Prevalence of Fungal Foot Infections in Patients with Diabetes Mellitus Type 1 – Underestimation of Moccasin-Type Tinea

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Article

Abstract

In diabetic patients, mycotic infections may increase the risk of developing diabetic foot syndrome. However, few data are available on the prevalence of fungal foot infections in patients with diabetes. During a conference attended by patients with long-term diabetes, 95 individuals with type 1 diabetes mellitus (52 men, 43 women, mean disease duration 35.8 years) were examined for fungal infections of the feet. As well as frequency of infection and risk profiles, the level of patient awareness and preventive measures taken were assessed by means of a questionnaire. Clinically, 78 patients (82.1%) showed probable pedal fungal infections, of which 84.6% (66/78) were mycologically confirmed by direct microscopy and/or culture. Skin mycoses were found in 9 patients (toe webs 5, soles 4), onychomycosis in 29 patients and simultaneous infection of nails and skin in 28 patients (toe webs 8, soles 20). Thirty-seven (47.4%) of these patients had positive cultures, particularly for the dermatophyte *Trichophyton rubrum* (69.2% of isolates). A significant correlation was found between infection and gender (men more frequently affected) and the age of the patients. The actual frequency of mycoses was underestimated by the patients. This correlated with the assessment of their own knowledge level concerning fungal infections: 83.2% of patients with skin mycoses and 88.4% of those with onychomycosis of the feet felt that they needed more information about their disease. Marked mycoses on the soles were often considered to be dry skin by the patients. The high number of infections detected is especially remarkable in that this group of patients were highly motivated. It therefore appears that diabetics require more diagnostic, therapeutic and preventive care in terms of mycotic diseases than has been previously thought.

Key words
Diabetes mellitus · fungal foot infections · mocassin-type tinea

Introduction

With an estimated 60 million people worldwide, all populations and age groups are affected by diabetes mellitus (DM) (Rich and Hare, 1999). The annual incidence of new cases of type 1 and type 2 diabetes mellitus in the USA is estimated to be 30000 and 625000, respectively (Gupta et al., 1998). Diabetic foot disease is a polyetiological disease of great importance; its prevention through inspection, hygiene, callus removal, appropriate shoe wear, awareness of neuropathy and peripheral arterial occlusive disease is crucial. Bacterial and mycotic infections may worsen diabetic foot syndrome (Wheat, 1980; Joshi, 1999). Pedal mycosis may become a potential entry site for bacterial infection, esp. cellulitis (Rich and Hare, 1999; Yosipovitch et al., 1998). Severe onychomycosis is particularly problematical in the presence of polyneuropathy, as pressure erosions of the nail bed and hyponychium may be noted late due to impaired sensation, increasing the risk of subsequent bacterial infections involving the bone. Di-

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abetics with onychomycosis show a higher rate for gangrene and diabetic ulcers (12.2%) compared to patients without onychomycosis (3.8%) (Gupta et al., 1998; Gupta and Humke, 2000). However, data on the prevalence of fungal foot infections in diabetic patients are rare and heterogeneous (Gupta et al., 1998; Gupta and Humke, 2000; Buxton et al., 1996; Alteras and Saryt, 1979; Levy 1997; Romano et al., 2001; Lugo-Somolinos and Sanchez, 1992).

During a meeting organized by the Diabetes Academy Bad Mergentheim we were able to assess the point prevalence of fungal foot infections in patients with type 1 diabetes mellitus. Apart from examining each patient's clinical situation, fungal spectrum, risk factors and complications, attention was focused on each patient's individual knowledge as well as the nature and scope of preventive measures taken by each patient.

