

A Clinical Study on Correlation of Fungal Infection in Diabetic Foot Ulcer and Its Management

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ABSTRACT

Background:

Over the past two decades, diabetes mellitus has surged globally, increasing from 30 million to 177 million cases. A key complication is diabetic foot ulcers (DFU), caused by hyperglycemia-induced neuropathy and poor circulation, often leading to infection and amputation. While bacterial DFU infections are well documented, fungal involvement remains understudied. This study assessed the prevalence of fungal species, especially *Candida*, in DFUs and compared healing outcomes between debridement alone and debridement with clotrimazole.

Methodology:

This prospective study at Meenakshi Medical College Hospital (Nov 2022–Apr 2024) included 80 diabetic patients with foot ulcers selected by purposive sampling. Exclusions were non-diabetic ulcers, cellulitis, and gangrene. Data collected included demographics, ulcer grading, and lab values (HbA1c, FBS, PPBS). Tissue samples were examined via KOH mount and cultured on Sabouraud Dextrose Agar. Patients with fungal DFU were randomized to receive either debridement alone or debridement with topical clotrimazole.

Results:

Fungal infections were detected in 27.5% of DFU cases, with *Candida albicans* being the most prevalent isolate. No significant association was found between fungal DFU and demographic or lifestyle factors, such as age, gender, or socioeconomic status. However, fungal DFUs were significantly associated with longer duration of diabetes, prolonged ulceration, and poor glycemic control ($p < 0.05$). Healing outcome is higher in debridement with topical clotrimazole.

Conclusion:

Poor glycemic control and long-standing diabetes are major risk factors for fungal infections in DFU. Early detection of fungal involvement and optimal blood sugar management are crucial in preventing complications. Demographic variables were not significantly linked to fungal DFUs, reinforcing the importance of metabolic control in diabetic wound care.

Keywords: Debridement, Diabetes, Fungus, Ulcer, Clotrimazole

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It encompasses various forms, including Type 1 and Type 2 diabetes, gestational diabetes, and secondary forms linked to endocrine dysfunction or drug use. Among these, Type 2 Diabetes Mellitus (T2DM) is the most prevalent, especially among middle-aged and elderly populations, driven largely by sedentary lifestyles and dietary habits. Globally, the prevalence of DM has surged over the last two decades, rising from 30 million cases to 177 million, with projections estimating that the number will exceed 700 million by 2045 [1].

A significant complication of poorly managed diabetes is the development of diabetic foot ulcers (DFU), which results from the combined effects of hyperglycemia-induced neuropathy, peripheral arterial disease, and immune dysfunction. DFUs significantly increase the risk of infections, amputations, and mortality. Approximately 15% of diabetic individuals are expected to develop DFUs during their lifetime, with 14–24% of these cases requiring amputations due to severe infections

or osteomyelitis [2].

Although bacterial pathogens are commonly implicated in DFUs, recent research highlights the substantial role of fungal organisms, particularly *Candida* species, in delaying wound healing and complicating management. Fungal infections in DFUs are frequently underdiagnosed, often coexisting with bacterial biofilms and contributing to chronic inflammation and poor outcomes [3]. Studies have reported fungal colonization rates in DFUs ranging from 20% to 30%, with *Candida albicans* being the most commonly isolated species [4].

Moreover, fungal infections pose diagnostic challenges due to their often non-specific clinical manifestations, which can mimic bacterial infections. This frequently leads to delays in appropriate antifungal therapy, prolonging healing and increasing the risk of complications such as osteomyelitis and limb amputation [5].

Despite the growing recognition of fungal involvement in DFUs, standardized guidelines for fungal diagnostics and treatment are lacking, resulting in suboptimal management. This study aims to evaluate the prevalence of fungal infections in diabetic foot ulcers, identify the common fungal species involved, and compare outcomes between debridement alone and debridement combined with topical antifungal therapy using clotrimazole.

2. MATERIALS & METHODS:

This prospective observational study was conducted at the Department of General Surgery, Meenakshi Medical College Hospital and Research Institute (MMCHRI), Kanchipuram, between November 2022 and April 2024. The study population included diabetic patients with diabetic foot ulcers (DFUs) who attended the department.

