



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Editorial

Cystic fibrosis microbiology research in Spain

Investigación de la microbiología de la fibrosis quística en España



Chronic respiratory infections in persons with cystic fibrosis (CF) has been for decades a topic of major research interest, including both evolutionary biology and clinical perspectives, in which Spanish microbiologists have been traditionally located in the frontier of the generation of knowledge.

In this issue of EIMC Maruri-Aransolo et al. present the results of a recent (2021) multicenter study involving 16 specialized CF Units in Spain.¹ The objectives of the study were to determine the prevalence of major CF pathogens as well as their antimicrobial susceptibility profiles and correlation with lung function; a comparison with a previous multicenter study carried out in 2013² was performed, in order to decipher the evolution of the disease in Spain during the last decade.

A total of 326 CF patients were included in the 2021 study, 3/4 of them showing the F508del mutation. The most common bacteria detected were *Staphylococcus aureus* followed by *Pseudomonas aeruginosa*; while *S. aureus* highest prevalence was detected in children under 10 years old, the age range with the highest prevalence of *P. aeruginosa* was between 41 and 45 years. *P. aeruginosa* colonization status was defined as chronic in 30% of the patients and intermittent in 17%. *Achromobacter xylosoxidans* and *Burkholderia cepacia* complex (BCC) were also more prevalent in samples obtained from adults, being more frequent in the 36–40 age groups and 41–45 respectively. Multilocus sequence typing (MLST) revealed that the most prevalent species of the BCC were *B. cepacia* and *Burkholderia contaminans* followed by *Burkholderia multivorans* and *Burkholderia vietnamiensis*. No isolates of *Burkholderia cenocepacia* were detected. *Mycobacteroides abscessus* was the most frequent non-tuberculous mycobacteria (NTM) species, detected in six patients, followed by *Mycobacteroides avium* in two and *Mycobacteroides lentiflavus* and *Mycobacteroides indicuspragensis* in one each.

Certainly, one of the most relevant findings of the study was the lower frequency of isolation of relevant CF pathogens, such as *S. aureus* and *P. aeruginosa*, in 2021 as compared with the data obtained in 2013.

Half of the patients had a positive culture for a single CF pathogen, whereas one third showed at least two. The association of *P. aeruginosa* and *S. aureus*, detected in over 10% of the patients, was that most frequently documented. Indeed, previous studies have identified both species in the same lobe of CF lungs, suggesting

that both pathogens are present in the same niche and may interact *in vivo*.³

The performed analysis of the colonization patterns vs pulmonary function revealed a tendency toward lower FEV1 values of patients positive for MRSA as compared with susceptible *S. aureus* as well as those showing acute exacerbation by *P. aeruginosa* as compared with those only colonized, confirming findings from previous studies.⁴

Regarding antimicrobial susceptibility patterns, 56% of the *P. aeruginosa* isolates were non-MDR, 11% MDR, 23% XDR and up to 10% PDR. The most active antibiotic was meropenem (79%) distantly followed by ceftazidime (27%). While novel β -lactams and β -lactam β -lactamase inhibitor combinations were not tested in this study, a recent publication from the same group revealed a relatively high activity for cefiderocol (92% susceptible) in *P. aeruginosa* CF isolates from three Spanish multicenter studies.⁵ The most active antibiotics against MRSA were linezolid (96%) and co-trimoxazole (100%), while resistance to macrolides and aminoglycosides was frequent and related to the received therapies. Among BCC, *A. xylosoxidans* and *S. maltophilia* isolates, highest activity was noted for meropenem, piperacillin-tazobactam and fluoroquinolones respectively. Overall, a similar pattern was observed when comparing the 2021 and 2013 studies, although the percentages of XDR and PDR *P. aeruginosa*, as well as BCC and *A. xylosoxidans* resistance seemed to have increased over the last decade.

Up to 86% of the patients had received an antibiotic treatment over the study period, most frequently by oral route followed by inhalation. A significant proportion of patients received antibiotics through multiple routes of administration. The most common combination was oral + inhaled administration, followed by inhaled + intravenous. Immunomodulatory azithromycin was administered orally in half of the patients. Dornase administration was significantly higher in patients with moderate-severe disease versus patients with mild disease. Up to 36% of the patients received CFTR modulators; the combination tezacaftor + ivacaftor was the most used modulator therapy, followed by ivacaftor and lumacaftor + ivacaftor. The newly approved modulator elxacaftor + tezacaftor + ivacaftor was administered to 15% of the patients. These drugs were not yet used in 2013.

