

MINISTRY OF EDUCATION
AND TRAINING

MINISTRY OF
HEALTH

NATIONAL INSTITUTE OF MALARIOLOGY,
PARASITOLOGY AND ENTOMOLOGY

**PREVALENCE, CLINICAL FEATURES, CAUSATIVE
AGENTS AND TREATMENT OUTCOMES OF TINEA
PEDIS AMONG SMALL TRADERS IN NGHE AN
PROVINCE IN 2022**

Major: Infectious and tropical diseases
Code: 972 01 09

THESIS SUMMARY

HANOI - 2024

THE THESIS WAS COMPLETED AT THE NATIONAL
INSTITUTE OF MALARIOLOGY, PARASITOLOGY AND
ENTOMOLOGY

Instructors:

Instructor 1. Assoc.Prof.Ph.D.Le Tran Anh

Instructor 2. Assoc.Prof.Ph.D. Tang Xuan Hai

Reviewer 1:

Reviewer 2:

Reviewer 3:

The thesis will be defended in front of the Institutional Defense
Committee at the National Institute of Malariology, Parasitology
and Entomology

at 8:00 on DEC 26, 2024

The thesis can be found at:

- Vietnam National Library;
- The Library of the National Institute of Malariology,
Parasitology and Entomology.

INTRODUCTION

Superficial fungal infection is one of the most common diseases in humans, causing damage to the skin, hair, and nails. It affects about 20-25% of the world's population, especially in countries with tropical and subtropical climates [1]. Tinea pedis (athlete's foot) has a high prevalence in the community, with up to 35% of people with foot diseases being clinically diagnosed with fungal infections [2]. Its causative agents consist of two main groups: filamentous fungi (dermatophytes, non-dermatophytes) and yeasts (*Candida*, *Malassezia*). The tropical, hot and humid climate in Vietnam is very favorable for fungal growth. The working and living conditions of small traders are greatly affected by the weather and climate conditions; therefore, they are at high risk of fungal infection.

Diagnosis of superficial fungal infections is mainly based on clinical examination combined with direct testing. Due to the lack of screening and early diagnosis procedures, treatment of superficial fungal infections still has many difficulties. Preventive measures often focus on infection prevention. Up to now, there have been few studies on tinea pedis in Vietnam; therefore, we conducted the study: "***Prevalence, clinical features, causative agents and treatment outcomes of tinea pedis among small traders in Nghe An province in 2022***" with the following objectives:

1. To determine the prevalence and some factors associated with tinea pedis among small traders in Nghe An province in 2022.
2. To describe clinical features and treatment outcomes of tinea pedis in the study subjects.
3. To identify the composition of fungal species by morphology and molecular biology.

NOVELTY OF THE THESIS

This is the first time a study on tinea pedis has been conducted in Vietnam. In addition, the study applied the traditional technique of morphology combined with the modern technique of molecular biology for species identification.

THESIS STRUCTURE

The thesis consists of 122 pages divided into the following sections: Introduction (2 pages); literature review (27 pages); study subjects and methods (26 pages); study results (39 pages); discussions (25 pages); conclusions (2 pages); and recommendations (1 page). There are 130 references, including 10 Vietnamese references and 120 English references.

Chapter 1

LITERATURE REVIEW

1.1. Overview of fungi and superficial fungal infections

Superficial (or cutaneous) mycoses are fungal infections that are confined to the outer layers of the skin, nail, or hair, (keratinized layers). Depending on the level of fungal penetration and the body's immune response, superficial mycoses have clinical manifestations as limited inflammation or obvious inflammation.

The foot is the part of the lower limb distal to the ankle joint.

1.2. Prevalence and factors associated with tinea pedis

1.2.1. Prevalence

The prevalence of superficial fungal infections in the world is about 20 to 25%. A study on 1303 elderly patients with skin diseases at a hospital in Bangladesh showed that the percentage of tinea pedis was 1.84%, tinea unguum 2.14%, and candidiasis 5.06%.

There have not been many in-depth studies on tinea pedis in Vietnam. Nguyen Canh Cau (2001), a study on 435 coal miners in Thai Nguyen, found that the rate of tinea pedis was 7.12%. Truong Quang Anh and Ton Nu Phuong Anh (2003), studying 199 cases of skin fungal infection showed that the proportion of lesions caused by tinea pedis was 7.04%.

With a study on 184 patients with skin fungal infection in Nghe An, Nguyen Thai Dung (2015 - 2016) found that the prevalence of fungal lesions on the feet was 4.35%.

1.2.2. Associated factors

The number of patients with superficial fungal infections

increases with age, and 80% of the elderly people over 60 years old get infected with tinea pedis. Tinea unguum is more common in men than in women with a ratio of 3:1.

People who are frequently exposed to water, such as fishmongers, dishwashers, salesperson, etc., are at high risk of *Candida* nail infection. People with regular wearing of shoes, such as soldiers, office workers, etc., are also at higher risk of getting tinea pedis.

Favorable factors for the transmission and development of superficial fungal infection include skin trauma, microtrauma, wet skin, unsanitary conditions, and genetic factors.