Inclusion Criteria

- Patients diagnosed with Type 2 Diabetes Mellitus.
- Patients with clinically confirmed diabetic foot ulcers, irrespective of the duration.
- Patients aged 18 years and above, who provided informed consent.

Exclusion Criteria

- Non-diabetic patients presenting with foot ulcers.
- Diabetic patients with cellulitis or gangrene without foot ulcers.
- Patients who refused to participate or were unable to provide consent.

Sampling Technique: A purposive sampling method was adopted, and 80 patients were enrolled based on the inclusion and exclusion criteria.

Data Collection

A structured proforma was used to collect the following information:

- Demographic data: Age, gender, place of residence, and socioeconomic status.
- Clinical data: Duration of diabetes mellitus, comorbidities (such as hypertension, neuropathy, peripheral arterial disease, retinopathy, and osteomyelitis), lifestyle habits (such as smoking and alcohol consumption), and treatment history for diabetes.
- Diabetic foot ulcer assessment: Ulcer grading was performed using Wagner's classification system.

Laboratory Investigations: Blood tests: Fasting blood sugar (FBS), postprandial blood sugar (PPBS), and glycated hemoglobin (HbA1c).

Microbiological evaluation: Tissue samples from the ulcer were collected aseptically. Direct microscopic examination was performed using potassium hydroxide (KOH) wet mount. The samples were cultured on Sabouraud Dextrose Agar (SDA) to isolate and identify fungal species. Fungal growth was confirmed based on colony morphology and microscopy.

Randomization and Treatment Groups

Patients who tested positive for fungal infections were randomized into two treatment groups:

- Group A: Received standard wound debridement alone.
- Group B: Received standard wound debridement plus topical clotrimazole (1%).

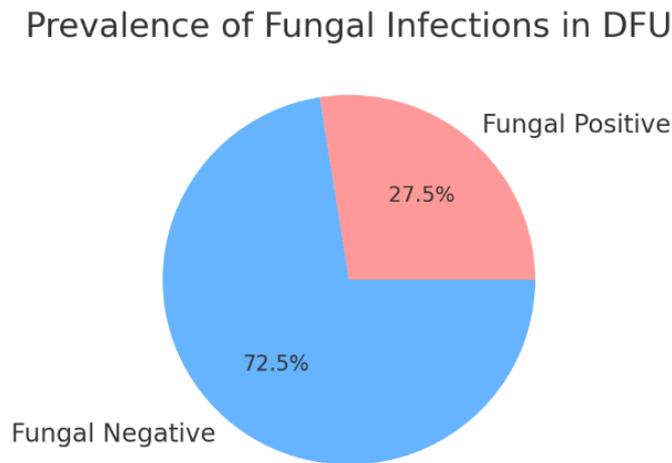
Outcome Measurement: The primary outcome measured was the duration of wound healing in both treatment groups. Secondary parameters included fungal species' prevalence, fungal infection association with patient demographics, glycemic control, and comorbidities.

Statistical Analysis: The data were analyzed using SPSS software version 26.0. Descriptive statistics were used to summarize the data. Associations between categorical variables were assessed using the Chi-square (χ^2) test. A p-value of <0.05 was considered statistically significant.

3. RESULTS:

Table 1 & Fig 1: Prevalence of Fungal Infections in DFU Patients

Fungal Infection	Number of Patients (n=80)	Percentage (%)
Present	22	27.5%
Absent	58	72.5%



Out of the 80 patients with diabetic foot ulcers (DFUs) who were included in the study, 22 patients (27.5%) had confirmed fungal infections based on culture results.

Table 2: Gender Distribution of Patients

Gender	Fungal DFU (n=22)	Non-Fungal DFU (n=58)	Total (n=80)
Male	14	38	52
Female	8	20	28

No statistically significant association was found between gender and fungal DFU ($p > 0.05$).

