

Trends and Associations of Chilblains Prevalence with Connective Tissue Diseases, Including COVID-19 Incidence

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Background: Chilblains, also known as perniosis, are inflammatory skin lesions that have long been associated with exposure to low temperatures. However, their co-occurrence with autoimmune illnesses and viral infections, particularly COVID-19, has received increased attention. This study was designed to examine chilblains' documented prevalence and association with autoimmune diseases and COVID-19.

Methods: This was a descriptive cross-sectional study carried out at Mass General Brigham (MGB), an extensive integrated healthcare system situated in Greater Boston, Massachusetts. The study included patients with a confirmed diagnosis of chilblains from 2014 to 2021 and COVID-19 from 2020 to 2021. The study was approved by the Mass General Brigham Human Research Committee, ensuring compliance with ethical standards.

Results: During the study, 24,711 charts were reviewed, identifying 1478 patients with chilblains, resulting in an overall registered prevalence of 0.02463%. The majority of chilblains patients were female (72.5%), with the highest proportion in the 31–30-year age group (31.3%). 169 (11.43%) patients were identified with autoimmune diseases, predominantly females (94.1%). The most prevalent condition among them was systemic lupus erythematosus (SLE) (52.6%). Among COVID-19-positive patients (n = 88,763), 30 were diagnosed with chilblains, leading to a prevalence of 0.033%. Females (66.7%) and individuals aged 40–50 (56.7%) were predominantly affected.

Conclusion: This study found a low prevalence primarily among young females and a significant correlation with connective tissue disorders like SLE. The study also notes a rare occurrence of chilblains in COVID-19 patients, suggesting a possible association that requires further investigation, particularly regarding demographic patterns within this subgroup.

Keywords: chilblains, autoimmune diseases, COVID-19, prevalence, connective tissue disorders, SLE

Introduction

Chilblains, also known as perniosis, have intrigued, and perplexed the medical community for centuries. Dermatologists in Europe noted a significant rise in chilblains at the beginning of 2020, with most cases reported from England, France, and northern Europe. However, current data also indicate an increasing number of cases from the United States.¹ These are inflammatory dermatoses that typically affect the dorsal feet or hands during damp and cold weather, not necessarily freezing conditions, and have been associated with COVID-19.^{2–6} Symptoms usually manifest within 12–24 hours after exposure and include swelling, burning, redness, itching, and painful toes.^{7,8} Although less common, lesions on the ears, nose, and trunk can also occur, with extremity lesions being the most prevalent.^{9,10} While chilblains are primarily linked to cold exposure, they can also arise from various underlying medical conditions.¹¹

Chilblains are typically classified into two categories: primary and secondary. Secondary chilblains are associated with conditions such as immune-mediated inflammatory diseases (IMIDs), infections (including hepatitis), hematological disorders, cancer, and drug-related factors. Primary chilblains usually resolve within a few days to three to four weeks. However, persistence of lesions, occurrence in warmer climates, or unusual features like ulceration or scarring may

warrant investigation for a secondary cause.⁷ Their association with connective tissue disorders (CTDs) such as systemic lupus erythematosus (SLE), systemic sclerosis, scleroderma, dermatomyositis, and Sjogren's syndrome has been studied, suggesting a potential but rare link.^{7,12}

The term "COVID toes" emerged during the pandemic to describe chilblain-like lesions observed in certain COVID-19 patients.^{3,13} The nature of COVID-19 toes remains debated; some scientists consider them a distinct condition, while others attribute them to the virus causing typical pernio. This study aims to analyze the documented prevalence of chilblains and its associations with connective tissue disorders from 2014 to 2021. Additionally, it seeks to explore the incidence rates of chilblains in correlation with COVID-19 cases between January 2020 and June 2021.

Materials and Methods

The research was carried out at Mass General Brigham (MGB), an extensive integrated healthcare system in Greater Boston, Massachusetts, covering the period from January 1st, 2014, to June 1st, 2021. The study included patients with a confirmed diagnosis of chilblains from 2014 to 2021 and COVID-19 from 2020 to 2021. Data collection was facilitated through the Research Patient Data Registry (RPDR) system. This system serves as a centralized clinical database that amalgamates information from multiple hospital systems within the MGB network, including Massachusetts General Hospital (MGH), Brigham and Women's Hospital (BWH), North Shore Medical Center (NSMC), Newton-Wellesley Hospital (NWH), Faulkner Hospital (FH), Spaulding Rehabilitation Hospital (SRH), Massachusetts Eye and Ear (MEE), Dana-Farber Cancer Institute (DFCI), Wentworth-Douglass Hospital (WDH), and Massachusetts College of Pharmacy and Health Sciences (MCPHS).

The RPDR incorporates data from various source systems such as the TSI Hospital and IDX physician billing systems from BWH and MGH (historical data), the Clinical Data Repository (CDR), Enterprise Master Patient Index (EMPI), and EPIC, which are all consolidated within the RPDR warehouse. Presently, this database encompasses clinical data for over 6 million patients affiliated with Mass General Brigham and offers access to more than 30 types of data tables that can be requested through the RPDR Data Request Wizard upon obtaining approval from the Institutional Review Board (IRB). The Mass General Brigham Human Research Committee approved the study, ensuring compliance with ethical standards.