1.3. Clinical and laboratory features and causative agents of tinea pedis

1.3.1. Clinical features and causative agents

- Tinea unguum

Functional symptoms: asymptomatic or pain, paresthesia at the damaged nail, difficulty wearing shoes.

Physical symptoms: Based on the location of fungal invasion, there are 4 clinical forms: distal lateral subungual onychomycosis (DLSO); superficial white onychomycosis (SWO); proximal subungual onychomycosis (PSO)

Causative agents: common yeasts, dermatophytes, filamentous fungi...

- Tinea pedis is a foot infection due to a dermatophyte fungus on the soles of the foot and between the toes. The infection on the instep of the feet is considered tinea corporis.

Typical dermatophytes causing tinea pedis include: *T. rubrum*, *Trichophyton interdigitale*...

Primary lesions consist of vesicles, pustules, bullae, scales, ulcers... Clinical manifestations include 4 types: interdigital type, scaling hyperkeratotic moccasin-type, inflammatory type (vesicular, bullae type), ulcerative type.

- Tinea corporis on the foot: Dermatophyte lesions appear on the instep of the foot, which may be accompanied with lesions on other smooth skin areas of the body.

+ Functional symptoms: itching and burning

+ Primary lesions are centrifugal and arcuate with varying sizes. Scaling is a common primary lesion, but may be minimal or absent when corticosteroids are used. Pustules develop at the margins of lesions. Vesicles and granulomas, papules may be seen.

- Interdigital form of cutaneous candidiasis

Functional symptoms are mainly itching and burning.

Primary lesions include white, thin, crumbly patches. *Candida* infection often occurs between toes 4-5, and may be accompanied by paronychia.

- Chronic mucocutaneous candidiasis

It is a chronic fungal infection of the skin, mucous membranes, and nails. The disease is often associated with genes, endocrine, and immune deficiencies. *Candida albicans* (*C. albicans*) is the most common causative species.

Primary lesions are red, hyperkeratotic, thickened patches of skin, mucous membranes, and possible nail damage.

- Tinea nigra: is caused by *Hortaea werneckii*, usually asymptomatic.

Primary lesions are burnings or gray-brown to green macules or plaques with clear borders. They appear in palms, soles, neck, or trunk.

1.3.2. Laboratory features

Superficial fungal infections often have diagnostic symptoms, but laboratory testing can aid in the diagnosis of cases with similar symptoms or atypical lesions due to previous treatment.

Diagnostic tests: direct testing, culture, molecular biology.

Species identification: by morphology and molecular biology. Species identification of the causative agent has been focused on to support treatment.

Direct testing:

This is a simple and widely used technique with quick results using 10 - 20% KOH solution.

Culture

Direct testing cannot provide accurate species identification, therefore fungal culture is required. Fungi are cultured at temperatures ranging from 25 to 30°C. Culture medium contains antibiotics to limit bacterial growth. Culture gives slower results than direct testing, but it can help identify the causative agents of disease.

Identification techniques

- Traditional techniques:

Identification of filamentous fungi is based on morphology.

Identification of yeast species is based on physical and physiological characteristics (ability to assimilate and ferment sugar, presence of certain enzymes such as urease, ability to form spores...).

- Modern techniques

+ Identification based on DNA: PCR-RFLP, Realtime PCR, sequencing. Up to now, studies on fungal species identification often focus on analyzing the ITS region. Compared with traditional techniques, molecular biology techniques based on DNA can provide faster results and accurate identification of rare species. The cost of this method is high and not all medical facilities are capable of performing it.

+Protein: MALDI-TOF

1.4. Treatment of tinea pedis

- *Topical treatment*: Traditional, non-specific topical medications include ASA alcohol, BSI2.5% alcohol, Whitfield 5% ointment, Salisilic 5% ointment... They are all effective after 2 - 4 weeks.

- *Systemic treatment*: Some medications used for treatment of superficial fungal infections include griseofulvin, azole, Allylamine.

Terbinafine is an allylamine which has a broad spectrum of antifungal activity. It inhibits squalene epoxidase, an enzyme that plays a key role in ergosterol biosynthesis in fungi.

There hasn't been any research on the treatment outcomes of tinea pedis with terbinafine in Vietnam.

1.5. Characteristics of the study subjects and study locations

Nghe An is the largest province among 63 provinces/cities of Vietnam. The living conditions, economic and social development in coastal plains and mountainous areas of Nghe An is obviously different. There are currently 370 markets in Nghe An province; however, the environmental sanitation in the markets still exposes many shortcomings, especially the markets in some rural areas and suburban areas. Although some markets have been upgraded and renovated, waste treatment areas, toilets and water systems serving market operations have not been improved. This results in the bad environment and unhygienic working conditions for small traders in the markets, creating favorable conditions for fungal disease development.

Chapter 2

STUDY SUBJECTS AND METHODS

2.1. Study subjects and methods for determination of the prevalence and associated factors

2.1.1. Study subjects

- Small traders at some markets in Nghe An province who met the selection criteria and agreed to participate in the research.

Inclusion criteria: Small traders, regardless of age, gender, education level..., who had worked in the markets for more than 6 months and agreed to participate in the study.