Research Design and Methods

A four-page questionnaire was sent to everybody who was going to attend the 15th meeting of long-term type 1 diabetes mellitus of the Diabetes Academy Bad Mergentheim. In addition to basic data (age, sex, duration of disease, current therapy, history of vascular disease and peripheral neuropathy) it contained questions about delegates' level of knowledge concerning frequency of, previous therapy for, and possible prevention of fungal infections. Following introductory lectures on the day of the event, patients were invited to have their feet examined for fungal infections. The size and distribution of skin and nail lesions were recorded by an experienced physician. The severity of onychomycosis was classified for all toenails as follows: minimal (< 20% involvement of nail bed and plate), moderate (20 – 60%) and severe (> 60%). Skin scrapings and nail clippings were taken from any lesions suggesting mycotic infection. If more than one of the toenails appeared clinically abnormal, the two toenails that were clinically most likely to have onychomycosis were sampled. To ensure data protection, the questionnaires submitted and the clinical/mycological findings were coded for blind evaluation and later assignment. Under their code, the patients could call for their results after 4 weeks. In our mycological laboratory in Giessen, the specimens were analyzed by direct microscopy (KOH and Uvitex 2 B) and conventional culture technique using Kimmig's agar and selective agar for pathogenic fungi (with chloramphenicol and cycloheximide) (both Merck, Darmstadt, FRG). Incubation was performed at 30 °C for 4 weeks. Differentiation of dermatophytes was based on gross and microscopic criteria according to Rebell (Rebell and Taplin, 1970). Differentiation of yeasts was made by means of rice agar and the ID32 C auxanogram (BioMérieux, Marcy-l'Etoile, France). Infection was considered to be present in subjects with positive microscopy and/or culture of a dermatophyte. According to Gupta (Gupta et al., 1998) in the case of a yeast or non-dermatophyte mould non-dermatophyte fungal spores, filaments or pseudomycelium have to be observed by microscopy, in addition to the culture being positive for these organisms. It was not within the scope of our study to summon patients for repeat sampling.

Statistics

Fisher's exact test, Pearson's test and the chi square test were used for statistical evaluation, and the program SPSS 6.1.3. was used for all statistical calculations.

Results

A total of 185 people attended the meeting. 95 volunteered to be examined, all Caucasians, and all with a diagnosis of type 1 diabetes mellitus: 52 men (age range 23 – 77 years, mean 58.88, median 60.5, SD 10.53) and 43 women (age range 23 – 82 years, mean 55.6 years, median 5, SD 10.94). Mean disease duration was 36.5 years in men (age range 1 – 65 years, mean 35.15, median 36.5, SD 14.35) and 37.6 in women (age range 7 – 60 years, mean 37.57, median 40, SD 3.52). Nineteen patients did not use any drugs other than insulin, most of the remaining took antihypertensives and one patient took prednisolone 15 mg/d for rheumatic disease. No clinical indication of foot mycosis was seen in 17 patients (17.9%), and sampling was deemed unnecessary. Of those in whom there was clinical suspicion of disease (82.1%, n = 78), 109 specimens were taken. In 65 patients (68.4%), either direct preparation or culture was found to be positive. Isolated skin mycoses were mycologically confirmed in 9 patients (5 toe webs, 4 soles), onychomycosis in 28, and combined skin and nail mycoses in another 28 patients (8 toe webs, 20 soles). Clinical suspicion of skin mycosis (n = 41) was mycologically confirmed in 90.2% (n = 37): direct microscopy was positive in 13, culture was positive in 1, both were positive in 23 cases. Clinical suspicion of onychomycosis (n = 64) was mycologically confirmed in 87.5% (n = 56): direct microscopy was positive in 33, culture was positive in 2, both were positive in 21 patients. The 3rd and 4th interdigital space and nails of the big toes were most often affected. Of the patients with onychomycosis (n = 64) diagnosed clinically, 25 were minimally affected, 16 were moderately affected and 23 were severely affected, in most cases with distal subungual onychomycosis (DSO) or total dystrophic onychomycosis (TDO) resp. Skin/nail mycosis was found to correlate significantly with increasing age (p = 0.03) and male sex (p = 0.01).

The relationship between clinical finding, mycological result and subjective patient assessment is shown in Fig. **1**. It is evident that in particular the actual frequency of onychomycosis is underesti-

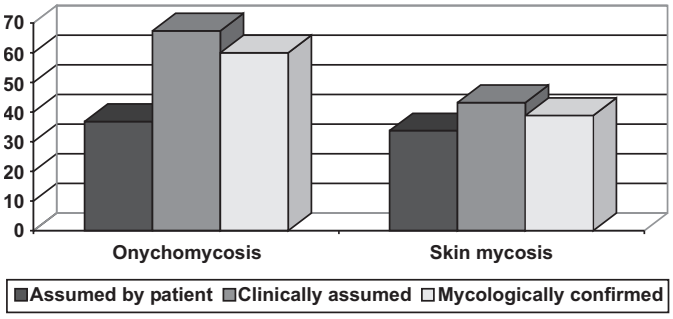

Fig. **1** The relationship between clinical findings, mycological results and subjective patient assessments (%).

