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PREVALENCE OF FUNGAL INFECTIONS AMONG DIABETIC FOOT ULCER PATIENTS IN A RURAL AREA IN SOUTH INDIA

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ABSTRACT

Introduction: Infections among the diabetic patients play a vital role in the morbidity and to an extent mortality of the diabetic patients. Among the bacteriology of diabetic foot ulcers which had been documented by various researchers mixed aerobic - anaerobic microbes seems to be more common. Fungal infections among immunocompromised patient's particularly diabetic patients are one of the major health concern in the world today. Very few studies in India was previously done on assessing the magnitude of fungal infections in diabetic foot ulcers particularly among the rural patients. This study was undertaken to assess the prevalence of infections among the diabetic patients with foot ulcers and see for the presence of fungal infections and to describe the spectrum of those fungal infections.

Material and Methods: A prospective study was carried out on diabetic patients with foot ulcer during the period of 1 year from June 2014 – May 2015 at Thanjavur medical college. A total of 100 cases with diabetic foot ulcers were included for the study. The power of the study was kept as 89.7%, which was calculated by using the formula of $Z_{power} = \text{test statistics} / S.E - 1.96$. Where the test statistics was taken as 0.2 and the SE was taken as square root of $0.5/n$ and where $n = 100$. Specimens (pus, wound, exudates or tissue biopsy) for microbiological studies were obtained from the ulcer region. All the 100 specimens were immediately transported to the microlab for further processing, culture and isolation. Identification of the microorganisms were done according to the standard microbiological procedures.

Results: Among the study subjects males constitutes to 83% and females 17%. The mean random blood sugar among the subjects was 316.35 ± 54 mgs/dl. The average duration of the foot ulcer among the study subjects was 13 ± 7.58 months. Of the various microorganisms which was found in the foot ulcer bacterial agents were present in almost 100% of the patients. The fungal growth was seen in 29% of the patients with foot ulcers. The most common fungus identified were *Aspergillus flavus* (17%), *Aspergillus fumigates* (5%), *Candida albicans* (6%) and *Mucor* (1%).

Conclusions: The present study insists on the evaluation of fungal pathogen for long standing diabetic foot ulcers even after effective treatment with antibacterial agents.

Keywords: Diabetes, fungal infection, foot ulcer, rural area, prevalence.

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INTRODUCTION

Diabetes mellitus (DM) is one of the most common non communicable disease in the developed and developing countries like India. The prevalence of type 2 DM is 11% in urban areas in comparison to 3-9% in rural areas and the number increases to 30 – 35% when we look at the age specific rates.¹ Infections among the diabetic patients play a vital role in the morbidity and to an extent mortality of the diabetic patients.²

Studies revealed that defect in the functions of WBC's are the most common reason for increase incidence of infections in diabetic patients.^{3,4} Few other studies had shown that low levels of leucotriene B₄, thromboxane B₂, and prostaglandin E can also be the triggering factor for the development of infections in the diabetic patients.⁵ Other studies showed decreased lymphocyte function and decreased levels of phagocytosis among the diabetic patients had led

to the incidence of infections in them.⁶ As their glycemic status improves, the cellular immunity also improves leading on to the control of the infections which had already occurred.⁷ Although DM is very common in south India, studies on type of infections in patients with DM from rural south Indian areas are lacking. Among the bacteriology of diabetic foot ulcers which had been documented by various researchers mixed aerobic - anaerobic microbes seems to be more common. However studies done on the prevalence of fungal infections among the diabetic patients are very limited. Many studies had quoted that *Candida* species is the most commonly isolated yeast from the diabetic foot ulcers.⁸ Although few studies have reported *Candida albicans* as the most prevalent species, others had proven that even nonalbicans species found to be more common.^{9,11} The increased incidence of fungal infections in the inter-digital spaces and nails in the toes of diabetic patients leads to the development of severe and deep inflammatory processes in feet. Fungal infections among immunocompromised patients particularly diabetic patients are one of the major health concern in the world today,¹¹ but the spectrum of fungi infecting the diabetic foot wounds and their pathogenicity was not studied thoroughly. Many of the clinicians treating the diabetic foot wounds usually suspect bacterial infections and treat them accordingly.¹² They do not routinely send deep tissue for fungal culture and sensitivity. A recent study had shown 27.9% positive fungal cultures in 318 diabetic patients with foot ulcers.¹³ The opportunistic fungi usually invade deep into the wounds and contribute to the delayed wound healing. Very few studies in India were previously done on assessing the magnitude of fungal infections in diabetic foot ulcers particularly among the rural patients.

This study was undertaken to assess the prevalence of infections among the diabetic patients with foot ulcers and see for the presence of fungal infections and to describe the spectrum of those fungal infections.

