeal/metatarsophalangeal joint (9.5%), split-thickness skin graft (7.5%) were performed. We noted clinical improvement in 99.0% patients. **Conclusion:** Diabetic foot infections are most common in patients with diabetes mellitus. Mixed infections require combination therapy including appropriate broad-spectrum antimicrobials. Surgical procedures may be needed to control infection. **Key Word:** Antimicrobials, diabetes mellitus, diabetic foot infections, prescription analysis.

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INTRODUCTION

The therapeutic goal in the management of Diabetes mellitus (DM) is aimed not only at the disease control but also at the management of associated morbidity. Infections are a frequent associate of DM as diabetic patients are at greater risk^{1,4} with those with type 1 at a greater risk of developing severe infections. ⁵Defective immune defense mechanism in DM, make them prone for developing infections^{6,8}, however, lack of preventive care, difficulty in accessing medical care may be the most significant factors of late presentation and poor outcome in the tropics.⁹ Often, these infections are the reason for hospitalization in these patients, adding to the existing disease and economic burden. Community-acquired

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infections, infections of the skin and soft tissue, genitourinary, gastrointestinal and respiratory system are common in diabetic patients.

Diabetic foot infections are a common, complex and costly affair for diabetic patients^{10,13} in terms of severe morbidities and diabetes-related hospital bed-days.¹⁴ Apart from the disease progression and complications, patient disability, mal-adaptive patient behaviour (inadequate precautions, unhygienic measures, poor treatment compliance, excessive weight bearing, and ill-fitting footwear), inadequate blood glucose monitoring and inadequate patient education are well-documented risk factors for the occurrence of infection in diabetic patients. The primary goal in the disease management of the infection is to determine the clinical extent and the invading microbial flora, the biology and the pathogenesis of the wound, altered foot biomechanics, peripheral arterial disease and the presence/absence of any systemic consequences of the underlying infection. The primary focus of our study was to determine the prescription pattern of antimicrobials, analyse the risk factors, cover the general management of diabetic skin and soft tissue infections, analysing the most common microbes infecting diabetic wounds, various surgical procedures carried out, wound care, diagnostic testing and adjunctive treatments in diabetic patients with various skin and soft tissue infections.

MATERIAL AND METHODS

This retrospective observational, descriptive study was conducted by the department of pharmacology of a teaching hospital, in coastal southern India between May 2011 and May 2012. The Institutional Ethics Committee approved this study. Analysis of the prescription pattern of antimicrobial drugs in diabetic patients with infection was our primary objective; to study the clinical presentation, associated risk factors in the skin and soft tissue infections, Establishing the microbiological aetiology, and outcome of the treatment were secondary objectives. We collected the data of diabetic patients with skin and soft tissue infections, aged >18 years, treated for five years (2006-2010) from the medical records department of our hospital. Information collected included the type of clinical presentation, associated risk factors, laboratory investigations, culture reports, anti-microbial, anti-diabetic treatment, the procedures carried out and other supportive measures carried out during the patients' course of stay in the hospital. Collected data captured on Microsoft Excel 2007 worksheets were analysed. Chi-square test was used as applicable. Descriptive statistics was used, and results were expressed as frequency, percentage, range, mean; tables, and figures were done as appropriate.

RESULTS

We analysed the prescriptions of 200 patients meeting the selection criteria. There were 134 (67.0%) men and 66 (33.0%) women. Mean age of patients was 58 years, with an age range of 28-88 years; patients in 50-60 years comprised 42.0% of the study population (Table 1).

Table 1: Age-wise distribution among the study population

Age group (years)	n(%)	Gender	
		Male n(%)	Female n(%)
<30	6 (3.0%)	1 (16.7%)	5 (83.3%)
30-40	14(7.0%)	9 (64.3%)	5 (35.7%)
40-50	13(6.5%)	2 (15.4%)	11 (84.6%)
50-60	84(42.0%)	47 (56.0%)	37 (44.0%)
60-70	34(17.0%)	28 (82.4%)	6 (17.6%)
70-80	24(12.0%)	23 (95.8%)	1 (4.2%)
>80	25(12.5%)	24 (96.0%)	1 (4.0%)
Total	200 (100.0%)	134 (67.0%)	66 (33.0%)

There were 199 (99.5%) patients with type 2 DM, and only one patient had type 1 DM. Only nine (4.5%) were smokers, and two (1.0%) consumed alcohol; three were both smokers and consumed alcohol. One hundred and eighty-six patients were non-smokers and non-alcoholics. Retired personnel (n=70, 35.0%), homemakers (n=64, 32.0%) and farmers (n=46, 23.0%) comprised major proportion of study population (Table 2).

