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Prevalence of Diabetic Peripheral Neuropathy (DPN) in Diabetic Foot Infection (DFI) and Clinical Response of Clindamycin in DPN Positive DFI

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ABSTRACT

Background: Diabetic foot infection is one of the major complications of diabetes and that it is largely preventable.
Materials and Method: This was an observational study in which we recruited patients >18 years of age, with Diabetic foot infection. Detailed history and clinical examination of all patients were taken at admission. Patients were classified as per IDSA classification of Diabetic Foot Infection. The patient data including the diabetic status, antibiotic therapy, neuropathy, along with glycemic control were recorded. All the data were subjected to statistical analysis and p-value was calculated.
Results and Conclusion: The mean age of male patients was found to be 57.8±9.3 years and that of female patients was found to be 54.5±15.9 years. Higher numbers of patients were found in 50-70 years age group which comprised of 16 (59%) patients. The prevalence of diabetic peripheral neuropathy in Diabetic foot infection patients was found to be 63%. The mean± SD for duration of total antibiotic therapy among the DPN positive and negative patients was 7.41±3.10 and 5.10±2.13 respectively. In our study, according to IDSA classification majority of patients were found having moderate DFI (44.4%). We conclude that DPN positive patients require higher duration of antibiotic therapy and individualized regimen to improve wound healing and reduce the risk of amputation.

Keywords: IDSA, Diabetic Peripheral Neuropathy, Diabetic foot infection, Diabetic foot ulcer, clindamycin, antibiotics

INTRODUCTION

Foot infections usually begin with skin ulceration and are the most recurrent and severe among diabetes mellitus patients. ulcers and infection of foot are considered to be leading cause of morbidity in diabetic population. [1] Risk factors related to presence of peripheral vascular disease in the affected limb are Poor glycemic control, Loss of protective sensation (i.e., neuropathy), Traumatic foot wound, Ulceration > 30 days, History of recurrent foot ulcers, Previous lower-extremity amputation, Improper footwear and Wounds that penetrated to bone. [2] The major predisposing factor for diabetic patients with foot infections are unknown other immunologic disturbances, such as impaired polymorphonuclear leukocyte migration, phagocytosis, intracellular killing, and chemotaxis can play role in causing infection. The Ketosis, impairs leukocyte function. Some evidence revealed that in diabetic patients, cellular immune responses, monocyte function, and complement function are decreased as well. *Staphylococcus aureus* is found in higher rates in the treatment of several types of skin and nail disorders, may be associated with increased risk of skin and soft-tissue infections in diabetic patients. Enhanced atherosclerosis, especially of the arteries between the knee and ankle, increases the likelihood of ischemia at the infection site. The anatomy of the foot, with its various compartments, tendon sheaths, and

neurovascular bundles, may cause proximal spread of infection and favors ischemic necrosis of the confined tissue. [3] Treatment of foot problem are based on (e.g. pain, swelling, ulceration) or a systemic disorder (e.g. fever, malaise, poor glycemic control. In an acute diabetic foot infection (DFI), there is frequently a delay in the identification of the causative organism, which may compel use of empirical antimicrobial therapy. Ulcers which are uninfected also needs antibiotics with Sharp debridement combined with pressure offloading, management of infection to optimize glycaemia, cardiovascular risk, assess potential revascularization and surgical intervention are considered to be the basis of ulceration. [1]

The infection can break-through the layers of deeper tissues, including fascia, muscle, joint and bone with the risk of microvascular and macrovascular complications. Other diabetes foot ulcer (DFU) is affiliated with an increased risk of lower extremity amputation and death. [2]

METHODOLOGY

Inclusion and exclusion criteria

Patients ≥18 years of age diagnosed with Diabetic foot infection. Patients with conditions mimicking Diabetic foot infection such venous stasis ulcers, deep vein thrombosis, Charcot arthropathy. Patients receiving clindamycin as the primary/mainstay treatment were included. Patients who died while receiving antibiotic therapy, as well as to whom the clindamycin wasn't prescribed or to whom clindamycin wasn't the primary/mainstay of antibiotic therapy were also excluded from the study. Patients with traumatic ulcers were excluded from the study.

Study Population

This study includes all in-patient diabetes mellitus patients diagnosed with diabetic foot infections at a tertiary care hospital in Hyderabad.