MATERIAL AND METHODS

A prospective study was carried out on diabetic patients with foot ulcer during the period of 1 year from June 2014 – May 2015 at Thanjavur medical college and Hospital. The study was carried out

after getting the clearance from the institutional ethical committee and the informed consent was obtained from all the patients who were involved in the study. Foot ulcers in diabetic patients were categorized into six grades (Grade 0 – Grade 5) based on Meggit Wagner classification system. Patients with grade 1 or more were included in the study. However all patients with grade 0 or limb amputations were excluded from the study group. Details regarding type of diabetes, its duration, treatment, compliance by the patient, awareness about complications, personal habits like smoking, alcohol consumption were recorded by using a semi-structured questionnaire. Meticulous clinical examination was done on all the patients.

Cases with ulcers on the other foot also were considered as a separate case. A total of 100 cases with diabetic foot ulcers were included for the study. Neuropathy assessment was done by using 10 gram monofilament and presence of ischemia was tested by feeling for pulsations in dorsalis pedis and posterior tibialis arteries, while osteomyelitis was diagnosed by using x-rays.

Specimens (pus, wound, exudates or 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 in 93 patients and 7 patients respectively which was then transported in a clean and sterile test tube. All the 100 specimens were immediately transported to the microlab for further processing, culture and isolation. Identification of the microorganisms were done according to the standard microbiological procedures. All the data were entered in SPSS version 16 and Chi-square test was used for deriving the statistical significance.

RESULTS

The age and sex wise distribution of the study population shows that majority of the study population were in the age group between 50 – 70 years with a mean age of 59.07±9.09 years. Among the study subjects males constitutes to 83% and females were only 17% (table1). The mean duration of diabetes in the study subjects was 5.53±2.97 years. The mean random blood sugar among the subjects was 316.35±54 mgs/dl. The most common site of ulcer among the study patients was right foot (45%) followed by left foot (40%), ankle(10%) and right leg(5%).

Table 1: Age and Sex wise distribution of the study population

Age group (in years)	Gender		Total
	Male	Female	
30 – 40	4 (4.8%)	0	4 (4%)
41 – 50	13 (15.6%)	3 (17.6%)	16 (16%)
51 – 60	30 (36.1%)	6 (35.2%)	36 (36%)
61 – 70	31 (37.3%)	5 (29.4%)	36 (36%)
>70	5 (6.02%)	3 (17.6%)	8 (8%)
Total	83 (100%)	17 (100%)	100 (100%)

Table 2: Distribution of microorganisms in the foot ulcer among the diabetic patients

Type of microorganism	Name of microorganisms	Frequency	Percentage
Bacterial	Staphylococcus	74	74%
	Pseudomonas	9	9%
	Klebsiella	14	14%
	E.Coli	3	3%
Fungus	Aspergillus flavus	17	17%
	Aspergillus fumigatus	5	5%
	Candida albicans	6	6%
	Mucor	1	1%
	No growth	71	71%

Table3: Duration of diabetes and the fungal growth among the diabetic foot ulcer patients

Duration of diabetes	Presence of fungal growth	Percentage	P value
6 months – 1 year (n=16)	1	6.25%	Chi-square value= 9.929 d.o.f= 5 p value = 0.047
1 year – 2 years (n=19)	3	15.7%	
2 year – 3 years (n=15)	4	26.6%	
3 year – 4 years (n= 20)	8	40%	
4 year – 5 years (n=13)	6	46.1%	
>5 years (n=17)	7	41.1%	

Table 4: Duration of foot ulcer and the fungal growth among the diabetic patients with foot ulcers

Duration of foot ulcer	Presence of fungal growth	Percentage	P value
<6 months (n=28)	3	10.7%	Chi-square value = 8.244 d.o.f= 4 p value = 0.083
6 months – 1 year (n=31)	9	29%	
1 year – 2 years (n=17)	6	35.2%	
2 years – 3 years (n=19)	8	42.1%	
>3 years (n=6)	3	50%	

Table 6: Gender wise distribution according to presence of microorganisms

Gender	Presence of bacterial organisms	Presence of fungal organisms
Male (n=83)	83 (100%)	26 (31.3%)
Female (n=17)	17 (100%)	3 (17.6%)
P value	1.000	Chi-square value = 1.282 d.o.f= 1 p value = 0.258

Table 7: Agewise distribution according to presence of microorganisms

Age group	Presence of bacterial organisms	Presence of fungal organisms
30 – 40 (n=4)	4 (100%)	0 (0.0%)
41 – 50 (n=16)	16 (100%)	1 (6.25%)
51 – 60 (n=36)	36 (100%)	10 (27.7%)
61 – 70 (n=36)	36 (100%)	12 (33.3%)
>70 (n=8)	8 (100%)	5 (62.5%)
P value	1.000	Chi-square value = 10.542 d.o.f= 4 pvalue = 0.032

The average duration of the foot ulcer among the study subjects was 13±7.58 months. More than 90% of the patients were taking only oral hypoglycemic agents before the onset of foot ulcer whereas after the development of foot ulcer almost 100% of the patients were taking both insulin and oral hypoglycemic agents. Of the various microorganisms which was found in the foot ulcer bacterial agents were present in almost 100% of the patients and the most common agents identified were staphylococcus (74%), pseudomonas (9%), klebsiella (14%) and E.coli (3%). The fungal growth was seen in 29% of the patients with foot ulcers and the most common fungus identified were Aspergillus flavus (17%), Aspergillus fumigates (5%), Candida albicans (6%) and Mucor (1%) (table2).

