

## ONYCHOMYCOSIS AND CHILDREN – A MULTICENTER STUDY

L. Zisova<sup>1</sup>, A. Chokoeva<sup>1</sup>, E. Sotiriou<sup>2</sup>, V. Valtchev<sup>3</sup> and D. Gospodinov<sup>3</sup>

<sup>1</sup>Department of Dermatology and Venereology, Medical University, Plovdiv, Bulgaria

<sup>2</sup>First Dermatology Department, Aristotle University, Thessaloniki, Greece

<sup>3</sup>Department of Dermatology and Venereology, Medical University, Pleven, Bulgaria

**Summary.** Onychomycosis is a chronic disease caused by dermatophytes, yeasts and molds, which leads to destruction of the nail plate of the fingernails and toenails. The incidence of onychomycosis in children is considerably smaller compared with that in adults. Onychomycosis in children under 6 years of age is particularly unusual. The trauma and the hyperhidrosis after puberty are the major predisposing factor for fungal nail infection in childhood. Some systemic diseases and congenital syndromes have a crucial role for the development of onychomycosis in children. Wearing infected socks and shoes of other family members, family history for fungal infection of the nails, reduced hygiene and onychophagia are other important predisposing factors. Dermatophytic species *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Epidermophyton floccosum* are the most frequent causative agents of onychomycosis in adults and much less common yeast of the genus *Candida*. A retrospective study for a period of 11 years was performed (2003-2013) investigating 292 children aged 0 to 18 years with proven onychomycosis (123 – from Plovdiv, Bulgaria, 94 – from Plevan, Bulgaria, and 75 – from Thessaloniki, Greece). *Candida albicans* was the main etiologic agent in onychomycosis in children under 18 years of age, according to the performed retrospective study. The diagnose was made by direct microscopic examination and fungal culture on Sabouraud agar media.

**Key words:** *onychomycosis, children*

### INTRODUCTION

Onychomycosis, also known as *Tinea unguium* is a chronic, slowly progressing disease leading to destruction of the nail plate. The infection may be localized only on the nail, but it is most often combined with *Tinea pedum*, or *Tinea manum*. Invasion of the nail plate usually begins from the lateral nail fold or from the free edge of the nail – so called lateral or distal subungual onychomycosis [1, 2, 3].

The disease can have certain negative consequences for patients, such as pain, and can potentially undermine work and social lives. Although not life-threatening, onychomycosis constitutes an important public health problem because of its high prevalence and associated morbidity [1].

This kind of nail infection is a common disease with worldwide distribution. It affects 5.5% of the world population, accounts for 20-40% of all nail disorders and about 30% of all fungal infections [4].

In childhood, however, onychomycosis is rare, as its incidence reaches only 0.3-0.44% of all skin pathology. It is particularly unusual in children under 6 years [4] – Figs. 1, 2.



**Fig. 1.** Toenail onychomycosis in children, caused by *Candida* spp.



**Fig. 2.** Toenail onychomycosis in children, caused by *M. gypseum*

Trauma is a major predisposing factor for fungal infection of the nail in childhood, as well as hyperhidrosis that appears after puberty [5]. Significant role in the development of onychomycosis in childhood have some systemic diseases (diabetes, psoriasis, etc.) and congenital syndromes (primary and secondary immunodeficiencies, Down syndrome, etc.) [5, 6, 7, 8, 9]. Therapeutic immunosuppression during treatment of oncohematological diseases is an important risk factor for the development of onychomycosis in children [5]. Other important predisposing factors are wearing of infected socks and shoes of other family members, decreased hygiene and biting of the nails, also called onychophagia [9]. It is also known that sport activity increases the risk of onychomycosis [6]. This could be explained by the chronic microtrauma of the nail plate in athletes, especially football players, but a high incidence is found among swimmers as well [10].

The most common causative agents of onychomycosis are the dermatophytes and *Candida* species. Less common are certain types of moulds (nondermatophyte moulds or NDMs). In approximately 60-80% of the cases, onychomycosis is due to dermatophytes [3]. However, it has been established that the most prevalent isolated etiological agent shows some variability related to different geographic areas, significant differences between different age groups as well as seasonality [11]. In the early childhood, *Candida* spp are the most common isolated agent, while dermatophyte species and *Trichophyton rubrum* in particular, occupies a major part in the etiology of onychomycosis in the middle-aged children [11]. According to some authors, the frequency of its isolation reaches 51% between 3 and 12 years of age, followed by *Trichophyton mentagrophytes* and *Epidermophyton floccosum* [12].