Duration of study: 8 months

Severity of Diabetic Foot Infection Based on IDSA classification

Uninfected - No symptoms or signs of infection. Mild - Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer. Moderate - Local infection with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs. Severe - Local infection (as described above) with the signs of SIRS, as manifested by ≥2 of the following: Temperature >38°C or <36°C, Heart rate >90 beats/min, Respiratory rate >20 breaths/min or PaCO2 <32 mm Hg, White blood cell count >12 000 or <4000 cells/μL or ≥10% immature (band) forms.

Diagnosis of Diabetic Peripheral neuropathy

Diagnosis of DPN was done if the patient had at least one manifestation such as numbness, freezing, burning pain, vibration from the skin, extreme sensitive to touch, muscle weakness, and lack of coordination.

Data collection

On admission clinical investigation of patients were done such as complete blood picture, ESR, GRBS, HbA1C, culture and sensitivity of pus or tissue samples, X-ray were done. To rule out DVT in suspected individuals. Other details such as mode of diabetic control, history of diabetes, co-morbid conditions, duration of diabetic foot infection/ulcer. Clindamycin was the being given as the mainstay of treatment. Other alternative antibiotics such as piperacillin-tazobactam, metronidazole, and amikacin were also given to patients failing to clinical response or showing poor prognosis towards infection. Duration of antibiotic therapy of all the patients in whom clindamycin was mainstay of therapy was taken. The duration of which was based on the severity of infection ranging from 5 – 14 days. Surgical debridement, fasciotomy, and/or amputation were also done based on patients' condition.

Statistical analysis

All statistical analyses were performed based on the parameters. Unpaired student t test was used to calculate the duration of diabetes, duration of foot ulcer, Glycated Hb and duration of antibiotic therapy in DPN positive and negative individuals. A descriptive statistical analysis was also performed were necessary and results are reported as mean±SD for scale variables and as counts (%) for nominal variables.

RESULTS

A total of 27 patients were enrolled during the study period. The mean age of male patients was found to be 57.8±9.3 years and that of female patients was found to be 54.5±15.9 years. This proportion was found to be not significant. The duration of Diabetes in male patients was found to be 10.8±5.96 years and that female patients was found to be 10.7±7.04 which was also found to be not significant. However, this can be seen in table 1.

Table.1. Demographic data and clinical characteristics of patients

		Male	Female	P-value
No. of patients n (%)		17(63)	10(37)	-
Age (years) mean±SD		57.8±9.3	54.5±15.9	0.4993
Duration of diabetes mellitus (years). Mean±SD		10.8±5.96	10.7±7.04	0.9433
Duration of foot ulcer mean± SD		11.9±13.39	8.8±8.03	0.5087
Mode of diabetic control, n (%)	Diet only Oral agents only Insulin Newly diagnosed	0 14(82) 4(23) 0	1 10(100) 0 0	- - - -
Glycated Hb (HbAlc%)		6.62±0.86	7.03±1.62	0.3912
Location of infection, n (%) Right Left		 9(60) 7(41)	 5(50) 6(60)	 - -
Comorbid conditions Hypertension		 17(63)	 9(33)	 -

***Significant at p<0.05**

Table 2.Age distribution of patients according to gender

Age Groups, n (%)	Male	Female
30-40	1(6)	2(20)
40-50	3(18)	2(20)
50-60	6(35)	3(30)
60-70	6(35)	1(10)
70-80	1(6)	2(20)

After categorizing the data into various age groups, the higher proportion of individuals were in the age group between 50 – 70 which is tabulated as table 2.

The clinical signs and symptoms such as local swelling, local tenderness, local warmth and erythema was present in all the patients. The proportion of all the signs and symptoms is depicted in the figure 1.

