

Pediatric Non-Cystic Fibrosis Pulmonary Nontuberculous Mycobacterium Infections: A Global Population Based Study

Marina Bahaa Monir Zakhary Gad El Sayed¹, Dennis Tai^{2,*}, Lucy Yu^{3,*}, Daniel Novak¹, Amrita Dosanjh⁴

¹School of Medicine, University of California Riverside, Riverside, CA, USA; ²Department of Biology, Brown University, Providence, RI, USA; ³School of Public Health, Brown University, Providence, RI, USA; ⁴Pediatric Respiratory, Affiliated Rady Children's Hospital, San Diego, CA, USA

*These authors contributed equally to this work

Correspondence: Amrita Dosanjh, Pediatric Respiratory, Affiliated Rady Children's Hospital San Diego, San Diego, CA, USA, Email pulmdl@gmail.com

Background: Nontuberculous mycobacteria (NTM) are Mycobacterial pathogens that cause pulmonary infections among children, particularly those with underlying lung conditions or immunosuppression. Clinical presentations include chronic cough, weight loss, and fatigue. Diagnosis involves clinical assessment, radiographic imaging, and microbiological confirmation, while treatment often requires prolonged, multidrug antibiotic regimens. This study aimed to analyze the epidemiology and clinical outcomes of pulmonary NTM infections in a non-cystic fibrosis pediatric population from four distinct age groups.

Methods: A retrospective study as cross-sectional design for data collection from the TriNetX platform, a global electronic health record database. Inclusion criteria targeted pediatric patients aged 0–18 years with pulmonary NTM, while exclusion criteria included cystic fibrosis, tuberculosis, smoking history, and cutaneous NTM infections. The cohort comprised 109 cases among 0–2 years (mean age 2 years), 401 cases among 3–5 years (mean age 4 years), 1,074 cases among 6–12 years (mean age 9 years), and 760 cases among 13–18 years (mean age 15 years). Demographics, comorbidities, and inflammatory markers were analyzed. Logistic and binomial regression models were used to evaluate associations between age group and five-year outcomes of pediatric pulmonary NTM, reporting odds ratios (OR), risk ratios (RR), 95% confidence intervals (CI), and p-values.

Results: Of the total 2,344 records of pediatric patients examined, the most common comorbidities included malignancies (36%), acute pharyngitis (78%), asthma (46%), unspecified pneumonia (46%), and immunodeficiencies (22%). Female patients represented 53.31% of cases. Key inflammatory markers (eg C-reactive protein (CRP), mean white blood cell count, ferritin) were elevated among older age groups.

Conclusion: This study highlights age-specific variations in risk factors, clinical outcomes, and inflammatory responses, offering potential insights for improved diagnosis and management of NTM in children. These results underscore the importance of further research in pediatric cohorts with NTM to better understand its role in pediatric pulmonary conditions and comorbidities.

Keywords: non-tuberculous mycobacteria, non-cystic fibrosis, pulmonary, pediatric, NTM-PD

Introduction

Nontuberculous mycobacteria (NTM) are environmental pathogens with over 190 identified species,¹ primarily affecting individuals with preexisting lung disease or immunodeficiency.² There is a rising trend in incidence of infection and mortality globally, including among younger populations. Among children, the infection may occur with or without preexisting lung disease.³ Risk factors among adults have been well studied, but there are fewer pediatric studies in this area of study.⁴ Past research has found that immunodeficiency, the developing immune system, and chronic lung disease heighten the risk of NTM infections in the pediatric population.⁵ NTM infections are especially prevalent because of their ability to inhabit common soil and water sources such as water distribution systems, allowing repeated environmental

exposures to invade the lungs through bioaerosols.⁵ It is also thought that different species and subspecies of mycobacteria containing genetic differences manifest themselves differently in infection and clinical response.⁶ For example, two of the most common NTM species *Mycobacterium avium* and *Mycobacterium abscessus* differ in their infections with the former being characterized by slow growth, greater general prevalence, and weaker biofilm formation,⁷ while the latter is associated with significant morbidity/mortality, is clinically resistant to most antibiotics, and shows greater general immune responses throughout the course of infection.⁸ Infections from different types of these bacteria can vary by geographic location⁵ with *Mycobacterium abscessus* being commonly observed in East Asia and *Mycobacterium avium complex* and *Mycobacterium kansasii* occurring most commonly in many parts of the US. In Europe, Asia, and partially in Australia, increases in latitude generally see higher rates of *Mycobacterium avium complex*.

