



Retrospective Analysis of Onychomycosis Risk Factors Using the 2003-2014 National Inpatient Sample

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ABSTRACT Introduction: Onychomycosis, a fungal nail infection, is associated with significant morbidity and negative impact on quality of life. Therefore, understanding associated risk factors may inform onychomycosis screening guidelines.

Objectives: This retrospective study investigated common demographic and comorbidity risk factors among hospitalized patients using the National Inpatient Sample.

Methods: The 2003-2014 National Inpatient Sample (NIS) database was used to identify onychomycosis cases and age and sex matched controls in a 1:2 ratio. Chi-square tests and T-tests for independent samples were utilized to compare categorical and continuous patient factors. Demographic and comorbidity variables significant ($P < 0.05$) on univariate analysis were analyzed via a multivariate regression model with Bonferroni correction ($P < 0.0029$).

Results: 119,662 onychomycosis cases and 239,324 controls were identified. Compared to controls, onychomycosis patients frequently were White (69.0% versus 68.0%; $P < 0.001$), Black (17.9% versus 5.8%; $P < 0.0001$), and insured by Medicare or Medicaid (80.1% versus 71.1%; $P < 0.0001$). Patients had greater hospital stays (9.69 versus 5.39 days; $P < 0.0001$) and costs (\$39,925 versus \$36,720; $P < 0.001$) compared to controls. On multivariate analysis, onychomycosis was commonly associated with tinea pedis (odds ratio [OR]: 111.993; $P < 0.0001$), human immunodeficiency virus (OR: 4.372; $P < 0.001$), venous insufficiency (OR: 6.916; $P < 0.0001$), and psoriasis (OR: 3.668; $P < 0.001$).

Conclusions: Onychomycosis patients had longer hospital stays and greater costs compared to controls. Black patients were disproportionately represented among cases compared to controls. Onychomycosis was associated with tinea pedis, venous insufficiency, human immunodeficiency virus, psoriasis, obesity (body mass index [BMI] ≥ 30 kg/m²), peripheral vascular disease, and diabetes with chronic complications, suggesting that inpatients with onychomycosis should be screened for these conditions.

Introduction

Onychomycosis, a fungal nail infection, is the most frequent nail condition seen in the clinical setting worldwide [1-4]. Onychomycosis is not just a cosmetic problem, and patients often have poor quality of life both physically and psychologically. Fortunately, timely and adequate treatment treats diseases and alleviates patient distress [5-7]. Onychomycosis prevalence is more common among men⁸ and increases with older age [8-10], and was the most common nail diagnosis among ambulatory care patients in the United States from 2007-2016 [11]. Previous studies have analyzed associations of comorbidity risk factors with onychomycosis and their impact on prognosis [12-18]. A comprehensive analysis of risk factors among a large, matched, and nationally representative cohort of hospitalized onychomycosis patients may help to develop screening guidelines in the United States.

Objectives

The primary objective was to identify risk factors associated with development of onychomycosis among hospitalized patients compared to age and gender matched controls. The secondary objective was to characterize demographics of onychomycosis patients compared to controls.

Methods

The 2003-2014 National Inpatient Sample (NIS) database, a publicly available all-payer inpatient healthcare database developed for the Healthcare Cost and Utilization Project (HCUP) that contains unweighted data for about 7 million hospital stays each year [19], was utilized for this retrospective analysis. NIS was queried using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 110.1 for “Dermatophytosis of nail”, yielding 119,687 cases. Cases were matched to controls in a 1:2 ratio by age and sex. We analyzed demographics (age, sex, race), other patient information (quarter of discharge, length of stay, hospital costs/deaths, hospital region, insurance type), and associated comorbidities.

The most common comorbidities associated with a diagnosis of onychomycosis from available variables in the National Inpatient Sample were identified through a descending counts frequency analysis. Co-morbidities of interest that were unavailable through NIS including tinea pedis, hyperhidrosis, venous insufficiency, and psoriasis were identified through ICD-9-CM codes which were recoded into new variables (Table 1).

Statistical analyses were completed using IBM SPSS software v28.0.1.1. Patient distribution of demographic factors (age, sex, race), other patient information (quarter of discharge, hospital deaths, hospital region, insurance type), and