Exclusion criteria: Small traders with painted toenails; patients using systemic or topical antifungal medication for 1 month.

2.1.2. Study methods

- *Study design:* Cross-sectional descriptive research method

- *Sample size:* The following formula was used for calculating the sample size in a prevalence study:

$$n = Z^2_{1-\alpha/2} \frac{(1-p)}{p\varepsilon^2} \times DE$$

Where: n is the minimum sample size. p : is the estimated prevalence of tinea pedis in the population. Because there had been no research on tinea pedis in Nghe An province in particular and Vietnam in general, we chose $p = 50\%$ ($p = 0.50$). $Z_{1-\alpha/2}$: is the confidence coefficient; With a 95 percent confidence interval, the value of $Z_{1-\alpha/2}$ is 1.96; ε : is the relative error, choose $\varepsilon = 0.1$. DE is the effective coefficient, take $DE=2$.

With the selected values, the calculated sample size was 768. In fact, 787 small traders agreed to participate in the study.

- *Sampling method*: Cluster random sampling.

- *Research content*:

Determination of the characteristics of the study subjects: demographic characteristics (age, gender, education level); nature of work; business items; behavioral characteristics, habits, prevalence...

Determination of the prevalence

Determination of associated factors

- *Techniques used in the study*

Interviewing and determination of height and weight

Examination performed by dermatologists to detect lesions.

Sample collection

Transportation of specimens and culture tubes according to Decision No. 57/QĐ-DP of the Ministry of Health in 2017 on the guidelines for sampling, packaging, preservation and transportation of infectious disease specimens

Direct potassium hydroxide (KOH) testing for fungal detection

Fungal culture in Sabouraud Agar and Mycosel Agar

The fungal culture is positive when fungal colonies grow on inoculated tissues. The fungal culture is negative after 5 weeks of no colony growth.

Variables, research indexes: variables on demographics, behavior, environment, history, prevalence...

Criteria for determining tinea pedis: having suspicious lesions and positive test results.

2.2. Study subjects and methods for description of clinical

features and treatment outcomes

2.2.1. Study subjects

- The patients with tinea pedis in the study

2.2.2. Study methods

- *Study design:*

For clinical characterization study: Cross-sectional descriptive method

For treatment outcome research: Non-randomized, non-controlled, longitudinal, interventional study.

- *Sample size*

All the patients diagnosed with tinea pedis.

- *Sampling method:* Total population sampling

- *Research content:*

+ Description of demographic characteristics of the patients with tinea pedis

+ Description of clinical features: duration, functional and physical symptoms (location of lesions, primary lesions, clinical form, severity).

+ Determination of treatment outcomes and adverse effects of medications.

- *Techniques used in the study*

+ Interviewing: for evaluation of duration and functional symptoms

+ Examination and description of lesions

+ Determination of clinical forms and the severity of the disease according to Decision No. 75/QĐ-BYT of the Ministry of Health dated January 13, 2015 on the Guidelines for diagnosis and treatment of dermatological diseases.

+ Selection of treatment regimen: follow the regimen of the Ministry of Health at Decision No. 75/QĐ-BYT of the Ministry of Health dated January 13, 2015.

+ Evaluation of treatment outcomes according to the Vietnam Dermatology Association, interviewing for adverse effects of medications.

- Variables, indexes: functional symptoms, location of

lesions, primary lesions, severity of lesions, recovery rate, adverse effects...

2.3. Study subjects and methods for species identification

2.3.1. Study subjects

Fungal samples isolated from the patients participating in the study objective 1

2.3.2. Study methods

Study design: Laboratory Experiment

Sample size and sampling method:

- Species identification by morphology: all positive fungal culture.

- Species identification by PCR – RFLP: all isolated yeast samples.

- Species identification by gene sequencing:

+ For the samples of filamentous fungi: Representative strains are selected and sequenced.

+ For the samples of yeast: When morphological identification and PCR-RFLP provides the same results, sequencing is performed for confirmation.

When morphology and PCR-RFLP produces different results, gene sequencing is conducted on the samples that are not identified by morphology and PCR-RFLP for determination.

Research content: Identification of fungal species by morphology and molecular biology; species distribution by disease and disease form.

Techniques used in the study

+ Macroscopic observation: daily check of culture samples, observation and description of colonies using magnifying glass.

+ Microscopic observation: Based on macroscopic morphological characteristics, microscopic classification of filamentous fungi is conducted using identification keys:

+ Yeast identification:

Morphology: culture in Chrome agar

- Techniques used in PCR identification

DNA extraction using the Kit by Norgen Biotek Corp. (Canada)

PCR running with primers ITS1, ITS4

Cleaving with enzyme *MspI*

Species identification based on PCR products and restriction enzyme cleavage

Representative sample taken for sequencing; comparison of the obtained sequence with the genebank for determination of fungal species. (Appendix 2)

2.4. Data analysis and processing

Statistical analyses were performed using SPSS 20.0. Quantitative variable description included mean value and standard deviation. Qualitative variable description included number and percentage. Analysis of the relationship between variables employed Pearson's chi-squared test or Fisher's exact test for categorical variables in univariate analysis, multivariate logistic regression analysis for significant related variables in univariate analysis. A p value <0.05 was considered statistically significant.