NTM pulmonary disease is frequently misdiagnosed as tuberculosis due to similar symptoms, leading to delays in appropriate treatment. One of the most common signs of NTM infection in healthy children is cervical lymphadenitis, but its clinical presentation is indistinguishable from that of cervical lymphadenitis in regular tuberculosis.⁹ Pulmonary infection, while less commonly associated may be more difficult to treat. This is especially problematic in countries with high tuberculosis rates, where NTM testing methods are resource limited.^{10–12} Industrialized nations often report higher NTM incidence than tuberculosis, although pediatric prevalence globally is not well studied.^{13,14}

This study was conducted to investigate pediatric pulmonary NTM infections among the non-cystic fibrosis population. The global incidence of NTM infections is increasing, and more studies are needed to better understand the disease among the pediatric population.¹⁵ Unlike Cystic Fibrosis patients, who are known to have higher susceptibility to pulmonary infections,¹⁶ the risk factors and clinical manifestations in non-cystic fibrosis pediatric population remains poorly understood. This study aims to investigate the epidemiology, clinical comorbid condition, and five year clinical outcomes of non CF pulmonary NTM infections in distinct pediatric age groups. We hypothesize that there are important differences in these key areas among pediatric age groups. This may lead to the identification of characteristics that could guide clinical decision-making and potentially improve patient outcomes.

The study further hypothesizes that: i) BMI percentiles mediate susceptibility to NTM infections in children, ii) common comorbidities are expected to be significant risk factors for pediatric pulmonary NTM infections, iii) pediatric pulmonary NTM may predispose patients to future lung disease.

Methods

The TriNetX Clinical Data Platform

We utilized the TriNetX research platform to select our patient cohorts from a total of 152,714,105 collected, de-identified patient records on the Global Collaborative Network containing 127 health-care organizations from the following 17 countries: United States, Canada, United Kingdom, Germany, France, Italy, Spain, Netherlands, Denmark, Australia, Singapore, Japan, Brazil, Mexico, Israel, South Korea, and Switzerland. TriNetX deidentifies and aggregates electronic health record (EHR) data from health-care systems, primarily drawing from large academic medical institutions across the USA. It organizes diagnoses under specific ICD codes and stores information such as demographics, medications, lab results, procedures, and vital signs. The platform provides a secure, web-based access to patient-level analyses and interpretation. It reports updated population-level data while ensuring Health Insurance Portability and Accountability Act (HIPAA) compliance.

Data Collection and Stratification

From the TriNetX Global Collaborative Network, the pediatric patient population was stratified into four groups: i) 0–2 years, ii) 3–5 years, iii) 6–12 years, and iv) 13–18 years based on age. The inclusion criteria were: i) subjects with pulmonary NTM infection, and ii) ages 0–18 years. The exclusion criteria were: i) Cystic Fibrosis, ii) Tuberculosis, iii) smoking history, iv) cutaneous non-mycobacterial infections, and v) adult patients. The total cohort (0–18 years) consisted of 2,344 NTM cases from a larger population base of over 23 million pediatric patients collected on July 13, 2024. The distribution among the four groups was expressed both numerically and as a percent of patients in each respective age group with NTM.

