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Microbiological Pattern and Antibiotic Sensitivity in Diabetic Foot Ulcer in a Tertiary Care Center- A Cross Sectional Study

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Abstract
The problem of Diabetes is rapidly growing worldwide, making it the most challenging health problem of present century. The burden is supposed to rise from 382 million adults in 2013 to 592 million adults by 2035.The organism associated with diabetic foot ulcer varies in different geographical location. The aim of the present study is to describe the pattern of microbiological spectrum in the diabetic foot ulcers. In addition, we aimed to compare the difference in various variables between the mono microbial and microbial infections in the diabetic foot ulcers and associate these with different grades of the SINBAD grading.
After a priori sample size calculation was done, 100 consecutive patients were recruited for the study. All diabetic foot ulcer patients aged more than 30 years were included in the study. Data analysis was done using R statistical software. Continuous data was summarized with mean (±) and standard deviation or median and interquartile range. Categorical data were summarized with proportion and %cent ages. Difference in the mean (±) s were analyzed with t test and Mann Whitney test. Chi square test was used to test categorical variables.
Using a pretested well-structured data collection form, patient's data were taken. All variables needed for the SINBAD grading were recorded. Sixty four percent of the study population were males. The average age of the patients was 58.1 years (SD=9.59). The median duration of diabetes was 10 years (IQR 5.75-15). The most common site affected was mid foot/hind foot. Most of the lesions (48%) occurred spontaneously, followed by trauma in 44% of the patient (Table1.) In addition, there were statistically significant difference in ulcer area when ulcer characteristics are compared across the type of microbial organisms obtained as per culture and sensitivity
In the 91 patients with infection, gram positive organism was present in 35(38.5%) of the patients, mixed organisms in 32(35.2%) and gram negative in 24(26,4%) of the patients. Proteus, citrobacter and klebsiella were the most common organisms in the mixed category. Ploy microbial organism constituted 39 % of the patients and 61 % mono microbial. Most sensitive antibiotic in our study is Gentamycin (24%) followed by Cloxacillin(17%) and Amikacin (16%). Moreover, mono microbial group was sensitive to these antibiotics. Our analysis shows that an FBS > 200 mg/dl is an important factor for development of foot ulcer.Males are more affected than females. Both aerobic & anaerobic pathogens are involved in diabetic wound Infection, but among them staph aureus is more common. Common site of ulcer in foot was mid/hind foot, developing spontaneously in a background of neuropathy & vasculopathy.
The first requirement in the management of DFU is strict control of diabetes, & early detection and treatment of lesions; after identifying the organism & its antibiotic sensitivity. Regular foot care is also important. The importance of grading ulcer& treating with appropriate antibiotic according to culture & sensitivity is essential for controlling infection and progression of ulcer and thereby preventing limb amputation.

Introduction

The problem of Diabetes is rapidly growing worldwide, making it the most challenging health problem of the present century. The number of diabetics is supposed to rise from 382 million adults in 2013 to 592 million adults by 2035, and is further aggravated by changing population demographics, urbanization, and lifestyle factors [1]Prevalence of DFU is estimated to be 4—10% of total diabetics, with a life time risk to develop DFU is 25%). Foot ulceration increases the risk of lower limb amputation. Almost 85% of amputation is preceded by foot ulceration that later progress to spreading infection or gangrene. DFU affects both physical and mental health of patient leading to poor quality of life[2], Moreover, this imposes a substantial economic burden, where cost of hospitalization and amputation account for more than 50% of money spent[3]

Of the various causes of diabetic foot ulcers, infection contributes to an important role. Ulcer is not directly due to infection[2], but once an ulcer is complicated by infection, the risk for amputation increases; especially in ischaemic and neuroischaemic ulcers. Diabetic neuropathy, which occur in 25% of diabetic patients; in the presence of hyperglycemia, with or without significant vascular impairment, can form a bed for the entry of bacterial pathogens and the progression of the infection. In the present scenario, foot infection is the most common diabetic complication leading on to hospitalization and lower limb amputations[4],[5],[6,7].