The Institutional Review Board (IRB) waived the requirement for patient consent to review medical records as the study involved retrospective data collection. All patient data were handled with strict confidentiality, anonymized before analysis, and securely stored to prevent unauthorized access. This study used the ethical principles outlined in the Declaration of Helsinki.

The data extracted from the RPDR comprise demographic details of patients, including age, gender, ethnicity, and autoimmune diseases associated with chilblains. Informed consent was obtained from the study participants.

Data were analyzed using SPSS version 26. Descriptive data were spread out to recapitulate. The mean and standard deviation ($\pm$ SD) were calculated for every quantitative variable. The frequency and percentages were calculated for qualitative variables.

Results

A total of 24,711 charts were reviewed during the study period, including 1478 patients diagnosed with chilblains, equating to an overall registered prevalence of 0.02463%. Among these patients, the majority were female, comprising 1071 individuals (72.5%), while the remaining 407 (27.5%) were male. Regarding age distribution, the most significant proportion of patients, 463 (31.3%), fell within the 31–30-year age group, followed by those over 60 years old, accounting for 295 (19.9%). The 31–40-year age bracket comprised 252 (17.1%), while individuals aged 51–60 years represented 230 (15.6%) patients.

Regarding racial demographics, the sample exhibited diversity, with the majority being white, consisting of 1247 (84.3%) patients. This was followed by Black 45 (3.1%), Hispanic 16 (1.1%), Asian 86 (5.8%), and other 84 cases (5.7%). [Table 1](#).

A total of 169 patients were identified with autoimmune diseases with prevalence of 11.43%, with a higher representation of females, 159 (94.1%). Among the age groups, aged 20–30 years formed the largest cohort with 48

Table 1 Demographic Characteristics of the Patients with Chilblains (n = 1478)

Demographics	Frequency	Percentages
Gender		
Male	407	27.5
Female	1071	72.5
Age group		
0–20 years	129	8.7
21–30 years	463	31.3
31–40 years	252	17.1
41–50 years	109	7.4
51–60 years	230	15.6
>60 years	295	19.9
Ethnicity		
White	1247	84.3
Black	45	3.1
Hispanic	16	1.1
Asian	86	5.8
Other	84	5.7

(28.4%), followed by those over 60 years 39 (23%), 51–60 years 36 (21.4%), 31–40 years 26 (15.4%), and those aged 41–50 years 20 (11.8%).

In terms of racial demographics, the majority of patients identified as White, comprising 133 (78.7%), while smaller proportions identified as Black 13 cases (7.7%), Hispanic 4(2.4%), Asian 9(5.3%), and individuals from other racial backgrounds with 10 (5.9%). [Table 2](#).

Table 2 Demographic Characteristics of Patients with Autoimmune Disease in Chilblains (n = 169)

Variables	Frequency	Percentages
Gender		
Male	10	5.9
Female	159	94.1
Age group		
20–30 years	48	28.4
31–40 years	26	15.4
41–50 years	20	11.8
51–60 years	36	21.4

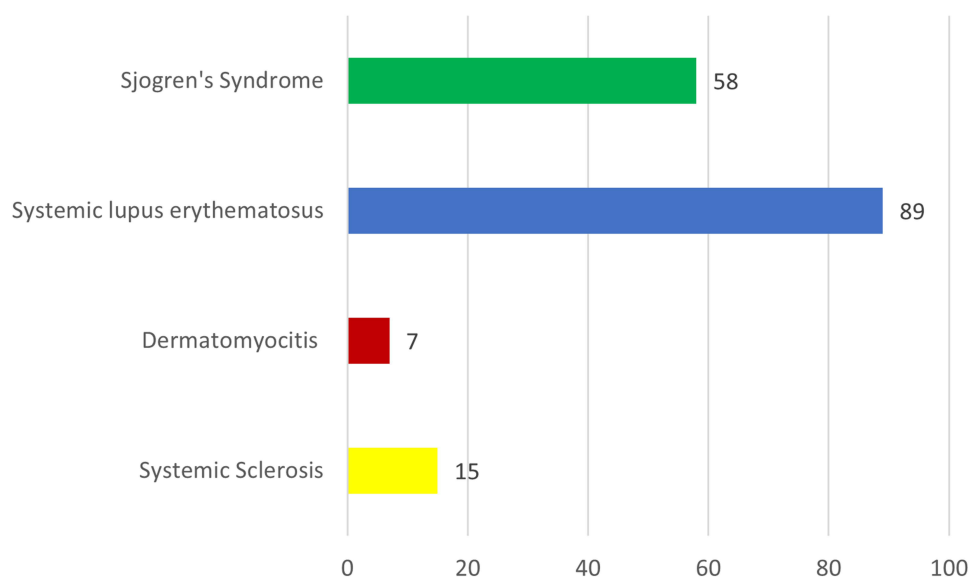
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Table 2 (Continued).

