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# Microbial Evaluation of Sputum of Cystic Fibrosis Patients

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***Abstract***

***Background*:** Cystic fibrosis disease is a common hereditary autosomal recessive disorder in which loss of lung function caused by infectious factors is the most common cause of the patient's death. In this study, the microbes in sputum of the cystic fibrosis patients have been studied during relapses of the disease.

***Materials and Methods*:** In this cross-sectional study, 129 sputum cultures of the patients with cystic fibrosis, who were hospitalized in Mofid Children's Hospital in Tehran during 2004-2009 with relapse of disease, were studied. The data were collected through census method and based on the information concerning (gender, age, type of germ and the appropriate antibiotics).

***Results*:** The most common germs in the sputum of these patients are *Pseudomonas aeruginosa* (approximately 36%) and then respectively *klebsiella* (13%), *Staphylococcus aureus* (9.3%) and *Streptococcus pneumoniae* (5.4%). Examination of antibiogram showed that these germs give an appropriate response to antibiotics such as Ceftazidime, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin and largely to aminoglycosides.

***Conclusion*:** Considering the more prevalence of *Pseudomonas aeruginosa*, combined therapy with ceftazidime or imipenem along with aminoglycoside and further treatment with oral azithromycin are recommended. More studies in this area are necessary.



## Introduction

Cystic fibrosis is an inherited disease that affects several organs including the digestive system, sweat glands and the reproductive system and causes a progressive disease in respiratory system that eventually will be one of the main causes of death in these patients. The hereditary pattern of this disease is autosomal recessive and its prevalence is different in various races from about 1 in 2500 to 1 in 32000 live births and carrier's frequency has been reported to be about 1 in 25 patients (4%). Cystic fibrosis disease occurs due to mutations in the large single gene on chromosome seven that encodes the CFTR protein. Most mutations are related to exon 10 of this gene. In patients with cystic fibrosis (CF), any disorder in chloride sodium transport through respiratory epithelium causes thick and sticky secretions in the airways and it leads to chronic infection of the respiratory system and ultimately, will create progressive respiratory failure. Loss of lung function in cystic fibrosis patients is the most common cause of their death [1,2].

The prevalence of airway colonization with *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Burkholderia cepacia* is common in children with CF [1]. Essentially, the immune system of CF patients is normal. Nutritional disorders such as fatty acid deficiency increase the susceptibility to respiratory infection [1,3]. Patients with CF usually have no problems with appetite, but there is difficulty in absorption. Finding of *S. aureus* and *Pseudomonas aeruginosa* in culture of the secretions obtained from the lower parts of the airways (e.g., sputum), strongly suggests the diagnosis of CF [2]. Finding of *Burkholderia Cepacia* should also suggest the diagnosis of CF [4]. The other organisms which are obtained especially in advanced pulmonary disease include a variety of gram negative rods, fungi and non-tuberculosis mycobacterium species [5,6]. Failure to improve respiratory symptoms with regular antibiotics necessitates the test for mycoplasma and viruses [1,5]. These patients should be treated completely and comprehensively. Due to the frequent relapse of infections, it is very important to take quick hospital actions and care for proper nutrition in these children, because it reduces the severity of lung damage. Antibiotic are the basis of treatment to control the advancement of lung infections and eventually lung damage. The goal of treatment is to reduce the severity of bronchial infection and delay the progression of lung damage. Antibacterial prophylaxis is effective in prevention of *Staphylococcus aureus* infection [1,2]. Using nebulizer aminoglycoside, especially tobramycin, helps to prevent and reduce infection. Gentamicin can also be used as the helper aminoglycoside [7,8].

It is hard to take drugs and medical interventions for long, but it can keep the child asymptomatic and give an almost normal life to the patient. There are simple measures to reduce the risk of expansion of the germs

causing infection in CF patients. Medications should be taken constantly. Given that the most common cause of mortality in CF patients is pneumonia [2,9], and considering the short lifespan of these patients if the infections are not treated appropriately and on the other hand, significant improvement in quality and quantity of life of these patients with treatment, this study was designed and implemented to examine the type of microbes in the sputum of cystic fibrosis patients after relapses, the patients who referred to Mofid hospital in Tehran during 2004-2009.