2.5. Error elimination

The selection and screening of patients were well conducted, and the minimum sample size was ensured to minimize errors in the study.

2.6. Ethics in research

The study had been approved by the Scientific and Ethical Review Board of National Institute of Malariology, Parasitology and Entomology according to Decision No. 303/QĐ-VSR dated 3 March 2019. The study subjects were well informed of the purpose of the study, voluntarily provided information, and were tested and treated free of charge. Their information was kept confidential and used for research purposes only.

Chapter 3 STUDY RESULTS

3.1. Prevalence and some factors associated with tinea pedis among small traders in Nghe An, 2022

3.1.1. Prevalence of tinea pedis

Table 3.3: Prevalence of tinea pedis

Population	Population sample size	Number of cases or suspected cases	Percentage (%)
Suspicious lesions in the population	787	231	29.4
In the study subjects	787	124	15.8
In the subjects with suspicious lesions	231	124	53.7

The proportion of study subjects with suspicious lesions was 29.4%. The prevalence of tinea pedis was 15.8%. And the prevalence among the subjects with suspicious lesions was 53.7%.

3.1.2. Factors associated with tinea pedis

Table 3.4: Prevalence of tinea pedis by age

Age group	Number	Infected	Percentage (%)
15 - < 39	122	7	5.7
40 – 49	244	26	10.
≥ 50 – 77	252	91	36.1
Total	787	124	
Mean age ($X \pm SD$)		53.87 ± 9.71	

The results showed that the prevalence of tinea pedis increased with age.

Table 3.10: Multivariate analysis of factors associated with tinea pedis in the study subjects

Factor		Infected		OR (95% CI)	P
		Yes	No		
Living in the mountains	Yes	75	307	0.68 0.49 – 1.03	0.069
	No	49	356		
Business items	High	102	609	1.32	0.341

	NC			0.75– 2.34	
	Low NC	22	54		
≥ 50 years old	Yes	91	330	2.65	<0.001
	No	33	333	1.70 – 4.13	
Selling aquatic products and seafood	Yes	24	77	1.79	0.034
	No	100	586	1.04 – 3.08	
Frequent contact with water	Yes	69	305	1.37	0.175
	No	55	358	0.87 – 2.17	
Wearing closed toe boots, shoes, sandals	Yes	102	609	1.06 0.35 – 3.22	0.916
Habit of going barefoot	Yes	28	69	1.94	0.206
	No	96	594	0.70 – 5.40	
Hard work	Yes	40	139	1.30	0.259
	No	84	524	0.82– 2.06	
Commonly used nail clippers	Scissors	21	71	1.25	0.433
	Others	103	592	0.71 - 2.20	
Previous use of immunosuppressants	Yes	9	20	1.81	0.179
	No	115	643	0.76 – 4.31	

People aged ≥ 50 years old and working in seafood business were at risk of tinea pedis; the difference was statistically significant, $p < 0.05$.

3.2. Clinical features and treatment outcomes of tinea pedis

Table 3.12: Gender and age of the patients with tinea pedis

Features	Number	Percentage (%)
-----------------	---------------	-----------------------

Gender	Male	2	2.4
	Female	121	97.6
Age group	< 40	7	5.6
	40 – 49	26	21.0
	≥ 50	91	73.4
	Total	124	100
Youngest – Oldest		15 – 77	
Mean age (X± SD)		53.87 ± 9.71	

Most of the patients (97.6%) were females. The number of patients aged 50 years old or more accounted for 73.4%. The mean age was 53.87 ± 9.71

- Location of lesions

Table 3.14: Location of lesions in the patients with tinea pedis (n=124)

Location	Location	Number	Percentage (%)
Nails only	Nails	97	78.2
Skin only	Interdigital clefts of toes	19	15.3
	Sole	1	0.8
Nails and skin	Nails and around nails	5	4.0
	Interdigital clefts of toes and nails	2	1.6
Total		124	100

Of 124 patients with tinea pedis, there were 104 cases of nail lesions, 27 cases of skin lesions, and 21 cases of interdigital lesions.

- Characteristics of nail lesions

+ Most patients (93.3%) with tinea pedis suffered from the disease for more than 6 months, with no cases of less than 3 months.

+ 100% of the patients had no functional symptoms.

+ Physical symptoms: Analysis of 104 patients with nail lesions showed the following results:

Table 3.15: Primary lesions of tinea pedis (n=104)

Symptoms	Number	Percentage (%)
Color change	99	95.2
Subungual hyperkeratosis	21	20.2
Onycholysis	21	20.2
Nail dystrophy	32	30.8
Sunken, lusterless nails	37	36.6
Paronychia	5	4.8

The majority (95.2%) of patients with tinea pedis had changes in nail color.

