

The Incidence of Asymptomatic Onychomycosis in Diabetes mellitus

Rathur HM¹, Housley A² and Rajbhandari SM^{1,3}

¹Diabetes Unit, Lancashire Teaching Hospital, Chorley, United Kingdom

²Podiatry Department, Lancashire Care Foundation Trust, United Kingdom

³University of Central Lancashire, United Kingdom

*Corresponding author: Satyan M Rajbhandari, Honorary Clinical Professor, University of Central Lancashire, Tel: 441257 245028; Fax: 441257 245208; E-mail: Satyan.rajbhandari@lthtr.nhs.uk

Received date: July 14, 2015; Accepted date: August 27, 2015; Published date: August 30, 2015

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Abstract

In people with diabetes mellitus (DM), fungal infection is believed to occur more frequently. Toenail onychomycosis (TOM), a common type of fungal infection is asymptomatic in most cases. In order to study the incidence and prevalence of previously undiagnosed TOM in a population of subjects with DM attending for routine annual foot screening, nail plate and sub-ungual tissue samples were collected for microbiological analysis. Examining clinicians also made a graded visual diagnosis of onychomycosis at the same visit. Various blood samples markers of diabetes and its associated complications were also reviewed. 88 consecutive subjects with diabetes [mean age 78.4 (\pm SD 10.2) and duration 7.9 (\pm SD 8.1) years] were recruited to the study, and 29.5% had a positive (laboratory) diagnosis of TOM. There was no correlation with the incidence of TOM and duration of diabetes, other demographic data, or various biochemical parameters, but there was a trend for association of TOM to reduced sensation in healthy people with diabetes. Clinician were making more accurate (82%) diagnosis of TOM than that of healthy nail plate (53.8%) when compared with microbiological studies. As TOM is very common and the benefit of its treatment has not been confirmed, the value of routine laboratory screening for TOM as part of annual assessment of diabetes is not established. Our study shows that TOM is very common so further studies are needed to see if screening and treatment of TOM will prevent future secondary foot and leg infection in people with diabetes.

Keywords: Toe; Onychomycosis; Diabetic foot; Fungal infection

Introduction

Diabetes mellitus (DM) is a common metabolic problem and its global prevalence is rising day by day [1]. As a result we are seeing more complications related to diabetes. Individuals with diabetes have an increased susceptibility to infections [2]. In vitro evidence shows that neutrophil function is compromised and that antioxidant systems and humoral immunity may be depressed in people with diabetes [3]. Therefore unusual infections are frequently seen in people with diabetes [4]. Fungal infection is believed to occur more frequently in subjects with diabetes and is an important factor in the development of cellulitis [5].

Fungal infection is common in general population. In one large epidemiological study of 90,000 people attending their general practitioners and dermatologists in 16 European countries, almost a third had fungal foot infection [6]. Most fungal foot infections were caused by *Trichophyton* species but *Candida* species and *Aspergillus* species were also frequently isolated [6]. *Trichophyton* causes toe nail onychomycosis (TOM), which accounts for about one third of the cutaneous fungal skin infections [7]. Similar result was seen in recent study too [8]. Diabetes was one of the risk factors for the development of fungal infection [6,9]. Many other studies have also highlighted an increased incidence of onychomycosis and other superficial fungal infections in these patients [10,11]. Although hyperglycaemia is believed to be the cause of increased fungal infection in diabetes, there is no clear evidence if TOM is more common with poor metabolic control or with any other associated risk factors.

Aims

The aim of this study was to assess the prevalence of toe nail onychomycosis (TOM) in asymptomatic patients with diabetes attending annual foot screening programme and to identify risk factors associated with it.

Patients and Methods

Patients were recruited from community annual diabetic foot screening clinic in which all patients with diabetes attends once a year. Over a period of 18 month all consecutive subjects attending this clinic were approached by a single podiatrist for this study. In our area all podiatrists are trained to perform annual diabetic foot screening and their screening results are regularly audited as per screening programme. Subjects with symptomatic onychomycosis, defined by those who consulted their general practitioner to seek treatment for the appearance of their toe nail and those who were on anti-fungal treatment were excluded from the study. Similarly patients who had amputation of more than 2 toes were also excluded as the subungal samples were collected for the study. The local Research and Ethics committee reviewed and approved this study.