Table 1. Comorbidity Variables Including Relevant ICD-9 Codes

Variable	ICD-9 Codes for Each Variable
Tinea Pedis	110.4
Hyperhidrosis	780.8, 705.21, 705.22
Diabetes with chronic complications	Co-morbidity variable provided by the National Inpatient Sample database
Diabetes without chronic complications	Co-morbidity variable provided by the National Inpatient Sample database
Human Immunodeficiency virus/AIDS	042, V08
Peripheral Vascular Disease	Co-morbidity variable provided by the National Inpatient Sample database
Venous insufficiency	454.0, 454.1, 454.2, 454.8, 454.9, 459.10, 459.11, 459.12, 459.13, 459.19, 459.2, 459.30, 459.31, 459.32, 459.33, 459.39, 459.81, 459.89
Obesity (body mass index \geq 30 kg/m ²) [‡]	Co-morbidity variable provided by the National Inpatient Sample database
Psoriasis	696.0, 696.1
Deficiency Anemias	Co-morbidity variable provided by the National Inpatient Sample database
Hypertension	Co-morbidity variable provided by the National Inpatient Sample database
Chronic Pulmonary Disease	Co-morbidity variable provided by the National Inpatient Sample database
Congestive Heart Failure	Co-morbidity variable provided by the National Inpatient Sample database
Depression	Co-morbidity variable provided by the National Inpatient Sample database
Hypothyroidism	Co-morbidity variable provided by the National Inpatient Sample database
Renal Failure	Co-morbidity variable provided by the National Inpatient Sample database
Fluid and Electrolyte Disorders	Co-morbidity variable provided by the National Inpatient Sample database

associated comorbidities were compared between cases and controls using chi-square tests with a 0.05 level of significance. T-tests for independent samples were used to compare distributions of continuous variables including length of stay and hospital costs between cases and controls with a 0.05 level of significance. Demographic factors including age, sex, and race as well as co-morbidity variables were analyzed using univariate logistic regression with a 0.05 level of significance. Variables significant on univariate logistic regression were included in the multivariate regression model, performed with Bonferroni correction ($P < 0.0029$).

The authors confirm that the ethical policies of the journal have been followed. As this study was IRB exempt due to utilization of publicly available and deidentified data, no ethical approval was needed.

Results

We identified a total of 119,662 onychomycosis cases and 239,324 controls (Table 2). Age and sex were matched between onychomycosis cases and controls with 56.7% males ($P = 1.000$) and 63.1% being 65 years or older ($P = 1.000$). Onychomycosis versus control patients were most frequently White (69.0% versus 68.0%; $P < 0.001$), followed by Black (17.9% versus 5.8%; $P < 0.0001$) and Native American (0.5% versus 0.3%; $P < 0.001$), and were less likely to be Hispanic (9.1% versus 17.4%; $P < 0.0001$) and Asian or Pacific Islander (1.0% versus 6.7%; $P < 0.0001$). There was an even distribution of quarter of discharge between cases and controls though onychomycosis cases were slightly more likely to be discharged in the winter months

Table 2. Patient Descriptive Factor Distributions among Onychomycosis Patients Compared to Controls (1:2)

Variable	Onychomycosis Cases (N = 119662)	Matched Controls (N = 239324)	P value
Sex (N, %)			
Male	67807 (56.7%)	135614 (56.7%)	1.000
Female	51855 (43.3%)	103710 (43.3%)	
Age group (years) N, %			
0-17	427 (0.4%)	854 (0.4%)	1.000
18-64	43713 (36.5%)	87426 (36.5%)	1.000
65+	75522 (63.1%)	151044 (63.1%)	1.000
Race (N, %)			
White	69285 (69.0%)	157723 (68.0%)	<0.001
Black	18001 (17.9%)	13482 (5.8%)	<0.0001
Hispanic	9121 (9.1%)	40385 (17.4%)	<0.0001
Asian or Pacific Islander	995 (1.0%)	15599 (6.7%)	<0.0001
Native American	465 (0.5%)	645 (0.3%)	<0.001
Other	2567 (2.6%)	4226 (1.8%)	<0.001
Quarter of Discharge (N, %)			
1 (January-March)	31706 (26.5%)	60321 (25.2%)	<0.001
2 (April - June)	29752 (24.9%)	59652 (24.9%)	0.884
3 (July-September)	29123 (24.4%)	59021 (24.7%)	0.062
4 (October-December)	28891 (24.2%)	60330 (25.2%)	<0.001
Hospital data			
Length of stay (days \pm standard error (SE))	9.69 \pm 0.041	5.39 \pm 0.016	<0.0001
Hospital costs (dollars \pm SE)	39925 \pm 187.920	36720 \pm 119.819	<0.001
Hospitalization deaths (N, %)	1624 (1.4%)	9793 (4.1%)	<0.0001
Hospital region N, %			
Northeast	31453 (26.3%)	4606 (1.9%)	<0.0001
Midwest or North Central	39012 (32.6%)	1292 (0.5%)	<0.0001
South	33116 (27.7%)	8297 (3.5%)	<0.0001
West	16081 (13.4%)	225129 (94.1%)	<0.0001
Insurance type (N, %)			
Government	95833 (80.1%)	170119 (71.1%)	<0.0001
Medicare	83313 (69.6%)	147636 (61.7%)	<0.0001
Medicaid	12520 (10.5%)	22483 (9.4%)	<0.01
Private	17104 (14.3%)	54550 (22.8%)	<0.0001
Other type	6552 (5.5%)	14552 (6.1%)	<0.001

Table 3. Patient Comorbidity Distribution among Onychomycosis Patients Compared to Controls (1:2)