Table 3.16: Changes in nail color in the patients with tinea pedis

Color	Number	Percentage (%) (n=99)	Percentage (%) (n=124)
White	21	21.2	16.9
Yellow	32	32.3	25.8
Black	25	25.3	20.2
Brown	18	18.2	14.5
Blue	3	3.0	2.4

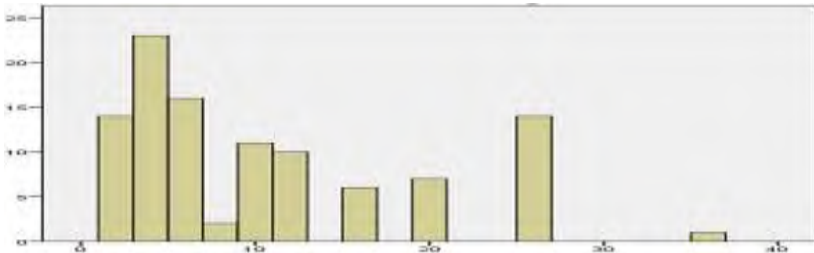
Nail discoloration in fungal lesions was diverse: yellow (32.3%), black (25.3%), and white, brown, blue.

Table 3.19: Number and location of nail lesions (n=104)

Lesions	Characteristics	Number	Percentage (%)	Percentage (%) of lesion side
Unilateral	Right	19	18.3	46.2
	Left	31	29.8	53.8
Bilateral		54	51.9	
Number of damaged nails	One	47	45.2	
	Two	48	46.2	
	Three	9	8.6	

Damaged toenails could be unilateral or bilateral, in which the nails of the left foot was more infected (53.8%).

- **Assessment of the clinical severity of tinea pedis using OSI score**

**Figure 3.2: OSI score of the patients with tinea pedis**

The mean OSI score was 10.26 ± 8.05 .

Table 3.19: Clinical form of tinea pedis (n=104)

Clinical form	Number	Percentage (%)
DSLO	88	84.6
PLO	2	1.9
SWO	9	8.7
CO	5	4.8
Total	104	100%

Distal lateral subungual onychomycosis (DLSO) was the most common clinical form of tinea pedis with a rate of 84.6%.

Table 3.21: Percentage of fungal nail lesions by clinical form

Primary lesions	DSLO (n=88)	Percentage (%)	Other forms (n= 18)	Percentage (%)
Color change	84	95.5	15	83.3
Subungual hyperkeratosis	18	20.5	3	16.7
Onycholysis	17	19.3	4	22.2
Nail dystrophy	21	23.9	11	61.1
Sunken, lusterless nails	33	37.5	4	22.2

Clinical forms of DSLO were diverse, in which color change was the most common primary lesion (95.5%).

- Characteristics of skin lesions in the patients with tinea pedis

The study of 27 cases with skin lesions showed that 100% of the patients suffered from the disease for less than 3 months.

Table 3.22: Location of skin lesions in the patients with tinea pedis (n=27)

Location	Number	Percentage (%)
Interdigital clefts of the toes	21	77.8
Around the toenails	5	18.5
Sole	1	3.7
Total	27	100

Lesions in the interdigital clefts of the toes accounted for the highest proportion of 77.8%, followed by lesions around the toenails and soles of the feet.

The majority of clinical lesions on the skin had unclear boundaries (24/27).

Table 3.29: Location of interdigital lesions on the feet (n=21)

Interdigital clefts of the toes	Left	Right	Total	Percentage (%)
1-2	1	1	2	9.5
2-3	1	1	2	9.5
3-4	4	4	8	38.1
4-5	2	7	9	42.9
Total	8	13	21	100
Percentage (%)	38.1	61.9	100	

The most common location of lesions was the cleft between toes 4-5 (42.9%), followed by toes 3-4 (38.1%), and toes 1-2 and 2-3 (9.5% both).

Treatment outcomes

Among six patients accepting medication and follow-up, one patient was completely cured with combination treatment of topical and oral terbinafine, and five patients with interdigital *candidiasis* were completely cured with the treatment of topical terbinafine.

No adverse effects were recorded.