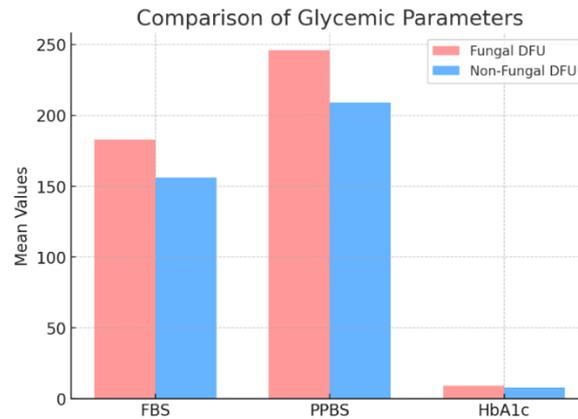
Table 3: Residence-wise Distribution

Residence	Fungal DFU (n=22)	Non-Fungal DFU (n=58)	Total (n=80)
Urban	10	22	32
Rural	12	36	48

The distribution was higher in rural areas but without significant association ($p > 0.05$).

Table 4 & fig 2: Glycemic Parameters Comparison

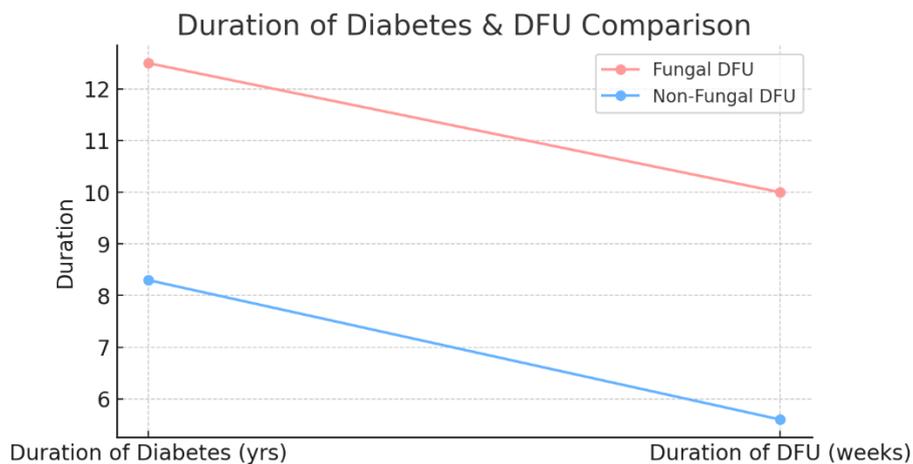
Glycemic Parameter	Fungal DFU (Mean ± SD)	Non-Fungal DFU (Mean ± SD)	p-value
FBS (mg/dL)	183 ± 32	156 ± 25	<0.05
PPBS (mg/dL)	246 ± 45	209 ± 37	<0.05
HbA1c (%)	9.2 ± 1.3	7.8 ± 1.1	<0.05



Patients with fungal DFUs had significantly higher FBS, PPBS, and HbA1c compared to non-fungal cases.

Table 5 & Fig 3: Duration of Diabetes and DFU

Parameter	Fungal DFU (Mean ± SD)	Non-Fungal DFU (Mean ± SD)	p-value
Duration of Diabetes (yrs)	12.5 ± 4.1	8.3 ± 3.8	<0.05
Duration of DFU (weeks)	10 ± 3.2	5.6 ± 2.7	<0.05

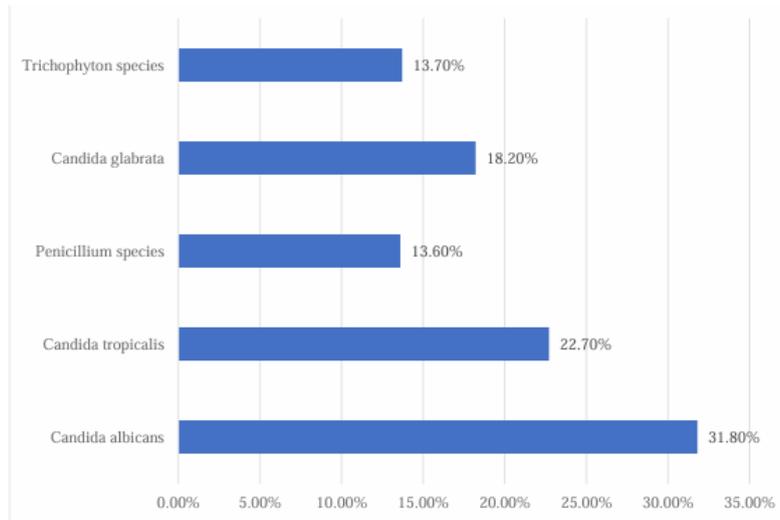


Fungal DFU patients had a significantly longer history of both diabetes and ulcer duration.