Table 1 Inclusion and Exclusion Criteria Entered into TriNetX

Must Have	Cannot Have
– Mycobacteria culture – Mycobacterium gordonae rRNA [Presence] in Specimen by Probe – Infection due to other mycobacteria – Disseminated mycobacterium avium-intracellulare complex (DMAC) – Mycobacterial infection, unspecified – Pulmonary mycobacterial infection – Infection due to other mycobacteria – Other mycobacterial infections – Pulmonary mycobacterial infection	– Cutaneous mycobacterial infection – Cystic fibrosis – Cystic fibrosis, unspecified – Mycobacterium tuberculosis tuberculin stimulated gamma interferon [Presence] in Blood – Mycobacterium tuberculosis DNA [Presence] in Specimen by NAA with probe detection – Tuberculosis – Mycobacterium tuberculosis DNA [Presence] in Sputum by NAA with probe detection – Cutaneous mycobacterial infection – Smoking and tobacco use cessation counseling visit

Note: Criteria sought to include all NTM-related search terms and exclude tuberculosis-related cases.

Data Analysis

Data analysis focused on patient demographics, clinical characteristics, comorbidities, and outcomes of the 2,344 NTM cases, with particular attention to odds ratios and lab values associated with these infections. Descriptive analysis for this data included prevalence, mean values, and standard deviation within the age cohorts. Demographic information included age, sex, ethnicity, and race. Comorbidities were identified in our analysis. Clinical data were collected including mean values for BMI and oxygen saturation.

Statistical analysis was performed to compare the prevalence and outcomes of NTM across the different age groups, and to evaluate the different comorbidities experienced by each age group. Specifically, the six most common five-year outcomes were compared across the cohorts, assessing risk difference, confidence interval, risk ratio, odds ratio, and statistical significance to determine risk levels between pairs of groups. The analysis was conducted through the built-in analytics tools in the TriNetX software where a p value of <0.05 was defined as statistically significant. Our patients were selected using the inclusion and exclusion criteria outlined in Table 1. Descriptive statistics (mean, SD, proportion) were reported for demographics and clinical features. Comparative analysis across age groups was conducted using Chi-square tests for categorical variables and Student's *t*-test or ANOVA for continuous variables. To evaluate associations between NTM and clinical outcomes across age groups, we conducted: Logistic regression analysis for binary outcomes to generate odds ratios (OR), Binomial regression to estimate risk ratios (RR) when appropriate. All models were adjusted for key covariates including age, sex, race, and comorbidity burden. Point estimates were reported with 95% CI.

Ethics

The University of California, Riverside IRB determined that the current study was exempt from further ethics review as it did not fit under the federal definition of human subjects research [DHHS 45 CFR46.102(e), 46.102(l)] or clinical investigation [FDA 21 CFR 50.3(c), 56.102(c)].

Results

Demographics

The demographic data provided insight into the prevalence and distribution of pediatric pulmonary NTM infections among the age cohorts, and with respect to sex, race and ethnicity. The study cohort comprised 2,344 cases stratified across four age groups: 0–2 years, 3–5 years, 6–12 years, and 13–18 years. The majority of NTM cases were observed in the 6–12 year age group at 1074 (734/100,000), followed closely by the 13–18 year age group at 760 (848/100,000). The 3–5 year age group had 401 patients (1261/100,000) and the 0–2 group had 109 patients (689/100,000) (Table 2). There were gender differences in the prevalence of pediatric pulmonary NTM lung infections (Table 3). There was a higher mean prevalence of NTM infections among females compared to males 53.31% vs 46.29% among all age groups. There

Table 2 Age Demographics of Our Study Cohort, Including the Number of Patients in Each Age Cohort

Age Cohort	Mean Age Years	Total # Patients
0-2	2	109
3-5	4	401
6-12	9	1074
13-18	15	760

Table 3 Sex Demographics of Our Study Cohort, Stratified by Age

Sex	0-2 Years	3-5 Years	6-12 Years	13-15 Years
Male	44.54	44.75	46.92	48.95
Female	54.54	54.75	52.88	51.05
Unknown	9.09	2.50	0.93	0

Note: All cases without sex information were included as "Unknown".

