



Difference analysis of cutaneous sporotrichosis between different regions in China: a secondary analysis based on published studies on sporotrichosis in China

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Background: Cutaneous sporotrichosis is prevalent worldwide and a common subcutaneous fungal disease in northeast China. The incidence of cutaneous sporotrichosis in southern China cannot be ignored. Previous studies have revealed differences between different regions in China regarding populations susceptible to infection, cause of infection, and pathological mechanisms of sporotrichosis. Therefore, This study aimed to analyze the differences in the epidemiological characteristics of cutaneous sporotrichosis in different regions of China to provide a reference for regional prevention, control, and treatment.

Methods: We searched PubMed, EMBASE, Cochrane Library, CNKI, WanFang Data, and VIP for published reports on cutaneous sporotrichosis in China. The information about the characteristics of populations getting cutaneous sporotrichosis, causes of infection, disease types, and treatment regimens was extracted from studies to construct a knowledge database of cutaneous sporotrichosis in China. Taking the Qinling Mountains-Huaihe River line as the boundary to divide China into the northern and southern, the epidemiological characteristics of cutaneous sporotrichosis in two parts of China were analyzed.

Results: In northern China, more women than men get cutaneous sporotrichosis (60.4% *vs.* 39.6%), while it is the other way around in southern China (men *vs.* women: 50.6% *vs.* 49.4%). In northern China, the incidence of this disease was more concentrated in spring (34.0%) and winter (35.7%), while in southern China, this disease frequently spread in spring (48.1%) and summer (26.9%). In the north, cutaneous sporotrichosis usually affected the face (50.1%) and limbs (45.3%), while in the south, it targets limbs (72.6%). In northern China, potassium iodide (30.5%) and combination therapy (37.8%) were preferred, while in southern China, potassium iodide (86.0%) was the main choice. Although there was a significant difference in treatment regimens ($P < 0.05$), no significant difference emerged in cure rates between northern and southern China (98.5% *vs.* 98.4%, $P > 0.05$).

Conclusions: It is the first retrospective study on sporotrichosis in China. It describes the prevention of sporotrichosis in China since it was first reported and also reflects the differences in sporotrichosis between the northern and southern of China. This study provides a valuable reference for the prevention, control, and treatment of sporotrichosis in different regions of China.

Keywords: Sporotrichosis; epidemiology; China; northern and southern regions; difference analysis

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Introduction

Fungi are eukaryotes found in nature that appeared about 1.6 million years ago and have the important function of returning nutrients removed by plants to the soil (1). Research has found that fungi are the main pathogens of plants, rotifers, insects, and amphibians, and relatively few fungi can cause human infections. However, the transformation of the natural environment by humans has exacerbated the spread of fungal infections (2). So far, about 400 kinds of fungi have been reported to be pathogenic to human beings, and the number of pathogenic fungi has increased year by year (3). Sporotrichosis is a subcutaneous fungal disease caused by the type 2 fungus *Sporothrix schenckii*; it can infect the skin, subcutaneous tissue, mucous membranes, and the local lymphatic system and occasionally spread throughout the body, causing systemic damage (4). This disease mainly invades the skin. If the disease is mainly seen in the exposed parts of the skin, it is called cutaneous sporotrichosis, which can be divided into 3 types: fixed, lymphatic vessel, and skin disseminated. Cutaneous sporotrichosis is the most common type (5,6). Any organ can be infected, such as in the case of pulmonary sporotrichosis. Compared with the skin type, pulmonary sporotrichosis is a less well-known clinical manifestation, but its prevalence may increase (7).

Although sporotrichosis occurs on a global scale, it

has certain regional characteristics. The disease is rare in Europe, with occasionally sporadic cases, but it is relatively severe in areas such as South America and Asia (8). Since the first case of sporotrichosis was reported in China, the incidence of sporotrichosis has increased in some areas of China, among which provinces such as Jilin and Liaoning have more serious cases. Geographically, the Qinling Mountains-Huaihe River line is the boundary between China's warm temperate zone and subtropical zone. The geographical environment on both sides differs, so the north and south of China are divided on this basis (9).

