An epidemiological and pharmacotherapy study on diabetic foot infections

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Abstract

Objectives: To assess the epidemiology, risk factors and pharmacotherapy pattern and to provide patient education regarding care to be taken in diabetic foot infections.

Methods: A prospective observational study was carried out on 122 diabetic foot infection patients after obtaining the consent, from the surgery department of a tertiary care hospital. Socio-demographic data, laboratory data and pharmacotherapy data were documented in a self-structured data collection form and analyzed.

Findings: It was observed that male patients between the age group of 61-70 years and patients with long standing diabetes along with peripheral neuropathy were mostly affected. Risk factors included uncontrolled hyperglycemia and walking barefoot. Cephalosporin class of drugs followed by fluroquinolones and penicillins were the chief drug classes used in therapy. Patient education was provided using designed patient information leaflets.

Conclusion: Diabetic patients are at an increased risk for developing foot infections. Clinical pharmacists can play an active and responsible role in providing education for self-care and medication adherence to the patients.

Keywords: Peripheral neuropathy, hyperglycemia, walking barefoot, cephalosporins, patient information leaflets.

1. Introduction

Diabetic foot infections (DFI) are infections that can develop in the skin, muscles, or bones of the foot as a result of the nerve damage and poor circulation that is associated with diabetes. Various foot abnormalities result from peripheral neuropathy, macro-angiopathy, and other consequences of metabolic disturbances in patients with diabetes. Foot problems and amputations are very common in India, as we have a greater population living with diabetes [1].Men and patients over 60 years of age are prone to a greater extent in developing diabetic foot problems. According to International Diabetic Federation, 1 in 11 people were diabetic in 2015 and it is estimated that 1 in 10 people will have diabetes by 2040. Over the past 2 decades the threat of diabetes mellitus has shown substantial rise. According to the epidemiological studies, the number of diabetic patients rocketed/ dramatically increased from 30 million cases in 1985 to 177 million in 2000, followed by increase to 285 million in 2010, and is roughly estimated be reach 642 million by 2040[2,3].India having a diabetic population of about 50.8 million, is expected to grow to 87 million by 2030[4]. Presently in India, (approx.) 3-4% of all diabetic patients have foot problems, utilizing 12-15% of the health care resources. With regard to the etiology of foot ulceration, 45–60% of ulceration is thought to be purely neuropathic, 10% purely ischemic and 25–40% mixed neuroischemic in nature. People in developed countries tend to be more often neuroischemic [5]. Several risk factors are associated with diabetic foot ulcers[6-8]. They are gender (male), duration of diabetes longer than 10yrs, advanced age, high body mass index, race, poor glycemic control, peripheral neuropathy, retinopathy, nephropathy, biomechanical factors, fungal infection of web space, smoking, obesity, h/o previous foot ulceration and amputation, socio-cultural factors (bare foot walking, religion, improper foot care, customs) [2,9]. Polymicrobial pattern of foot infections are prevalent in diabetics with a combination of gram-positive and gram-negative aerobes with anaerobes at the site of infection[10,11]. Staphylococcusaureus and the hemolytic streptococci are the most commonly isolated pathogens. Clinical laboratory tests that may be necessary in the appropriate clinical situations include: Fasting or random blood glucose, glycosylated hemoglobin (HbA1C), complete blood count (CBC) including differential count, erythrocyte

sedimentation rate (ESR), serum chemistries, wound and blood cultures. The most prognostic sign of infection severity is recalcitrant hyperglycemia despite normal anti-hyperglycemic regimens [12]. Plain radiography and MRI may be used to diagnose the condition. The treatment in DFI patients depends on the severity of infection. In mild infection empiric oral antibiotic treatment is preferred mostly targeting the causative pathogens like Staphylococcus aureus/ Streptococci. Drugs preferred for mild infection include amoxicillin/clavulanate, cefdinir, cephalexin, clindamycin, diclocycline, doxycycline, levofloxacin, linezolid, monocyline and trimethoprim/sulfamethoxazole. In moderate to severe infection empiric broad spectrum parenteral antibiotic treatment is aimed at the most common organisms including g+ve, g-ve and anaerobic bacteria and include the following drugs:ampicillin/sulbactum, cefoxitin. ceftriaxone, clindamycin, daptomycin, ertapenem, imipenem/cilastin, linezolid, moxifloxacin. pipercillin/tazobactam, ticarcillin/clavulanate, tigecycline and vancomycin [13]. As the most accessible health care professional, the pharmacist has significant position in providing health care and helping prevent DFI. Pharmacists should frequently remind their diabetic patients to wear socks and properly fitting closed-toe footwear, to moisturize and visually inspect their feet every day, and to see a physician for evaluation of cracks, sores, and other injuries. Once a foot infection develops, the pharmacist should assist the health care professionals to select the most appropriate anti-microbial regimen for the patient, including dosage, route of administration, frequency, and duration of therapy.