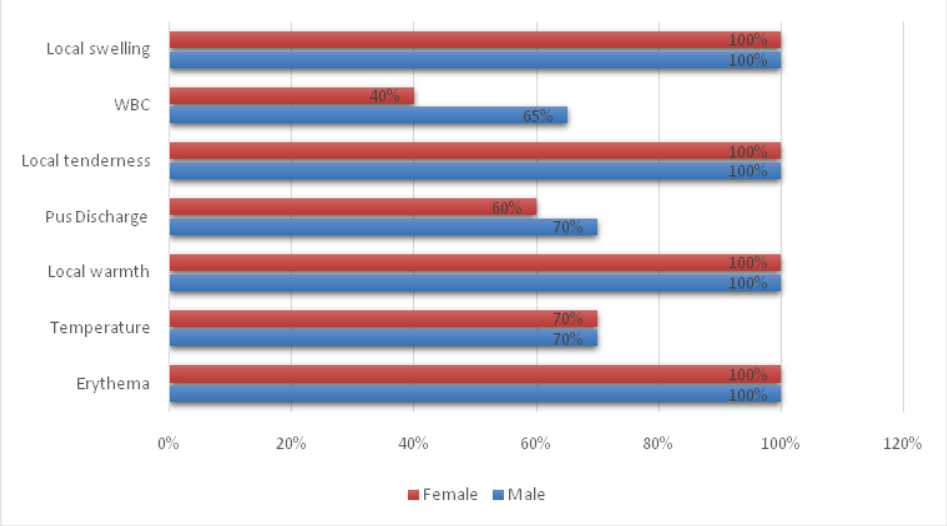

Figure 1. Clinical presentation of patients with DFI

Categorizing patient's severity condition according to IDSA, it was found that higher preponderance of both male (47%) and female (40%) patients were in moderate group which is shown in the figure 2.

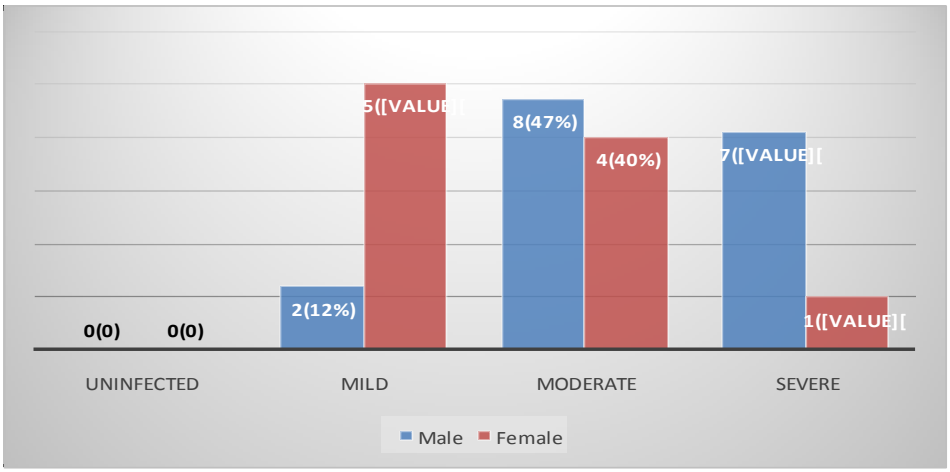

Figure 2. Stages of patients with DFI based on IDSA classification

The culture and sensitivity reports revealed positive cultures in 22(%) patients. The proportion of which is shown in figure 3.

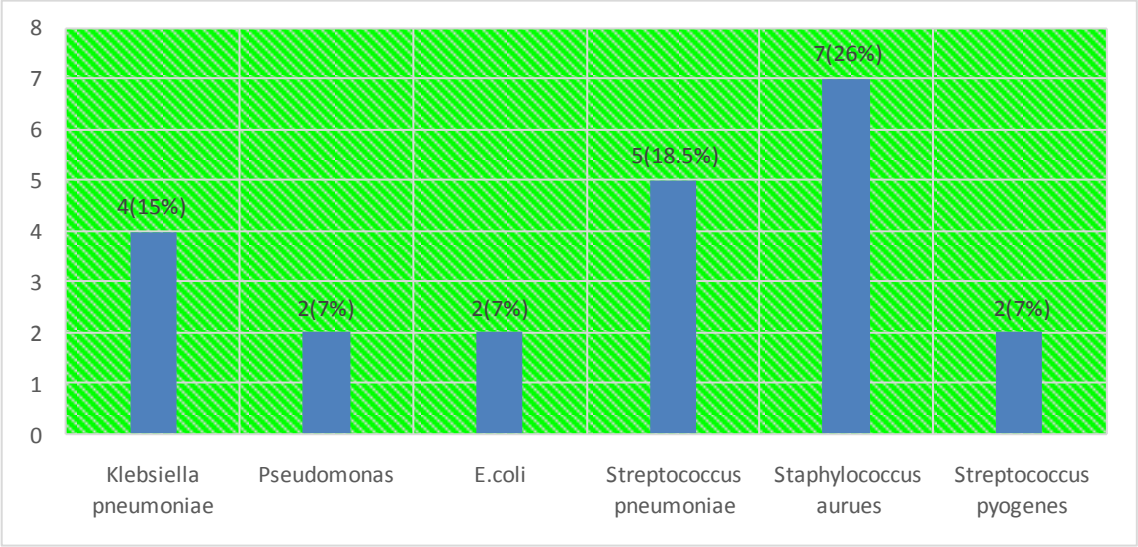

Figure 3. Microbiological profile of patients

The mean±SD for duration of total antibiotic therapy among the DPN positive and negative patients is shown in table 3. P value for which was found to be significant which is 0.0482. This indicates that the DPN positive patients required higher duration of antibiotic therapy when compared to DPN negative individuals. Complications observed were osteomyelitis in 15 (55.5%) patients. Debridement was done in 95% of patients.