Various grading and classification system are used to categorize and prognosticate the diabetic ulcers. There is no well accepted classification system for diabetic foot ulcers. A clinical classification should be relatively flexible and descriptive, but the one used for auditing must be more structured and simple enough for use in larger populations. One used for prospective research should be selective and exclusive. To compare outcomes among different countries, a new scoring system was developed and- the "SINBAD "scoring system; which is a clinical classification that includes various factors important in the healing of a diabetic ulcer.

The organism associated with diabetic foot ulcer varies in different geographical location. There is a paucity of studies that elucidate the microbiological spectrum in diabetic foot ulcers in various SINBAD grades. The aim of the present study is to describe the pattern of microbiological spectrum in the diabetic foot ulcers. In addition, we aimed to compare the difference in various variables between the mono microbial and poly microbial infections in the diabetic foot ulcers and associate these with different grades of the SINBAD grading.

Materials and Methods

We conducted this hospital-based cross-sectional study at the department of surgery medical college, Trivandrum. Ethics committee approval was obtained before starting the study. A formal priori sample size calculation was done. Thereafter, 100 consecutive patients were recruited for the study. All diabetic foot ulcer patients aged more than 30 years were included in the study. Vascular disorders like vasculitis and neurological disorders like leprosy were excluded from the study. Those patients with co existing renal diseases were excluded from the study.

Using a pretested well-structured data collection form, patient's data were taken. All variables needed for the SINBAD grading were recorded. Detailed history and clinical examination were done in all patients. Specimens (pus, wound exudates, tissue biopsy) for microbiological studies were obtained from the ulcer region. Pus and exudates were collected from the margins and the base of the ulcer using a sterile swab stick, which was then transported in a clean and sterile test tube soon after collection. Tissue biopsy was taken with a sterile blade/knife in wedge shape, including base and margin of ulcer along with wound swabs from the same site and was then transported in sterile solution of normal saline and sterile test tube respectively. These specimens were immediately transported to the microbiology laboratory and identification of microorganisms

were done according to the standard microbiological procedures.

Data analysis was done using R statistical software. Continuous data was summarized with mean and standard deviation or median and interquartile range. Categorical data were summarized with proportion and percentage. Differences in the means were analyzed with t-test and Mann-Whitney test. Chi-square test was used to test categorical variables.

Results

In this study, we enrolled 100 diabetic patients with foot ulcers. Table 1 shows the baseline demographic features of the patients. Sixty-four percent of the study population were males. The average age of the patients was 58.1 years (SD=9.59). The median duration of diabetes was 10 years (IQR 5.75-15). The most common site affected was mid foot/hind foot. Most of the lesions (48%) occurred spontaneously, followed by trauma in 44% of the patient (Table1.)

