

# Is Diabetes mellitus a risk factor for tinea pedis and onychomycosis?

## Diyabet mellitus onikomikoz ve tinea pedis için bir risk faktörü müdür?

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### SUMMARY


**Objective:** The objective of this study was to determine the frequency of onychomycosis and tinea pedis in patients with diabetes mellitus compared to non-diabetic control group with similar age and gender, to evaluate diabetic and epidemiological risk factors, and to determine the pathogens in onychomycosis and tinea pedis.


**Method:** A total of 167 patients followed-up for diabetes were enrolled in the study. The control group comprised 150 individuals with similar age and gender characteristics with the diabetic group. The demographic data for each subject were recorded in a questionnaire form by face-to-face interview with the consent of the patient. Data recorded in this questionnaire included age, gender, type and duration of diabetes, and hemoglobin A1c (HbA1C) levels. Clinical samples were collected separately from the toenails and the surrounding area and from the plantar and interdigital area of the feet for direct microscopic examination and culture.

**Results:** The co-occurrence of diabetes and tinea pedis was significantly increased in this study. *T. rubrum* growth was seen in a substantial proportion of the cases and intertriginous type was the most frequently observed type, similar to normal population. In this study, the correlation between diabetes types and onychomycosis or tinea pedis was not significant while longer duration of diabetes was found to increase susceptibility to fungal infections.

**Conclusions:** It was concluded that the frequency of onychomycosis and tinea pedis, as an important cause of morbidity in diabetes, should routinely be surveyed, any infections should be treated, and patients should be given training regarding the protective measures and risk factors.

**Keywords:** Diabetes mellitus, tinea pedis, onychomycosis

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### ÖZET

**Amaç:** Bu çalışmada diyabet mellituslu hastalarda onikomikoz veya tinea pedis sıklığının, diyabetik olmayan benzer yaş ve cinsiyete sahip kontrol grubu ile karşılaştırılarak belirlenmesi, diyabetik ve epidemiyolojik risk faktörlerinin değerlendirilmesi, onikomikoz ve tinea pedis etkenlerinin saptanması amaçlandı.

**Yöntem:** Diyabet tanısı ile takip edilen toplam 167 hasta çalışmaya alındı. Kontrol grubunu ise diyabet grubuyla benzer yaş ve cinsiyet özelliklerine sahip 150 hasta oluşturdu. Ayak tabanı, ayak parmak arası, tırnak ve çevresinden direkt mikroskopik inceleme ve kültür ekimi için her bölgeden ayrı ayrı olmak üzere klinik örnekler toplandı.

**Bulgular:** Çalışmamızda onikomikoz verilerimize benzer şekilde diyabet ile tinea pedis birlikteliği de anlamlı olarak artmıştı. Normal popülasyondaki oranlara benzer şekilde en sık intertriginöz tip görüldü ve olguların önemli bir kısmında *T. rubrum* üredi. Bu çalışmada onikomikoz ve tinea pedis ile diyabet tipi anlamsız bulunurken diyabet süresinin uzun olmasının fungal enfeksiyonlara eğilimi arttırdığı saptandı.

**Sonuç:** Diyabette önemli bir morbidite sebebi olan onikomikoz ve tinea pedis sıklığı rutin olarak araştırılmalı, mevcut enfeksiyon tedavisi edilmeli ve hastaların uymaları gereken koruyucu önlemler ve risk faktörleri hakkında eğitimleri gerektiği sonucuna varılmıştır.

**Anahtar sözcükler:** Diabetes mellitus, tinea pedis, onikomikoz

## INTRODUCTION

Diabetes is an important disease with a frequency of 7.2% that leads to mortality and morbidity and impairs quality of life. The prevalence of skin symptoms in diabetes is 30% and a significant proportion of these are skin infections.<sup>1</sup> Hyperglycemia and insulin deficiency promote the occurrence of cutaneous fungal and bacterial infections in patients with diabetes mellitus by cellular immunity impairment and affecting polymorphonuclear leucocytes, thereby leading to phagocyte dysfunction.<sup>2,3</sup>

Onychomycosis and tinea pedis constitute 30% of cutaneous fungal infections that occur in patients with diabetes. These infections may lead to serious bacterial infections, foot ulcers and more importantly diabetic foot as a result of impaired skin integrity, if left untreated.