In the above context this study was planned and carried out to assess the epidemiology and risk factors in DFI, to review the pharmacotherapy pattern and educate the patients regarding the clinical condition.

2. Materials and methods

A prospective observational study was conducted in Surgery Department of KIMS Hospital and Research Centre, Bengaluru for a period of 1 year. The study was carried out on 122 in-patients after inclusion criteria had been satisfied and after taking an informed consent. The study criteria included, all patients identified with Diabetic foot infections and receiving pharmacotherapy while patients with a complication of diabetic nephropathy were excluded. The patient relevant data were collected from the sources like patient case notes, laboratory test data, follow up data and patient/caregiver's interview wherever necessary. The data was documented in a self-designed structured and standardized data collection form. The documented data included admission details, socio demographic details, family history, risk factors, relevant laboratory findings, pharmacotherapy given and discharge medications. The study was conducted after obtaining the ethical clearance from Human ethics committee of Visveswarapura Institute of Pharmaceutical Sciences (VIPS/ 2015/01).

Patient information leaflets were designed in both English and local language (Kannada) to provide education to the patients and the care givers regarding the foot care and life style changes. The documented data was analyzed for assessing the treatment pattern and to determine the epidemiology and risk factors using suitable statistical tests. Descriptive statistical analysis was used to analyze the documented data. MS Excel 2013 was used to draw the tables and figures. Results on categorical measurements are expressed in terms of number and percentage while results on continuous measurements are presented in terms of mean ± standard deviation.

3. Results

The present study included 122 in-patients with diabetic foot infection. Table 1 shows the distribution of study patients based on age and gender, the majority being males and the age group 61-70 years. From the above findings it can be said that age and gender of the patient are important predisposing factors for DFI. 37% and 31% of patients had primary and no formal education respectively as shown in Table 1.

Table 2 summarizes the socio-demographic and risk factors of study patients. About 80 patients reported to have an income of less than 10,000 INR. 23 patients had the habits of smoking and alcohol consumption. Peripheral neuropathy, foot ulcers, hyperglycemia, walking barefoot were the most common risk factors observed as shown in Table 2.

The past medical and medication history of enrolled study patients are depicted in table 3. 83 patients were diabetic only, while the rest were diabetics with other co-morbidities. Accordingly these patients were prescribed medications for the corresponding comorbid conditions apart from antidiabetic drugs. The duration of diabetes ranged from less than 1 year to greater than 15 years with 31% patients having diabetes from 6-10 years. During the study the mean duration of hospital stay of the patients was calculated and it was found to be 12.15±9.2 days as shown in Table 3.

Age (yrs)	Total						
	Number		Percentage (%)		Number	Percentage (%)	
	М	F	м	F	M+F		
<20yrs	0	0	0	0	0	0	
21-30	0	2	0	0.9	2	2	
31-40	4	3	0	1.3	7	6	
41-50	22	4	2	1.7	26	21	
51-60	28	6	3	2.6	34	28	
61-70	35	6	4	2.6	41	34	
71-80	9	2	1	0.9	11	9	
>80	1	0	0	0.0	1	1	
Total	99	23	100	100	122	100	

Table 1. Age and gender distribution of the patients

*M- male; F- Female

Table 2. Socio-demographic details and risk factors

Socio- demographics and risk factors		Number	(%)
		33	27
Occupation	Agriculture		37
	Self-employed		20
	In service		14
	Housewife		2
	None		
	Total	122	100
Income in		80	66
	<10,000	22	18
	10,000-20,000		6
INR	>20,000	13	11
	Nil		
	Total	122	100
Social	Smoking	9	7
	Alcohol		5
habits	Smoking + Alcohol		19
	None	84	69
	Total	122	100
	Peripheral neuropathy	23	10
	Peripheral vascular disease		2
	Infection	7	3
Risk factors	Recurrent foot ulcers	16	7
	foot ulcer> 30 days		20
	Hyperglycemia		19
	Wound extended to bone		1
	Degenerative joint disease		0
	Walking bare foot	26	11
	Peripheral arterial disease	5	2
	Any other	57	25
	Total	232	100

Laboratory findings regarding fasting, post prandial, random blood sugar levels were indicative of uncontrolled glycemic levels in the study patients. The mean and the standard deviation values of these are shown in figure 1. The mean HbA_{1c} values were 9.3±2.41% in males and 9.47±2.36% in females. The total leucocyte count were elevated (males-12224±5935 cells/mm³, females- 9759±3173 cells/ mm³). The mean neutrophil values were 76.48±11.03% and 70.80±8.41% in males and females respectively. The ESR values were also elevated in males (70.03±34.56 mm/hr) and females (59.87±28.36 mm/hr) as shown in Figure 1.