Comorbidities	Onychomycosis Cases (N = 119662)	Matched Controls (N = 239324)	P value
Tinea Pedis	8204 (6.9%)	167 (0.1%)	<0.001
Hyperhidrosis	54 (<0.01%)	114 (<0.01%)	0.743
Diabetes with chronic complications	14942 (12.6%)	11425 (4.8%)	<0.0001
Diabetes without chronic complications	26505 (22.3%)	44934 (18.8%)	<0.001
Human Immunodeficiency virus/AIDS	1457 (1.2%)	715 (0.3%)	<0.001
Peripheral Vascular Disease	17681 (14.9%)	13884 (5.8%)	<0.0001
Venous insufficiency	9987 (8.3%)	2362 (1.0%)	<0.0001
Obesity (body mass index \geq 30 kg/m ²)	17940 (15.1%)	12448 (5.2%)	<0.0001
Psoriasis	1286 (1.1%)	678 (0.3%)	<0.001
Deficiency Anemias	26423 (22.2%)	36525 (15.3%)	<0.0001
Hypertension	72414 (60.8%)	118352 (49.5%)	<0.0001
Chronic Pulmonary Disease	27023 (22.7%)	42336 (17.7%)	<0.001
Congestive Heart Failure	16846 (14.2%)	23461 (9.8%)	<0.0001
Depression	11928 (10.0%)	15476 (6.5%)	<0.0001
Hypothyroidism	13846 (11.6%)	22312 (9.3%)	<0.001
Renal Failure	15925 (13.4%)	14130 (5.9%)	<0.0001
Fluid and Electrolyte Disorders	30396 (25.5%)	44586 (18.6%)	<0.0001

from January to March (26.5% versus 25.2%; $P < 0.001$) and less likely to be discharged in the fall season from October to December (24.2% versus 25.2%; $P < 0.001$). Onychomycosis patients were also more likely to be publicly insured by Medicare (69.9% versus 61.7%; $P < 0.0001$) and Medicaid (10.5% versus 9.4%; $P < 0.01$) and less likely to have private insurance (14.3% versus 22.8%; $P < 0.0001$) than controls. Furthermore, onychomycosis patients versus controls had greater lengths of stay (9.69 versus 5.39 days; $P < 0.0001$), greater hospital costs (39,925 versus 36,720 dollars; $P < 0.001$), but fewer hospitalization deaths (1624 versus 9793 deaths; $P < 0.0001$). A majority of onychomycosis cases were seen in hospitals in the Northeast (26.3% versus 1.9%; $P < 0.0001$), Midwest or North Central (32.6% versus 0.5%; $P < 0.0001$), and Southern United States (27.7% versus 3.5%; $P < 0.0001$).

A descending counts frequency analysis used to identify the most common comorbidities associated with onychomycosis from variables available in NIS showed that hypertension (60.8%), fluid and electrolyte disorders (25.5%), chronic pulmonary disease (22.7%), diabetes without chronic complications (22.3%), deficiency anemias (22.2%), obesity (defined as a body mass index (BMI) of greater than 30 kg/m²) (15.1%), peripheral vascular disease (14.9%), congestive heart failure (14.2%), renal failure (13.4%), diabetes with chronic complications (12.6%), hypothyroidism (11.6%), depression (10.0%), and venous insufficiency (8.3%) were most represented and were included in the analysis. Using Chi-square analysis, onychomycosis versus control patients more often

had all associated comorbidities studied compared to controls (Table 3). The most commonly represented comorbidities in onychomycosis versus control patients included hypertension (60.8% versus 49.5%; $P < 0.0001$), fluid and electrolyte disorders (25.5% versus 18.6%; $P < 0.0001$), chronic pulmonary disease (22.7% versus 17.7%; $P < 0.001$), diabetes without chronic complications (22.3% versus 18.8%; $P < 0.001$), and deficiency anemias (22.2% versus 15.3%; $P < 0.0001$).

Using univariate and multivariate logistic regression models, Black (odds ratio [OR]: 2.734; $P < 0.0001$) and Native American (OR: 1.430; $P < 0.001$) individuals had greater risk of having onychomycosis than White individuals (Table 4). All comorbidities were significantly associated with greater risk of onychomycosis except hyperhidrosis (OR: 0.947; $P = 0.743$). The comorbidities most commonly associated with onychomycosis included tinea pedis (OR: 111.993; $P < 0.0001$), venous insufficiency (OR: 6.916; $P < 0.0001$), human immunodeficiency virus (OR: 4.372; $P < 0.001$), psoriasis (OR: 3.668; $P < 0.001$), obesity (OR: 2.407; $P < 0.0001$), peripheral vascular disease (OR: 2.294; $P < 0.0001$), and diabetes with chronic complications (OR: 2.047; $P < 0.0001$).