The most typical clinical form, as in adults but also in children is distal and lateral subungual onychomycosis [13, 12]. Proximal subungual onychomycosis represents about 0.4% of onychomycosis in all ages, but is extremely rare in children under 18 years of age [14]. The massive invasion of the nail often is favored by immunocompromised factor and leads to total dystrophic form which is casuistic for the pediatric population [15]. Available data that describe such cases is extremely poor, mainly in severely immunosuppressed individuals, as a sepa-

rate group of high risk patients with chronic mucocutaneous candidiasis, which often develop *Candida-onychomycosis* [16].

Male gender is affected from two to three times more often than females, as in childhood this ratio is most pronounced between 10 and 18 years of age [5, 6]. There is no significant difference regarding gender among younger children up to 1 years old [17].

Despite all the established facts, until nowadays there is no comparative multicenter study performed regarding onychomycosis in children.

## OBJECTIVES

The aim of this retrospectively performed study was to compare the incidence, etiological structure, gender distribution and the most common localization of onychomycosis in children between 0-18 years of age. The results from three mycological centers - Plovdiv (Bulgaria), Pleven (Bulgaria) and Thessaloniki (Greece) were analyzed.

## MATERIALS AND METHODS

This retrospective study was performed for a period of 11 years (2003-2013), and included 292 children aged 0 to 18 years, of which 139 were males and 153 females, with proven onychomycosis.

A total of 123 children from Plovdiv (Bulgaria), of which 52 boys and 71 girls, were included in the study and were distributed as follows: 0-1 years old – 7 children, 1-3 years old – 30 children, 3-12 years old – 48 children and 12-18 years old – 38 children.

A total of 94 children from Pleven (Bulgaria), of which 42 boys and 52 girls, respectively, were distributed as follows: 0-1 years old – 20 children, 1-3 years old – 4 children, 3-12 years old – 58 children and 12-18 years old – 12 children.

A total of 75 children from Thessaloniki (Greece), of which 45 boys and 30 girls, were distributed as follows: 0-1 years old – 3 children, 1-3 years old – 7 children, 3-12 years old – 27 children, 12-18 years old – 41 children.

The diagnosis was made by direct microscopic examination and culture on Sabouraud agar. Species typing of *Candida* spp. was performed with Chrom agar and Api *Candida* test.

None of the children, included in the performed study was suffering from psoriasis, neither had a positive history for onychodystrophy.

## RESULTS

The retrospective analysis for the 11-year period (2003-2013), revealed that the total number of patients with onychomycosis in the mycological center of Plovdiv (Bulgaria) was 1413, of which 91.3% (1290) were adults with onychomycosis and 8.7% (123) – children (Table 1).

Results from the mycological center of Pleven (Bulgaria) showed that the total number of patients with onychomycosis for the same period of time was 1296, of which 92.7% (1202) adults and 7.3% (94) – children (Table 1).

The total number of onychomycosis cases in the mycological center of Thessaloniki (Greece) was 3,555, of which 97.9% (3480) were adult patients and 2.1% (75) – children – (Table 1).

**Table 1.** The incidence of onychomycosis in the mycological centers of Plovdiv, Pleven and Thessaloniki

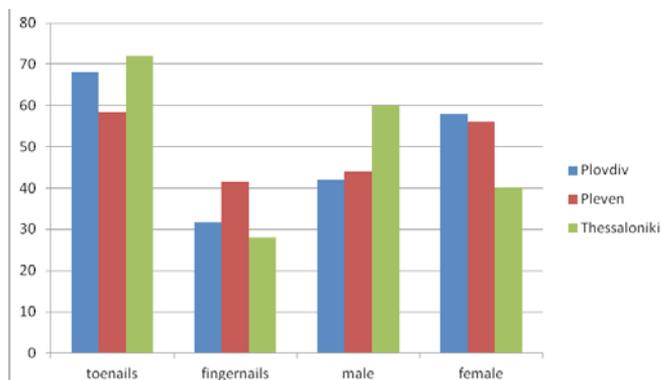
Mycological Center	Onychomycosis Total	ADULTS	CHILDREN
		Onychomycosis	Onychomycosis
Plovdiv	1 413	1 290 (91.3%)	123 (8.7%)
Thessaloniki	3 555	3 480 (97.9%)	75 (2.1%)
Pleven	1296	1202 (92.7%)	94 (7.3%)

According to our survey, among children from Bulgaria female gender is more often affected from onychomycosis. In Plovdiv (Bulgaria) the ratio was 52:71, in Pleven (Bulgaria) – 42:52 in favor of girls, as opposed to Thessaloniki (Greece), where the ratio was in favor of boys – 45:30 (Tabl. 2, Fig. 3).