Figure 1.Mean ± Standard deviation of blood sugar levels

The culture sensitivity test was carried out in 17 cases and the causative organisms identified were *Staph. aureus*, *Klebsiellaoxytoca*, *Pseudomonas* species, *Proteus species* and Gram negative and Gram positive bacilli and cocci.

The pharmacotherapy pattern of the study patients revealed that monotherapy with antibiotics was chosen in 54 (43.2%) patients closely followed by therapy with combination of two antibiotics in 53 (42.4%) patients. Only 5 (4%) patients received more than 3 antibiotic regimen. The preferred route of antibiotic administration was intravenous followed by oral.

Table 4 represents the therapy pattern with the class of antibiotics and specific drugs under the respective classes. Cephalosporins are the most preferred choice of antibiotics followed by penicillins and fluoroquinolones. It was also observed that metronidazole was another widely prescribed medication in DFI patients.

Class of antibiotic	Antibiotic	Number	Percentage
	Ceftriaxone	37	41.57
Cephalosporins	Cefixime	17	19.10
(N= 89)	Ceftazidime	15	16.85
	*Other cephalosporins	20	22.4
	Amoxicillin	36	61.02
Penicillins	Piperacillin + Tazobactam	21	35.59
(N= 59)	Benzyl penicillin	2	3.39
	Levofloxacin	23	48.94
Fluoroquinolones	Moxifloxacin	17	36.17
(N= 47)	**Other fluoroquinolones	7	14.8
	Metronidazole	55	76.3
Nitroimidazoles + other antibiotics (N= 72)	Clindamycin, linezolid, amikacin, faropenem, co-trimoxazole, tetracyclines, rifaximin	17	23.6

*other cephalosporins: cefpodoxime, cefuroxime, cefoperazone, cefpirome.

**other fluoroquinolones: ciprofloxacin, ofloxacin

^{*}FBS- Fasting blood sugar; PPBS- Postprandial blood sugar; GRBS- Glucometer random blood sugar

The patients received medications from the classes of proton pump inhibitor drugs, H₂ blockers apart from protein supplements, vitamin supplements in addition to the medications for respective comorbidities present along with diabetes. At discharge the clinicians prescribed antibiotics largely in the order of cephalosporins, fluoroquinolones, penicillins, drugs like co-trimoxazole and aminoglycoside group of drugs. Seventeen patients were not prescribed with any antibiotics at discharge.

As the other important objective of the study we educated the patients regarding the condition, its management and presentation through patient information leaflets designed in English and local language Kannada. The education provided were related to the importance of glycemic control, usage of appropriate foot wears at all times, avoiding foot trauma, daily self-examination of feet, and reporting any changes to health professionals. All the patients and their care givers expressed their satisfaction regarding the education provided to them as shown in Figure 2, 3.

4. Discussion

The present study included 122 patients with diabetic foot infection, all were in-patients, out of which were 99 (81.15%) male patients and 23 (18.85%) female patients. The study is similar to the study carried out by [14] who also reported that DFI was more common in males than in females [14]. In our study we found that majority of the patients belonged to the age group of 61-70 years, 51-60 years and 41-50 years (34%, 28% and 21% respectively) showing that older patients are more vulnerable to DFI. From the above findings it can be said that age and gender of the patient are important predisposing factors for DFI. About 68% of the study population were with literacy levels not higher than primary education. In [15] others state that association between health literacy and diabetes selfmanagement may not be directly related to one another. Factors like educational level, knowledge, perception, attitude, self-management behavior influence the level of health literacy which in turn shows implication on patient's ability towards self-management [15]. Hence, more repeated education in simplified version and preferably in the patient's own language would be required to improve the patients understanding towards his condition and lifestyle management. Patients were from the background of agriculture, self-employment, in service and most female patients were housewives. The self-reported income showed majority of the patients (66%) with < 10,000 INR per month. The social habits of smoking and/or alcohol were observed in 31% of patients while 69% of patients did not report any such habits. This observation indicates that there is an increase in the awareness regarding the ill-effects of such habits. In the study by [14], it was found that about 52% of the patients admitted with DFI reported regular ingestion of alcohol & tobacco etc. and leading unhealthy life style which are well recognized factors in increasing the risk of diabetic complications.