Although differences in populations subject to sporotrichosis, cause of infection, and pathological mechanisms of this disease have been demonstrated in previous study (8), the epidemiological characteristics of cutaneous sporotrichosis in different regions of China are poorly understood, possibly impeding the prevention and treatment of this disease. In this study, we searched published reports on the incidence of cutaneous sporotrichosis in China and analyzed the differences in the disease between north and south China to provide a valuable reference for the prevention, control, and treatment of the disease. We present the following article in accordance with the PRISMA reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-23-448/rc>).

Methods

Literature retrieval strategy

The search objects were the reports on cutaneous sporotrichosis in various regions of China. The databases PubMed, EMBASE, Cochrane Library, CNKI, WangFangData, and VIP were searched. The search time was set from the establishment of the database to July 2021. Chinese search keywords included “sporotrichosis”, “epidemiology”, “clinical analysis”, “treatment” and “curative effect”. The English databases were searched by subject words plus free words, and the subject words were “sporotrichosis” and “China”.

Literature inclusion and exclusion criteria

Inclusion criteria

P (Populations): Patients were diagnosed with cutaneous sporotrichosis, and studies in which the pathological type was not clarified were also included in our research.

E (Exposure): None.

Highlight box

Key findings

- There were significant differences in population characteristics, disease manifestations, and treatment methods of cutaneous sporotrichosis between the northern and southern of China, but the cure situation was similar.

What is known and what is new?

- Cutaneous sporotrichosis is prevalent worldwide and is a common subcutaneous fungal disease in northeast China.
- This study presents the epidemiological characteristics of cutaneous sporotrichosis in China up to July 2021 and demonstrates the differences in sporotrichosis between the northern and southern of China.

What is the implication, and what should change now?

- This study examines the disease prevention context of sporotrichosis in China since the first report of sporotrichosis and analyzes the differences between the disease in the north and south of China. In doing so, this study provides a valuable reference for the prevention, control, and treatment of sporotrichosis in different regions in China.

C (Control): None.

O (Outcome): Outcome measures are the number of cases with sporotrichosis, areas where the disease occurred, population characteristics, disease characteristics, and pathological types, given that this is a study on the epidemiological characteristics of cutaneous sporotrichosis in China.

S (Study design): Case-control studies, randomized controlled trials, cross-sectional studies, and cohort studies were included in this research.

Exclusion criteria

P (Populations): Patients got other forms of sporotrichosis except for cutaneous sporotrichosis, such as pulmonary sporotrichosis.

E (Exposure): None.

C (Control): None.

O (Outcome): None.

S (Study design): (I) conference abstracts or animal experiments whose full texts were not available; (II) a molecular identification test of sporothrix; (III) studies with repeated collection of cases (studies investigating more extensive cases or more recently published were eligible). Repeated collection of cases was defined as the A and B study collection cases originating from the same unit, with the A study case collection time being a subset of the B study.

Literature screening and data extraction

Retrieved articles were imported into the software Endnote X9.0 for removing duplicate publications, and then titles and abstracts of articles were reviewed to get candidates for full-text screening. Finally, studies meeting the predefined inclusion criteria were obtained. Two researchers independently extracted data from the literature, mainly including the following information: (I) basic information of case collection, including the first author, year of publication, the province where the case was collected, case collection unit, and time of case collection; (II) Characteristics of the research population, including the age of onset of the patient, gender, course of the disease, and occupation; (III) disease manifestations, including onset season, inducement (mainly history of trauma), disease type, onset location, type of rash; and (IV) treatment and results, including treatment medication, course of treatment, and treatment outcome.