With regard to localization, onychomycosis in children was more often localized in toenails than in fingernails, in all of the three centers included in the study – Table 2, Fig. 3.

**Table 2.** Comparison of the results for onychomycosis in children in Plovdiv, Pleven and Thessaloniki, divided by the total number, gender predilection and localization

Year	Onychomycosis Total 0-18 year			Male: Female			Toenail: Fingernail		
	Plovdiv	Pleven	Thessaloniki	Plovdiv	Pleven	Thessaloniki	Plovdiv	Pleven	Thessaloniki
2003	3	6	6	1:2	2:4	4:2	3:0	1:5	4:2
2004	18	7	7	8:10	3:4	4:3	6:12	5:2	5:2
2005	3	15	5	0:3	8:7	3:2	1:2	11:4	3:2
2006	8	6	9	3:5	1:5	5:4	2:6	2:4	7:2
2007	10	5	7	4:6	3:2	4:3	10:0	4:1	5:2
2008	8	18	6	1:7	9:9	4:2	7:1	10:8	4:2
2009	10	5	8	3:7	1:4	4:4	8:2	2:3	6:2
2010	12	8	7	9:3	5:3	4:3	9:3	5:3	5:2
2011	17	15	9	7:10	7:8	5:4	13:4	10:5	7:2
2012	9	5	6	5:4	1:4	4:2	7:2	2:3	4:2
2013	25	4	5	11:14	2:2	4:1	18:7	3:1	4:1
Total:	123	94	75	52:71	42:52	45:30	84:39	55:39	54:21



**Fig. 3.** Comparison of localization and gender predilection of onychomycosis in childhood in Plovdiv, Pleven and Thessaloniki

**Combined onychomycosis** of fingernails and toenails occurs rarely in childhood. In Plovdiv, it was observed only in 4.1% of children (in 5 out of 123 children), in Thessaloniki – in 4% (3 of 75 cases), while in Pleven, the combined infection of fingernails and toenails was more common – 32.9% (31 of 94 cases).

Specific literature data on the incidence of combined onychomycosis in children were not found.

Not uncommon, the combined onychomycosis of fingernails and toenails has a different isolated pathogen. According to the results obtained in Plovdiv, it was observed in 100% (5 out of 5 children) of the cases – Table 3.

In Pleven, in 87.1% (27 out of 31) of the cases with combined onychomycosis on fingernails and toenails, were isolated yeasts of the genus and only 12.9% (4 out of 31) – *T. rubrum*.

In Thessaloniki, combined infection of the fingernails and toenails was established only in three male children, as the isolated pathogen was the same in all of them (100%) – *T. rubrum*.

**Table 3.** Combined onychomycosis in children in Plovdiv (Bulgaria)

Gender	Age	Toenails	Fingernails
Female	4 years	Aspergillus	<i>M. ferrugineum</i>
Male	5 years	Aspergillus + Candida	Penicillium + Candida
Female	6 years	<i>T. violaceum</i>	<i>Candida albicans</i>
Male	12 years	<i>Candida albicans</i>	<i>M. gypseum</i> + <i>Rhodotorulla</i>
Female	17 years	Aspergillus + Candida	<i>T. verrucosum</i>

The study of etiological structure of children onychomycosis in Plovdiv, Plevan and Thessaloniki showed significant differences in the occurrence of isolated pathogens in different age groups – Tabl. 4, Tabl. 5, Tabl. 6, Fig .4.