Table 4 BMI Percentiles of Each Age Cohort

Age Cohort Years	BMI Percentile
0-2	55
3-5	59.2
6-12	61.2
13-18	61.1

was no identified gender for 4.17% of the cohort. The majority of the cohort was identified as white 57.8%, followed by Black/African American, 8.88%, Asian, 4.49%, Native American, 2.83%, Native Hawaiian, 1.19%, another race, 8.52%, and unspecified race 21.6%. BMI percentiles were above the 50th percentile for all age groups, and this was statistically significant ($p < 0.05$) (Table 4).

Laboratory Findings

The data indicated a varying prevalence of NTM infections across the age groups, with the highest prevalence observed in children aged 6–12 years at 1,074 cases (0.007339%). Lab values, particularly those related to immune function, revealed a trend towards higher inflammatory markers among older children, possibly reflecting a more robust immune response or delayed diagnosis. There was an elevated mean white blood cell count in the 13–18 age group at $18.5 \times 10^3/\mu\text{L}$ compared to the expected range of $4.0 \times 10^3/\mu\text{L}$ to $11.0 \times 10^3/\mu\text{L}$ (Table 5). Similarly, CRP mean levels for this age group were significantly above the expected value of 1 mg/L at 26.8 mg/L. In the 3–5 year and 13–18 year cohorts, basophil levels were above the expected 0–1% at 2.68% and 1.83%, respectively. Ferritin levels were higher in the 6–12 year and 13–18 year groups at 546 ng/mL and 1758 ng/mL, respectively, compared to the normal range of 10–200 ng/mL. Among younger children, there were lower levels of inflammatory markers, which may suggest an underdeveloped immune response or early-stage infection.

Table 5 Comparison of Selected Inflammatory Markers by Age Cohort

Cell Marker	0-2 Years	3-5 Years	6-12 Years	13-18 Years
WBC cells/microliter	11	9.7	9.49	18.5
Neutrophils	217	25	62.9	45
Lymphocytes	51	45.7	42.1	35
Monocytes	8.61	8.4	7.78	7.81
Eosinophils	2.54	9.23	3.04	3.65
Basophils	0.513	2.68	0.981	1.83
ESR mm/hr	24.8	23.8	24.8	22.9
CRP mg/dL	11.6	12.4	20.1	26.8
Ferritin ng/mL	202	139	546	1578
Immunoglobulin G mg/dL	7.81	33.6	38	64.5

Note: Laboratory values demonstrate increased immune system activity in response to NTM infection.

Comorbid Conditions

Comorbidities such as acute pharyngitis, pneumonia, asthma, malignancy, and immunodeficiency were identified. (Table 6 and Figure 1). The most common comorbidity among the groups was acute pharyngitis in the 13–18 age group at 30% of the cohort. There was a higher burden of NTM infections among the older pediatric group, ages 13 to 18 years. This group also had the highest proportion of each comorbidity: 18% pneumonia, 22% asthma, 12% malignancy, and 11% immunodeficiency. The overall proportion of individuals with comorbidities was lower in the 6–12 year age group, still with acute pharyngitis leading at 19%, pneumonia at 12%, asthma at 13%, malignancy at 6%, and immunodeficiency at 7%. The 3–5 year old cohort had the following comorbid conditions: 11% acute pharyngitis, 7% pneumonia, 11% asthma, 5% malignancy, and 4% immunodeficiency. The 0–2 age groups saw a notable increase in acute pharyngitis, pneumonia, and malignancy at 18%, 9%, and 13%, respectively. The age 0–2 year old group had the highest percent of malignancy. Asthma and immunodeficiency data was not recorded for this age group likely due to reduced diagnosis of these issues at such ages. The most prevalent comorbidity was acute pharyngitis at 78% across all age groups, and no other comorbidity rose above 46%.

Table 6 Comparison of the Top Five Most Common Comorbidities by Age Cohort

Comorbidities	0-2 Years	3-5 Years	6-12 Years	13-18 Years
Acute pharyngitis	18	11	19	30
Pneumonia	9	7	12	18
Asthma	0	11	13	22
Malignancy	13	5	6	12
Immunodeficiency	0	4	7	11

Note: Values are presented as percentages of the total age cohort with the comorbidity.