Comorbidity Analysis

No statistically significant association was found between fungal infection and comorbidities such as neuropathy, PAD, retinopathy, or osteomyelitis (p > 0.05 for each).

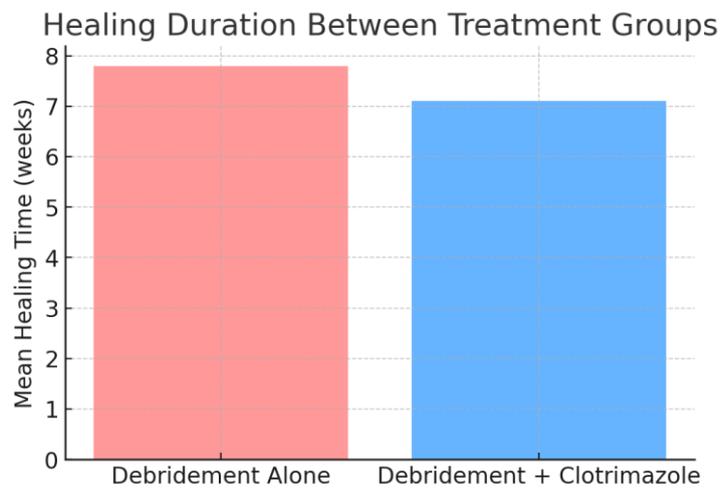
Figure 4: Frequency of Species (n = 22)



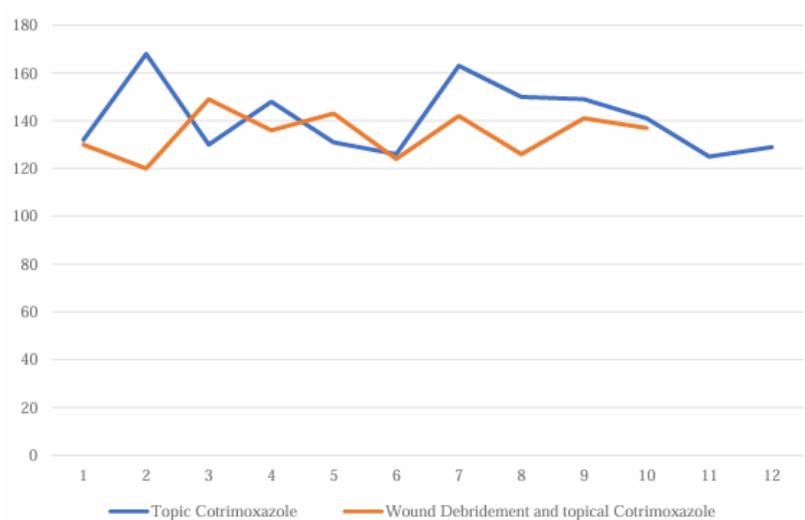
Our investigation identified *Candida albicans* as the predominant fungal species among patients diagnosed with fungal infections in Diabetic Foot Ulcers (DFU), followed by *Candida tropicalis*.

Table 6 & Fig 5: Duration of Wound Healing in Treatment Groups

Group	Mean Duration (weeks)	p-value
Debridement Alone (n=11)	7.8 ± 1.5	>0.05
Debridement + Clotrimazole (n=11)	7.1 ± 1.2	



Group B patients has slightly faster healing than group A.

Figure 6: Duration of Wound Healing (n = 22)

The mean duration for wound healing in patients receiving topical clotrimazole (Group A) was determined to be 141 ± 15.6 days, whereas in patients undergoing wound debridement and topical clotrimazole treatment (Group B), it was 135 ± 9.44 days. Notably, Group B exhibited a slightly faster healing rate compared to Group A; however, this difference did not achieve statistical significance.

Key Findings:

- Fungal DFU prevalence: 27.5%
- Most common fungal isolate: *Candida albicans*
- Significant association between fungal DFUs and poor glycemic control and longer duration of diabetes/ulcer.
- Group B patients has slightly faster healing than group A.