**Table 4.** Etiological structure of onychomycosis in children in Plovdiv, divided into age groups

0-1 year	1-3 years	3-12 years	12-18 years
<i>Candida</i> spp – 7 (100%)	<i>Candida</i> spp – 16 (53.3%)	<i>Candida</i> spp – 20 (41.6%)	<i>Candida</i> spp – 13 (34.2%)
<i>C. albicans</i> – 5 <i>C. nonalbicans</i> – 2	<i>C. albicans</i> – 14 <i>C. nonalbicans</i> – 2	<i>C. albicans</i> – 19 <i>C. nonalbicans</i> – 1	<i>C. albicans</i> – 12 <i>C. nonalbicans</i> – 1
Dermatophytes – 0 (0%)	Dermatophytes – 9 (30%)	Dermatophytes – 19 (39.6%)	Dermatophytes – 16 (42.1%)
	<i>T. rubrum</i> – 1 <i>T. violaceum</i> – 2 <i>T. mentagrophytes</i> – 1 <i>M. gypseum</i> – 2 <i>T. verrucosum</i> – 2 <i>M. ferrugineum</i> – 1	<i>T. rubrum</i> – 3 <i>T. violaceum</i> – 2 <i>T. mentagrophytes</i> – 4 <i>M. canis</i> – 2 <i>M. gypseum</i> – 4 <i>E. floccosum</i> – 1 <i>M. ferrugineum</i> – 3	<i>T. rubrum</i> – 3 <i>T. violaceum</i> – 2 <i>T. mentagrophytes</i> – 1 <i>M. canis</i> – 1 <i>T. verrucosum</i> – 4 <i>M. nanum</i> – 1 <i>M. ferrugineum</i> – 4
Molds – 0 (0%)	Molds – 5 (16.7%)	Molds – 9 (18.7%)	Molds – 9 (23.7%)
	<i>Aspergillus</i> 2 <i>Penicillium</i> 2 <i>Scopulariopsis</i> 1	<i>Aspergillus</i> – 5 <i>Penicillium</i> – 3 <i>Rhodotorulla</i> – 1	<i>Aspergillus</i> – 7 <i>Penicillium</i> – 2
Total:	7	30	48
			38

**Table 5.** Etiological structure of onychomycosis in children in Pleven, divided into age groups

year	1-3 years	3-12 years	12-18 years
Candida spp 20 (100%) C. albicans – 20	Candida spp 4 (100%) C. albicans – 4	Candida spp 22 (37,9%) C. albicans – 22	Candida spp 3 (25%) C. albicans – 3
Dermatophytes 0 (0%)	Dermatophytes 0 (0%)	Dermatophytes 36 (62,1%) T. rubrum – 36	Dermatophytes 9 (75%) T. rubrum – 9
Molds 0 (0%)	Molds 0 (0%)	Molds 0 (0%)	Molds 0 (0%)
Total: 20	4	58	12

**Table 6.** Etiological structure of onychomycosis in children in Thessaloniki, divided into age groups

year	1-3 years	3-12 years	12-18 years
Candida spp. 3 (100%) C.albicans – 3	Candida spp. 7 (100%) C.albicans – 2 C.parapsilosis – 3 C.guillermonti – 2	Candida spp. 3 (11.1%) C.albicans – 1 C.parapsilosis – 2	Candida spp. 6 (15.8%) C.albicans – 3 C.parapsilosis – 3
Dermatophytes: 0 (0%)	Dermatophytes: 0 (0%)	Dermatophytes: 24 (88.9%) T.rubrum – 24	Dermatophytes: 32 (84.2%) T.rubrum – 27 T.interdigitales – 5
Molds 0 (0%)	Molds 0 (0%)	Molds 0 (0%)	Molds 0 (0%)
Total: 3	7	27	38

**Up to 1 year of age** Candida spp were the main isolated pathogens of onychomycosis in children – in 100% of the cases, in all of the centers – Plovdiv, Pleven, Thessaloniki (Table 4, Table 5, Table 6, Fig. 4).

**In the age 1-3 years** Candida spp were again the most common isolated agent in 53.3% [16] of the cases in *Plovdiv*. However, in this age group in the same center, an increasing number of isolated dermatophytes was observed – 30.0% [9]. In 16.7% [5] of the patients in this group pathogenic molds were isolated as well (Table 4, Fig. 5).

*In Pleven and Thessaloniki*, Candida spp were the only pathogens isolated in 100% [4 and 7] of the cases in this age group. Dermatophytes and pathogenic molds were not observed (Table 5, Table 6).

**In the age group 3-12 years in Plovdiv**, Candida spp was the main etiological agent of onychomycosis – 41.6% [20] of the cases, but the percentage was close to that of the isolated dermatophyte types – 39.7% [19]. The presence of pathogenic molds was insignificantly increased – 18.7% [9] (Table 4).