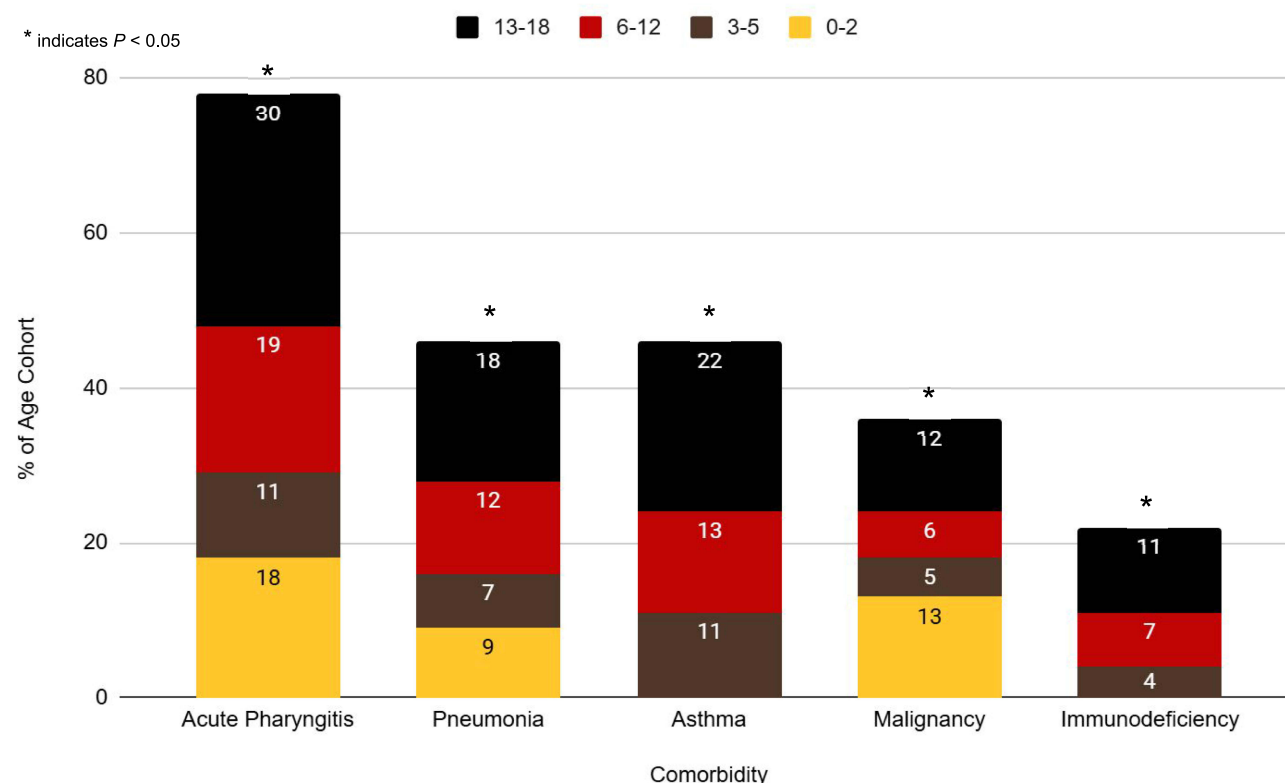


Figure 1 The five most common comorbidities associated with NTM infection as a percent of each age cohort. *indicates $P < 0.05$.