Relapse and reinfection are frequently observed once onychomycosis and tinea pedis occur in patients with diabetes due to immunopathy, vasculopathy and neuropathy.<sup>4</sup> There are many studies reporting either similar or increased prevalence of onychomycosis and tinea pedis in patients with diabetes compared to normal population.

## MATERIAL AND METHODS

The objective of this study was to determine the frequency of onychomycosis and tinea pedis in patients with diabetes mellitus compared to non-diabetic control group with matching age and gender, to evaluate diabetic and epidemiological risk factors, and to determine the pathogens in onychomycosis and tinea pedis.

A total of 167 patients followed-up for diabetes were enrolled in the study. The control group comprised 150 individuals with similar age and gender characteristics with the diabetic group. Informed consent form was taken from all patients. The demographic data for each subject were recorded in a questionnaire form by face-to-face interview with the consent of the patient. Data recorded in this questionnaire included age, gender, type and duration of diabetes, and hemoglobin A1c

(HbA1C) levels. Information on the diabetic complications of neuropathy and peripheral vascular system diseases were evaluated by reviewing available patient records. For this study an ethical committee approval had been received. All the data from the questionnaires were entered into Statistical Package for Social Sciences (SPSS) 11.5 statistical software. Fasting blood glucose levels were measured for all control subjects. The inclusion criteria for both groups were established as not having been treated with oral and/or topical antifungal agents within the last two months, absence of a dermatological disease that may affect the nails and/or feet such as psoriasis, eczema or lichen planus, and absence of an immunosuppressive condition.

Clinical samples were collected separately from the toenails and the surrounding area and from the plantar and interdigital area of the feet for direct microscopic examination and culture. Slides prepared using potassium hydroxide (KOH) were examined first under X10 and then X40 magnification. The samples were inoculated into Sabouraud Glucose Agar (SGA) (Oxoid) media and Sabouraud Glucose Agar containing cycloheximide-chloramphenicol-gentamicin (SGA-CCG). Yeast colonies were determined at species level by appearance in SGA medium as well as structural characteristics in Jerm tube test corn meal Tween 80 medium and by color and shape in CCA.

Species were determined based on characteristics seen in lactophenol cotton blue stain and BCPMSG (Bromcresol purple milk solid glucose agar) medium. Hair perforation test and urea test were also used.

Statistical analysis of the data was performed using SPSS 11.5 software. A p-value <0.05 was considered statistically significant. Mean  $\pm$  standard deviation was provided for numerical variables as descriptive statistics.

## RESULTS

Hyphe and/or spores were seen in 64 (38.4%) of 167 subjects in the KOH examination of samples

collected from nails of the hands and feet while in the control group, positive KOH examination was found in 36 (24.0%) of 150 subjects. The difference between the two groups was statistically significant ( $p < 0.05$ ) (Table 1).

No statistically significant difference was found

between diabetic group and controls in terms of types and pathogens of onychomycosis. The most common type of onychomycosis in patients with diabetes mellitus is distal subungual onychomycosis (DSO) and most common fungus species are *Trichopyton rubrum* ( $p > 0.05$ ) (Table 2).

**Table 1:** Prevalance of onychomycosis in control and diabetic group

Gender	Diabetic group		Control group	
	OM (+) (%)	OM (-) (%)	OM (+) (%)	OM (-) (%)
Male	37 (22.2)	40 (24.0)	24 (16.0)	51 (34.0)
Female	27 (16.2)	63 (37.7)	12 (8.0)	63 (42.0)
Total	64 (38.4)	103 (61.7)	36 (24.0)	114 (76.0)

P değeri: 0,017 ( $p < 0,05$ )

P değeri: 0,022 ( $p < 0,05$ )