The abovementioned literature screening and data

extraction were carried out independently by two researchers, and cross-checking was done. If there was any dispute, the third researcher was asked to assist in the ruling. Discussion among researchers was undertaken to resolve any disagreements.

Statistical analysis

The Qinling Mountains-Huaihe River line was regarded as the boundary to divide China into northern or southern China. Differences in the epidemiological characteristics of sporotrichosis between the northern and southern regions of China were analyzed according to the regional distribution of sporotrichosis in China based on where the cases in included studies came from. Count data were obtained from included studies and they were represented by n (%). The Chi-square test or Fisher's exact test was used to analyze the abovementioned differences between northern and southern China. Statistical analysis was carried out using the software SPSS (version 23.0).

Results

Literature search results

A total of 1,677 articles were originally retrieved for the first time, and 1,151 articles remained after deleting duplicates. After screening these articles by title and abstract, 155 articles remained. A full-text analysis of the remaining 155 articles was carried out, and 99 articles were excluded. The reason for the exclusion was that 37 were molecular identification tests of sporothrix, and 62 were repeated collections of case documents. Finally, 56 articles were included in this study, including 16,465 patients with cutaneous sporotrichosis from all over China (*Figure 1*).

Distribution of sporotrichosis cases

In the literature included in this study, the collection period of sporotrichosis cases was from 1955 to 2019, with a total of 16,465 sporotrichosis patients. The cases were distributed in 16 provinces/municipalities directly under the Central Government, 35 articles were in the north, with 15,391 (93.48%) cases in the north and 21 articles with 1,074 (6.52%) cases in the south. This distribution illustrates that sporotrichosis in China is prevalent in the northern regions, especially in the provinces mainly engaged in agriculture and animal husbandry (*Table 1; Figure 2*).

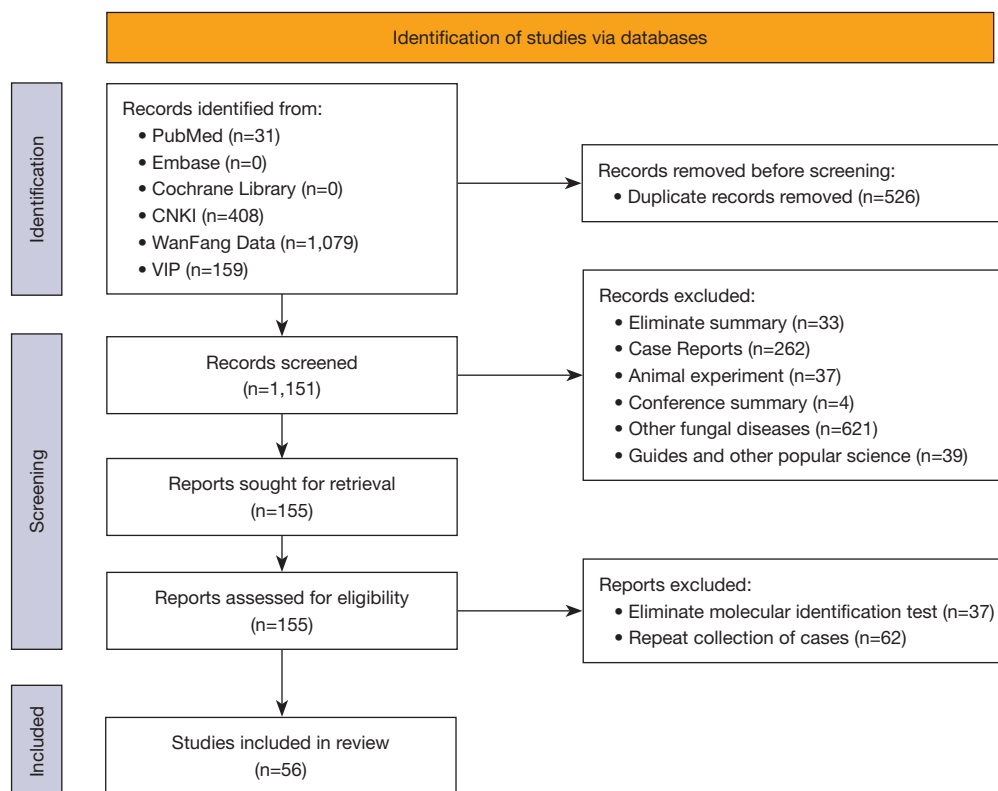


Figure 1 Document retrieval process.