Table 3. Antibiotic therapy and surgical therapy in DPN positive and negative patients

	DPN POSITIVE	DPN NEGATIVE	P-VALUE
NO. OF PATIENTS, n (%)	17(63)	10(37)	-
DURATION OF ANTIBIOTIC THERAPY, MEAN±SD	7.41±3.10	5.10±2.13	0.0482
DEBRIDEMENT, n (%)	15(88)	9(90)	-
FASCIOTOMY, n (%)	1(6)	1(10)	-
AMPUTATION, n (%)	5(29)	2(20)	-

DISCUSSION

Out of the total study population, 17(63%) patients were male and 10(37%) patients were female. This was similar to the study carried out by Sangeerabanoo et.al. revealed 65% males and 35% females. [4] Similar proportion was found in various literatures. [5, 6] The mean age in our patients was 56.59 ± 12.03 years which was similar to that previously reported in the literature. [7, 8] Higher numbers of patients were found in 50-70 years age group which comprised of 16 (59%) patients. Study published by TwahaKisozi et.al revealed similar predominance. [9] Our diagnosis of DPN was found to be similar to that followed by Tesfamichael G. Mariam et.al. [10] In our study, out of 17(63%) DPN positive patients, 10(59%) were male and 7(42%) were female. This predominance of male patients in similar to those published in the literatures. [11,12]

The mean duration of DM in our study was 10.8±5.96years in male patients and 10.7±7.04 years in female patients. However, there were not significant differences. According to IDSA classification of severity of DFI there was a majority of patients with moderate DFI (44.4%) in this study. These similar preponderances were found in this study. [6] The glycemic control was found to be moderately controlled with mean HbA1c 6.62±0.86in males and 7.03±1.62 in females. This was found to be not significant ($p<0.05$).

In our study, the gram-positive organisms were isolated in 14 (52%) patients and gram-negative organisms were isolated in 8 (48%) patients. However, the study published by Ramakant P et.al. revealed higher preponderance of gram-negative organisms. [8] Staphylococcus aureus was found to be isolated in majority of patients with gram-positive Diabetic foot infections, being present in 7(50%) patients.

As DFI is multifactorial, neuropathy is one of the risk factors for DFI. [13] The prevalence of diabetic peripheral neuropathy in DFI patients was found to be 63%(17 patients).The duration of antibiotic therapy was calculated. DPN positive patients had been for 7.41±3.10days on antibiotic therapy and DPN negative patients for 5.10±2.13days. Higher duration of antibiotic therapy is because of the slow wound healing observed in DPN positive patients. And that the proportion of amputation in DPN positive individuals was 29%(n=5) and DPN negative individuals was 20%(n=2).Debridement to 24(89%) patients, fasciotomy to 2(7%) patients and amputation to 7(26%) patients was performed based on patient condition. This is also evident from the study published by Elroy P Weledji et.al, Hunt D. [14,15]

It should be noted that self-assessment and foot examination is important for the identification of potential infection, particularly in patients with diabetes diagnosed with peripheral neuropathy. Early intervention and care of a diabetic ulcer will avoid complications from developing and save the feet from eventual amputation. [16]

CONCLUSION

The risk of occurrence of DFI is higher in patients in the age group of 50s and 60s and that its prevalence is higher in males than females. This predominance is similar in DPN patients also wherein males have more preponderance rate of occurrence of diabetic peripheral neuropathy. Adequate glycemic control, foot hygiene and patient's education are very essential in patients with diabetes and especially in DPN positive Diabetic individuals. The main limitation of our study is the sample size and hence further study has to be done in this area of research. As diabetic neuropathy is one of the etiological factors for diabetic foot infections, routine examination of foot and early intervention is necessary to avoid DFI and subsequently amputation. Nevertheless, optimum drug therapy shall be planned in such patients based on the characteristics of the diabetic foot ulcer and presence/absence of infection or ischemia.

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