Conclusions

In this representative inpatient cohort, we found that onychomycosis was most commonly associated with tinea pedis, human immunodeficiency virus, venous insufficiency, psoriasis, and diabetes mellitus. Given the longer hospital stays and

Table 4. Regression Analysis of Onychomycosis Patients Compared to Matched Controls (1:2)

Variable	Univariate	P value	Multivariate	P value
Sex				
Male	Reference	-	-	-
Female	1.000 (0.986-1.014)	1.000	-	-
Age group (yrs)				
0-20	Reference	-	-	-
21-64	1.000 (0.890-1.124)	1.000	-	-
65+	1.000 (0.890-1.124)	1.000	-	-
Race				
White	Reference	-	Reference	-
Black	3.039 (2.967-3.113)	<0.0001	2.734 (2.663-2.807)	<0.0001
Hispanic	0.514 (0.502-0.527)	<0.0001	0.472 (0.460-0.486)	<0.0001
Asian or Pacific Islander	0.145 (0.136-0.155)	<0.0001	0.143 (0.134-0.153)	<0.0001
Native American	1.641 (1.456-1.850)	<0.001	1.430 (1.254-1.630)	<0.001
Other	1.383 (1.316-1.453)	<0.001	1.377 (1.304-1.453)	<0.001
Comorbidities				
Tinea Pedis	105.410 (90.422-122.882)	<0.0001	111.993 (95.611-131.180)	<0.0001
Hyperhidrosis	0.947 (0.685-1.310)	0.743	-	-
Diabetes without chronic complications	1.239 (1.218-1.261)	<0.001	1.209 (1.184-1.235)	<0.001
Diabetes with chronic complications	2.864 (2.792-2.937)	<0.0001	2.047 (1.983-2.113)	<0.0001
Hypertension	1.588 (1.566-1.611)	<0.0001	1.302 (1.279-1.324)	<0.001
Obesity (body mass index \geq 30 kg/m ²)	3.235 (3.158-3.313)	<0.0001	2.407 (2.340-2.477)	<0.0001
Human Immunodeficiency Virus/AIDS	4.113 (3.760-4.500)	<0.001	4.372 (3.950-4.839)	<0.001
Peripheral Vascular Disease	2.833 (2.767-2.900)	<0.0001	2.294 (2.232-2.357)	<0.0001
Venous Insufficiency	9.135 (8.730-9.560)	<0.0001	6.916 (6.578-7.271)	<0.0001
Psoriasis	3.824 (3.483-4.198)	<0.001	3.668 (3.295-4.083)	<0.001
Depression	1.611 (1.571-1.652)	<0.001	1.504 (1.460-1.548)	<0.001
Renal Failure	2.462 (2.404-2.521)	<0.0001	1.715 (1.666-1.767)	<0.001
Hypothyroidism	1.280 (1.252-1.309)	<0.001	1.200 (1.169-1.232)	<0.001
Deficiency Anemias	1.584 (1.557-1.613)	<0.0001	1.291 (1.264-1.319)	<0.001
Chronic Pulmonary Disease	1.367 (1.343-1.390)	<0.001	1.193 (1.169-1.217)	<0.001
Congestive Heart Failure	1.517 (1.485-1.549)	<0.0001	1.094 (1.066-1.122)	<0.001
Fluid and Electrolyte Disorders	1.498 (1.473-1.523)	<0.0001	1.441 (1.412-1.470)	<0.001

greater costs among the onychomycosis cohort as compared to controls, understanding associated demographics and comorbidities may be used to develop onychomycosis screening guidelines among hospitalized patients.

With multivariate analysis, we found that onychomycosis patients were more often Black compared to patients of other races. A 2023 study from the All of Us initiative linking survey and electronic health record data also found that Black individuals (OR: 1.29; 95% confidence interval [CI]: 1.23-1.36) were more likely to develop onychomycosis compared to White individuals [20]. In contrast, this same study found that Hispanic individuals (OR: 1.24; 95% CI: 1.17-1.31) were more likely to develop onychomycosis compared to White individuals. A 2021 systematic review of onychomycosis clinical trials demonstrated that only 32/182 (17.5%) of onychomycosis trials reported race and/or ethnicity, with only 1613/8270

(19.5%) non-white participants represented among studies between 2005-2020 [21]. Since our data, as well as previous research found that Blacks were more likely to have onychomycosis compared to other races, our study highlights the need to include more diverse participants in onychomycosis clinical trials.

We also found that the majority of onychomycosis patients versus controls presented in hospitals in the Northeast, Midwest or North Central, and Southern United States. In contrast, in a study analyzing data from the Porter Novelli summer 2022 ConsumerStyles survey, there was no difference (P = 0.621) in proportions of onychomycosis cases (N = 415) versus controls (N = 3727) by census regions, specifically in the Northeast (18.1% versus 17.2%), Midwest (18.1% versus 21.0%), South (38.1% versus 38.2%), and West (25.8% versus 23.7%) [22]. The difference between

our 2003-2014 results and the 2022 ConsumerStyles data might suggest that onychomycosis prevalence has changed over time and has now taken on a roughly equal distribution by region or that there are differences between the inpatient and outpatient burdens of onychomycosis.