Hypertension was the more common comorbidity with diabetes, others being conditions like IHD, asthma, cardiomyopathy etc. Accordingly the patients had the medication history with the drugs for respective comorbidity along with antidiabetic agents. It was observed that 12% of the study patients were diagnosed with diabetes for less than 12 months, 31% were diabetic for 6- 10 years, 18% for 11 - 15 years and 14% of the patients were diabetic for more than 15 years. In the study by [14], it was found that patients lived with diabetes for a mean duration of 15.3 years (SD = 9.39 years) [13]. From the study carried out by [4] it was found that the mean duration of diabetes ranged from less than a year to 20 years with a mean duration of 5.9 years (SD = 5.5 years)[4].

Major risk factors observed were hyperglycemia (19%), walking bare foot (11%), infection (3%) and others (25%). Other risk factors reported were peripheral neuropathy (10%), recurrent foot ulcers (7%), foot ulcer >30days (20%), peripheral vascular disease (2%), wound extended to the bone (1%) and peripheral arterial disease (1%). The clinical practice guideline by [12], states that presence of peripheral neuropathy, shoe related trauma (ill-fitting shoes), peripheral vascular disease, poor diabetes control, infection, and hyperglycemia are the main predisposing factors leading to DFI's [8].Other risk factors were found to be wound, bleb, boil, maggot infestation, trauma, Hansen's disease (leprosy) & pigmentation/blackish discoloration of foot.

The mean duration of hospital stay was 12.15±9.2 days. In a study by [16], the mean duration of hospitalization in DFI patients was found to be 22.5 days[16].

In our study culture test and sensitivity pattern were performed only in 17 cases. Hence the choice of the pharmacotherapy pattern was largely based on clinicians' experience. Diabetic foot infection being most commonly polymicrobial in nature, the therapy with antibiotics needs to be evidence based. The laboratory test performed confirmed uncontrolled glycemic index, elevated levels of infection markers like total leucocyte count, ESR etc.

The therapy pattern in the study patients showed the cephalosporins as the first choice of drugs in the treatment of DFI with ceftriaxone as the most prescribed drug. Penicillins and fluoroquinolones were the next preferred class of drugs with amoxicillin, piperacillin + tazobactam and levofloxacin as the chosen drugs under these categories [17]. Certain class of drugs like fluoroquinolones is more likely to facilitate emergence of bacterial resistance and therefore it is important to carefully monitor the effectiveness of treatment. Monotherapy with antibiotics was closely followed by two drug combination therapy and I.V. route was the most preferred. At discharge, cephalosporins were again the preferred drug.

Diabetic foot ulcerations cause intense suffering and huge economic burden on the patient, the family and society at large. In diabetic patients with neuropathy, low intensity traumatic conditions like use of ill-fitting shoes, walking barefoot or any injury can be the cause of ulceration. A holistic approach encompassing prevention, education of patient and all health care professionals, pharmacotherapy and lifestyle management can reduce and control recurrence of infection [13]. The objective for DFI treatment is to reduce the tissue damage by the causative organisms, to categorize the DFI as mild, moderate and severe. Points to be noted include when to commence the treatment, necessity for an immediate surgical procedure, the choice and route of administration of antibiotics, either empirically or chosen specifically based on sensitivity results. Basic laboratory tests like complete haemogram, ESR and inflammatory markers like C- reactive protein are helpful in the assessment of infection. The empirical treatment with antibiotics should take into consideration the patient's comorbid conditions and past antimicrobial treatment. Antibiotic therapy in mild infectious conditions can be oral, while in moderate or severe conditions the initial choice of therapy is by parenteral route and subsequently oral route. Appropriate specimens from the wounds should be taken for culture and sensitivity test and based on the results the switch over from the empirical antibiotic regimen to accurate specific antibiotic regimen should be considered. The pharmacotherapy chosen should be cost effective, consider the comorbidities in the patient to assess for any drug interactions involving antibiotics with other medications as well as long term therapy with antibiotics which may lead to antibiotic resistance[17]. Diabetic patients in general and patients with DFI specifically need to be educated about the self-responsibility towards their wellbeing. The education given to these patients should emphasize on risk factors for DFI, importance of foot care, proper maintenance of foot hygiene, use of appropriate fitting footwear and most importantly optimal control of blood sugar levels [3]. The patients should be informed not to use chemical agents or plasters to remove corn, keep skin optimally moisturized and to cut the toe nails straight across. Self-management of foot by diabetic patients is an integral part of their lifestyle [18].

5. Conclusion

The microbial spectrum in diabetic foot infection varies largely inter-individually. In a country like India, with different cultures and huge population load it is a great challenge for all the members of the healthcare team to optimize the treatment and arrive at an outcome which is both clinically and economically beneficial to the affected patients. Assessing the clinical status, use of appropriate pharmacotherapy and continuous patient education are essential.

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