Study population characteristics

In the literature included in this study, the proportion of women with sporotrichosis in the country was higher (59.7%) than that of men. The majority of patients with sporotrichosis in the northern region were women (60.4%), while the proportion of men in the southern region was slightly higher (50.6%), and there was a significant difference ($P < 0.05$). The youngest age of onset was one month old, and the oldest was 92 years old. The main age group of onset was young adults (64.3%). The occupations of patients were mainly farmers (76.8%) and workers (8.3%). The proportion of farmers in the south was lower than that in the north, while the proportion of workers was the opposite. The course of the disease was mainly concentrated in 2 to 6 months. There were significant differences in the age of onset, occupation, and disease course of sporotrichosis patients in the northern and southern regions ($P < 0.05$; *Table 2*).

Disease manifestations

In the literature included in this study, the main onset

seasons of sporotrichosis across the country were spring and winter. The main onset seasons of sporotrichosis in the north were spring and winter, while those in the south were spring and summer. There were significant differences in the onset seasons between the northern and southern ($P < 0.05$).

In rural areas of China, 18.2% of patients with sporotrichosis had a history of trauma. Only 16.9% of patients in the northern region had a history of trauma, while those in the southern region accounted for 45.3%. There were significant differences in the history of trauma between the northern and southern ($P < 0.05$).

The main type of sporotrichosis in China was the fixed type (62.8%), followed by the lymphatic type (35.1%) and the disseminated type (1.0%). The disease types of patients in northern China were mainly the fixed type, followed by the lymphatic type and the disseminated type. In southern China, the lymphatic type was the main type (51.1%), followed by the fixed type (46.2%) and the disseminated type (0.5%). There were significant differences in disease types between the northern and southern ($P < 0.05$).

Sporotrichosis patients across the country were mainly

Table 1 Distribution of sporothrix

Province/city	Case collection time	Total number of people (example)	Composition ratio (%)
Heilongjiang (10-17)	1994–2018	1,891	11.48
Jilin (18-29)	1987–2019	10,797	65.58
Liaoning (30-36)	1972–2017	960	5.83
Inner Mongolia (37-40)	1991–2016	1,609	9.77
Beijing (41)	2008–2015	20	0.12
Shandong (42)	2015–2017	61	0.37
Henan (43)	2002–2009	35	0.21
Ningxia (44)	1994–1998	18	0.11
Jiangsu (45-49)	1974–2006	303	1.84
Hubei (50)	1988–1999	62	0.38
Zhejiang (51)	–2003	25	0.15
Fujian (52-54)	1979–1996	69	0.42
Guangdong (55-57)	1973–2012	160	0.97
Guangxi (58-60)	1955–2008	292	1.77
Chongqing (61)	2006–2010	64	0.39
Sichuan (62-65)	1985–2005	99	0.60
Northern region	1972–2019	15,391	93.48
Southern region	1955–2012	1,074	6.52
Total	–	16,465	100.00