Discussion

The findings of this study demonstrate an age-based differential presentation of Pulmonary NTM infection among the cohort studied. This study highlights the need for age-specific approaches to the diagnosis and management of pediatric pulmonary NTM infections. Our study adds novel data regarding the global prevalence of NTM pulmonary infections among a Pediatric population. The varying prevalence and outcomes across age groups suggest that different factors, such as immune development and environmental exposure, play significant roles in the susceptibility to and progression of these infections. It is important to understand the mechanisms of these differences. Further studies will be completed to better understand the age-based differential of disease prevalence.¹⁷ The top five comorbidities we identified were acute pharyngitis, unspecified pneumonia, asthma, malignancy and immunodeficiency. The presence of these comorbidities also correlated with a higher burden of NTM infection in the older pediatric groups, suggesting that these children might have prolonged exposure to risk factors or delayed diagnosis.¹⁸ This increased susceptibility is thought to be related to damaged respiratory mucosa, promoting NTM attachment and infection.¹⁹ Our observed comorbidity of asthma drew our attention to the fact that children with underlying chronic lung diseases may have a higher likelihood of severe outcomes, including prolonged hospitalizations and the need for intensive care.²⁰ There was a higher odds ratio (OR) of developing more severe lung disease, such as pneumonia, pulmonary fibrosis, lung abscess, bronchiectasis, interstitial lung disease upon NTM infection among 0–2 year olds compared to older age groups (Table 7). This is also supported by several reports of some of these outcomes occurring in various age groups.^{21,22} Immunodeficiency, whether congenital or acquired, tends to be associated with a more complicated clinical course and higher mortality rates, and we also observed it as a comorbidity.²³ Specifically, this immunosuppression allows for extrapulmonary NTM disease to develop and spread by escaping the body's immune cells and entering the lymphatic system and bloodstream.²⁴ The finding of lung or mediastinal abscess as a five year outcome heightens our clinical concern among this cohort, especially when considering clinical uncertainty in treatment of NTM.²⁵ The analysis of racial and ethnic data was limited in this study due to potential incomplete availability of documentation of some demographics in the electronic health records, which may

