Onychomycosis is the most common fungal infection seen by podiatrists today. It comprises about one-third of all skin fungal infections, and 50% of all nail disorders. The importance of diagnosing and treating onychomycosis in the diabetic population is becoming increasingly recognized. It is much more common than previously thought. The risk/odds ratio for diabetic subjects having toenail onychomycosis is 2.77 times that of normal individuals.

A recent study showed the prevalence of onychomycosis in patients with diabetic foot complications to be 53.3%, compared to 22.7% in matched control subjects (P < .001). Patients with diabetes are also at increased risk of developing complications. They often present with impaired ability to detect injury as a result of peripheral neuropathy, retinopathy; and obesity may impair foot inspection.

If ignored, their onychomycosis can result in damage to skin and nails leading to an increased chance of secondary bacterial infection and resultant lower limb cellulitis, necrosis, and diabetic foot infection. Diabetic patients with onychomycosis have a two to three times greater rate of secondary infection compared to those without onychomycosis.

In addition, onychomycosis is now considered an important predictor of diabetic foot infection, with a three-fold higher risk in diabetics of gangrene or foot ulcers. The morbidity linked to onychomycosis, the ever-growing size of the diabetic population, and the high frequency of foot disorders in diabetics present a considerable health problem. Diabetic patients also have an impaired ability to fight infection due to elevated blood glucose levels which may cause an altered immune function. Timely diagnosis and treatment can help to prevent serious consequences of neglecting onychomycosis.

The risk odds ratio for diabetic subjects having toenail onychomycosis is 2.77 times that of normal individuals.
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consequences in these patients.7

This review focuses on the size of the problem and provides an overview of the studies carried out to date in treating onychomycosis in a diabetic population.

Prevalence of Onychomycosis in Diabetics

The prevalence of onychomycosis in patients with diabetes depends on a number of factors including age, gender, background illnesses, occupation, climate, environment, trauma to the nails, lack of hygiene, humid environment, and the repeated contact of nails with water, in addition to the diagnostic criteria used.12 Indeed, it has been suggested that better diagnostic methods are needed, especially considering the high risks involved and investigator variability in diagnosis.19 Therefore, prevalence rates vary significantly.

Quoted prevalence rates generally range from 1.2–26%.1,14,15 In a prospective study, the prevalence of onychomycosis in type II diabetics was 22%; most infections were due to dermatophytes, and only in four patients were yeasts identified.18 Higher prevalence rates have been reported. In a study of 1,245 Taiwanese patients with diabetes mellitus, onychomycosis prevalence was over 30%.16

Older age, being male, metabolic syndrome, obesity, elevated triglyceride levels, and poor control of blood sugar levels (elevated HbA1c) were all associated with onychomycosis.19

However, studies looking at the association between glycemic control and prevalence of onychomycosis have produced conflicting results.16-18 This could be due to the different cut-off values for HbA1c or different laboratory measures being used, since methodological details were not provided. Data on the relationship between the prevalence of onychomycosis and the period of time that patients have had diabetes have also provided conflicting results.17,21

The severity of onychomycosis is significantly associated with the duration of diabetes.3 One study found out of 95 patients with type I diabetes (average duration of disease: 35.8 years), 82.1% had changes affecting their feet suggestive of mycosis; in 84.6%, fungal infection was confirmed by a plain specimen and mycological culture.19 Twenty-eight patients had a fungal nail infection, and another 28 had both cutaneous and nail infections.

In a cross-sectional study conducted in Japan, 51.3% of patients with diabetes had onychomycosis of the toenails.22 Nail thickness was significantly correlated with an elevated HbA1c value. Onychomycosis was significantly more common if the feet were not washed on a daily basis.

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Treatment of Onychomycosis in a Diabetic Population

Before reviewing the clinical data on the treatment of onychomycosis in a diabetic population, it is important to stress that educating patients on the importance of foot and nail care forms an essential component of their diabetes management. This is especially important in patient groups at a higher risk for the development of onychomycosis, such as elderly diabetics, and can help reduce recurrence and prevent foot ulcers.23,24

It is often suggested that patients with diabetes are more resistant to antifungal treatment than non-diabetic patients.25 It is certainly the case that elderly diabetic patients’ nails may grow even slower and require a longer duration to treat.3 Many studies have evaluated the treatment for onychomycosis in the general pop-

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once daily). At week 48, mycologic cure rates were 88.2% and 79.3% respectively (no significant difference between the two groups). Effective cure (defined as mycologic cure with ≤10% nail plate involvement) was seen in 52.9% and 51.7% of patients (again not significant between groups).28

In an unpublished study by Bohannon and Streja, the results in 81 diabetic patients were compared with those from a much larger cohort of non-diabetic patients receiving terbinafine for their onychomycosis. There were no significant differences in mycologic cure between diabetic and non-diabetic patients (64% vs. 73%).29

In an open-label non-comparative study of 49 type 2 diabetic patients with mild to moderate onychomycosis, treatment with once daily ciclopirox 8% nail lacquer for 48 weeks resulted in a 54.3% mycologic cure rate. Complete cure rates were achieved in only 4.4% of patients.30

A post-marketing observational study with ciclopirox 8% nail lacquer included 215 patients with diabetes. However, data on mycologic and complete cure are lacking, and the population included patients with both fingernail and toenail onychomycosis.31

Recently, a post-hoc analysis of 112 diabetic patients with onychomycosis treated with efinaconazole topical solution, 10% daily for 48 weeks resulted in a mycologic cure rate of 56.5% and complete cure rate of 13.0% (Figure 2). Compared to the larger study population of onychomycosis patients without co-existing diabetes, there was no statistical difference between the two populations for any efficacy endpoint. Treatment success (defined as ≤10% nail plate involvement) was reported in 40.8% and 47.7% of patients respectively.32

Conclusions

Recognition and early intervention in treating onychomycosis is important because of the potential progressive nature of the fungal infection, and the potentially serious sequelae associated with persistence of untreated infected nails. The consequence of neglecting onychomycosis carries a significant risk for diabetic patients.28 Yet, the clinical data we have in diabetic patients who have onychomycosis is sorely limited.

Two studies have shown similar efficacy in diabetic and non-diabetic populations,29,32 although one of these remains unpublished.29 Both were post-hoc analyses of larger studies, and not specifically set up to study diabetic patients with onychomycosis. The remaining studies also suggest that cure rates are comparable to those seen in onychomycosis patients who do not have diabetes. However, study limitations in terms of enrollment, study design, and disease assessment limit the reliability of these findings.

Figure 1: Mycological cure rates following systemic therapy in diabetic patients with onychomycosis.

Figure 2: Mycologic and complete cure rates following topical therapy in diabetic patients with onychomycosis.
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ability of any study comparisons. Further research is urgently needed, especially in patients more representative of the general diabetic population. This will allow us to evaluate effective management strategies that might include combination therapy, maintenance strategies to avoid recurrence, and mechanical debridement. PM

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