Written consent was obtained for this study following which annual foot screening examination was performed that involved brief history about present and past foot problems and clinical examination. Foot examination was performed with inspection for the presence of ulcers, deformities, calluses and condition of skin. Vascular assessment was done by palpation of dorsalis pedis and posterior tibial arteries on both sides. Absence of more than one pulse was classified as ischaemia. Neurological examination was performed by testing pressure sensation

using 5.07 Semmes-Weinstein monofilament and pain sensation using neuro-tip at 8 predetermined anatomical sites. Absence of sensation on more than 3 areas was classified as neuropathy. A composite score, which is used locally for screening, was used to determine whether the patient was in high, medium or low risk category. The clinician inspected the toenails and made the clinical probability of diagnosis of onychomycosis by using a 4 point score (unlikely, less likely, likely and most likely to have TOM) during the study. Subungual material and nail clippings were collected from the great and the 4th toe on each side and transported to the laboratory in a sterile pot as per standard clinical practice. Once the sample was received in the microbiology department, part of the sample was digested in 20% KOH for microscopy and remaining sample cultured on Sabouraud's agar with chloramphenicol and actidione.

Asymptomatic toe nail onychomycosis (TOM) was defined as the presence of fungus on microscopy and/or growth of typical dermatophytes on culture in the screened patients as they did not have any symptoms related to TOM. Isolation of other fungus on culture was considered contamination in the absence of positive microscopy. Laboratory staff that performed these tests was blinded to the clinical data. The result of HbA_{1c}, lipids, creatinine and microalbuminuria performed within last year were obtained from central pathology database. No treatments were offered to subjects with TOM as the benefit of treating asymptomatic cases has not been established.

Statistical analysis

Mann-Whitney test was used to compare continuous data between subjects who did and did not have onychomycosis. Chi square test and Fischer exact test was used to compare association between various risk factors and onychomycosis.

	Normal	Onychomycosis
Number	62	26
Sex M:F	25:37:00	14:12
Mean age (years)	69.7 (± 10.9)	73.7 (± 7.5)
Mean diabetes duration (years)	7.3 (± 7.1)	9.5 (± 10.0)
Mean HbA _{1c} (%)	7.0 (± 1.7)	6.8 (± 0.9)
Mean HbA _{1c} (mmol/mol)	53 (± 19)	51 (± 10)
Data are expressed as mean ± standard deviation		

Table 1: Characteristics of the patients (n=88).

Results

94 subjects were recruited for the study but 6 were excluded as they did not have diabetes or were recruited twice. The results of 88 consecutive patients with diabetes [mean age 78.4 (± SD 10.2) and duration 7.9 (± SD 8.1) years] were analysed. Of this 23 were treated with diet alone 48 with oral hypoglycaemic agents, 15 subjects were treated with insulin and the treatment was not recorded in 2 subjects. Onychomycosis was present in 26 (29.5%) subjects. There were no differences in age, duration of diabetes and HbA_{1c} between subjects with and without onychomycosis (Table 1). There was also no difference (p>0.05) between male and females, absent foot pulses, foot deformity and history of foot ulcers in subjects with or without

onychomycosis (Figure 1). However there was a trend for absent mono-filament sensation to be more prevalent in subjects with onychomycosis (42.3% Vs 21.0%; p=0.06). There was no difference in the prevalence of asymptomatic onychomycosis between subjects with low, medium or high risk diabetic foot (Table 2). The sensitivity and specificity of examining podiatrists making clinical diagnosis of onychomycosis was 53.8% and 82.3% and the positive and negative predictive value of clinical diagnosis was 56% and 81% respectively.

	Normal (63)	Infected (25)
Low	20 (31.7%)	6 (24%)
Medium	32 (50.8%)	11 (44%)
High	11 (17.5%)	8 (32%)

Table 2: There was no difference (p>0.05) in the prevalence of asymptomatic neuropathy between low risk (no peripheral vascular disease, deformity or neuropathy), medium risk (one risk factor) or high risk (more than one risk factor and/or history of foot ulcers) group patients.