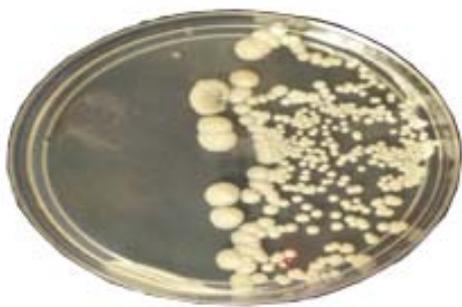


Fig. 4. *Candida albicans* – culture on Sabouraud agar



Fig. 5. *Trichophyton rubrum* – culture on Sabouraud agar

*In Pleven and Thessaloniki* however, the dermatophyte species prevailed as the etiologic agent in this age range and consisted of 62.1% [36] and 88.9% [24] of the cases, respectively.

*Candida* spp were isolated in 37.9% [22] cases in Pleven and in 11.1% [3] of the cases in Thessaloniki. Pathogenic molds again were not observed as a cause of onychomycosis among 3-12 year old patients in these centers – Table 5, Table 6.

In the last *age group 12-18 years*, the proportion of isolated agents was approaching that of adult population.

Dermatophytes appeared to be the main cause of onychomycosis in the age group 12-18 years, as they represented 42.1% [16] of the cases in Plovdiv, 75% [9] in Pleven, and 84.2% [32] of the cases in Thessaloniki – Table 4, Table 5, Table 6.

*Candida* spp. were isolated in 34.2% [13] of the cases in Plovdiv, 25% [3] of the children in Pleven and only in 15.8% [6] of pediatric patients in Thessaloniki.

Pathogenic molds were isolated only in Plovdiv, in 23.7% [9] of the investigated children (Table 4, Table 5, Table 6).

*M. ferrugineum*, *T. verrucosum*, *T. rubrum*, *T. mentagrophytes*, *T. violaceum*, *M. canis*, *M. Nanum* were the main dermatophytes species, as causative agents of onychomycosis in children in the age group 12-18 in Plovdiv.

*In Pleven*, *T. rubrum* was cultivated in 100% of the cases of onychomycosis with dermatophytic etiology (Fig. 6). *T. rubrum* was the main representative agent of dermatophyte species also in *Thessaloniki*. In this center, *T. rubrum* was isolated in 5 of 32 clinical cases of onychomycosis with dermatophyte etiology (Table 4, Table 5, Table 6).

The predominant type of *Candida* was *C. albicans* in all age groups as in the mycological center of Plovdiv, as well as in Pleven (Fig. 5).

In the mycological center of Thessaloniki, predominant type of *Candida* was *C. albicans* in the age group 0-1 year, while in the group 1-3 years and 3-12, *C. nonalbicans* species were dominating and in 12-18 age group, the ratio *C. albican*: *C. non albicans* was equal – Table 4, Table 5, Table 6.

According to the results of the performed study, **molds** were observed only in Plovdiv, with incidence similar to that in the adult population. The main part of that percentage was occupied by genus *Aspergillus*, followed by genus *Penicillium*, *Scopulariopsis* and *Rhodotorulla*- Table 4.

## DISCUSSION

In children, the incidence of onychomycosis is significantly smaller compared with that in adults [4].

The results from our retrospective, multicenter comparative study are confirmatory, regarding this statement. According to our results, the incidence of onychomycosis in children up to 18 years was 8.7% in the center of Plovdiv (Bulgaria), 7.3% in the center of Pleven (Bulgaria) and 2.1% in the center of Thessaloniki (Greece).

*Candida spp. is a prevalent causative agent in the etiology of onychomycosis in children [5, 6].*

According to the literature data, *Candida albicans* is pointed as the main etiological agent of onychomycosis in children (10%), as its incidence in children under 1 year of age is approximately 90%, followed by non-*albicans* species – *C. parapsilosis* (5.1%), *C. tropicalis* (2.6%), *C. guilliermondii* (2.6%), whose prevalence has increased considerably in recent years (6.12%).

Our study is confirmatory. The performed retrospective analysis indicates that *Candida spp. are the main causative agent of onychomycosis in children up to 18 years of age - as Candida albicans prevails over non albicans species.*

*For children up to 1 year, Candida spp is the main etiologic agent of onychomycosis – in 100% of the cases in all of the three investigated centers, which could be explain with the frequent scratches of the fingers at this age.*

In the age 1-3, the yeast of the genus *Candida* is also a major etiological agent, but in this group, in addition to *Candida spp.*, the number of isolated dermatophytes is increasing. Pathogenic molds are also added in this group. In this age, nail biting, or so called onychophagia is also a major predisposing factor.