Newborn screening programs and patient registry data collection have significantly improved in recent years.⁶ In the Spanish 2021 CF registry, 2578 patients were included, 56% of whom being adults, just like in the present study. Recent European data, including Spain, show a stable prevalence of CF among children but a

See related article: <https://doi.org/10.1016/j.eimc.2024.08.013>

<https://doi.org/10.1016/j.eimc.2025.04.003>

0213-005X/© 2025 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

notable increase in adults, reflecting an increasing trend in patient survival. Indeed, a lower rate of exacerbations and hospitalizations were documented in 2021 compared to 2013, possibly linked to the introduction of CFTR modulator treatments. Likewise, remarkably, a lower prevalence of *S. aureus* and *P. aeruginosa* isolation was documented in 2021 as compared with 2013, fact that could perhaps be explained by the improvement in patient's management or the implementation of newborn screening after 2013. Another factor to consider is that the number of recruited patients in 2021 was lower than that obtained in 2013, likely due to COVID-19 pandemic. Thus, restrictive measures that were introduced during the pandemic may have caused a potential bias, positively decreasing the number of bacterial transmissions. Nevertheless, the data obtained were fully representative and in line with Spanish Registry data, so they probably address accurately the evolution of CF disease in Spain. The prevalence of BCC (7%) was also lower in 2021 as compared with 2013 (12%) but still high, indicating a significant deviation from the expected prevalence compared to other European countries. However, close to half of the patients positive for BCC came from a single center, thus likely reflecting an ongoing outbreak situation rather than a global national trend.

Thus, altogether this study provides a further relevant step forward on the investigation of the microbiology of CF patients from Spain, following the trend of previous multicenter studies^{2,7,8} and early pioneer works, such as those helping to establish the bronchopulmonary colonization-infection patterns in these patients^{9,10} or the discovery of the high prevalence and major role in adaptation, persistence and antimicrobial resistance of hypermutable (mutator) pathogens in chronic infections, key milestone currently celebrating its 25th anniversary.¹¹

References

1. Maruri-Arnsolo A, Quintana E, Michelena-González M, Pastor-Viverod MD, Álvarez A, Girón R, et al. Bronchopulmonary colonization patterns in Spanish people with cystic fibrosis: Results of a national multicentre study. *Enferm Infect Microbiol Clin*. 2025;43:309–16, <http://dx.doi.org/10.1016/j.eimc.2024.08.013> [in press].
2. de Dios Caballero J, Del Campo R, Royuela A, Solé A, Máiz L, Oliveira C, et al. Bronchopulmonary infection-colonization patterns in Spanish cystic fibrosis patients: results from a national multicenter study. *J Cyst Fibros*. 2016;15:357–65, <http://dx.doi.org/10.1016/j.jcf.2015.09.004>.
3. Camus L, Briaud P, Vandenesch F, Doléans-Jordheim A, Moreau K. Mixed populations and co-infection: *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Adv Exp Med Biol*. 2022;1386:397–424, http://dx.doi.org/10.1007/978-3-031-08491-1_1.
4. Thornton CS, Parkins MD. Microbial epidemiology of the cystic fibrosis airways: past, present, and future. *Semin Respir Crit Care Med*. 2023;44:269–86, <http://dx.doi.org/10.1055/s-0042-1758732>.
5. Maruri-Arnsolo A, López-Causapé C, Hernández-García M, García-Castillo M, Caballero-Pérez JD, Oliver A, et al. In vitro activity of cefiderocol in *Pseudomonas aeruginosa* isolates from people with cystic fibrosis recovered during three multicentre studies in Spain. *J Antimicrob Chemother*. 2024;79:1432–40, <http://dx.doi.org/10.1093/jac/dkac126>.
6. European Cystic Fibrosis Society. ECFSPR 2021 annual data report; 2023. <https://www.ecfs.eu/sites/default/files/Annual%20Report.2021.09Jun2023.pdf>
7. Maruri-Arnsolo A, Hernandez-García M, Barbero R, Michelena M, Pastor-Vivero MD, Mondejar-Lopez P, et al. Genomic characterization of MRSA recovered from people with cystic fibrosis during two Spanish multicentre studies (2013 and 2021). *JAC Antimicrob Resist*. 2024;6:dlae160, <http://dx.doi.org/10.1093/jacamr/dlae160>.
8. López-Causapé C, de Dios-Caballero J, Cobo M, Escribano A, Asensio Ó, Oliver A, et al. Antibiotic resistance and population structure of cystic fibrosis *Pseudomonas aeruginosa* isolates from a Spanish multi-centre study. *Int J Antimicrob Agents*. 2017;50:334–41, <http://dx.doi.org/10.1016/j.ijantimicag.2017.03.034>.
9. Oliver A, Alarcón T, Caballero E, Cantón R. Microbiological diagnosis of bronchopulmonary colonization-infection in cystic fibrosis. *Enferm Infect Microbiol Clin*. 2009;27:89–104, <http://dx.doi.org/10.1016/j.eimc.2008.05.004>.
10. Cantón R, Cobos N, de Gracia J, Baquero F, Honorato J, Gartner S, et al. Antimicrobial therapy for pulmonary pathogenic colonisation and infection by *Pseudomonas aeruginosa* in cystic fibrosis patients. *Clin Microbiol Infect*. 2005;11:690–703, <http://dx.doi.org/10.1111/j.1469-0691.2005.01217.x>.
11. Oliver A, Cantón R, Campo P, Baquero F, Blázquez J. High frequency of hypermutable *Pseudomonas aeruginosa* in cystic fibrosis lung infection. *Science*. 2000;288:1251–4, <http://dx.doi.org/10.1126/science.288.5469.1251>.

Antonio Oliver
Servicio de Microbiología, Hospital Son Espases, IdISBa, CIBERINFEC,
Palma de Mallorca, Spain
E-mail address: Antonio.oliver@ssib.es