Table 1 Baseline characteristics of 100 patients with diabetic foot ulcer

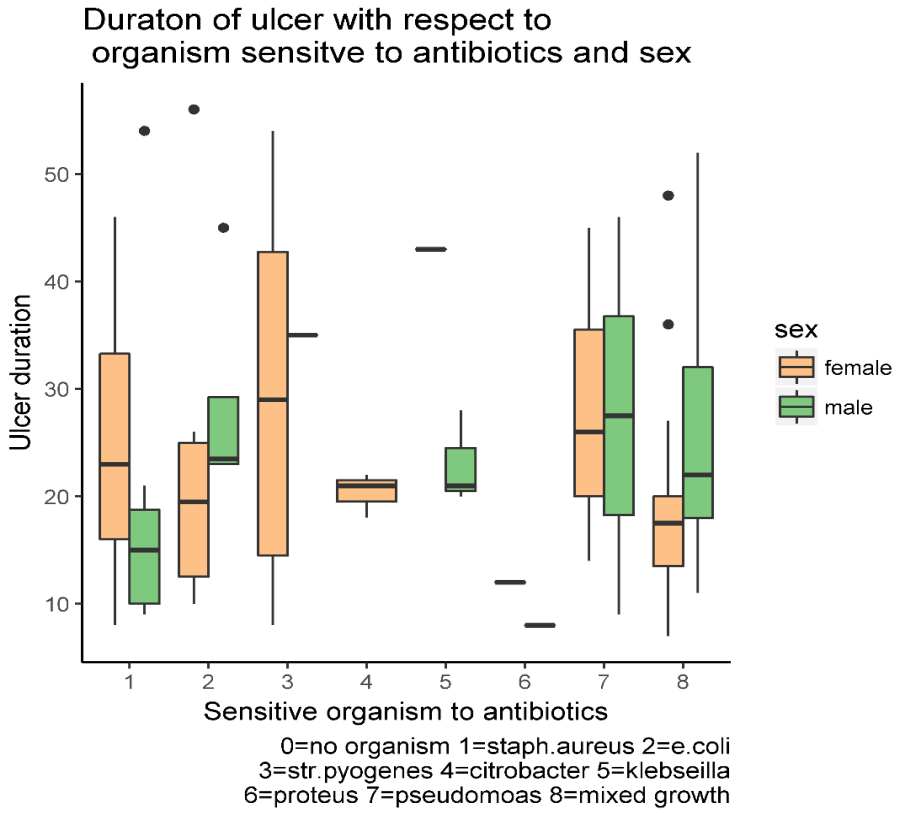
	[ALL] N=100
Age	58.1 (9.59)
Sex:	
Male	64 (64.0%)
Female	36 (36.0%)
Type of DM:	
I	1 (1.00%)
II	99 (99.0%)
Duration of DM	10.0 [5.75;15.0]
Treatment:	
Irregular	40 (40.0%)
Regular	60 (60.0%)
Medication:	
OHA	56 (56.0%)
Insulin	14 (14.0%)
OHA plus insulin	30 (30.0%)
Smoker:	
Non smoker	66 (66.0%)
Smoker	34 (34.0%)
Alcoholic:	
Non alcoholic	65 (65.0%)
Alcoholic	35 (35.0%)
FBS:	
70-110	29 (29.0%)
110-200	40 (40.0%)
>200	31 (31.0%)

The details of the patients with microbiological spectrum and culture positivity are summarized in table2. Comparison of various baseline features across monomicrobial and ploy microbial organisms shows statistically significant difference only in duration of diabetes mellitus (figure 1 and 2).

Table 2: comparison of baseline features across monomicrobial vesus poly microbial

	[ALL] N=100	Monomicrobial N=61	Polymicrobial N=39	p.overall
Age	58.1 (9.59)	59.4 (10.5)	56.2 (7.79)	0.085
Sex:				0.293
Male	64 (64.0%)	42 (68.9%)	22 (56.4%)	
Female	36 (36.0%)	19 (31.1%)	17 (43.6%)	
Type of DM:				1.000
I	1 (1.00%)	1 (1.64%)	0 (0.00%)	
II	99 (99.0%)	60 (98.4%)	39 (100%)	
Duration	10.0 [5.75;15.0]	12.0 [7.00;16.0]	8.00 [3.00;12.0]	0.007
Treatment :				0.706
Irregular	40 (40.0%)	23 (37.7%)	17 (43.6%)	
Regular	60 (60.0%)	38 (62.3%)	22 (56.4%)	
Medication :				0.664
OHA	56 (56.0%)	32 (52.5%)	24 (61.5%)	
Insulin	14 (14.0%)	9 (14.8%)	5 (12.8%)	
Both	30 (30.0%)	20 (32.8%)	10 (25.6%)	
Smoker:				0.742
No	66 (66.0%)	39 (63.9%)	27 (69.2%)	
Yes	34 (34.0%)	22 (36.1%)	12 (30.8%)	
Alcoholic:				0.074
No	65 (65.0%)	35 (57.4%)	30 (76.9%)	
Yes	35 (35.0%)	26 (42.6%)	9 (23.1%)	
FBS:				0.546
0 to 110	29 (29.0%)	18 (29.5%)	11 (28.2%)	
110-200	40 (40.0%)	22 (36.1%)	18 (46.2%)	
>200	31 (31.0%)	21 (34.4%)	10 (25.6%)	

Figure 2



In addition, there was statistically significant difference in ulcer area when ulcer characteristics are compared across the type of microbial organisms obtained as per culture and sensitivity (table 3) (figure3).