**Table 2:** Types of onychomycosis in patients with diabetes mellitus and distribution of pathogen agents

Fungal pathogen	Onychomycosis type				
	DSO (%)	WSO (%)	PSO (%)	TDO (%)	Total (%)
Dermatophytes					
Trichopyton rubrum	15 (37.5)	1 (2.5)	1 (2.5)	8 (20.0)	25 (62.5)
Trichopyton mentagrophytes	1 (2.5)	1 (2.5)	0 (0)	1 (2.5)	3 (7.5)
Yeasts					
Candida albicans	4 (10.0)	0 (0)	0 (0)	1 (2.5)	5 (12.5)
Candida parapsilosis	2 (5.0)	0 (0)	0 (0)	0 (0)	2 (5.0)
Candida crusei	1 (2.5)	0 (0)	0 (0)	1 (2.5)	2 (5.0)
Molds					
Fusarium sp	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2.5)
Alternaria sp	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2.5)
Aspergillus sp.	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2.5)
Total	26 (65.0)	2 (5.0)	1 (2.5)	11 (27.5)	40 (100.0)

DSO: Distal subungual onychomycosis

WSO: White superficial onychomycosis

PSO: Proksimal subungual onychomycosis

TDO: Total distrofik onychomycosis

Hyphe and spores were seen in 61 (36.6%) of the samples collected from plantar and interdigital areas of 167 subjects with diabetes while KOH positivity was found in 39 (26.0%) control subject. The difference between the two groups was statistically significant ( $p < 0.05$ ). The most common type of tinea pedis in patients with diabetes mellitus is intertriginous type and most common fungus species are *Trichopyton rubrum*. No statistically significant difference was found between the groups in terms of tinea pedis types

and pathogens (Table 3).

In subjects with diabetes, no statistically significant difference was found between onychomycosis and tinea pedis and the type of diabetes and HbA1c levels ( $p > 0.05$ ). However, there was a significant association between the frequency of onychomycosis and tinea pedis and the duration of diabetes ( $p < 0.05$ ), where there was a significant increase in patients with more than 10 years of diabetes (Table 4).

**Table 3:** Types of tinea pedis in patients with diabetes mellitus and distribution of pathogen agents

Fungal pathogen	Tinea pedis types				
	Intertriginous (%)	Hyperkeratotic (%)	Vesiculobullous (%)	Hyperkeratotic + intertriginous (%)	Total (%)
<b>Dermatophytes</b>					
Trichopyton rubrum	7 (21.2)	8 (24.3)	0 (0)	3 (9.1)	18 (54.6)
Trichopyton mentagrophytes	2 (6.1)	1 (3.0)	0 (0)	0 (0)	3 (9.1)
<b>Yeasts</b>					
candida albicans	8 (24.2)	0 (0)	0 (0)	0 (0)	8 (24.2)
candida parapsilosis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Candida crusei	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Molds</b>					
Fusarium spp.	2 (6.1)	0 (0)	0 (0)	0 (0)	2 (6.1)
Skorulopsus bv.	1 (3.0)	0 (0)	0 (0)	0 (0)	1 (3.0)
Aspergillus spp.	1 (3.0)	0 (0)	0 (0)	0 (0)	1 (3.0)
<b>Total</b>	<b>21 (63.0)</b>	<b>9 (27.0)</b>	<b>0 (3.0)</b>	<b>3 (18.0)</b>	<b>33 (100)</b>

T.rubrum: Trichopyton rubrum

T.mentagropytes: Trichopyton mentagropytes

C. albicans: Candida albicans

**Table 4:** Risk factors associated with diabetes mellitus in onychomycosis

Risk factors associated with diabetes mellitus		OM (-)		OM (+)		Total (%)	P value
		N	%	N	%		
Type of diabetes	Tip 1	15	9	5	3	20 (12)	P=0,2
	Tip 2	91	54,5	56	33,5	147 (88)	P>0,05
Diabetes duration	0-1	10	6,0	0	0	10 (6,0)	P=0,000 P<0,05
	2-5	24	14,4	5	3,0	29 (17,4)	
	6-10	32	13,8	16	9,6	48 (23,4)	
	11-20	44	26,3	34	20,4	78 (46,7)	
	20 yıldan fazla	2	1,2	9	5,4	11 (5,6)	
HbA1c	Normal	9	5,4	2	1,2	11 (6,6)	P=0,155
	High	94	56,3	62	37,1	156 (93,4)	P>0,05

## DISCUSSION

The relationship between diabetes and onychomycosis is still controversial despite many controlled<sup>4,5,6,7,8,9</sup> and uncontrolled<sup>10,11,12</sup> studies investigating co-occurrence of diabetes and onychomycosis. The rates show a wide range and the frequency of onychomycosis is reported to be 6-85% in these studies. Diabetes is mentioned as a facilitator factor for onychomycosis in some studies, while others have reported that the frequency of onychomycosis in diabetes is similar to non-diabetic controls (Table 5).