The isolated pathogens in the age group 1-3 years in Plovdiv shows a ratio of 41.6%:39.6%:18.7% for *Candida spp.*, dermatophytes and molds, respectively. In Pleven and Thessaloniki, the results observed in the same age group was 100% in favor of *Candida spp.*

*Candida spp* is a major etiological agent of onychomycosis in patients in the age group 3-12 years in Plovdiv – 41.6%, but the percentage is close to that of isolated dermatophytes – 39.6%. The percentage of pathogenic molds is insignificantly increased only in Plovdiv – 18.7%, while dermatophyte species prevail as an etiologic agent in this age group in Pleven – 62.1% and in Thessaloniki – 88.9%.

*In the group of older children 12-18, the ratio is similar to that of the patients in the adult population – dermatophytes appear to be the main causative agent of onychomycosis.*

The etiological structure of onychomycosis in children for the age group 12-18 years in Plovdiv indicates a ratio of isolated pathogens *Candida spp.*, dermatophytes and molds equal to 34.2%:42.1%:23.7%, respectively, while in Pleven that ratio is 25%:75%:0%, respectively, and for Thessaloniki – 15.8%:84.2%:0%, respectively.

*In Plovdiv, the isolated pathogens in age group 12-18 were different dermatophytes with almost equal incidence – M. ferrugineum, T. verrucosum, T. rubrum, T. mentagrophytes, T.violaceum, M. canis, M. nanum.*

*In Pleven, T. rubrum is representative of the dermatophyte species in 100% of cases.*

*In Thessaloniki T. rubrum also dominates among isolated pathogens of onychomycosis in children.*

About 15% of onychomycosis in elderly are caused by molds - *Aspergillus*, *Scopulariopsis*, *Penicillium* and others [1]. But molds are uncommon causative pathogens for childhood, and this percentage decreased to 3% [11]. According to our results, molds are isolated only in Plovdiv, but they are not presented in the etiological structure in the group up to 1 year. In the age group 1-3, the pathogenic molds in Plovdiv are 16.7% and in older children 3-12 years – 18.7%, while in the group of 12-18 year olds, they represented 23.7%. Because of the nature of our study, it is difficult to state whether they are real pathogens of onychomycosis in all of the cases. It is possible that in a proportion of cases, molds were superposed, or simply were laboratory contaminants, which would explain this relatively high rate. In Thessaloniki, patho-

genic molds have been isolated only in 3 of 75 cases, as a combined, or superposed cause of onychomycosis in older children (15-16 years), together with the Dermatophyte.

Unlike the established literature data [5,6], according to our study, *females are more often affected by onychomycosis in Bulgaria*, while in Greece, males are more often being affected. We found no specific data that could explain these established differences in gender predilection in Bulgaria.

Toenails are affected about 7 times more frequently in comparison with the fingernails. This is favored by the fact that they grow about 3 times slower than the fingernails [11]. The results of our retrospective study are confirmatory, which lead to the conclusion that the speed of nail growth, in combination or not with a higher incidence of minor trauma from shoes or spur, is relevant to higher incidence of development of toenail onychomycosis.

*Isolated infection of toenails*, occupies the majority of cases of onychomycosis in children [18, 19, 20]. According to results of other studies, it constitutes about 66% of this pathology [15, 21]. It is most typically manifested at the age between 16 and 18 years, where it represents almost 80% of the cases, followed by the incidence in the patients from 8 to 11 years, while in children between 3 and 7 years, this percentage declines to 10 % [18, 19].

According to the analysis of our results, the affection of the toenails dominates in all three investigated centers.

*The infection of the fingernails* is most frequent manifested in children up to 3 years and in cases of patients up to 1 year, this localization represents nearly 100%, while for the age group 4-7 years, it consist about 34%. Cases with such localization are rare between the ages of 16 and 18 [15].

Isolated infection of fingernails among the examined patients constitutes 33.9% of onychomycosis in children up to 18 years of age (99 of 292 children). According to our data, it is most pronounced in the age up to 1 year. Although it constitutes a small part of onychomycosis in children, the percentage of affection of fingernails in children is quite bigger than the same in adults [12]. It is assumed that this is due to some pernicious habits such as „paw fingers“ and „biting of the fingernails“ – also known as onychophagia [8].

*Combined onychomycosis of the fingernails and toenails* is most typical presented in the age 8-12 years [6, 12]. In our study, the combined infection represent 13.4% of the cases [39 of the total 292 children] as it is most often observed in patients in Pleven – 32.9% [31 of 94 cases]. It is possible that the combined onychomycosis of fingernails and toenails is caused by a different pathogen [6, 13, 20]. Such etiology occurred in 100% of cases of combined onychomycosis in Plovdiv – in all 5 of 123 children.