Furthermore, compared to controls, onychomycosis patients were more likely to be discharged between January and March which is typically winter season. Similarly, a retrospective study of 59 pediatric (age <18 years) onychomycosis patients seen at a dermatology clinic in Dongguk University Gyeongju Hospital, Korea found that a majority (N = 22, 37.3%) of patients developed onychomycosis during the winter months (December through February) [23]. Greater discharge frequency during the colder months may be partly attributed to dampness experienced in the winter season along with wearing closed-toed shoes which may increase risk of onychomycosis.

With multivariate analysis, tinea pedis was the most commonly represented comorbidity among onychomycosis patients in our cohort, which is consistent with a 1999-2004 retrospective study analyzing 311 toenail clippings, in which, of thirty-three toenail clippings from patients who also had tinea pedis, 23 showed presence of dermatophytes and ten lacked dermatophytes [24]. Therefore, with concomitant tinea, odds of having versus not having onychomycosis was 2.73 (P < 0.001). Similarly, in a prospective epidemiological study on the prevalence of tinea pedis and concurrent onychomycosis among males residing in two boarding schools in Turkey found that among 410 males, 51.5% (N = 211) of residents had tinea pedis with 14.2% (N = 30) of tinea pedis cases having concurrent toenail onychomycosis [25]. In a 2015 multicenter, double-blinded, 48-week randomized (3:1) controlled trial of 1,655 patients assessing efinaconazole efficacy compared to vehicle for onychomycosis treatment, there was a 29.4% (P = 0.003) versus 16.1% (P = 0.045) cure rate with efinaconazole when treating versus not treating coexisting tinea pedis, respectively [26]. Therefore, early identification of tinea pedis may reduce onychomycosis risk and treatment of coexisting tinea pedis improves outcomes for onychomycosis patients.

We also found a significant correlation between venous and peripheral vascular disease with onychomycosis, consistent with prior studies. In a 2005 cross-sectional study, among 42 outpatient onychomycosis patients and 39 controls, venous insufficiency was more frequent among onychomycosis patients versus controls (15/42, 35.7% versus 6/39, 15.4%; P = 0.037) [27]. Furthermore, in a 2000 prospective epidemiological study of 254 patients presenting to a vascular clinic, there was a significant association between onychomycosis and peripheral arterial disease (ROR: 4.8, P = 0.02) [28].

Obesity was relatively common in onychomycosis patients compared to controls with multivariate regression analysis. In a 2002 Hong Kong epidemiological study of 1014 patients with foot diseases, including onychomycosis, risk factors included vascular disease, diabetes, and obesity [29]. Similarly, in a 2009-2010 study of adult patients hospitalized in inpatient clinics at the Haydarpaşa Numune Training and Research Hospital in Turkey, onychomycosis was more prevalent among the obese patients (BMI \geq 30 kg/m²) as compared to controls (91/250, 36.4% versus 19/120, 15.8%; P < 0.001) [30]. In addition, in a 2004-2005 nested case-control study of 1245 patients with type 2 diabetes mellitus from a Taiwanese clinic, in onychomycosis patients, odds of obesity (BMI \geq 27 kg/m²) versus normal weight was 2.31 (95% CI: 1.45-3.13; p=0.001) [31]. Therefore, we propose for obese patients to be screened for onychomycosis.

Human immunodeficiency virus (HIV) was also significantly associated with onychomycosis risk in our study, similar to previous literature. In a 2011 study of 100 HIV and acquired immunodeficiency syndrome (AIDS) patients attending Hospital Correia Picanço in Brazil, 32 were diagnosed with onychomycosis [32]. In a 2011 retrospective chart review study of 280 Mexican patients with HIV, 20% (N = 54) had onychomycosis [33]. In another observational cross-sectional study of 205 Mexican patients attending an HIV/AIDS clinic, 26.3% (N = 54) had onychomycosis, and HIV+ patients with versus without onychomycosis had lower CD4+ cell counts at 379.5 cells/ μ L versus 448 cells/ μ L respectively (no p-value reported) [34]. Therefore, our study corroborates that HIV infection may be a risk factor for onychomycosis, which may help to inform screening guidelines.

We also found that psoriasis was associated with a greater risk of onychomycosis. The relationship between onychomycosis and psoriasis remains controversial [35,36]. Some studies have found a positive association between onychomycosis and psoriasis. For example, in a 2017-2018 Brazilian cross-sectional outpatient study of 38 patients with psoriasis, 57.9% (N = 22) of patients had onychomycosis [35]. In a 2003-2005 prospective study of 113 psoriatic patients and 106 non-psoriatic controls, 47.6% and 28.4% (P = 0.0054) were diagnosed with toenail onychomycosis respectively [37]. However, other studies have shown a lesser prevalence of onychomycosis among psoriasis patients. For example, a prospective controlled trial of psoriasis patients seen at a dermatology outpatient clinic in Turkey found that, of the 168 psoriasis patients and 164 controls, 13.1% (N = 22) and 7.9% (N = 13) of patients had onychomycosis, respectively (P > 0.05) [38].