Variables	Frequency	Percentages
>60 years	39	23.0
Ethnicity		
White	133	78.7
Black	13	7.7
Hispanic	4	2.4
Asian	9	5.3
Other	10	5.9

Out of 169 patients, systemic lupus erythematosus (SLE) emerged as the most prevalent condition, affecting 89 (52.6%) patients. Among the SLE cases, the majority were female patients, 86 (50.8%) falling within the age group of 20 to 40 years. Dermatomyositis was identified in 7 patients (8.33%), of whom 5 were female, and these cases were primarily observed in individuals over 60 years old. Systemic sclerosis was manifested in 15 (4.14%), all of whom were female and concentrated within the age group of 50 years. Furthermore, Sjogren's syndrome was detected in 58 patients (34.31%), with majority female 55 (90%) and predominantly in the age group of 40 to 60 years. [Figure 1](#)

During the same study period, there were 88,763 COVID-positive patients, among whom 30 presented with chilblains. This indicates a prevalence of chilblains in COVID patients of 0.033%. Among those with both COVID and chilblains, the majority 20 (66.7%) were female, while males accounted for only 10 (33.3%). Furthermore, a majority of cases 17 (56.7%) fell within the age group of 40 to 50 years, and 23 (76.7%) cases were among individuals of white ethnicity.

**Figure 1** Distribution of autoimmune disease with chilblains (n = 169).

Discussion

This study examined the occurrence of chilblains from 2014 to 2021 and its associations with COVID-19 and connective tissue diseases (CTDs). In our study population, the prevalence of chilblains was notably low, at 0.02463%, consistent with prior research indicating its limited prevalence.^{14,15} Chilblains are typically more prevalent in women,¹ aligning with our findings and previous reports that women have a significantly higher prevalence of chilblains compared to men.^{14,16–18} This gender disparity may stem from various factors such as the slender body habit common among young girls and the likelihood of young individuals working in poorly heated environments after leaving school. Additionally, immunological differences between genders or fluctuations in hormone levels could also play a role,⁷ although further investigation is needed to elucidate these underlying causes.

One unexpected finding was that the age group of 31 to 40 years old had the highest occurrence of chilblains, contrary to the long-held belief that children and young individuals are more susceptible to chilblains.^{14–17} This disparity may be attributed to changes in how chilblains present over time or potential underreporting in younger age groups, highlighting the need for continued research to better understand these trends.

The majority of chilblains cases are considered idiopathic. However, previous research has linked chilblains to various CTDs such as antiphospholipid syndrome, rheumatoid arthritis, SLE, cryofibrinogenemia, as well as blood dyscrasias and Raynaud's disease.^{1,14,19,20} The observed correlation of 11.43% between chilblains and CTDs in this study is consistent with other findings suggesting a possible connection, although it underscores how rare this association is.^{1,7} Specifically, SLE emerged as the most common CTD linked to chilblains, particularly among younger women, reaffirming the known demographic overlap between chilblains and SLE.^{16–18,21,22}

The second most common syndrome associated with chilblains, primarily affecting women in their 40s and 60s, was Sjogren's syndrome. Conversely, dermatomyositis was uncommon and mainly impacted women over 60, while systemic sclerosis was predominantly found in women over 50. These findings suggest a potential correlation between age, gender, and specific autoimmune and inflammatory disorders (AIDs) when chilblains are present. It is crucial for healthcare providers to recognize chilblains as a potential indicator of underlying CTDs, especially SLE, particularly in high-risk patients.

The study revealed an uncommon association with the notably low co-occurrence rate (0.033%) of chilblains in COVID-19 positive patients. This finding aligns with previous research indicating rare instances of chilblains in COVID-19 positive individuals.^{3–5,23} Further investigation is warranted to explore this potential link, given that the exact mechanism connecting COVID-19 and chilblains remains elusive. Additional research is necessary to determine whether the demographic trends observed in this subgroup, characterized by a predominance of white ethnicity and female gender, signify a genuine association or merely reflect the demographics of the COVID-19 population.

This study's strengths lie in its size, community-based approach, utilization of a historical control group, validation through a review of medical records, and a design that incorporates regional variations in weather patterns by utilizing location-month as the unit of observation. However, there are limitations to consider, including the absence of access to reliable testing and the study population's restriction to a specific northeastern United States healthcare system, which could affect generalizability. Additionally, the study did not assess the duration or severity of chilblains, which could be valuable information for future research and follow-up studies.

Conclusion

In conclusion, this research sheds light on the epidemiology and associations of chilblains within the context of autoimmune diseases and COVID-19. The study revealed a low prevalence of chilblains, with a notable predominance among young females. Connective tissue disorders, especially SLE, showed a significant correlation with chilblains, emphasizing the importance of considering underlying autoimmune conditions in chilblains patients. The study also highlighted a rare co-occurrence of chilblains in COVID-19 positive patients, indicating a potential but not fully understood association. Further investigation is warranted to elucidate the mechanisms linking COVID-19 and chilblains, especially regarding demographic patterns observed in this subgroup.

Disclosure

The author reports no conflicts of interest in this work.

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