3.3. Composition of fungal species causing tinea pedis

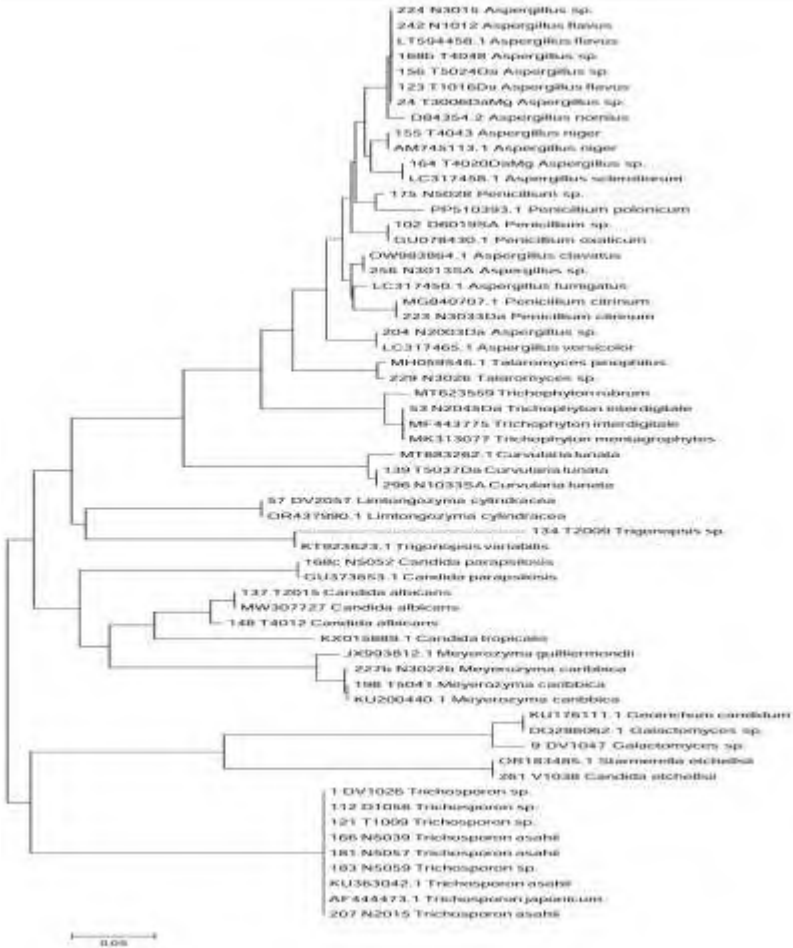


Figure 3.12: Phylogenetic tree showing relationships between fungal species sequenced in the study

Table 3.34: Results of species identification (n=126)

Genera	Species	Number	Percentage (%)
--------	---------	--------	----------------

Genera	Species	Number	Percentage (%)
<i>Candida</i>	<i>C. albicans</i>	58	46.0
	<i>C. tropicalis</i>	3	2.4
	<i>C. parapsilosis</i>	6	4.8
	<i>C. guilliermondii</i>	1	0.8
	<i>C. cylindracea</i>	1	0.8
	<i>Starmerella etchellsii</i>	3	2.4
<i>Trichosporon</i>	<i>T. asahii</i>	13	10.3
	<i>Trichosporon japonicum</i>	4	3.2
<i>Meyerozyma</i>	<i>Meyerozyma caribbica</i>	2	1.6
<i>Geotrichum</i>	<i>Geotrichum candidum</i>	2	1.6
<i>Trigonopsis</i>	<i>Trigonopsis variabilis</i>	1	0.8
Yeast		94	74.6
<i>Aspergillus</i>	<i>Aspergillus sclerotiorum</i>	1	0.8
	<i>A. flavus</i>	8	6.3
	<i>A. nomius</i>	3	2.4
	<i>A. clavatus</i>	1	0.8
	<i>A. niger</i>	4	3.2
	<i>A. versicolor</i>	1	0.8
<i>Penicillium</i>	<i>Penicillium citrium</i>	5	4.0
	<i>Penicillium oxalicum</i>	1	0.8
	<i>Penicillium polonicum</i>	1	0.8
<i>Trichophyton</i>	<i>Trichophyton interdigitale</i>	2	1.6
<i>Curvularia</i>	<i>Curvularia lunata</i>	3	2.4
<i>Fusarium</i>	<i>F. solani</i>	1	0.8
<i>Talaromyces</i>	<i>Talaromyces pinophilus</i>	1	0.8
Filamentous fungi		32	25.4

Among 126 different fungal samples isolated from 124 patients, a total of 11 genera and 24 species were identified. Yeast was the most common pathogen (74.6%). *Candida* was the most common genus (57.2%), followed by *Aspergillus* (14.2%).

Chapter 4

DISCUSSIONS

4.1. Prevalence and some factors associated with tinea pedis among small traders in Nghe An

- **Prevalence:** Among 787 small traders, 29.4% had suspicious lesions. Test results showed that 124 patients were infected with tinea pedis, accounting for 15.8%. There have been few studies on the prevalence of tinea pedis in the world. The Achilles project in Europe revealed that about ¼ of the total populations were screened for tinea pedis and more than half of the total subjects had or were suffering from the disease. A study in Madrid, Spain in the community in 1997 showed a much lower prevalence of tinea pedis (2.9%) and tinea unguum (2.8%). In our study, the prevalence of tinea pedis among the subjects with suspicious lesions was 53.7%. This high prevalence may result from the climate of Vietnam, which is tropical, hot and humid, with a lot of rain; working and living conditions of small traders in markets are not good enough, especially in mountainous markets.

Some epidemiological studies show that the prevalence of toenail fungus in the general population is about 5.5%. A 2013 systematic review based on 11 community studies and 21 hospital studies revealed that the average prevalence of toenail fungus in North America and Europe was 4.3%, and in hospital studies it was 8.9%. As such, the prevalence of toenail fungus in small traders is higher than in studies around the world. In addition to differences in geography, geographical conditions, and natural disposition, the nature of work is also a factor contributing to this inconsistency.

It can be seen that toenail fungus has a high prevalence in the community. Elderly people or those with underlying diseases such as psoriasis, diabetes... need to examine and take care of their feet regularly

- *Associated factors*

In our study, the prevalence of tinea pedis differed by age, with 5.7% in the age group of below 40 years old, 10.7% in the age group of 40 to 50 years old, and 36.1% in those over 50 years

old. Multivariate analysis showed that people over 50 years old had a 2.65 times higher risk of tinea pedis than those under 50 years old. This finding is quite similar to Nourrchène Toubraki et al. (2013 - 2014) which found that the frequency of tinea pedis increased with age. The highest prevalence was found in the 41 to 50 year old group (23.1%), followed by the 51 - 60 year old group (21.9%); the difference was not statistically significant ($p = 0.066$). And this result is also proven by many other studies in the world.