Table 7 Pulmonary Health Outcomes by Age Cohort

Age Comparison (Year)	Pneumonia	Bronchiectasis	Chronic Resp. Failure	Pulmonary Fibrosis	Interstitial Lung Disease	Abscess of Lung and Mediastinum
0-2 vs 3-5	RD: -0.067 CI: (-0.125, -0.0089) p = 0.003** RR: 0.290 (0.124, 0.677) OR: 0.270 (0.109, 0.667)	RD: -0.066 CI: (-0.122, -0.009) p = 0.002** RR: 0.285 (0.122, 0.668) OR: 0.266 (0.108, 0.657)	RD: -0.066 CI: (-0.122, -0.009) p = 0.002** RR: 0.285 (0.122, 0.668) OR: 0.266 (0.108, 0.657)	RD: -0.066 CI: (-0.122, -0.00906) p = 0.00225** RR: 0.285 (0.122, 0.668) OR: 0.266 (0.108, 0.657)	RD: -0.0656 CI: (-0.122, -0.00906) p = 0.00225** RR: 0.285 (0.122, 0.667) OR: 0.266 (0.108, 0.657)	RD: -0.0656 CI: (-0.122, -0.00906) p = 0.00225** RR: 0.285 (0.122, 0.668) OR: 0.266 (0.108, 0.657)
0-2 vs 6-12	RD: -0.062 CI: (-0.119, -0.005) p = 0.001** RR: 0.340 (0.171, 0.677) OR: 0.319 (0.151, 0.672)	RD: -0.074 CI: (-0.129, -0.020) p = 0.0000018*** RR: 0.190 (0.090, 0.401) OR: 0.176 (0.079, 0.391)	RD: -0.075 CI: (-0.130, -0.021) p = 8.64E-07*** RR: 0.179 (0.084, 0.382) OR: 0.166 (0.074, 0.372)	RD: -0.0821 CI: (-0.137, -0.0275) p = 5.23E-10*** RR: 0.106 (0.0449, 0.248) OR: 0.0968 (0.0393, 0.238)	RD: -0.0821 CI: (-0.137, -0.0275) p = 5.23E-10*** RR: 0.106 (0.0450, 0.248) OR: 0.0968 (0.0393, 0.238)	RD: -0.0821 CI: (-0.137, -0.0275) p = 5.23E-10*** RR: 0.106 (0.0449, 0.248) OR: 0.0968 (0.0393, 0.238)
0-2 vs 13-18	RD: -0.0660 CI: (-0.123, -0.00882) p = 0.000988*** RR: 0.301 (0.143, 0.634) OR: 0.281 (0.126, 0.626)	RD: -0.0651 CI: (-0.121, -0.00971) p = 0.000536*** RR: 0.290 (0.140, 0.604) OR: 0.271 (0.123, 0.595)	RD: -0.0678 CI: (-0.123, -0.0125) p = 0.000195*** RR: 0.261 (0.124, 0.551) OR: 0.243 (0.109, 0.542)	RD: -0.0784 CI: (-0.133, -0.0236) p = 3.84E-07*** RR: 0.145 (0.0618, 0.341) OR: 0.134 (0.0542, 0.329)	RD: -0.0784 CI: (-0.133, -0.0236) p = 3.84E-07*** RR: 0.145 (0.0618, 0.341) OR: 0.134 (0.0542, 0.329)	RD: -0.0784 CI: (-0.133, 0.0236) p = 3.84E-07*** RR: 0.145 (0.062, 0.341) OR: 0.134 (0.0542, 0.329)
3-5 vs 6-12	RD: -0.00456 CI: (-0.0247, 0.0156) p = 0.667 RR: 0.857 (0.423, 1.735) OR: 0.853 (0.413, 1.763)	RD: 0.00887 CI: (-0.009, 0.0267) p = 0.286 RR: 1.512 (0.704, 3.247) OR: 1.526 (0.698, 3.337)	RD: 0.00983 CI: (-0.00794, 0.0276) p = 0.229 RR: 1.601 (0.740, 3.467) OR: 1.618 (0.734, 3.565)	RD: 0.0166 CI: (-0.00051, 0.0336) p = 0.0187* RR: 2.723 (1.142, 6.490) OR: 2.769 (1.143, 6.706)	RD: 0.0166 CI: (-0.00051) p = 0.0187* RR: 2.723 (1.142, 6.490) OR: 2.769 (1.143, 6.706)	RD: 0.0166 CI: (-0.000512, 0.0337) p = 0.0187* RR: 2.723 (1.142, 6.490) OR: 2.769 (1.143, 6.706)
3-5 vs 13-18	RD: -0.00102 CI: (-0.0221, 0.0201) p = 0.925 RR: 0.964 (0.450, 2.066) OR: 0.963 (0.440, 2.110)	RD: -0.00042 CI: (-0.0213, 0.0193) p = 0.967 RR: 0.984 (0.465, 2.082) OR: 0.984 (0.456, 2.123)	RD: 0.00224 CI: (-0.01714, 0.02163) p = 0.818 RR: 1.094 (0.510, 2.346) OR: 1.096 (0.501, 2.400)	RD: 0.0129 CI: (-0.0051, 0.0309) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)	RD: 0.01288 CI: (-0.0051, 0.03086) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)	RD: 0.0129 CI: (-0.0051, 0.03086) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)
6-12 vs 13-18	RD: -0.009 CI: (-0.023, 0.005) p = 0.184 RR: 0.654 (0.349, 1.23) OR: 0.648 (0.340, 1.230)	RD: -0.009 CI: (-0.023, 0.005) p = 0.184 RR: 0.654 (0.349, 1.23) OR: 0.648 (0.340, 1.230)	RD: -0.008 CI: (-0.021, 0.006) p = 0.259 RR: 0.687 (0.356, 1.323) OR: 0.681 (0.349, 1.331)	RD: 0.0129 CI: (-0.0051, 0.0309) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)	RD: 0.01288 CI: (-0.0051, 0.03086) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)	RD: 0.0129 CI: (-0.0051, 0.03086) p = 0.119 RR: 1.969 (0.827, 4.689) OR: 1.995 (0.823, 4.835)

Notes: *p < 0.05, **p < 0.01, ***p < 0.001. Bolded values indicate statistically significant differences.