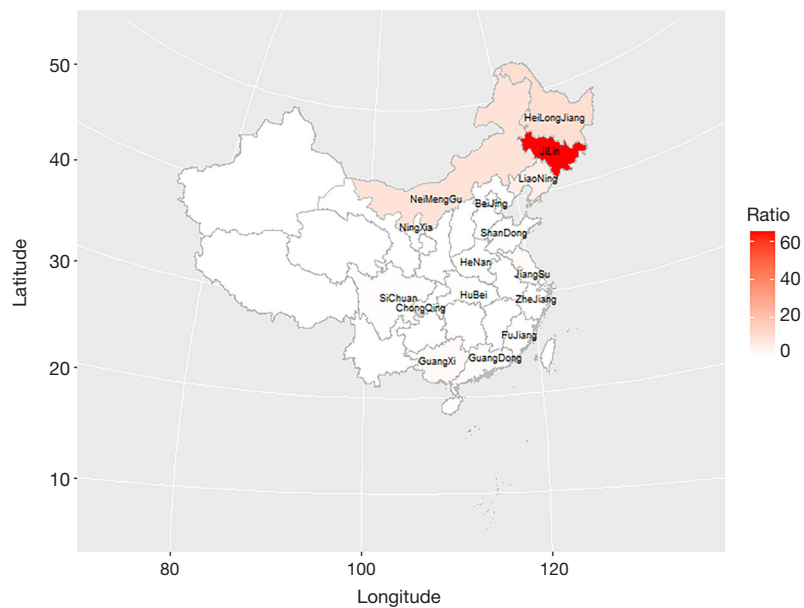
**Figure 2** Distribution area of sporothrix case reports in our country. Only the provinces/municipalities where reports of Sporothrix appeared are marked in the figure.

Table 2 Basic information on patients with sporotrichosis

Basic patient information	Total number of case reports	Northern region	Southern region	χ^2	P value
Gender	16,451	15,377	1,074	56.369	<0.001
Male	6,628 (40.3%)	6,085 (39.6%)	543 (50.6%)		
Female	9,823 (59.7%)	9,292 (60.4%)	531 (49.4%)		
Age of onset	11,480	10,833	647	29.315	<0.001
Children (<14 years old)	1,754 (15.2%)	1,692 (15.6%)	62 (9.6%)		
Young adults (14–59 years old)	7,413 (64.3%)	6,935 (64.0%)	478 (73.9%)		
Elderly (≥ 60 years old)	2,363 (20.5%)	2,256 (20.8%)	107 (16.5%)		
Profession	11,520	10,604	916	204.741	<0.001
Preschooler	308 (2.7%)	278 (2.6%)	30 (3.3%)		
Student	710 (6.2%)	638 (6.0%)	72 (7.9%)		
Farmer	8,852 (76.8%)	8,277 (78.1%)	575 (62.8%)		
Worker	960 (8.3%)	827 (7.8%)	133 (14.5%)		
Staff and officials	326 (2.8%)	302 (2.8%)	24 (2.6%)		
Housewife	85 (0.7%)	76 (0.7%)	9 (1.0%)		
Other	279 (2.4%)	206 (1.9%)	73 (8.0%)		
Course of disease	4,148	3,865	283	45.824	<0.001
<2 months	429 (10.3%)	414 (10.7%)	15 (5.3%)		
2–6 months	2,705 (65.2%)	2,552 (66.0%)	153 (54.1%)		
7–12 months	645 (15.5%)	572 (14.8%)	73 (25.8%)		
>12 months	369 (8.9%)	327 (8.5%)	42 (14.8%)		

affected by the face and limbs, of which the face accounted for the highest proportion (48.5%), followed by the limbs (46.9%). In northern areas, the incidence of patients was also concentrated on the face and limbs, with the face accounting for 50.1%. In the south, the extremities accounted for the highest proportion (72.6%), and the face only accounted for 24.7%. There was a significant difference in the location of the patients with sporotrichosis between the northern and southern ($P < 0.05$).

The types of skin rashes of patients with sporotrichosis across the country were only shown in studies in the northern region. The types of rashes were mainly nodules, plaques, and nonsingle skin rashes, altogether accounting for more than 70% of the reported cases (*Table 3*).