Table **1** Relationship between subjective patients' assessment and mycological result, interestingly there was a marked underestimation of skin mycosis (results proven by direct microscopy and/or culture)

	Assumed by patient	*Correctly Yes*	*Wrong/ false*
Skin mycosis	Yes (n = 25)	13 (52%)	12 (48%)
	No (n = 49)	16 (32%)	**33 (67%)**
	no statement (n = 21)		
Onychomycosis	Yes (n = 33)	27 (82%)	6 (18%)
	No (n = 38)	18 (47%)	20 (53%)
	no statement (n = 24)		

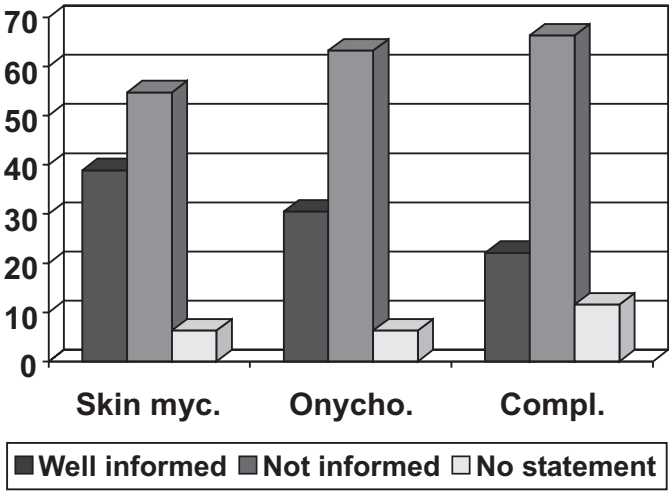

Fig. **2** Patients' level of information concerning skin mycosis, onychomycosis and complications of fungal infections (data in %, n = 95).

mated, and that patients have difficulty assessing the presence or absence of skin mycoses (Table **1**). Of those patients who thought they had skin mycoses, only 52% were correct. For onychomycosis, the percentage of "correctly yes" (related to total yes) was 81.8%, of "correctly no" (related to total no) 52.6%. With regard to skin mycoses it appears especially interesting that most of those who had no suspicion but positive mycology (n = 18) had mycoses on the soles (n = 11) rather than in the toe webs (n = 5).

These results also correlate with patients' assessment of their own level of, and need for information about fungal diseases (Fig. **2**). A need for information was stated by 83.2% of patients with skin mycosis and by 88.4% with onychomycosis. The great interest in these conditions was reflected by the fact that 64.1% of the patients called for their laboratory findings after 4 weeks.

In the questionnaire, 82.1% of the patients said that they had previously suffered from mycosis and 62.1% had experienced repeated fungal infections. In 53.8% the diagnosis had been established by a physician, 37.2% had diagnosed the infection themselves, and 9% were diagnosed by a chiropodist or friends. 85.5% of these patients had foot/foot nail infections. Asked for details of previous therapy, 64.5% of patients said that they treated the disease topically with creams, lotions, powder or lacquer. 11.4% had undergone systemic therapy with tablets or capsules, another 24.1% had had a combination of both treatments. Of the 75 patients who answered the question about successful therapy, 34.7% reported rapid healing, 32.2% lengthy but finally successful treatment, and 24% no healing. In 9.3% the success of therapy was not determined. Two patients reported the development of erysipelas as a complication of fungal infection.

Table **2** Relationship between mycological findings (skin and/or nail mycosis) and regular skin care (n = 91)

	*Onychomycosis**	*Skin mycosis**
n = 13 visiting a doctor	9 (69.2%)	4 (30.8%)
n = 21 visiting a chiropodist	14 (66.7%)	5 (23.8%)
n = 18 visiting both	11 (61.1%)	7 (38.9%)
n = 39 visiting neither	18 (46.1%)	16 (41%)

* direct microscopy and/or culture positive

32.6% of patients reported receiving regular medical care with attention to fungal infections, most of them 2 – 4 times a year. 41% said that they were regularly treated by a chiropodist. The mycological results for patients with active prevention are shown in Table **2**. It is remarkable that diabetics who had neither medical care nor treatment by a chiropodist did not show worse results.

64.2% of the patients said that they examined their feet every day for injuries/infections. 73.7% used skin cream or oil for foot care. Antifungal preparations were applied preventively by 17.9%. All these patients were clinically suspected of having mycotic infections. Only one was mycologically negative, in 11 direct microscopy was positive, and in 5 both direct microscopy and culture were positive (3 soles, 1 nail and 1 sole and nail). Prophylaxis had mainly concentrated on the toe webs. Another two patients had taken systemic antimycotics because of onychomycosis (itraconazole and terbinafine, respectively); both had positive direct microscopy.