Table 3: comparison of features of ulcers in mono microbial versus Polymicrobial.

	[ALL] N=100	Monomicrobial N=61	Polymicrobial N=39	p.overall
Ulcer duration	20.0 [14.0;27.2]	22.0 [14.0;34.0]	18.0 [14.5;24.0]	0.233
Area	9.00 [6.00;14.2]	12.0 [6.00;15.0]	6.00 [4.00;10.0]	0.024
Mode :				0.285
Trauma	44 (44.0%)	24 (39.3%)	20 (51.3%)	
Spontaneous	48 (48.0%)	33 (54.1%)	15 (38.5%)	
Weight bear	7 (7.00%)	4 (6.56%)	3 (7.69%)	
Injury	1 (1.00%)	0 (0.00%)	1 (2.56%)	
Site:				1.000
Forefoot	22 (22.0%)	13 (21.3%)	9 (23.1%)	
Mid/hindfoot	78 (78.0%)	48 (78.7%)	30 (76.9%)	
Ulcer area:				0.296
Less than 1cm	4 (4.00%)	1 (1.64%)	3 (7.69%)	
More than 1cm	96 (96.0%)	60 (98.4%)	36 (92.3%)	
Depth:				1.000
superficial	5 (5.00%)	3 (4.92%)	2 (5.13%)	
Deep	95 (95.0%)	58 (95.1%)	37 (94.9%)	

Figure 3

In the 91 patients with infection, gram-positive organism was present in 35(38.5%) of the patients, mixed organisms in 32(35.2%) and gram negative in 24 (26.4%) 4% of the patients. Proteus, Citrobacter, and Klebsiella were the most common organisms. Poly microbial organism constituted 39 % of the patients and 61 % mono microbial.

Sensitivity of the microorganisms to various antibiotics are given in table4.

Table 4: Antimicrobial sensitivity of different organisms

	[ALL] N=100	Monomicrobial N=61	Polymicrobial N=39	p.overall
Pencilllin :				0.154
Sensitive	4 (4.00%)	4 (6.56%)	0 (0.00%)	
Resistant	96 (96.0%)	57 (93.4%)	39 (100%)	
Gentamycin:				0.001
Sensitive	24 (24.0%)	22 (36.1%)	2 (5.13%)	
Resistant	76 (76.0%)	39 (63.9%)	37 (94.9%)	
Piperacllin-Tazobactum:				0.153
Sensitive	5 (5.00%)	5 (8.20%)	0 (0.00%)	
Resistant	95 (95.0%)	56 (91.8%)	39 (100%)	
Amikacin :				0.008
Sensitive	16 (16.0%)	15 (24.6%)	1 (2.56%)	
Resistant	84 (84.0%)	46 (75.4%)	38 (97.4%)	
Nitrofurantoin:				0.079
Sensitive	6 (6.00%)	6 (9.84%)	0 (0.00%)	
Resistant	94 (94.0%)	55 (90.2%)	39 (100%)	
Cloxacillin:				0.537
Sensitive	17 (17.0%)	12 (19.7%)	5 (12.8%)	
Resistant	83 (83.0%)	49 (80.3%)	34 (87.2%)	
Ceftriaxone:				0.011
Sensitive	9 (9.00%)	9 (14.8%)	0 (0.00%)	
Resistant	91 (91.0%)	52 (85.2%)	39 (100%)	

Discussion

In this study, we aimed to find out the microbiological pattern in diabetic foot ulcers in our setting, a tertiary care teaching center. Our study has shown that diabetic foot ulcers are more commonly involved with mono microbial organisms. Out of this, gram positive constitute the major part. Another important finding we observed is that there is a statistically significant difference in the area of the ulcer and duration of diabetes in the mono microbial group. There was a reduction of about 50% in the ulcer size in the ploy microbial group.