Furthermore, in our study, patients with diabetes had increased risk of onychomycosis development similar to previous literature. For example, in a 2016 Italian retrospective

study including 668 non-diabetic and 47 diabetic patients, 55.3% (N = 26) of diabetic patients and 25.2% (N = 169) of non-diabetic patients were diagnosed with onychomycosis (P < 0.0001) [39]. In a 2008-2009 Japanese cross-sectional observational study of 71 patients, an unadjusted multiple logistic regression model found that not washing feet every day was associated with a significantly increased risk of onychomycosis among diabetic patients (OR: 3.45, 95% CI: 1.24-9.65; P = 0.018), though data was not significant in the age and sex adjusted model (OR: 2.37; 95% CI: 0.76-7.33; P = 0.136) [40]. We found a greater risk of onychomycosis among patients with diabetes with chronic complications compared to those without chronic complications, suggesting that better diabetic control may decrease onychomycosis risk.

We also found significant relationships between onychomycosis and depression, deficiency anemias, and fluid and electrolyte disorders. These comorbidities and their mechanisms leading to onychomycosis development have not been studied extensively, and may be a topic for future research.

Limitations of this study include its retrospective nature and inclusion of only inpatient data. Therefore, these trends, common risk factors, and the overall burden of onychomycosis may not be generalizable to the outpatient setting. In addition, onychomycosis cases were not necessarily mycologically confirmed. Data on diagnosing physician specialty were unavailable. Furthermore, we used International Classification of Diseases, 9th edition codes to create the comorbidity variables for tinea pedis, human immunodeficiency virus, hyperhidrosis, and psoriasis. Consequently, cases with the comorbidity that were not classified within the ICD-9 codes we included may have been missed. There may also have been missing data among the variables we included using the National Inpatient Sample. Further, inaccurate ICD-9 coding of conditions could have affected our data by including cases that were incorrectly classified as onychomycosis in our analysis. Our study was limited to NIS data 2003-2014, and studies analyzing more recent data are warranted.

In sum, in this inpatient cohort, we identified numerous comorbidity risk factors associated with an increased risk of developing onychomycosis among hospitalized patients including tinea pedis, venous insufficiency, human immunodeficiency virus, psoriasis, obesity, peripheral vascular disease, and diabetes with chronic complications. Black patients were disproportionately represented among onychomycosis cases compared to controls. Onychomycosis patients were more likely to have longer hospital stays and greater costs. As onychomycosis has significant impact on quality of life, understanding associated risk factors may help formulate onychomycosis screening guidelines, initiate early treatment/intervention, and alleviate the burden of onychomycosis in the inpatient setting.

References

1. Falotico JM, Lipner SR. Updated Perspectives on the Diagnosis and Management of Onychomycosis. *Clin Cosmet Investig Dermatol*. 2022;15:1933-1957. DOI: 10.2147/CCID.S362635. PMID: 36133401. PMCID: PMC9484770.
2. Gupta AK, Stec N, Summerbell RC, et al. Onychomycosis: a review. *J Eur Acad Dermatol Venereol*. 2020;34(9):1972-1990. DOI: 10.1111/jdv.16394. PMID: 32239567.
3. Christenson JK, Peterson GM, Naunton M, et al. Challenges and Opportunities in the Management of Onychomycosis. *J Fungi (Basel)*. 2018;4(3):87. DOI: 10.3390/jof4030087. PMID: 30042327. PMCID: PMC6162761.
4. Falotico JM, Lipner SR. Poor Antifungal Coverage for Onychomycosis in a Cross-Sectional Analysis of Medicaid Formularies. *J Am Podiatr Med Assoc*. 2022;112(5):21-221. DOI: 10.7547/21-221. PMID: 36251605.
5. Drake LA, Scher RK, Smith EB, et al. Effect of onychomycosis on quality of life. *J Am Acad Dermatol*. 1998;38(5 Pt 1):702-704. DOI: 10.1016/s0190-9622(98)70199-9. PMID: 9591814.
6. Stewart CR, Algu L, Kamran R, et al. Effect of onychomycosis and treatment on patient-reported quality-of-life outcomes: A systematic review. *J Am Acad Dermatol*. 2021;85(5):1227-1239. DOI: 10.1016/j.jaad.2020.05.143. PMID: 32502586.
7. Gupta AK, Mays RR. The Impact of Onychomycosis on Quality of Life: A Systematic Review of the Available Literature. *Skin Appendage Disord*. 2018;4(4):208-216. DOI: 10.1159/000485632. PMID: 30410887. PMCID: PMC6219228.
8. Gregoriou S, Mpali N, Vrioni G, Hatzidimitriou E, Chryssou SE, Rigopoulos D. Epidemiology of Onychomycosis in an Academic Nail Unit in South Greece during a Three-Year Period. *Skin Appendage Disord*. 2020;6(2):102-107. DOI: 10.1159/000504812. PMID: 32258053. PMCID: PMC7109406.
9. Svejgaard EL, Nilsson J. Onychomycosis in Denmark: prevalence of fungal nail infection in general practice. *Mycoses*. 2004; 47(3-4):131-135. DOI: 10.1111/j.1439-0507.2004.00968.x. PMID: 15078429.
10. Rafat Z, Hashemi SJ, Saboor-Yaraghi AA, et al. A systematic review and meta-analysis on the epidemiology, casual agents and demographic characteristics of onychomycosis in Iran. *J Mycol Med*. 2019;29(3):265-272. DOI: 10.1016/j.mycmed.2019.05.004. PMID: 31285126.
11. Lipner SR, Hancock JE, Fleischer AB. The ambulatory care burden of nail conditions in the United States. *J Dermatolog Treat*. 2021;32(5):517-520. DOI: 10.1080/09546634.2019.1679337. PMID: 31613182.
12. *J Clin Aesthet Dermatol*. 2015;8(11):38-42. PMID: 26705439. PMCID: PMC4689496.
13. Bang CH, Yoon JW, Lee HJ, Lee JY, Park YM, Lee SJ, Lee JH. Evaluation of relationships between onychomycosis and vascular diseases using sequential pattern mining. *Sci Rep*. 2018;8(1):17840. DOI: 10.1038/s41598-018-35909-z. PMID: 30552340. PMCID: PMC6294792.
14. Pichardo-Geisinger R, Mora DC, Newman JC, Arcury TA, Feldman SR, Quandt SA. Comorbidity of tinea pedis and onychomycosis and evaluation of risk factors in Latino immigrant poultry processing and other manual laborers. *South Med J*. 2014;107(6):374-379. DOI: 10.14423/01.SMJ.0000450705.67259.26. PMID: 24945173.