Considering the high incidence of mycoses among adults, it should be noted that the family history appears to be also an important risk factor for the development of onychomycosis in children, as it occurs in 13% of the pediatric patients [4, 5]. Debatable is the question whether it is mainly due to infectious factor as a result from infestation of common objects in everyday life. According to some studies, genetic factors are the dominant risk factor and they are the basis of the high percentage of family history [19, 22, 23]. Results from recent studies in this area indicate that there are genetic mutations and genotypes that contribute to the familial and the individual susceptibility to onychomycosis [24, 24, 25]. Specific genotypes of the human leukocyte antigen, are established, which are more frequently observed in individuals and families with a higher incidence of onychomycosis [26]. Family history of onychomycosis and *Tinea pedum* are considered as a potential etiological factor for the development of the same in children and it is found and proved to be a leading predisposing factor in most of the cases with very early clinical manifestation and unusual progression [27, 28].

Numerous studies of the incidence and the prevalence of onychomycosis in different regions of the world are established, by which the epidemiological evolution structure, the

change of leading etiological agent during different periods in different countries and the increasing incidence of onychomycosis among population during the processes of urbanization is also set [29, 30].

However, no specific literature data with enough evidence exist to explain the differences in the incidence, the epidemiological and the etiological structure of onychomycosis, which was established in Bulgaria and Greece. Probably, it is essential to have in consideration the spatial characteristics as well as cultural differences of two neighboring countries.

In conclusion, our retrospective, multicenter study found significant differences in the incidence of onychomycosis in children from Bulgaria and Greece, as well as a difference in the etiological structure, gender distribution and the most common localization of onychomycosis in children up to 18 years old in Bulgaria and Greece.

Knowledge of the risk factors and the specific clinical manifestations of onychomycosis in children, as well as determining the exact causative agent is essential for proper treatment and prevention of recurrence of the disease.

## CONCLUSION

Onychomycosis is rare in childhood. The lowest incidence rate of onychomycosis in children was observed in Thessaloniki – 2.1%. *Candida* spp. are the leading causative agent in the etiology of childhood onychomycosis in the group of children up to 3 years old, as *Candida albicans* prevails over the non *albicans* species. Dermatophytes were the leading causative agent in the group after 3 years old, and *Trichophyton rubrum* was estimated as the most common isolated agent among them. Non-significant differences were established between the frequency and etiological structure of children onychomycosis in Bulgaria and Greece. Probably, from an essential importance was the influence of the territorial specificities in one hand, as well as the cultural differences of the two neighboring countries.

A significant difference in the predisposing factors, the incidence and the etiological structure of onychomycosis in childhood, was established, compared to the same in adults.

## REFERENCES

1. Westerberg D P, Voyack M J. Onychomycosis: Current trends in diagnosis and treatment. *Am Fam Physician*. 2013;88(11):762-70.
2. Elewski, B. E. Onychomycosis: Pathogenesis, Diagnosis, and Management. *Clin Microbiol Rev*. 1998; 11(3): 415-429.
3. Tchernev G, Penev P K, Nenoff P, Zisova L G, Cardoso J C, Taneva T, Ginter-Hanselmayer G, Ananiev J, Gulubova M, Hristova R, Nocheva D, Guarneri C, Martino G, Kanazawa N. Onychomycosis: modern diagnostic and treatment approaches. *Wien Med Wochenschr*. 2013;163(1-2):1-12.
4. Nenoff P, Krüger C, Schaller J et al. Mycology – an update part 2: dermatomycoses: clinical picture and diagnostics. *J Dtsch Dermatol Ges*. 2014; 12(9):749-77.
5. Mallory S., Bree A., Chern P. *Illustrated manual of Pediatric dermatology-diagnosis and management*. Taylor&Francis, United Kingdom; 2005
6. Gupta, A. K. P. Chang, J. Q. Del Rosso et al. Onychomycosis in Children: Prevalence and Management. *Pediatric Dermatology*, 1998; 15, 6:464-471.
7. Dong Min Kim, Moo Kyu Suh, Gyoung Yim Ha. Onychomycosis in Children: An Experience of 59 Cases. *Ann Dermatol* 2013; Vol 25, 3:327-334.
8. Gupta A K., Humke S. The prevalence and management of Onychomycosis in diabetic patients. *Eur J Dermatol*. 2000;10(5):379-84.
9. Zisova L, Valtchev V, Sotiriou E, Gospodinov D, Mateev G. Onychomycosis in patients with psoriasis--a multicentre study. *Mycoses*. 2012;55(2):143-7.