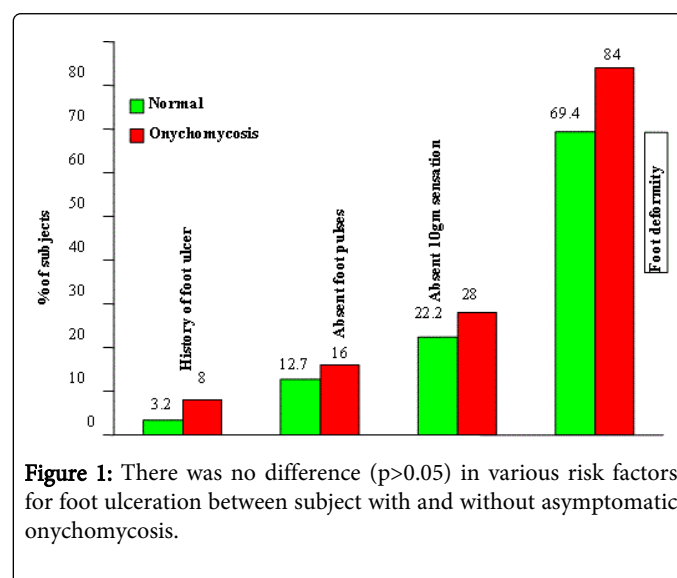


Figure 1: There was no difference (p>0.05) in various risk factors for foot ulceration between subject with and without asymptomatic onychomycosis.

Discussion

Various epidemiological studies in general population shows the prevalence of TOM to vary between 2.7% to 11.1% [12-14]. There are limited studies on the prevalence of onychomycosis in people with diabetes. In our study, we did not include subjects without diabetes because the samples were collected during annual diabetic foot examination. We found that almost a third of asymptomatic diabetic population had onychomycosis which is much higher than these published observations. In one multicentre study conducted in USA, onychomycosis was present in 26% asymptomatic subjects with diabetes consulting dermatologists, which is similar to our finding of 29.5% when they were assessed during routine foot screening [15]. In Denmark, onychomycosis was present in 30.5% of subjects with type 1 diabetes [16]; however in our study majority had type 2 diabetes.

We found that clinical observation was good to exclude diagnosis of onychomycosis but not good for diagnosis. The clinical appearance of the nail varies with the nature of the infecting organism. Similarly

several conditions such as previous trauma, onychogryphosis, psoriasis, lichen planus etc. may be associated with nail dystrophy. Many conditions such as bacterial infection, yellow nail syndrome can cause a change in the appearance of the nail [17]. In a study in Belgium, the positive predictive values of the dermatologist's diagnoses of onychomycosis performed by two independent dermatologists were 57.8% and 35.6%, and the negative predictive values were 85.0% and 90.5% [18]. This is consistent with our finding that clinical appearance may not be accurate for diagnosis but is good for exclusion of onychomycosis.

In few studies, old age, male gender and peripheral vascular disease were associated with increased prevalence of onychomycosis [14-19]. We did not find any such association, however we found a trend for higher prevalence of onychomycosis in subjects who had absent monofilament sensation. We failed to find any association between other risk factors for foot ulceration such as foot deformity, visual impairment, inappropriate footwear and previous ulceration. In one Danish study onychomycosis was associated with increasing age but not with gender, type of diabetes, lower extremity arterial disease, neuropathy, toe amputation or oedema [20].

We could not compare people with diabetes with healthy control as these do not routinely attend podiatry clinics. We did not collect data on recent use of antibiotics or the type of foot wear which might affect the prevalence. We used clinical examination to diagnose ischaemia and neuropathy which is the most commonly used method in the diabetic annual foot screening programme. We used only one fully trained clinician to collect data and to diagnose TOM clinically to avoid inter-observer variation, despite these, there is still a possibility of variation in collecting clinical data which are mostly subjective. In conclusion, we found asymptomatic onychomycosis to affect about a third of the population with diabetes and not to be associated with known risk factors of foot ulceration. Therefore routine screening and treatment for onychomycosis as suggested by some authors [21] may not be necessary. Further prospective studies are needed to assess if the treatment of asymptomatic TOM will prevent the future complications of bacterial infection in foot and leg of these patients.

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