41% of patients undertook regular sporting activities, 50.5% using public showers and swimming baths, and 87.5% wearing bathing shoes. Occurrence of fungal infections in family members was reported by 24.2% and denied by 43.2%; 32.6% made no statement. The most frequently reported complications included disturbed circulation (n = 25), changes in foot shape (n = 23) and polyneuropathy (n = 20). Only one patient suffered from a diabetic ulcer. Table **3** shows the frequency of foot and nail mycoses in these subgroups. The results are not different from those obtained in the overall group.

Results of Mycological Examination

Of 48 relevant organisms isolated, 41 were dermatophytes, with *T. rubrum* predominating in both skin and nail mycoses (Table **4**). *T. rubrum* and *T. interdigitale* occurred together in one patient

Table **3** Frequency of onychomycosis and skin mycosis in patients suffering complications of diabetes

Complication	*Positiv mycological finding*	
	Onychomycosis	*Skin mycosis*
Polyneuropathy (n = 20)	13 (65%)	5 (25%)
Circulatory disturbance (n = 25)	16 (64%)	8 (32%)
Foot deformity (n = 23)	16 (69%)	10 (43%)

Table **4** Spectrum of fungal pathogens isolated

Pathogen	*Total number of isolates*	*In skin mycoses*	*In onycho-mycosis*
T. rubrum	36	17	19
T. interdigitale	5	3	2
C. guilliermondii	4	0	4
C. parapsilosis	3	1	2
Trichosporon mucoides	4	1	3

with onychomycosis. The yeasts *C. guilliermondii, C. parapsilosis* and *Tr. mucoides* are well known pathogens in onychomycosis (Haneke, 1991; Mayser et al., 1996). In one case of onychomycosis each they were isolated together with *T. rubrum.*

Discussion

Our study assessed the prevalence of pedal skin and nail mycoses in long-term type 1 diabetes mellitus. Our data are supplemented by the results of a questionnaire evaluating patients' knowledge of their condition. The results are surprising in several respects, as our group of patients was highly motivated as demonstrated by their attendance at the diabetes meeting, showing their interest by attendance and a high level of cooperation. In this group, 78 patients (82.1%) showed lesions suspicious of fungal infection, which were mycologically confirmed by direct microscopy and/or culture in 84.6% of these patients (66/78). Organisms were cultured in 47.4% (37/78) of the patients, *Trichophyton rubrum* predominating with 69.2%. Our results are in accordance with previous investigations (Gupta et al., 1998; Buxton et al., 1996; Alteras and Saryt, 1979; Levy, 1997; Romano et al., 2001; Lugo-Somolinos and Sanchez, 1992). Significant relationships were found with regard to gender (men more frequently affected) and age of the patients. The unexpectedly high number of mycoses in a highly motivated group of type 1 diabetes mellitus patients is particularly remarkable because 64.2% of them examined their feet daily for injuries or infections; 32.6% received regular medical care with attention to fungal infections, and 41% were regularly treated by a chiropodist. The probable reason for this is that even marked mycoses on the soles ("moccasin-type tinea"), which were mycologically confirmed in 24 patients, were often misinterpreted as dry skin, which is a well-known symptom of diabetic polyneuropathy. This might explain why moccasin-type tinea was misjudged even by experienced specialist physicians and chiropodists. On the other hand, the patients reported no acute infections in the days leading up to examination. Infections of the plantar skin caused by the anthropophlic fungus *T. rubrum* have a particularly aphlegmatic course, and the chronicity of these diseases is shown by the high co-occurence with onychomycosis in our group. Concerning prophylaxis, while 73.7% of the patients regularly performed foot skin care, only 17.9% reported using topical antimycotics prophylactically, and only one of these patients had a negative mycological diagnosis. This was probably due to the fact that prophylaxis mainly concentrated on the toe webs, while mocassin-type tinea was not recognized. It may also reflect the fact that in cases of severe moccasin-type tinea, topical therapy is rarely curative because of the thick horny layer of the soles. However, the newer systemic antimycotics (itraconazole, fluconazole, terbinafine) are effective and safe drugs in diabetes (Gupta and Humke, 2000; Farkas et al., 2002).