## Materials and Methods

In this descriptive-analytical study, the study population included files of all children with cystic fibrosis, who were hospitalized at Mofid hospital during 2004-2009 after relapses of the disease. The patients referring to children pulmonary ultra-specialized clinic who were treated as outpatients were excluded from this study. First, the files of CF patients admitted during 2004-2009 were specified and reviewed. Then, according to the results of cultures and other required data, the respective data form was completed. The sputum samples sent to culture and smear were taken after physical therapy and their culture results were presented in their file. The method is disk diffusion antibiogram and the medium was McFarland and Molar and Molar Khondar. Data was collected using data from including the questions such as age, gender, type of microorganisms, duration of therapy, the most appropriate antibiotic, diagnosis age and referral age. In addition, sputum culture and smear of the secretions of sputum and throat the results were conducted for these patients, whose results were also evaluated. The data obtained from the questionnaires were analyzed using SPSS-15 software. When entering the data into the software, since a patient might have been tested several times, each time was considered as a separate record. Frequency of the obtained Microorganisms was calculated as the relative frequency and frequency of the operating microorganisms in different classes of variables were calculated by $\chi^2$ test. Variable of duration was measured as the mean. The relationship between various independent variables and dependent variables were examined by regression analysis. The necessary permits were obtained from the Ethics Committee to use patient's files.

## Results

According to the variables assessed in this study, the average age of CF diagnosis in these patients was 4.9 months, the average age of onset of pulmonary symptoms was 9.3 months, the age of admission of patients in the lung unit was 75.6 months, and the average duration of therapy based on culture results and clinical symptoms improvement was 12.9 days in the hospital. Among the samples who had the inclusion criteria, 60% were male and 40% were female. Given the expansion of the study and to simplify large volumes of data, the subjects were divided into two age groups of less than 24 months and more than 24 months. Percentage frequency distribution of the geographic location of patients was considered in three categories of Tehran and suburbs, rural areas and other cities. The results showed a higher frequency of *Pseudomonas aeruginosa* bacteria (46 cases) (Fig. 1).

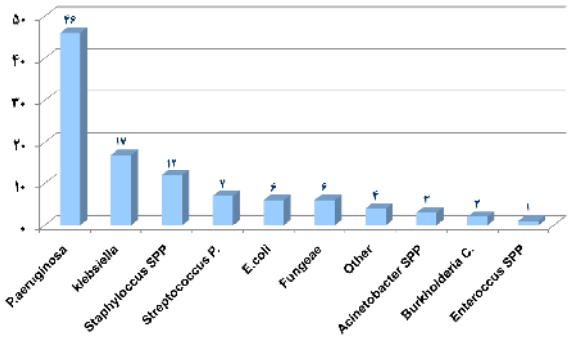


**Figure 1.** Frequency distribution of the microorganisms reported in culture of the studied patients

Examination of the frequency of the microorganisms obtained from cultures in two age groups (less and more than 24 months) shows that *Klebsiella* was more prevalent in patients less than 24 months and *Pseudomonas aeruginosa* was more prevalent in patients more than 24 months (Fig. 2).

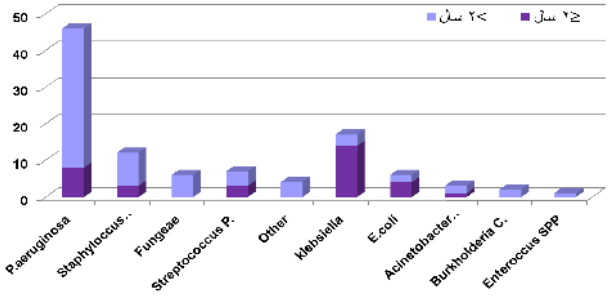


**Figure 2.** Frequency distribution of the microorganisms reported in culture of the studied patients separated by age group

The examination of reaction of aeruginosa bacteria based on antibiogram revealed that this bacterium was most sensitive to the antibiotics of ciprofloxacin, imipenem and ceftazidime and most resistant to antibiotics of ampicillin, oxacillin, penicillin, cephalotin, cefixime, ceftriaxone and cotrimoxazole (Fig. 3).