Treatment methods

In the literature included in this study, most treatment

methods were medication, and only a small proportion of patients required surgical resection. Regarding medication, the common drugs were potassium iodide, itraconazole, and terbinafine. In terms of usage, single drugs or combination drugs were often selected. The combination drugs were mainly potassium iodide + itraconazole and potassium iodide + terbinafine. Other drugs were not excluded. For example, the patients with an obvious bacterial infection in the included literature would choose to use metacycline in combination, and ketoconazole, and traditional Chinese medicine would be selected in other cases (66). This study showed that the proportion of combined medications in the treatment of sporotrichosis patients in the northern region was the highest, followed by potassium iodide alone, both of which accounted for 68.3% of the patients in the northern region. In the southern region, patients were mainly treated with potassium iodide alone, accounting for 86.0%.

The treatment course of patients with sporotrichosis

Table 3 Basic information on patients with sporotrichosis

Disease manifestations	Total number of case reports	Northern region	Southern region	χ^2	P value
Onset season	10,161	10,005	156	48.176	<0.001
Spring	3,481 (34.3%)	3,406 (34.0%)	75 (48.1%)		
Summer	1,450 (14.3%)	1,408 (14.1%)	42 (26.9%)		
Autumn	1,633 (16.1%)	1,621 (16.2%)	12 (7.7%)		
Winter	3,597 (35.4%)	3,570 (35.7%)	27 (17.3%)		
Trigger (clear history of trauma)	15,454	14,750	704	15454.000	<0.001
Yes	2,814 (18.2%)	2,495 (16.9%)	319 (45.3%)		
No	12,640 (81.8%)	12,255 (83.1%)	385 (54.7%)		
Type of disease	15,915	14,937	978	135.506	<0.001
Lymphatic type	5,591 (35.1%)	5,091 (34.1%)	500 (51.1%)		
Fixed type	10,001 (62.8%)	9,549 (63.9%)	452 (46.2%)		
Disseminated	154 (1.0%)	149 (1.0%)	5 (0.5%)		
Other	169 (1.1%)	148 (1.0%)	21 (2.1%)		
Disease site	15,464	14,534	930	279.628	<0.001
Face	7,506 (48.5%)	7,276 (50.1%)	230 (24.7%)		
Neck	308 (2.0%)	306 (2.1%)	2 (0.2%)		
Trunk	269 (1.7%)	260 (1.8%)	9 (1.0%)		
Limbs	7,259 (46.9%)	6,584 (45.3%)	675 (72.6%)		
Other	122 (0.8%)	108 (0.7%)	14 (1.5%)		
Type of rash	5,681				
Nodules	2,533 (44.6%)				
Granuloma	100 (1.8%)				
Plaque	830 (14.6%)				
Cyst	52 (0.9%)				
Satellite	57 (1.0%)				
Verrucous	136 (2.4%)				
Acne	60 (1.1%)				
Erythrophosene	442 (7.8%)				
Papules	269 (4.7%)				
Nonsingle skin lesion	750 (13.2%)				
Other	452 (8.0%)				

The types of rashes in the table are only described in research reports in northern regions.

Table 4 Treatment methods for patients with sporotrichosis

Treatment	Northern region		Southern region		Total	
	Number of cases (cases)	Composition ratio (%)	Number of cases (cases)	Composition ratio (%)	Number of cases (cases)	Composition ratio (%)
Potassium iodide	2,791	30.5	753	86.0	3,544	35.3
Itraconazole	1,532	16.7	15	1.7	1,547	15.4
Terbinafine	1,193	13.0	15	1.7	1,208	12.0
Combination medication	3,467	37.8	38	4.3	3,505	34.9
Other medications	180	2.0	51	5.8	231	2.3
Surgery	2	0.0	4	0.5	6	0.1
Total	9,165		876		10,041	

varied in length in the literature included in this study. The shortest course of treatment was one month, and the longest was one year. The treatment course was most often 6 to 12 weeks long. The cure rate was 98.4% in the north and 98.5% in the south (*Table 4*).