15. Dogra S, Kumar B, Bhansali A, Chakrabarty A. Epidemiology of onychomycosis in patients with diabetes mellitus in India. *Int J Dermatol*. 2002;41(10):647-651. DOI: 10.1046/j.1365-4362.2002.01528.x. PMID: 12390186.
16. Fukunaga A, Washio K, Ogura K, et al. Onychomycosis as a warning sign for peripheral arterial disease. *Acta Derm Venereol*. 2013;93(6):747-748. DOI: 10.2340/00015555-1576. PMID: 23529206.
17. Sigurgeirsson B, Steingrímsson O. Risk factors associated with onychomycosis. *J Eur Acad Dermatol Venereol*. 2004;18(1):48-51. DOI: 10.1111/j.1468-3083.2004.00851.x. PMID: 14678531.
18. Szepletowski JC, Reich A, Garlowska E, Kulig M, Baran E; Onychomycosis Epidemiology Study Group. Factors influencing coexistence of toenail onychomycosis with tinea pedis and other dermatomycoses: a survey of 2761 patients. *Arch Dermatol*. 2006;142(10):1279-1284. DOI: 10.1001/archderm.142.10.1279. PMID: 17043182.
19. Overview of the National (Nationwide) Inpatient Sample (NIS). Healthcare Cost & Utilization Project. Accessed May 15, 2023. Available from: <https://hcup-us.ahrq.gov/nisoverview.jsp>.
20. Moseley I, Ragi SD, Ouellette S, Rao B. Onychomycosis in under-represented groups: an all of us database analysis. *Arch Dermatol Res*. 2023;315(3):647-651. DOI: 10.1007/s00403-022-02413-4. PMID: 36261664.
21. Chang MJ, Qiu Y, Lipner SR. Race reporting and representation in onychomycosis clinical trials: A systematic review. *Mycoses*. 2021;64(8):954-966. DOI: 10.1111/myc.13262. PMID: 33655595.
22. Benedict K, Gold JAW, Wu K, Lipner SR. High Frequency of Self-Diagnosis and Self-Treatment in a Nationally Representative Survey about Superficial Fungal Infections in Adults-United States, 2022. *J Fungi (Basel)*. 2022;9(1):19. DOI: 10.3390/jof9010019. PMID: 36675840. PMCID: PMC9860956.
23. Kim DM, Suh MK, Ha GY. Onychomycosis in children: an experience of 59 cases. *Ann Dermatol*. 2013;25(3):327-334. DOI: 10.5021/ad.2013.25.3.327. PMID: 24003276. PMCID: PMC3756198.
24. Walling HW, Sniezek PJ. Distribution of toenail dystrophy predicts histologic diagnosis of onychomycosis. *J Am Acad Dermatol*. 2007;56(6):945-948. DOI: 10.1016/j.jaad.2006.06.003. PMID: 17368630.
25. Erbagci Z, Tuncel A, Zer Y, Balci I. A prospective epidemiologic survey on the prevalence of onychomycosis and dermatophytosis in male boarding school residents. *Mycopathologia*. 2005;159(3):347-352. DOI: 10.1007/s11046-004-5493-2. PMID: 15883717.
26. Markinson B, Caldwell B. Efinaconazole Topical Solution, 10% Efficacy in Patients with Onychomycosis and Coexisting Tinea Pedis. *J Am Podiatr Med Assoc*. 2015;105(5):407-411. DOI: 10.7547/14-088. PMID: 26429609.
27. Kulac M, Acar M, Karaca S, et al. Venous insufficiency in patients with toenail onychomycosis. *J Ultrasound Med*. 2005;24(8):1085-1089. DOI: 10.7863/jum.2005.24.8.1085. PMID: 16040823.
28. Gupta AK, Gupta MA, Summerbell RC, et al. The epidemiology of onychomycosis: possible role of smoking and peripheral arterial disease. *J Eur Acad Dermatol Venereol*. 2000;14(6):466-469. DOI: 10.1046/j.1468-3083.2000.00124.x. PMID: 11444267.