The fungal diabetic foot ulcer seems to be more common among the patients with diabetic status of 3 years and more and less common in patients with a diabetic status of less than 3 years and this difference was found to be statistically significant (P =0.047) (table3). Similarly diabetic patients with foot ulcers of more than 1 year shows more incidence of fungal growth when compared to the foot ulcers presenting with less than 1 year and the difference was found to be statistically significant (P=0.083) (table 4). So this infers that diabetic patients presenting with foot ulcers for more than 1 year even after effective antibiotics with both systemic and topical application should always be investigated for fungal growth. Male gender and advanced age group population were found to be additional risk factor in the development of fungal infections in the foot ulcer (table5 and 6) but male gender did not show statistical significant association in the development of fungal foot ulcer (p=0.258). Early interventions in the form of systemic anti-fungals might prevent the patients going on to below ankle amputations due to foot

ulcers. Of all the 100 patients majority of them required only wound debridement and dressing (92%), and only 5 patients had undergone below ankle amputation and 3 patients underwent transmetatarsal amputation.

DISCUSSION

Among the 100 patients with diabetic foot ulcer, the prevalence of fungal ulcer was found to be 29% and among the various fungal organisms identified the most common was *Aspergillus flavus*. The epidemic of diabetes mellitus is on a tremendous rise over the past 2 decades and this had led to the increase in the prevalence of complications due to diabetes, and diabetic foot ulcer is one of the most common complication among them. Lack of awareness about self care practices in diabetes, particularly the foot care is the major reason for the development of foot ulcers among the diabetic patients and peripheral neuropathy being the major precursor for this condition.

In our study out of 100 diabetic foot ulcer patients 83 were males and only 17 were females and the microorganisms, particularly bacteria were almost equally distributed in both the gender groups whereas the fungus was more prevalent among the males when compared to the females (table 5) and our results were almost in par with the studies done at Saudi,¹⁴ Nepal¹⁵ and Africa.¹⁶ In their results they highlighted that males have dominated in the incidence of fungal foot ulcers and also quoted that males tend to have the practice of walking bare foot than the females and this would be the reason for the increased incidence of fungal infection among them.

The present study had shown that the fungal infection was more common in the age group of 50 and above when compared to lower age group and similar type of findings was shown by Piérard and Piérard-Franchimont,¹⁷ and the explanation quoted by them was advanced age might lead on to reduced immunity making them more prone to develop fungal foot ulcers.

In our study the commonest bacterial pathogen present in the foot ulcer was staphylococcus (74%) followed by klebsiella (14%) and the results are almost in par with the studies done by Cincholika et al¹⁸ and Adler et al¹⁹. Our study had shown that the overall prevalence of fungal infections among the diabetic foot ulcer was 29%

and it is similar to the studies done by Nithiyalakshmi et al (27.46%)²⁰, Gopi Chellan et al (20.84%)²¹ and Saba Fata et al (19.9%)²².

Aspergillus was found to be the most common fungal pathogen among the diabetic foot ulcer patients in our study whereas most of the other studies had shown *Candida albicans* as the commonest fungal pathogen in the foot ulcer of diabetic patients except few study done by Gadepalli et al²³ and Gonzalez et al²⁴.

The duration of diabetes in our patients seems to be a factor for the development of fungus in the foot ulcer, longer the duration of diabetic status they were more prone to develop fungal foot ulcer and the similar type of results was also quoted by Mehamud et al²⁵. In our study we found that foot ulcers of longer duration had shown a significant positivity in fungal growth.

In the present study the longer the duration of foot ulcer had shown increase in the incidence of fungal infection and a similar type of result was also shown by the study done by Saravanan Sanniyasi et al²⁶. He also quoted in that study that prolonged usage of antibacterial agents might be the triggering factor for the development of fungal infection in these patients.

CONCLUSIONS

The present study shows the prevalence of fungal infections among the diabetic foot ulcer patients was 29% and *Aspergillus flavus* seems to be the most common pathogen which was detected among the patients with diabetic foot ulcers. The present study insists on the evaluation of fungal pathogen for long standing diabetic foot ulcers even after effective treatment with antibacterial agents. So the clinicians should initiate antifungal treatment for long standing nonhealing diabetic foot ulcers which might prevent the patients from amputations due to chronic non healing foot ulcers. One of the limitation of the present study is the drug sensitivity for the fungal pathogen which was detected in our study was not investigated. The effectiveness of antifungals in the curing of the infection will be the future perspective of this study.

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