have introduced bias in the interpretation of these variables. However, our demographic data supports our initial hypothesis that even a mildly elevated BMI may increase susceptibility for pediatric NTM.²⁶ While current literature supports lower BMI as a significant risk factor for NTM infection,²⁷ one possible explanation is the susceptibility of the host in states of malnutrition. Individuals with higher BMI are more likely to be diagnosed with chronic inflammatory or autoimmune conditions²⁸ which are commonly treated using immunosuppressive corticosteroids,²⁹ potentially increasing the risk for NTM infection.^{30,31} In addition to BMI, other physical conditions and comorbidities, particularly chronic lung diseases and immunodeficiency, underscore the need for vigilant screening and management in at-risk populations. The significant odds ratios associated with future 5-year outcomes in older children (Table 7) suggest that more aggressive diagnostic and therapeutic strategies may be warranted in these age groups.³² Our findings show that the majority of NTM cases were observed in the 6–12 year age group and the highest percent of cases were observed in the 3–5 year age group. This finding shows that school-aged children and adolescents are more likely to be diagnosed with NTM infections, potentially due to increased exposure to environmental reservoirs of NTM, such as water and soil, and higher rates of outdoor activities compared to toddlers.³³ Abnormal inflammatory marker values among the 13–18 age group were also a notable age cohort-based finding. Particularly, the elevated white blood cell count, ferritin levels, and CRP in older children suggest a more pronounced inflammatory response in the adolescent age group with NTM infections. These findings are distinct from the data that has been found from a previous study done in Wisconsin. In the Wisconsin study, the isolates were based on statewide data, rather than a global database, and this study included non Pulmonary infections. Our study is the first to our knowledge to analyze a global database, with a focus on Pediatric non CF Pulmonary infections. The data in the Wisconsin study included Cystic Fibrosis patients. Since CF is a known risk factor for Pulmonary NTM, our study design focused on non CF patients.³² From our demographic data, we also found that there were significant differences in the gender of infected patients. This trend aligns with existing adult literature that suggests females may have a higher susceptibility to pulmonary infections due to differences in immune response, hormonal influences, or behavioral factors, such as a greater likelihood of engaging in activities that increase exposure to NTM.³⁴ There were statistically significant differences in NTM infection rates among different racial groups, which has to our knowledge not been studied utilizing a global EHR database. The available data from diverse populations shows that certain racial and ethnic groups might be disproportionately affected by NTM infections, potentially due to disparities in healthcare access, environmental exposures, or genetic predispositions.³⁵ This finding highlights the need for more comprehensive data collection and medical record documentation in future studies to better understand the role of race and ethnicity in the epidemiology of pediatric pulmonary NTM infections.

Limitations

This study has several limitations, including its retrospective nature and reliance on data from the TriNetX platform, which may introduce selection bias. Additionally, the reliance on electronic health record data may result in incomplete or inaccurate documentation of clinical characteristics and outcomes. The platform's retrospective nature may introduce selection bias, affecting the generalizability of the results. Additionally, differences in cohort sizes can impact comparison results. TriNetX also anonymizes data by replacing counts of 1–10 with “10” to protect patient privacy, which limits the statistical analysis of rare outcomes. Furthermore, patients who move to non-TriNetX facilities are lost and not included in the outcome comparisons. There may also be comorbidities that were documented in patients' records in institutions not participating in TriNetX. The study also did not account for the potential impact of socio-economic factors, geographic location, or variations in healthcare access, which could influence the prevalence and outcomes of NTM infections.^{36,37} Despite these limitations, our study has provided an extensive analysis of global data in this area of study, utilizing a novel EHR based database.^{38,39} Additionally, more advocacy is needed to ensure that NTM is properly documented, species-wise in the EHR to ensure that future epidemiological studies can be done effectively.

Conclusions

Our study uniquely provides an analysis of global prevalence of non CF Pediatric Pulmonary NTM infections. The study contributes to current knowledge in the field and identifies selected future five year outcomes. We also compared the associated risk for the specific age cohorts studied. This study thus adds to current understanding of the incidence and

characteristics of Pediatric NTM non CF pulmonary disease. Future studies to develop treatment strategies and age based considerations are therefore important in the management of Pediatric pulmonary NTM infection.

Disclosure

The authors report no conflicts of interest in this work.

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