Age, in addition to the risk factor of tinea pedis, has also been shown to be a factor that increases the risk of toenail fungus by many studies around the world. Our study showed that small traders selling aquatic and seafood products had a significantly higher risk of contracting the disease with $p < 0.05$ (OR 1.79). This result is consistent because the traders frequently contacted with water and dirt, which increased the exposure to daily detergents, and wearing closed toe boots and sandals created favourable conditions for fungal growth. Research in Japan on the correlation between the environment in footwear and tinea pedis showed that high temperature/humidity and high dew points significantly increased the risk of contracting the disease.

4.2. Clinical features and treatment outcomes of tinea pedis

78.2% of the patients had clinical lesions on the nails, besides interdigital lesions, skin lesions, combined lesions of the nails and around the nails. Toenail fungus was the most common form of superficial fungal infections (82.26%), followed by interdigital *candidiasis* with 15.32%. Most patients with toenail fungus suffered from the disease for more than 6 months, accounting for 93.3%, and no cases of lesions of less than 3 months.

In our study, the main clinical symptom of toenail fungus was color change (95.2%).

- Number and location of damaged nails

Damaged toenails could be unilateral or bilateral, in which the nails of the left foot was more infected (53.8%). 46.2% of the

patients had lesions on 2 or more nails, which is quite similar to a study on 417 patients with nail fungus in Brazil, reporting 62.59% of cases with damage on the big toe.

The mean OSI score in our study was 10.26 ± 8.05 , which means the disease is moderate. This result is not similar to some studies in the world. The study on 417 patients with toenail fungus in Brazil showed the mean OSI score of 16.67 ± 7.80 , corresponding to a severe disease. Studies have also shown that the OSI score will vary in different study subjects.

Most of the patients (75.0%) had mild and moderate nail lesions. This result is similar to a study in the Netherlands, showing 51.1% of moderate lesions, 34.3% of severe lesions. In a study in Spain, the OSI score was used to analyze the severity of 50 cases of toenail fungus by experienced clinicians, and the proportion of severe cases was 80%, followed by mild cases (10%) and moderated cases (8%). This is a clinically based score, easy to use, and should be used widely in scientific research as well as clinical practice. DSLO was the most common clinical form (84.6%), and PSO was the least common (1.9%). This finding is similar to studies in Tunisia and Turkey.

- Characteristics of skin lesions in the patients with tinea pedis

In our study, 100% of the patients had lesions for less than 3 months. This result is different from the study by Raghavendra RM et al. in 2018, which showed up to 60% of the patients having lesions for more than 60 days, 28% of the patients having lesions for 41 - 50 days, and 12% of the patients having symptoms for 11 - 21 days.

Interdigital lesions between the toes accounted for the highest proportion of 77.8%, besides lesions around the nails and on the sole of the feet. Most patients (81.5%) suffered from itching while others were asymptomatic.

The main clinical symptoms were white, pustular patches, accounting for 66.7% of the cases. This result is consistent with documents referring to the primary lesions of interdigital type. In our study, 75% of the study subjects with suspicious lesions in the

interdigital clefts of the toes were confirmed to have interdigital candidiasis. Many studies in the world show that, in addition to lesions caused by yeast, bacteria or other fungi are also the cause of similar lesions in this location.

- ***Treatment outcomes***

The number of patients accepting treatment was low (6/124). The reason may be the disease had few functional symptoms; despite free treatment and follow-up, the prolonged use of oral antifungals made the patients hesitate about using medications, have a doubt on the effectiveness of the treatment as well as the risk of adverse effects.

There was only one case adhering the combination of topical and oral treatment. As a result, the patient was completely cured and had no adverse effects during the treatment. The cure rate in clinical studies worldwide was 66% with terbinafine. Undesirable effects included headache, gastrointestinal problems, and rashes. A systematic review shows that terbinafine is one of the most effective medications.

However, there is another aspect related to the effectiveness of treatment that the risk factors of nail fungus such as peripheral vascular disease, immunodeficiency, peripheral neuropathy... are difficult to be completely cured. This is one of the issues that clinicians need to pay attention to when giving advice to patients.

100% (5/5) of the patients with interdigital candidiasis in our study were cured after 1 week of treatment with topical terbinafine. This result is similar to many studies in the world, and topical antifungal is still an effective treatment option for interdigital candidiasis.

4.3. Composition of fungal species causing tinea pedis

Among 126 positive culture specimens, we detected 11 genera and 24 fungal species causing tinea pedis. Yeasts accounted for the highest proportion (74.6%), and filamentous fungi made up 25.4%. In previous studies, the most common causative agents of tinea pedis were dermatophytes, then yeasts [115]. The pathogens that are yeasts and filamentous fungi other than dermatophytes are always performed clinical and laboratory

tests in combination [106]. Unlike dermatophytes, yeasts and NDM are opportunistic fungi, often present on the body surface and in the environment without causing disease. Therefore, fungal diagnosis must be extremely strict [118].