29. Cheng S, Chong L. A prospective epidemiological study on tinea pedis and onychomycosis in Hong Kong. *Chin Med J (Engl)*. 2002;115(6):860-865. PMID: 12123553.
30. Doner NYS, Ekmekci TR. Evaluation of obesity-associated dermatoses in obese and overweight individuals. *Turkderm*. 2011;45(3):146-151. DOI:10.4274/turkderm.00908.
31. Chang SJ, Hsu SC, Tien KJ, Hsiao JY, Lin SR, Chen HC, Hsieh MC. Metabolic syndrome associated with toenail onychomycosis in Taiwanese with diabetes mellitus. *Int J Dermatol*. 2008;47(5):467-472. DOI: 10.1111/j.1365-4632.2008.03606.x. PMID: 18412863.
32. Cambuim II, Macêdo DP, Delgado M, et al. Avaliação clínica e micológica de onicomicose em pacientes brasileiros com HIV/AIDS [Clinical and mycological evaluation of onychomycosis among Brazilian HIV/AIDS patients]. *Rev Soc Bras Med Trop*. 2011;44(1):40-42. DOI:10.1590/s0037-86822011000100010
33. Moreno-Coutiño G, Arenas R, Reyes-Terán G. Clinical presentation of onychomycosis in hiv/aids: a review of 280 mexican cases. *Indian J Dermatol*. 2011;56(1):120-121. DOI: 10.4103/0019-5154.77577. PMID: 21572813. PMCID: PMC3088923.
34. Flores-Bozo LR, Méndez-Flores S, Olvera-Rodríguez V, et al. Nail Changes in People Living with Human Immunodeficiency Virus: Observational and Cross-Sectional Study in a Third-Level Hospital. *Skin Appendage Disord*. 2022;8(5):368-375. DOI: 10.1159/000524257. PMID: 36161090. PMCID: PMC9485993.
35. Alves NCP, Moreira TA, Malvino LDS, et al. Onychomycosis in Psoriatic Patients with Nail Disorders: Aetiological Agents and Immunosuppressive Therapy. *Dermatol Res Pract*. 2020;2020:7209518. DOI: 10.1155/2020/7209518. PMID: 32411192. PMCID: PMC7212309.
36. Tsentemeidou A, Vyzantiadis TA, Kyriakou A, Sotiriadis D, Patsatsi A. Prevalence of onychomycosis among patients with nail psoriasis who are not receiving immunosuppressive agents: Results of a pilot study. *Mycoses*. 2017;60(12):830-835. DOI: 10.1111/myc.12681. PMID: 28877373.
37. Leibovici V, Hershko K, Ingber A, Westerman M, Leviatan-Strauss N, Hochberg M. Increased prevalence of onychomycosis among psoriatic patients in Israel. *Acta Derm Venereol*. 2008;88(1):31-33. DOI: 10.2340/00015555-0323. PMID: 18176747.
38. Kaçar N, Ergin S, Ergin C, Erdogan BS, Kaleli I. The prevalence, aetiological agents and therapy of onychomycosis in patients with psoriasis: a prospective controlled trial. *Clin Exp Dermatol*. 2007;32(1):1-5. DOI: 10.1111/j.1365-2230.2006.02215.x. PMID: 16824053.
39. Trovato L, Calvo M, De Pasquale R, Scalia G, Oliveri S. Prevalence of Onychomycosis in Diabetic Patients: A Case-Control Study Performed at University Hospital Policlinico in Catania. *J Fungi (Basel)*. 2022;8(9):922. DOI: 10.3390/jof8090922. PMID: 36135647. PMCID: PMC9500927.
40. Takehara K, Oe M, Tsunemi Y, et al. Factors associated with presence and severity of toenail onychomycosis in patients with diabetes: a cross-sectional study. *Int J Nurs Stud*. 2011;48(9):1101-1108. DOI: 10.1016/j.ijnurstu.2011.02.005. PMID: 21367414.