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Letter to the Editor

Etiology of bronchopulmonary infections in Bulgarian cystic fibrosis patients

Dear Editor,

Cystic fibrosis (CF) is an autosomal recessive inherited disorder characterized by abnormal secretory function of all exocrine glands. Clinical symptoms vary with the severity of the disease and according to the organs involved, but the most common ones are pathological lung changes mainly presented as chronic infections. These bronchopulmonary infections (BPI) are the major reason for both progressive decreasing of lung function and mortality.

The aim of this study was to explore and analyze the etiological structure of BPI in Bulgarian CF patients according to the patient's age and gender.

During 2006–2011 period we examined 108 patients (46 females and 62 males), aged 5–27 years, with genetically confirmed CF disease. Sputum samples were plated and incubated at 37 °C for 24–48 h. BPI pathogens were identified by a BBL Crystal ID system (Becton Dickinson). From the sputum, genomic bacterial DNA was extracted and amplified by PCR employing two sequence-specific targets, namely (i) the *Pseudomonas aeruginosa* exotoxin A locus, and (ii) the *Burkholderia cepacia* complex *recA* gene using specific primers and conditions as previously described.^{1,2} Statistical analysis was performed by Student's t-test.

The etiologic agents of BPI are shown in Fig. 1. The leading pathogens causing BPI were *P. aeruginosa* and *Staphylococcus aureus*, followed by *Candida* spp., *Klebsiella-Enterobacter-Serratia* group, and *Haemophilus influenzae*. Co-infection of 2 or 3 microorganisms was found in 44 patients (40.7%).

The frequency of the infections caused by *P. aeruginosa* (57.4%) was very close that reported by the USA Cystic Fibrosis Foundation in 2009–2010 (51.7%). On the contrary, the frequency of *S. aureus* (35.2%) is lower compared to those in the USA – 51.3% (2009) and 67.0% (2010). Our established frequency of *B. cepacia* complex (5.5%) was slightly higher than in the USA in 2009–2010 (2.7% and 2.5% respectively), whereas the 3.3% of *Stenotrophomonas maltophilia* was lower (12.7% and 13.8% respectively).^{3,4}

Regarding *P. aeruginosa* we found that patients of 10-years old and younger were significantly less colonized (42.1%) than

patients over 16 years of age (83.3%) [$p < 0.01$]. In the younger patients *S. aureus* was isolated in 42.1%, compared to 25%, among patients aged 16 years or more. *Candida* spp. was isolated in 21% of those aged less than 10 years and in 41.7% in adolescent/adult age group (16+ years).

In comparison with data from the USA, the rate of colonization by *P. aeruginosa* abruptly increases from 25% at the age of 6 years to 65% among 18 year-old patients, and up to 80% in those patients older than 25 years. Respiratory tract colonization with *S. aureus* (around 70% in those aged between 6 and 17 years) steadily increases up to the 10th year and then slowly decreases between the 11th and 17th year followed by a significant decrease after the age of 17 years.⁴

The prevalence of *P. aeruginosa* infections was significantly higher in girls (73.9% vs. 45.2% among boys – $p < 0.05$). Likewise, *S. aureus* infections predominated among females (43.5%/29.0%) and so did *Candida* spp. infections (43.5%/19.4%). The frequency of BPI, caused by the *Klebsiella-Enterobacter-Serratia* group of pathogens was similar in both genders (8.7% in girls and 12.9% in boys).

Well documented by other authors gender difference in the onset of chronic infection by *P. aeruginosa* – average 1 year and 7 months earlier for the girls,⁵ could explain higher percentage of *P. aeruginosa* in girls compared to the boys of our results.

A recently carried on survey of annual hospitalization records of Scandinavian CF patients aiming to search for gender differences in clinical characteristics and treatment plans revealed a higher frequency of new chronic infection by *P. aeruginosa* in females (30.3%) compared to males (7.1%) in a 1-year period. Furthermore, in adult female patients a higher risk for infections caused by *P. aeruginosa* and *Burkholderia* spp. was established.⁶

The current study confirms the global trends of the leading etiologic pathogens in the airways and the dynamic changes found in respiratory microbial flora as the CF patients age – a considerable increase in *P. aeruginosa* colonization and decrease in *S. aureus* colonization after 16 years of age. Successful eradication of the initial and subsequent BPI in the early years of CF patients improves the quality of life and survival of these individuals.

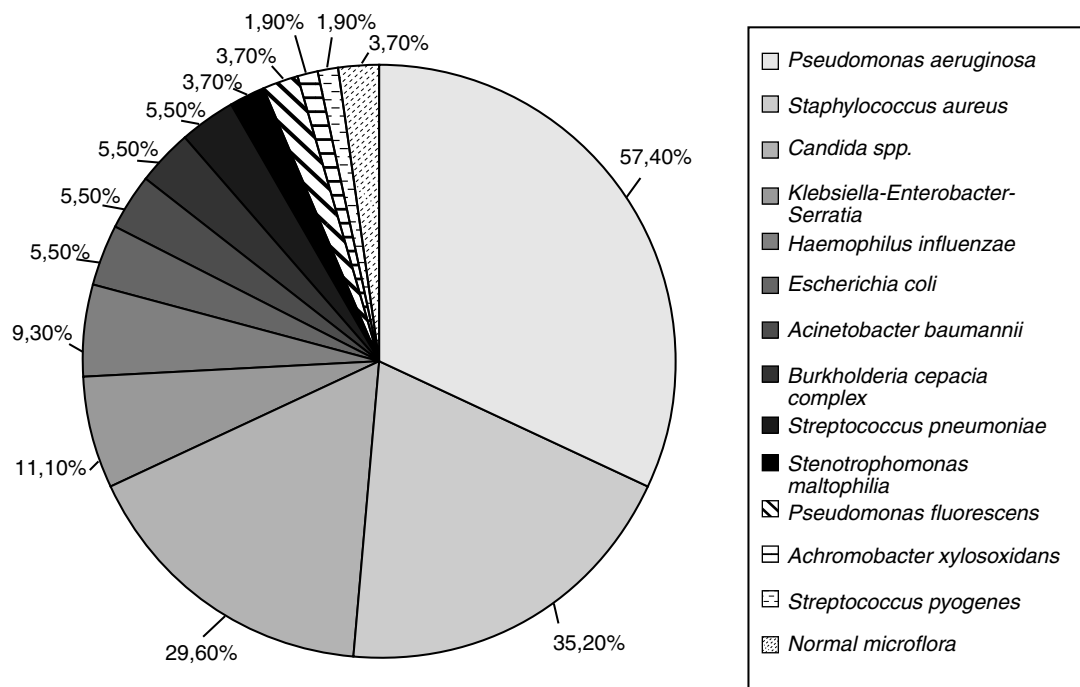


Fig. 1 – Total etiology of BPI in Bulgarian CF patients. BPI, bronchopulmonary infections; CF, cystic fibrosis.

Conflict of interest

The authors declare no conflicts of interest.

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