4. DISCUSSION:

In this study, the prevalence of fungal infections in diabetic foot ulcers (DFUs) was found to be 27.5%, which is consistent with existing literature where prevalence rates range between 20% and 30% [1,2]. The most commonly isolated fungus was *Candida albicans*, which is also the most frequently reported organism in other national and international studies [2,3].

The association between poor glycemic control and the occurrence of fungal DFUs was evident in this study. Patients with fungal DFUs exhibited significantly higher FBS, PPBS, and HbA1c levels compared to those without fungal infections ($p < 0.05$), confirming that chronic hyperglycemia predisposes patients to fungal colonization and infection [4,5]. Similar findings were reported by Kalan et al., who observed that impaired immunity and altered wound microenvironments due to uncontrolled blood sugar favor fungal growth in chronic wounds [6].

Interestingly, no significant correlation was observed between fungal DFU and demographic variables such as age, gender, residence, and socioeconomic status ($p > 0.05$), a finding also supported by Ahmed et al. [3] and Devasia et al. [7]. This highlights the possibility that glycemic dysregulation and prolonged disease duration play more decisive roles in the development of fungal infections in diabetic wounds than demographic factors alone.

Additionally, longer diabetes duration and longer ulcer duration were significantly associated with fungal infections ($p < 0.05$), which corroborates earlier findings from Musyoki et al. [2] and Mishra et al. [8]. The chronicity of the ulcer and prolonged exposure to high glucose levels likely enhance fungal colonization and biofilm formation.

In terms of comorbidities such as neuropathy, retinopathy, PAD, and osteomyelitis, no significant association with fungal DFUs was observed in this study, contrasting with some previous reports which suggested peripheral arterial disease may exacerbate fungal wound colonization due to ischemic environments [9]. However, this discrepancy could be due to sample size differences or population-specific factors.

Regarding treatment outcomes, both groups (debridement alone vs. debridement plus clotrimazole) demonstrated comparable wound healing durations without a statistically significant difference ($p > 0.05$). Although antifungal treatment logically reduces fungal burden, wound healing is multifactorial and dependent on glycemic control, vascular supply, and nutritional status [4,10]. This result aligns with Devasia et al., who observed similar wound healing durations with or without adjunct antifungal therapy, provided there was adequate ulcer debridement [7].

Finally, the findings reaffirm the underdiagnosis of fungal DFUs in routine clinical practice. Fungal cultures and KOH mounts remain indispensable, as clinical signs often mimic bacterial infections [5,11]. Timely fungal identification,

integrated management, and strict glycemetic control are critical to reduce diabetic foot ulcers (DFU).

5. CONCLUSION:

Our study found that 27.5% of patients with diabetic foot ulcers (DFU) developed fungal infections, predominantly caused by *Candida albicans*. Although demographic and lifestyle factors did not show a significant association with fungal DFUs, a longer duration of diabetes and poor glycemetic control emerged as notable risk factors. Effective diabetes management is therefore crucial in reducing the incidence of fungal infections in DFU patients. Additionally, the outcomes of topical clotrimazole therapy along with debridement were slightly faster wound healing and reduce the duration of wound healing as compared to debridement alone.

6. RECOMMENDATION:

Routine Fungal Screening: Incorporate fungal culture and KOH examination as part of the routine microbiological workup for all chronic or non-healing diabetic foot ulcers.

Strict Glycemetic Control: Emphasize tighter blood glucose control (FBS, PPBS, and HbA1c) as poor glycemetic regulation was significantly linked to fungal infections.

Early and Aggressive Debridement: Prioritize timely surgical debridement to reduce microbial load and biofilm formation, including fungal biofilms.

Consider Antifungal Therapy Selectively: Use antifungal agents, such as clotrimazole, in addition to debridement in patients with confirmed fungal DFUs or at high risk (e.g., long-standing ulcers or recurrent infections).

Multidisciplinary Approach: Implement a team-based care model involving surgeons, endocrinologists, infectious disease specialists, and podiatrists for comprehensive DFU management.

Further Research: Conduct larger, multicentric studies to evaluate antifungal therapy's long-term impact on DFU healing and amputation rates, considering emerging antifungal resistance patterns.

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