Although co-occurrence of diabetes and onychomycosis is still debated, our opinion is that diabetes promotes the development of onychomycosis. This may be accounted for by the

fact that factors that facilitate the occurrence of onychomycosis such as peripheral vascular disease, immunosuppression, trauma and peripheral neuropathy are more common than normal population<sup>13,18</sup>.

Similar to our data, the co-occurrence of diabetes and tinea pedis was significantly increased in this study. *Trichopyton rubrum* growth was seen in a substantial proportion of the cases and intertriginous type was the most frequently observed type, similar to normal population. Limited number of studies have been performed on this subject so far. In an uncontrolled study by Milnaric et al., the frequency of tinea pedis was found to be 24% and yeasts were the most frequently isolated pathogens<sup>19,20</sup>.

**Table 5:** Studies on the prevalence of onychomycosis in patients with diabetes mellitus

Author's name and year	Controlled/uncontrolled study	The association between diabetes and onychomycosis	Number of Cases	The most frequent agent	Ratios	
					Diabetes group (%)	Control group (%)
Somonolis et al.(4)	Controlled	Non significant	100	T. rubrum	31.0	33.0
Sert et al.(8)	Controlled	Non significant	180	T.rubrum	14.4	14.0
Romona et al..(12)	Controlled	Non significant	171	T. mentagropyhtes	12.0	11.0
Leelavathi et al.(13)	Controlled	meaningful	151	T. rubrum	22.0	11.0
Dogra et al.(5)	Controlled	Meaningful	400	Yeasts in subjects with DM, in controls T. rubrum	17.0	6.8
Saunte et al.(11)	Uncontrolled	Meaningful	278	Dermatophytes T. rubrum	22.0	----
Gupta et al(10)	Uncontrolled	Meaningful	550	T. rubrum	26.2	----
Buguerra et al.(14)	Uncontrolled	Meaningful	---	Dermatophytes	----	----
Aşçı et al.(4)	Controlled	Meaningful	40	T. rubrum	85.0	15.0
Mayser et al.[15]	Uncontrolled	Meaningful	95	T. rubrum	59.0	----
Josipovitch et al.(16)	Controlled	Meaningful	278	No cultures performed	6.0	----
Hekimsoy et al(17)	Uncontrolled	Meaningful	100	No cultures performed	18.0	----

In this study, the correlation between diabetes types and onychomycosis or tinea pedis was not significant while longer duration of diabetes was found to increase susceptibility to fungal infections, and our results were similar to the findings of Mil, Dogra et al. and Gülcan et al<sup>21,22</sup>. The frequency of tinea pedis and onychomycosis was particularly increased in patients with longer than 10 years of diabetes. Last studies determine that The development of onychomycosis or tinea

pedis was significantly related to type 2 DM, increasing age, and male gender. The most common isolate was *Trichophyton rubrum*<sup>7</sup>.

The incidence and morbidity of fungal infections in uncontrolled or undiagnosed diabetic patients may be reduced by controlling diabetes and using antifungal agents.<sup>23</sup> Based on this, it has been suggested that the possibility of other superficial fungal infections such as onychomycosis or tinea pedis will be lower in patients with normal levels

of HbA1c<sup>24</sup>.

While usually being asymptomatic in healthy individuals, onychomycosis or tinea pedis may lead to serious bacterial infections and foot ulcers due to impaired tissue integrity and most importantly may present with diabetic foot, when left untreated.<sup>25</sup> Therefore, it was concluded that the frequency of onychomycosis and tinea pedis, as an important cause of morbidity in diabetes, should routinely be surveyed, any infections should be treated, and patients should be given training regarding the protective measures and risk factors.

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