There could be multiple reasons for the drastic reduction almost by 50% in the ulcer area in the poly microbial group. The selective referral of patients with more severe ulcers may explain the increased prevalence of mono microbial infection in our group. Other factors like emergence of multidrug resistant bacteria, availability of over the counter, drugs and unscrupulous prescription of antibiotics could have resulted in the emergence of more virulent organisms. Most of the ulcers in the mono microbial group occurred spontaneously whereas trauma was the precipitating cause in most of the poly microbial group. The decreased immunity and trauma along with multiple organisms may be the cause in the second group. In addition, the duration of the diabetes was longer in the mono microbial group. This again would have reduced the immunity more compared to the other group. Longer duration and highly virulent organism may be the contributing factors in the first group.

In many studies in the literature, poly microbial infections are more prevalent than mono microbial infections. However, in our study mono-microbial infections are more common accounting for almost 61% of culture. Poly-microbial accounted only for 39. Staphylococcus aureus (26%) is the commonest organism in the present study. In the study conducted by Rajah et al, Staphylococcus constituted the major organisms (41%)[8]. In a study conducted by European society of clinical microbiology and infectious disease; Helsinki Finland, 65 % were gram-positive cocci, whereas Staphylococcus accounted for 42% cases[9]. This is mainly because skin lesions are mostly caused by gram-positive organisms. A variety of physiological and metabolic disturbances contribute to foot ulceration in diabetes patients. Endogenous bacterium that usually colonize a wound is potentially pathogenic in diabetic ulcers. Immunological disturbance also contributes to

pathophysiology of foot ulcer. These include abnormalities of migration, phagocytosis, intracellular killing, and chemotaxis. The cellular immune response and monocyte function are also reduced in diabetes.

Infection in diabetic foot can be aerobic or anaerobic; aerobic being the most common. The impact of anaerobes was first reported by Louie et al and subsequently by many researchers[10]. In the study by Edmonds et all, gram-positive cocci were the most prominent anaerobes[11] .Few reports are also available regarding the incidence of fungal pathogens in diabetic foot infections. As reported by Louie et al diabetic foot ulcer infection is usually poly microbial in nature[10]. E. coli, Streptococci & Pseudomonas (10 %, 9 %, 5 %) are the figures In our study.

The most sensitive antibiotic in our study is Gentamycin (24%) followed by Cloxacillin (17%) and Amikacin (16%). Moreover, mono microbial group was more sensitive to these antibiotics. In the study by Kavitha et al [12], local antibiotics like gentamycin were found to be effective in reducing the antimicrobial load in diabetic foot ulcers. However, most of the other literature does not show any evidence supporting the use of any local antibiotics in diabetic foot. In addition, our analysis shows that an FBS > 200 mg/dl is an important factor for development of foot ulcer.

According to Lehto et al, the risk of amputation increases proportionately with increase in plasma glucose level[13]. Boyko et al[5] reported an increase risk for diabetic foot ulcer with severe hypoglycemia. Chaturvedi et al reported an increased glucose level as a key risk factor for amputation[14]. Many studies have shown that increased levels of blood glucose over a long period of time, as assessed by HbAl C, is a better predictor for diabetic foot amputation.

Our study has a few limitations. One of the main limitations in our study is the hospital setting. A community-based study will better represent the true nature of microbiological pattern in the society. However, our results are pertinent in high-risk patients who are referred to tertiary care centers. Other potential drawbacks in our study are the relatively low sample size and cross-sectional nature of the study.

Conclusion

Diabetic foot ulcer is common in old age and is related to duration of diabetes. Males are more affected than females. Both aerobic & anaerobic pathogens are involved in diabetic wound infection but among them, staph aureus is more common. Common site of ulcer in foot was Common site of ulcer in foot was mid/hind foot, developing spontaneously in a background of neuropathy & vasculopathy. The first requirement in the management of DFU is strict control of diabetes, & early detection and treatment of lesions after identifying the organism & its antibiotic sensitivity. Regular foot care is also important. The importance grading of ulcer & treating with appropriate antibiotic according to culture & sensitivity is essential for controlling infection and progression of ulcer and thereby preventing limb amputation.

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