Original Article

Frequency of Cystic Fibrosis in Children with Recurrent Respiratory Infections by Sweat Chloride Testing: A Hospital-Based Cross-sectional Study

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Author's Contribution

[1,2,3,4,5,6] *Conception of study*
[2] *Experimentation/Study conduction*
[2,4] *Analysis/Interpretation/Discussion*
[1,3,4,6] *Manuscript Writing*
[1,3,5,6] *Critical Review*
[5,6] *Facilitation and Material analysis*

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Abstract

Objective: This study was designed to find out the frequency of cystic fibrosis in children with recurrent respiratory infections by performing a sweat chloride test.

Material and Methods: This cross-sectional study was carried out from 1st September 2015 to 28th February 2016 in the department of Pediatric Medicine at the Children's Hospital and the Institute of Child Health, Lahore after ethical approval. A total of 300 cases of recurrent respiratory tract infections were included. The sweat chloride test was done by using pilocarpine-induced iontophoresis and measuring chloride levels on the forearm or thigh by sweat analyzer at the time of induction. Cystic fibrosis was labeled if sweat chloride level ranges above 60 mEq/L. Data was collected on Performa and SPSS version 23 was used to analyze the data.

Results: Mean age of patients was 6.24 ± 2.7 years with 52.7% males and 47.3% females. Most patients (86.3%) have more than 5 episodes of respiratory infection in a year. Cystic fibrosis was diagnosed in 19 (6.3%) patients. There was no relationship between the frequency of respiratory infections in a year and cystic fibrosis (p-value 0.78).

Conclusion: This hospital-based study showed quite a high incidence of cystic fibrosis in our population. So facilities including neonatal screening along with sweat chloride testing and genetic analysis should be increased.

Keywords: Cystic fibrosis, sweat chloride test, screening, respiratory tract infections.

Introduction

Cystic fibrosis (CF) is the common fatal autosomal recessive disease in the European population with a frequency of 1 in 5000 live births.[1] The common presenting symptoms and signs include persistent chest infections, pancreatic insufficiency, and raised sweat chloride levels.[2] However, many patients manifest mild or atypical symptoms and clinicians should be alert to suspect CF even when only a few of the typical features are present.[3] The classic or typical form of CF is diagnosed if a patient demonstrates clinical disease in one or more organ systems and has elevated sweat chloride levels (≥60 mmol/L).[4] Most of these patients have disease manifestations in multiple organ systems (pancreas, upper and lower respiratory tract, and male reproductive tract). About 2% of patients fulfilling diagnostic criteria for CF have a normal or intermediate sweat chloride result. In these patients, the diagnosis of CF depends upon DNA analysis (two copies of a disease-causing mutation in the CFTR gene) or on the measurement of nasal potential difference. This disease pattern has often been termed "non-classic" CF. although current guidelines emphasize a wide spectrum of severity in CF and no clear distinction between "classic" and "non-classic" types.[5] The estimated prevalence and disease manifestations of non-classic CF may change in near future, as diagnostic methods for CFTR mutations and dysfunction become more sensitive and are broadly applied.[3,6] Most of the world has started neonatal screening based on immunoreactive trypsin (IRT) in capillary blood collected by heel prick after 72 hours of life. If IRT levels are high then further testing including sweat chloride and/or gene mutation analysis is done.[7] This aims to prevent early complications and timely management of these patients.

The prevalence of CF in the Pakistani population comprising individuals with diverse ethnic backgrounds is unknown.[8] All over the world more than 1900 mutations are found. Only a few centers in Pakistan are doing gene analysis of the most common mutation delta 508. Therefore sweat chloride analysis remains the main diagnostic approach to these patients. Pilocarpine induced iontophoresis is done to stimulate the sweat glands. Chloride concentration can also be directly measured on the skin by a potentiometer.[9] However, the sweat chloride concentrations do not correlate with the severity index and sweat chloride concentration does not predict milder pulmonary involvement in patients with cystic fibrosis.[10] In Pediatric Department in Jordan, a cross-sectional study involving 145 children with frequent chest infections were seen between January and December 2008 with age ranging from 2-12 years. 7.5% were diagnosed as having CF with a positive polymerase chain reaction. When the sweat chloride test was done, it showed a sensitivity of 100% and specificity was 90.3% at sweat chloride test>57 mEq/L.[11]

CF was previously taken as a disease of western countries[12,13] and frequently missed in the Pakistani population due to lack of appropriate diagnostic facilities in the public sector and also non-affordability.[8] Respiratory infections are one of three major killer diseases in Pakistani children and a major burden on the health care system. The current study will help us to find the prevalence of CF in children with recurrent respiratory infections in the referral center of Punjab i.e. Children's Hospital Lahore. The inclusion of CF in differential diagnosis by a pediatrician depends upon the real burden of disease. So, this study aimed to determine the frequency of CF in children presenting with recurrent respiratory tract infections using a simple diagnostic tool of sweat chloride test.