Table 2: Occupation of patients

Occupational history	n (%)
Bank worker	3 (1.5%)
Cobbler	1 (0.5%)
Cook	1 (0.5%)
Coolie	11 (5.5%)
Farmer	46 (23.0%)
Fisherman	1 (0.5%)
Housewife	64 (32.0%)
Priest	2 (1.0%)
Retired	70 (35.0%)
Shopkeeper	1 (0.5%)
Total	200 (100%)

There was no co-morbidity in 119 (59.5%) patients. Hypertension (26, 13.5%) was the most common comorbidity. Two patients had hypothyroidism; chronic kidney disease and benign prostatic hypertrophy, aortic stenosis, breast cancer (on treatment), human immunodeficiency virus infection, renal failure were noted in one patient each. Diabetic foot infections were common (n=179, 89.5%), followed by hand infections (n=10, 5.0%). Perianal abscess (n=7, 3.5%) and back infections (n=04, 2.0%) were other conditions. Hyperglycaemia(n=179, 89.5%), Peripheral neuropathy (both sensory and motor) (n=167, 83.5%) was the most common risk factors followed by maladaptive patient behaviour (n=91, 45.5%) and patient disabilities (n=32, 16.0%). None of our patients had peripheral autonomic

neuropathy and vascular insufficiency. Ulcer (n=84, 42.0%), cellulitis (n=48, 24.0%) and gangrene of foot (n=31, 15.5%), were common presentations (table 3)

Table 3: Common Clinical Presentation

Sl No	Clinical Presentation	n(%)
1.	Abscess	05 (2.5%)
2.	Abscess +cellulitis	11 (5.5%)
3.	Cellulitis	48 (24.0%)
4.	Diabetic foot	21 (10.5%)
5.	Gangrene	31 (15.5%)
6.	Ulcer	84 (42.0%)

Culture reports were negative in 130 patients. Presence of pus cells along with gram-positive cocci, gram-positive and negative bacilli was seen in 19 (9.5%) patients; pus cells along with gram-positive cocci, gram-negative bacilli were reported in 15 (7.5%) patients. Staphylococcus aureus was grown in 14 (7.0%) cultures (Table 4).

Table 4: Culture reports

Culture report	Frequency	Percent
Culture negative	130	65%
Citrobacter	1	0.5%
E coli, acintobacter, polymorphs	1	0.5%
Gram -ve bacilli	4	2%
Gram +ve cocci in pairs	1	0.5%
Pseudomonas sps grown	7	3.5%
Pus cells, gram+ve cocci, gram +ve bacilli, -ve bacilli	19	9.5%
Pus cells, gram -ve bacilli, gram +ve cocci	15	7.5%
Pus cells, gram -ve bacilli, gram +ve cocci	1	0.5%
Staph aureus, polymorphs	5	2.5%
Stap aureus , mixed infections of aerobic and anaerobic infections	1	0.5%
Staph aureus grown	14	7.0%
Staph aureus, gram positive and -ve cocci	1	0.5%

All patients received topical treatment and systemic medications. Of topical treatment, povidone iodine dressing was done on wounds for 160 (80.0%) patients, and 38 (19.0%) patients received glycerine magnesium sulfate dressing; Sitz bath was given for two patients with a perianal abscess. Of systemic medications, 70 (35%) patients received oral therapy (amoxicillin+ clavulanic acid 20%, metronidazole + cephadrine 12%, cefixime-3%) and 130 (65%) required parenteral administration of antibiotics. Of latter, ombination of Ceftriaxone and metronidazole was preferred in 66 (33.0%), ceftriaxone alone in 55 (27.5%), combination of metronidazole with amoxicillin clavulanate (n=39,19.5%),Cephadrine (n=24, 12.0%), cefotaxime (n=10, 5.0%) were prescribed. Combination of ampicillin with cloxacillin, amoxicillin-

clavulanate with cefixime and gentamicin were prescribed to two patients each.

Treatment duration: Parenteral therapy was administered for 7-10 days while oral therapy was given for seven days. Mild infection was controlled by oral therapy (amoxicillin+ clavulanic acid 2g x7 days, Metronidazole + Cephadrine 7.5mg/kg x7 days and Cefixime 400 mg x 7 days) while moderate infections required parenteral therapy followed by oral formulations. Severe infections were treated with parenteral antibiotics (ceftriaxone + metronidazole combination 1g intravenously (IV) once daily (OD) x10 days along with a loading dose of 15mg/kg IV, and maintenance dose of 7.5mg/kg IV x 7 days; Ceftriaxone 1g IV OD x 10 days; Ampicillin+ cloxacillin 1g IV+100mg/kg/day x 7 days; Gentamicin 4 mg/kg/day x10 days) Infection was controlled with antibiotics in 119 (59.5%) patients without any further procedure. Wound debridement was done in 32 (16.0%), disarticulation of left interphalangeal/metatarsophalangeal joint in 19 (9.5%), Split skin thickness graft (STSG) in 15 (7.5%) patients; incision and drainage (n=08, 4.0%), amputation of foot (n=04, 2.0%), disarticulation and amputation of toes (n=02) and drainage of gluteal abscess (n=01) were the other procedures performed. Clinical improvement was seen in 198 (99.0%) patients. There were two deaths; one each due to uncontrolled hyperglycemia and sepsis.