Candida was the most common genus (57.2%), followed by *Aspergillus* (14.2%), and *Trichosporon* (13.5%). *C. albicans* was the most common causative agent of tinea pedis (40.6%), followed by *T. asahii* (10.3%). Some rare species were also detected, including *Talaromyces pinophilus*, *Curvularia lunata*, *Penicillium polonicum*, *Trigonopsis variabilis*...

Our findings are not consistent with a study on morphological identification of fungal species causing tinea pedis by Fekih N.E. et al. (2009), which showed that dermatophytes were the main causative agents (57.1%), followed by *Candida* spp. (35.7%); *Trichophyton rubrum* and *C. parapsilosis* were the most common species of each group, respectively[22]. Many studies in the world also reveal that dermatophytes are the main causative agents of tinea pedis, possibly because of the nature of work, living habits, and natural disposition of small traders, which are favorable for yeast development and causing diseases. Therefore, it is necessary to study the factors affecting the occurrence of the disease.

CONCLUSIONS

1. The study was conducted on 787 small traders in Nghe An in 2022 to determine the prevalence of tinea pedis. The following conclusions were drawn:

- The prevalence of tinea pedis in the study subjects was 15.8%.
- The prevalence of tinea pedis in small traders with suspicious lesions was 53.7%. The prevalence increased with age.
- Factors that were statistically significantly associated with tinea pedis included age group ≥ 50 and seafood trading.

2. Clinical features and treatment outcomes of tinea pedis in the study subjects

The mean age of patients was 53.87 years old (15-77). Among 124 patients infected with tinea pedis, there were 117 cases of skin

or nail lesions only (94.35%); 104 cases of nail lesions (83.87%), 27 cases of skin lesions (21.77%); 7 cases of combined nail and skin lesions.

Toenail fungus had no functional symptoms, 93.3% of the patients had symptoms on the toenail for more than 6 months. Common physical symptoms included color change (95.2%), nail dystrophy (30.8%), subungual hyperkeratosis, onycholysis...; lesions mainly appeared on the big toe (92.4%). Distal lateral subungual onychomycosis (DLSO) was the most common clinical form with 84.6%. The mean OSI score was 10.26 ± 8.05 .

Skin lesions were mainly present in the interdigital clefts of the toes (21/27). Clinical symptoms included itching (22/27), white pustules (18/27)... The most common location of lesions was in the interdigital clefts of the toes 4-5 (9/20), and 3-4 (8/20).

The number of patients accepting treatment and follow-up was low (6/124). 6/6 patients were cured with terbinafine according to the Ministry of Health's protocol.

3. Among 126 different fungal samples isolated from 124 patients, a total of 11 genera and 24 species were identified. There were 5 genera of yeasts, including *Candida* (72/94, 76.6%), *Trichosporon* (17/94, 18.1%), *Meyerozyma*, *Geotrichum*, and *Trigonopsis*, and 11 species of yeasts, in which *Candida albicans* accounted for the highest proportion of 61.7%. Six genera of filamentous fungi were detected, including *Aspergillus* (18/32, 56.25%), *Penicillium*, *Trichophyton*, *Curvularia*, *Fusarium*, *Talaromyces*; *Aspergillus flavus* (8/32, 25.0%) was the most common species of filamentous fungi.

Yeast was the main causative agent of toenail fungus (70.2%), followed by filamentous fungi (29.8%). In the group of yeast agents, *C. albicans* accounted for the highest percentage (64.4%), while *A. flavus* was the most common filamentous fungal species (25.8%). Only one case of dermatophytosis caused by *T. interdigitale* was detected. All the patients with interdigital candidiasis were caused by yeast with *Candida albicans* as the most common species (52.4%). There was only one case of foot fungus caused by *Trichophyton interdigitale*.

RECOMMENDATIONS

1. Tinea pedis is a public health problem. It is necessary to strengthen health education and communication about the disease. Especially, small traders over 50 years old and selling seafood should adjust their working and daily living habits, avoid factors that increase the risk of tinea pedis, use personal protective equipment when working, and clean their feet daily...

2. When examining a patient with nail dystrophy, onycholysis, or white, crusty lesions between the toes, a dermatologist should refer to fungal lesions.

LIST OF PUBLICATIONS

1. Duong Thi Khanh Linh, Le Tran Anh, Tang Xuan Hai (2024), Prevalence and some factors associated with tinea pedis among small traders in Nghe An (2022), *Journal of Community Medicine*, Volume 65, pp.1-8.
2. Duong Thi Khanh Linh, Le Tran Anh, Tang Xuan Hai (2024), Clinical and laboratory features of tinea pedis among small traders in Nghe An (2022), *Journal of Community Medicine*, Volume 65, pp.9-18.
3. Duong Thi Khanh Linh, Le Tran Anh, Tang Xuan Hai (2024), Prevalence and composition of fungal species causing tinea pedis by morphology and molecular biology among small traders in Nghe An (2022), *Journal of Community Medicine*, Volume 65, pp.19-29.