Incidence, Prevalence and Patterns of Stenotrophomonas Maltophilia Infection in People with Cystic Fibrosis across Europe

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INTRODUCTION

Progressive airway disease with recurrent infections is a hallmark of cystic fibrosis (CF). While Pseudomonas aeruginosa and Staphylococcus aureus are the most common pathogens, emerging bacteria such as Stenotrophomonas maltophilia (SM), non-tuberculous mycobacteria, and Achromobacter species are increasingly identified. SM, a gram-negative bacterium, has been cultured from the sputum of people with CF (pwCF) with variable prevalence across countries. While its role remains debated, a 2012 review suggests that chronic SM may be a marker of more severe lung disease [1]. The clinical impact of Stenotrophomonas maltophilia in European pwCF remains underexplored, highlighting the need for better epidemiological data to guide research and care.

AIMS

Aims of this study are to estimate the prevalence and incidence of SM in Europe, to compare the clinical characteristics of pwCF according to their SM infection status and to characterize the most common patterns of infection during a period of 6 years (2018-2023).

METHODS

This longitudinal study is based on data provided by the European Cystic Fibrosis Society Patient Registry (ECFSPR), which collects demographic and clinical data of pwCF from 42 countries in Europe. Data are collected annually, according to specific inclusion criteria and standardized definitions.

In the ECFSPR, SM status is classified as negative, intermittent, or chronic, based on standardized criteria [2]. Demographics and clinical outcomes within SM-negative, intermittent, and chronic groups in 2023 were described and the differences among groups were assessed using Pearson's Chi-squared test for categorical and Kruskal-Wallis test for continuous variables.

SM overall incidence and prevalence from 2008 to 2023 were computed. Prevalence was the proportion of infected (both intermittent and chronic together) in each year, while incidence was the number of newly infected individuals divided by those uninfected in the previous year. To assess whether trends in prevalence and incidence over time were statistically significant, logistic regression models were applied, using infection status as the response variable and calendar year as a continuous explanatory variable. Additional models were then fitted, accounting for time of introduction of Cystic Fibrosis Transmembrane conductance Regulator (CFTR) modulators and COVID-19 pandemic (pre- or post- period).

Chronic and intermittent SM infection were used as response variables in further logistic regression models to assess whether a significant trend existed with age at follow-up, included as a continuous explanatory variable, also accounting for CFTR modulator use.

Infection patterns from 2018–2023 were used to classify patients accordingly.

Analyses were run using R Core Team versions 4.5.0.

RESULTS

In 2023, ECFSPR included 52977 pwCF, of whom 51566 (97.3%) had complete information regarding SM infection status.

The overall prevalence of SM (including both chronic and intermittent cases) in 2023 ranged from 0.26% in Romania to 19.3% in Serbia, accounting for 5.0% (95% CI: 4.8 to 5.2)

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across Europe. Four small countries did not report any SM detection.

Age, gender, BMI in adults, BMI z-score in children, and the country's income category (all p<.05) differed across the three infection groups: SM-negative (49010, 95%), intermittent (2000, 3.9%), and chronic (556, 1.1%). SM-chronic had the highest median age (28.7y) and lowest BMI (22.1 kg/m2), while SM-intermittent were the youngest (16.5y), and SM-negative had the highest BMI (22.5 kg/m2).

In contrast, genotype (p=0.7) and use of pancreatic enzymes (p=0.2) showed no significant differences. All concomitant infections—chronic P. aeruginosa, chronic S. aureus, MRSA, H. influenzae, Achromobacter spp., and nontuberculous mycobacteria—differed significantly across groups (all p<.001), with highest prevalence in those chronically infected with SM; only chronic Burkholderia cepacia complex showed a borderline difference (p=.041).

The prevalence of SM increases significantly with age (p<.001) in both the unadjusted model and the model adjusted with CFTR modulator use. The unadjusted model showed no significant trend in SM prevalence over time (p=0.609); however, after adjusting for CFTR modulator/COVID period (≤2019 vs >2019), a significant trend was observed (p<.001); furthermore, the stratified analysis revealed a significant rise in SM prevalence from 2008 to 2019 (p<.001), followed by a significant decline from 2020 to 2023 (p<.001).

Among 32,724 pwCF, 64 distinct infection patterns were identified. Most (24,594, 75.2%) showed no infection, while 24.8% (8,130) showed infection in at least one year and 11.1% (3640) for at least 2 years. Specifically, one year (13.7%), two years (5.3%), three years (2.8%), four years (1.5%), five years (0.8%), and six years (0.6%). Only 1.6% (524) of pwCF showed a continuous infection, remaining positive through 2023.

CONCLUSIONS

This large multinational analysis offers a detailed view of SM infection in the European CF population, revealing that while most individuals remained uninfected, nearly one-quarter experienced infection between 2018 and 2023. Chronic infection was strongly age-associated and consistently linked to a higher burden of co-infections. The shifting temporal trends—marked by a rise in prevalence up to 2019 and a subsequent decline during the CFTR modulator and post-COVID era—suggest that both medical advancements and broader changes in healthcare practices may significantly shape SM epidemiology. These findings highlight the need for continued surveillance to guide care and inform future research.

REFERENCES

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