DISCUSSION

Selection of appropriate antibiotic initially depends upon various factors such as the spectrum of microorganisms to be covered, the specific antibiotic drugs to administer and later choosing the definitive regimen and the duration of treatment. Initial treatment is generally empirical and is based on the severity of infection and microbiological data, if available.¹⁵Definite therapy must be started as soon as possible, immediately after the culture and sensitivity report. For severe, extensive, chronic moderate infections therapy with broad-spectrum agents should be commenced. These agents should have activity against gram-positive cocci (including Methicillin resistant staph aureus (MRSA) as well as gram-negative and obligate anaerobic organisms.¹⁶ Our study had male preponderance, similar to that reported by Morbach *Set al*^{17,18}, but there are reports of female preponderance as well. Hence, gender affliction can be considered inconclusive. In our study the prevalence of large group who were occupationally void either due to age (retired), choice (homemakers); surprisingly, a considerable proportion of study population included farmers (23%) and coolies (5.5%) who are physically active than the general population. The number of smokers and those who consumed alcohol regularly was less in our study.

Hypertension was the most common comorbidity present along with diabetes mellitus. Our study has proven again that hypertension and diabetes mellitus often co-exist. In our study, about 13.5% of the diabetic patients were hypertensive, comparable to the study by Shah A *et al.* (13.8%).¹⁹ Interestingly, hypothyroidism, the leading cause of metabolic syndrome²⁰ resulting in diabetes mellitus was seen only in two patients in our study. Lower limb was the most affected site in our study. Ulcer (diabetic foot with secondary infection), cellulitis, and gangrene were the common associated infections with DM noted in our study. Diabetic foot was a common infection even among the general population.¹⁰ Studies have shown that diabetic foot ulcers were the most common presentation of skin and soft tissue infections²¹ Lipsky *et al.*²² noted that foot infections in diabetic patients usually begin in skin ulceration. Culture and sensitivity are one of the key investigations in the management of infections. No organism was isolated in a more significant proportion of our study population (65%); mixed infection with gram-positive and negative organisms was common (18.5% of the study population and 52.86% of those with infection). Only 7% cultures isolated *Staphylococcus aureus*; staph aureus (2.5%) and gram-negative bacilli (2%) were isolated in fewer cultures. Local management of wounds is crucial in minimizing the spread of infection and disease complications. Iodine-based antiseptics are commonly used on diabetic wounds. A study conducted by Hilton *et al.*²³ 30% of the patients with diabetic ulcers received iodine based dressing. All our patients received local wound treatment; povidone iodine dressing (80%) was most preferred compared to glycerine magnesium sulfate dressing (19%). Most of our patients were treated with a combination of basic antibiotics. Single-drug was administered to 28.5% patients; remaining required two drug combinations to cover a broader spectrum of microorganisms. Our physicians preferred a combination of cephalosporins and nitroimidazoles; ceftriaxone was the most preferred first choice, and for combination, metronidazole was prescribed (ceftriaxone+metronidazole (33%) and amoxicillin-clavulanate + metronidazole (19.5%). Ceftriaxone alone was prescribed to 27.5% patients. Surgical procedures are often needed to clear the source of infection or arrest the progression of disease complication. Infection was controlled with medications in 59.5% patients; wound debridement (16%), disarticulation of left interphalangeal/metatarsophalangeal joint (9.5%) and STSG (7.5%) were the most opted surgical procedures. Clinical improvement was reported in 99% of study population. Many of the previous studies focused mainly on diabetic foot infections. Very few studies attempted to analyse the microbial data and

antibiotic prescription pattern in skin and soft tissue infections in patients with diabetes mellitus. We observed that despite the availability of advanced medical care infections, particularly of the lower limb, still needs patient and physician attention. The general rule for the use of antibiotics is to avoid antimicrobial therapy for uninfected ulcers. Unnecessary and inappropriate use of antibiotics encourages antimicrobial resistance, increases the cost and may cause drug-related adverse effects, so treatment of uninfected ulcers should be discouraged. However, it is necessary to note that uninfected diabetic foot ulcers are subclinically infected as they contain a massive "bioburden" of bacteria (usually defined as 10⁵ organisms per gram of tissue). That results in critical colonization of bacteria and hence decreases wound healing.²⁴⁻³⁰ Besides, higher glucose levels in diabetic patients' favors rapid development and spread of infection, thus, necessitating appropriate antibiotic therapy early. Physicians must confirm the presence of infection prior to initiating antimicrobial therapy.

CONCLUSION

Diabetic foot infections are the most common infections associated with diabetes mellitus. Mixed infections, requiring combination antimicrobial therapy needs physician's focus to select appropriate broadspectrum agents. Nevertheless, the role of local wound management cannot be ignored. Surgical procedures such as wound debridement may be needed in few to control infection.

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