10. Gunduz T, Metin D Y, Sacar et al. Onychomycosis in primary school children: association with socioeconomic conditions. *Mycoses*, 2006;49:431-433.
11. Singal A., Khanna D. Onychomycosis: Diagnosis and management. *Indian J Dermatol Venereol Leprol*. 2011;77(6):659-72.
12. Khebizi S, Mansouri R. Extensive inflammatory and childhood dermatophytosis caused by *Trichophyton rubrum*. *J Mycol Med*. 2014; 24(3):e131-6.
13. Hwang S M, Kim D M, Suh M K et al. Epidemiologic survey of onychomycosis in Koreans: multicenter study. *Korean J Med Mycol* 2011; 16:35-43.
14. Lateur N, Mortaki A, André J. Two hundred ninety-six cases of onychomycosis in children and teenagers: a 10-year laboratory survey. *Pediatr Dermatol* 2003; 20:385-388.
15. Gupta A K, Jain H C, Lynde C W et al. Prevalence and epidemiology of unsuspected onychomycosis in patient visiting dermatologists' ofices in Ontario, Canada-a multicenter survey of 2001 patients. *Int J Dermatol* 1997; 23:783-787.
16. Nenoff P, Ginter-Hanselmayer G, Tietz H J. Fungal nail infections – an update: Part 1 – Prevalence, epidemiology, predisposing conditions, and differential diagnosis. *Hautarzt*. 2012;63(1):30-8.
17. Chang P, Logemann H. Onychomycosis in children. *Int J Dermatol* 1994; 33:550-551.
18. Gupta A K, Sibbald R G, Lynde C W, Hull P R, Prussick R, Shear N H et al. Onychomycosis in children: prevalence and treatment strategies. *J Am Acad Dermatol* 1997;36:396-402.
19. Tosti A., Piraccini B M., Vincenzi C, Cameli N. Intraconazole in the treatment of two young brothers with chronic mucocutaneous candidiasis. *Pediatr Dermatology* 1997;14:146-148.
20. Lim SW, Suh MK, Ha GY. Clinical features and identification of etiologic agents in onychomycosis (1999-2002). *Korean J Dermatol* 2004;42:53-60.
21. William D. et al. *Andrews' Disease of the skin*. Clinical Dermatology; 11th ed., Saunders Elsevier 2011
22. Lange M, Roszkiewicz J, Szczerkowska-Dobosz A et al. Onychomycosis is no longer a rare finding in children. *Mycoses* 2006;49:55-59.
23. Abeck D. Typical nail alterations in childhood. *MMW Fortschr Med*. 2011; 153(8):44-5.
24. Zaias N, Tosti A, Rebell G et al. Autosomal dominant pattern of distal subungual onychomycosis caused by *Trichophyton rubrum*. *J Am Acad Dermatol*, 1996;34: 302-304.
25. Gupta A K, Simpson F C, Brintnell W C. Do genetic mutations and genotypes contribute to onychomycosis? *Dermatology*. 2014;228(3):207-10.
26. Rodríguez-Pazos L, Pereiro-Ferreirós M M, Pereiro M Jr, Toribio J. Onychomycosis observed in children over a 20-year period. *Mycoses* 2011;54:450-453.
27. Gunduz T, Metin D Y, Sacar T et al. Onychomycosis in primary school children: association with socioeconomic conditions. *Mycoses*. 2006;49(5):431-3.
28. Sachdeva S, Gupta S, Prasher P et al. *Trichophyton rubrum* onychomycosis in a 10-week-old infant. *Int J Dermatol* 2010; 49:108-109.
29. Seebacher C, Bouchara J P, Mignon B. Updates on the epidemiology of dermatophyte infections. *Mycopathologia*. 2008;166(5-6):335-52.
30. De Berker D. Childhood nail diseases. *Dermatol Clin*. 2006; 24(3):355-63.



*Corresponding author:*

Dr Anastasia Atanasova Chokoeva MD  
 University Clinic of Dermatology and Venereology  
 Department of Dermatology and Venereology  
 Medical University of Plovdiv, Bulgaria  
 15A Vasil Aprilov Blvd  
 e-mail: assia\_chokoeva@abv.bg