Discussion

Sporotrichosis was first reported by Shenck (67) in the United States in 1898, and the pathogen was then isolated. In China, Diao Xinde (68) discovered the disease for the first time, but the fungus was not cultivated. The disease mainly invades the skin (i.e., cutaneous sporotrichosis), and occasionally affects the internal organs (i.e., systemic sporotrichosis). There have been reports about bone/articular sporotrichosis, tracheal or pulmonary sporotrichosis, and ocular sporotrichosis.

Although sporotrichosis is distributed globally, the sporotrichosis species shows a high degree of endemicity. As of 2015, the data in the epidemiological literature of 8 fungal infections in China show that the most prevalent areas of sporotrichosis are Brazil, China, and South Africa (69). Our study shows that sporotrichosis has been reported in 16 provinces/municipalities directly under the Central Government in China, but the cases are mainly concentrated in Northeast and Inner Mongolia. The history of sporotrichosis in southern China cannot be ignored, mainly in Jiangsu, Guangxi, Guangdong, and Sichuan.

The main route of sporotrichosis infection is contact with materials contaminated by sporotrichosis after skin trauma, which is usually related to soil manipulation activities (70). Sporothrix is a kind of metatroph in nature. It is widely found in firewood, reeds, grain straw,

flowers, moss, grass charcoal, rotten wood, soil, and marsh muddy water. Therefore, farmers or people in rural areas, gardeners, and workers are susceptible groups. There are obvious differences in climate and geographical environment between the north and south of China. The north is the main agricultural and animal husbandry production area, and the number of people engaged in agriculture and animal husbandry is larger than that in the south, regardless of age or gender. There were significant differences in the age, sex, and occupation of patients with sporotrichosis in the northern and southern regions. Most patients in the north were women, while there was a slightly higher number of patients who were men in the south. Although the infected people in the north and south were mainly young and middle-aged farmers, the proportion of the elderly in the north was much higher than that in the south (71,72). Due to climatic reasons, there were also differences in the onset seasons between the 2 regions. The onset was mainly in spring and winter in the north and in spring and summer in the south. The number of people engaged in industrial activities in the south is larger than that in the north, and they are more likely to be injured during industrial activities. This also explains why the trauma history of patients with sporotrichosis in the south was significantly higher than that in the north. It also helps explain the difference in the location of the disease, which mainly occurred in the limbs of patients in the south and in the face of patients in the north (73,74).

There were significant differences in the types of diseases between the northern and southern. The fixed type accounted for the highest proportion in the north (63.9%), while the proportion of lymphatic vessels in patients in the south (51.1%) was slightly higher than that of the fixed

type. Therefore, in terms of treatment methods, there were also significant differences between the northern and southern, but the cure rate was very similar.

Despite the great harm inflicted on people, sporotrichosis can be prevented. We recommend the following preventive measures: keep the skin clean in daily life, especially skin that has experienced trauma; during outdoor activities, appropriate protective measures should be taken and strengthened, particularly for agricultural activities when people are likely to touch wildlife or rotten plants; prevent skin injury and treat any skin injury with frequent disinfection; in families with pets, pay attention to the cleaning of pets and environment, and regularly disinfect the environment; and avoid being scratched by animals.

This study had limitations. First, the participants of this study were patients with cutaneous sporotrichosis, and other sporotrichosis conditions were not considered, such as pulmonary sporotrichosis. Second, the research participants in this study came from published reports. There may be patients in some other areas that have not been reported. There were also a small number of cases that were repeated collections because these people might have been treated in different medical institutions.

Conclusions

The present study is the first retrospective study of sporotrichosis in China. This study examined the disease prevention situation of sporotrichosis in China since the first report of sporotrichosis. We analyzed the difference in the disease in the north and south of China to provide a valuable reference for the prevention, control, and treatment of sporotrichosis in different regions in China.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-23-448/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-23-448/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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