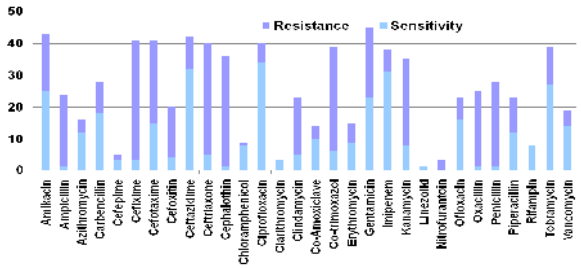


**Figure 3.** Frequency distribution of P. Aeruginosa resistance to the antibiotics studied in cystic fibrosis patients

The examination of reaction of *Klebsiella* based on antibiogram revealed that it was most sensitive to the antibiotics of vancomycin, rifampin, imipenem, azithromycin, ceftazidime, clarithromycin, ofloxacin and was most resistant to cefixime, ampicillin, cephalotin and pipracillin. Staphylococcus was most sensitive to the antibiotics vancomycin, tobramycin, imipenem, ceftazidime, amikacin and most resistant to ampicillin, co-amoxiclav, penicillin and ceftriaxone. Streptococci was most sensitive to the antibiotics vancomycin, rifampin, imipenem, ciprofloxacin and ofloxacin, and most resistant to ampicillin, cefixime, penicillin and ceftriaxone and finally E.coli was most sensitive to the antibiotics vancomycin, ofloxacin, cefotaxim, azithromycin, ceftazidime, ciprofloxacin, imipenem and amikacin and most resistant to antibiotics such as ampicillin, piperacillin, oxacillin, penicillin, carbenicillin and cefoxitin. There was no evaluable antibiogram regarding other microorganisms.

## Discussion

The results showed that the average CF diagnosis age of patients, 4.9 months, the average age of onset of pulmonary symptoms was 9.3 months, the age of admission of patients in the lung unit was 75.6 months, and the average duration of therapy based on culture results and clinical symptoms improvement was 12.9 days in the hospital and 60% were male and 40% were female. The studies conducted so far have shown that *Pseudomonas aeruginosa* is the most common germ affecting pulmonary system of cystic fibrosis patients [7,9,10].

In this study, *Pseudomonas aeruginosa* was also the most common germ affecting pulmonary system. Other important microorganisms which are isolated from the sputum of these patients in the relapse stage are respectively *Klebsiella*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Burkholderia cepacia* and other gram-negatives. The results showed that the incidence of microorganisms with greater sensitivity to antibiotics is more in the first two years of life and by increase of age in CF patients; the microorganisms resistant to different antibiotics such as *Pseudomonas aeruginosa* will become more prevalent.

The results of the studies of Alibakhshi [11,12] are consistent with the results of this study. In addition, the results obtained from the antibiogram of these cultures showed that totally there was more sensitivity to antibiotics such as ceftazidime, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin, and somewhat aminoglycosides to empirically treat more sensitive patients and there was more resistance to the antibiotics such as cefixime, penicillin, cotrimoxazole, ampicillin, ceftriaxone, cephalotin, piperacillin and oxacillin.

Other studies showed that the therapies combined with meropenem or imipenem and inhaled or intravenous tobramycin and inhaled or intravenous ceftazidime and aminoglycoside (with more inhaled effect) are most effective in improving the symptoms of CF patients [13,14]. The results showed that the most common germ extracted from the sputum culture of CF patients was *Pseudomonas aeruginosa* whose incidence increases with age increase, and drug resistance will be increased the same.

This study also showed that the patients admitted for pulmonary symptoms treatment are over 2 years old. This suggests poor diagnosis and referral system and that these patients who have given less medical care, have more severe disabilities. Trudy has claimed that the patients who enjoy appropriate medical services, education and occupation, will have higher FEV1, fewer hospitalizations, less *Pseudomonas aeruginosa* contamination, higher caloric intake, better performance and more favorable social conditions. Totally, the antibiotics such as ceftazidime, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin, and somewhat aminoglycosides showed a higher sensitivity for empirical treatment of patients.

According to the results of this study, it is suggested that longevity of CF patients, social, educational and occupational conditions of CF patients, bone densitometry of the CF patients over 8 years, different strains of *Pseudomonas aeruginosa* in CF patients (mucoid or non-mucoid), FEV1 measurement before and after antibiotic treatment, viral and fungal factors, and non-tuberculosis mycobacterium species (NTM) should be studied in CF patients.

CF patients should have two sputum samples during the admission (at first and during treatment) and they should have sputum samples for culture and antibiogram during their outpatient visits every 3 months and homogenizing should also be done in the culture and antibiogram results for further comparative studies. Since the number of these patients is not low in Iran and on the one hand, early diagnosis and appropriate treatment can improve the quantity and quality of their life and on the other hand, lack of treatment leads to early death, the studies in this field can be very valuable. It is important to have adequate monitoring of proper treatment based on antibiogram, that all these will be possible through the establishment of CF Association.

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