There are epidemiological implications of our results. Nearly 25% of our subjects told us that other members of their families also suffered from fungal infection of the feet. In addition, 41% of the patients played sport regularly, 50.5% of them using public showers and swimming baths. Whilst a high level of information about swimming pools as source of mycotic infections (Detandt, 1995) was suggested by the fact that 87.5% reported wearing bathing shoes, the unexpectedly high prevalence of foot mycoses raises concerns regarding the communal use of bathing and showering areas. Our results suggest a need for widespread education, which was confirmed by the patients: 83.2% said they needed more information about skin mycosis and 88.4% about onychomycosis. With this in mind, it appears remarkable that 37.2% of the patients had diagnosed their fungal disease themselves; only half of the diagnoses had been established by a physician. However, our study revealed a high proportion of false-positive and false-negative results for self-diagnosis of both onychomycosis and skin mycosis, carrying a risk of inappropriate treatment (Table **1**).

Apart from prevention, therapy seems to be also a problem. 82.1% of the patients said that they had suffered from mycosis in the past, 24% of these considered their previous treatment to be insufficient as it failed to achieve a cure. Considering the severity of mycoses observed in our study it is remarkable that 35.5% of the patients had undergone systemic antimycotic therapy with tablets or capsules and that 24.1% of them had received combined topical and systemic treatment. The actual number of therapy failures and reinfections is possibly higher than it should be due to insufficient education concerning disinfection of shoes, stockings, etc. In our study, no samples were taken from normal-appearing toenails. Interstingly Gupta found that in eight of 550 subjects (1.5%) the toenails appeared clinically normal: however, upon mycological examination there was evidence of onychomycosis (Gupta et al., 1998). Therefore, although not performed in our study, additional regular sampling from normal-appearing nails should perhaps be part of the check-up in diabetic foot care services.

In our group of subjects, skin and nail infections were often combined. The frequency of onychomycosis was only slightly higher in patients with diabetic complications such as polyneuropathy and disturbed circulation (approximately 64 – 69% affected) compared to the whole group (59% affected by onychomycosis).

Diabetic patients with onychomycosis were shown to have a higher rate of gangrene/diabetic ulcer (12.2%) than patients without onychomycosis (3.8%) (Gupta and Humke, 2000). As only one patient in our study was found to have diabetic ulcer, this again may reflect high motivation and disease self-management among this selective group.

Only two patients reported suffering from erysipelas, although this was not confirmed clinically. Considering the variety of mycoses and marked findings, this low number was most surprising to us.

Because of the study design (point prevalence) we were not able to generate matched pairs for our study population. Among dermatologic outpatients Abeck et al. found a prevalence of culture positive onychomycosis of 12.4% (Abeck et al., 2000). While looking for diabetic outpatients attending dermatologists (n = 550) Gupta (Gupta et al., 1998) found a prevalence of onychomyosis in 46 vs. 26% (clincical vs. mycologically confirmed). This roughly corresponds to our data of 58.9 vs. 26%. A correlation of onychomycosis with age and sex was also observed in the latter study. The odds ratio for toe nail onychomycosis was 2.77. In the subgroup of patients with type 1 diabetes mellitus, the rate of onychomycosis of 13% was lower than that in our study, but there are no details about the age breakdown. Yosipovitch (Yosipovitch et al., 1998) examined 238 type 1 diabetes mellitus patients and 122 healthy controls and found the prevalence of tinea pedis to be 32 vs. 7%. On the other hand, Buxton (Buxton et al., 1996) investigated 100 patients with type 1 diabetes mellitus and found that in well-controlled diabetics fungal infections are not commoner than in matched controls. The overall infection rate of both skin and nails was 19% and 17% in controls, but the study included the total body surface area as well as mucous membranes.

Among other studies that did not explicitly differentiate between types of diabetes mellitus, Lugo (Lugo-Somolinos and Sanchez, 1992) observed no difference in the frequency of onychomycosis in diabetes (29% in diabetics and 31% in controls). 12 of 31 diabetics had onychomycoses (39%). Romano (Romano et al., 2001) also reported only 7 positive results among 171 diabetics and thus no increased prevalence compared to 17/276 control patients. The percentage of patients with type 1 diabetes mellitus in this random sample survey was 9.4% (16/171). On the other hand, Alteras (Alteras et al., 1979) found that the frequency of onychomycosis increased in parallel with the level of blood glucose.

In summary, patients with diabetes would seem to have diagnostic, therapeutic and preventive needs with regard to mycotic diseases that have hitherto been underestimated. The patients themselves are highly interested in these matters. In particular, the frequency of moccasin-type tinea is underestimated apparently, because of the low grade of inflammation and the similarity to dry sebostatic skin often seen in diabetics. We recommend that family members of these high-risk patients be examined for mycosis. It would be interesting to compare our findings with results from less motivated groups of patients. We believe our results have important implications for the prevention, recognition and treatment of mycotic foot disease in diabetic patients.

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