Materials and Methods

The Descriptive Cross-sectional survey was carried out in the Department of Pediatric Medicine at the Children's Hospital and the Institute of Child Health, Lahore, Pakistan for 6 months from 1st September 2015 to 28th February 2016 after ethical clearance. 300 Children aged 12 months to 12 years of both genders having recurrent chest infections were included in the study. Recurrent respiratory tract infections were defined as 2 or more episodes in a single year or 3 or more episodes ever as determined by the history of high-grade fever, respiratory symptoms of difficulty breathing, or by labeling of lower respiratory tract infection by a registered medical practitioner.

The exclusion criteria included tuberculosis determined by history, examination, and laboratory investigations. Third-degree malnutrition is determined by history, examination according to WHO guidelines. Asthma determined by history, examination, and pulmonary function tests when possible, immunodeficiency determined by history and laboratory investigations, congenital heart disease determined by history, examination and echocardiography, congenital airway abnormalities determined by history, examination and laboratory

investigations and congenital Pulmonary/ Diaphragmatic defect determined by history, examination and laboratory investigations.

All patients underwent sweat chloride testing using Pilocarpine induced iontophoresis and measuring chloride levels on forearm or thigh by SM-01 Sweat Analyzer (SANASOL's, Hungary) in every patient at the time of induction. The recording was made by the researcher himself on the attached proforma. CF was labeled if sweat chloride levels range above 60 mEq/L on testing with SM-01 Sweat Analyzer.

Data analysis: The data was entered and analyzed using SPSS version 17.0. chai square test and independent t-test were used to determine the relationship between respiratory tract infections and the frequency of cystic fibrosis.

Results

A total of 300 patients were enrolled in the study. The mean age of the participants was 6.24 ± 2.7 with a range from 12 months to 12 years. 158 (52.7%) were male while 142 (47.3%) were female. The majority of the patients 259 (86.3%) had more than 5 episodes of respiratory infection in the last 12 months while 41 (13.7%) patients had less than 5 episodes of respiratory tract infections in the last 12 months.

19 (6.3%) were diagnosed as CF while 281 (93.7%) were negative for the sweat chloride test. there was no significant difference in frequency of cystic fibrosis 7.3% versus 6.2%, p-value .780 in patients with infection episodes less than 5, and infection episodes more than 5 respectively.

Mean episodes of respiratory tract infection in the last 12 months were 7.16 ± 1.4 in patients with CF and 7.41 ± 2.07 in patients without CF which was not statistically different (p = 0.605).

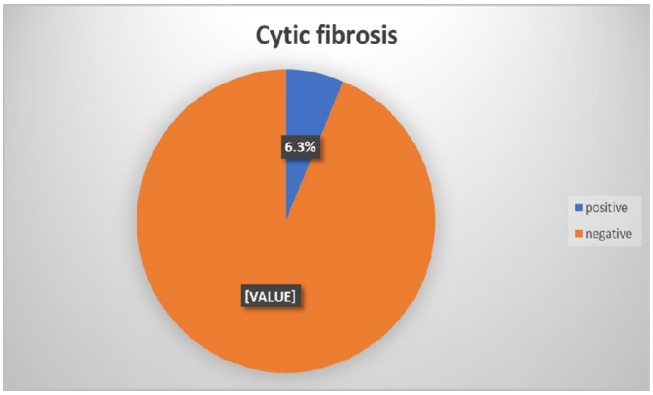

Figure 1: Frequency of cystic fibrosis in the study population

Table 1: Relationship between the frequency of cystic fibrosis and episodes of respiratory infections

	Total	Cystic fibrosis		P-value
		Yes	No	
Less than 5 episodes	41	3 (7.3%)	38 (92.7%)	**0.780**
More than 5 episodes	259	16 (6.2%)	243 (93.8%)	

Discussion

Our study gives details of patients with a history of recurrent respiratory infections coming to The Children's hospital/ICH, Lahore. CF was previously taken as a disease of western countries (14) and is frequently missed in the Pakistani population due to a lack of appropriate diagnostic facilities. Most countries are doing newborn screening to screen for cystic fibrosis[24,25] but in our country mainstay of diagnosis relies on sweat chloride analysis in patients who experience recurrent pneumonias.[21,23,26]

Recurrent respiratory infections are one of the three major killer diseases in Pakistani children and a major burden on the health care system by limiting the quality of life.[20] Although the sensitivity and specificity of the sweat chloride test is not too high[16,17] but this is a good diagnostic test when combined with gene mutation analysis.[19]

The results of our study matched those by Jordanian study[15] which showed a 7.5% prevalence of CF. Out of 300 patients, only 19(6.3%) were diagnosed as having a positive sweat chloride test. In our sampled population the male and female ratio was similar, (52.7%) were male while (47.3%) were female, showing that there are changes in health-seeking behavior in Pakistan with both male and female-presenting to our tertiary care hospitals. This prevalence of CF in our population therefore demands a population-wise screening program in the form of neonatal IRT analysis.[22] When we compare our prevalence with the United States, CF is found approximately one in 30,000 Americans.[18]

Similarly, to our surprise, respiratory tract infection is quite high in our population. 259 out of 300 individuals (86.3%) have five or more episodes in less than one year. This is an alarming situation and there should be reasonable preventing programs to reduce

the burden of respiratory tract infections in our population.

Although our study showed no relationship between the frequency of cystic fibrosis and the frequency and mean episodes of respiratory infections concluding that cystic fibrosis may not be associated with repeated respiratory tract infections.

Conclusion

It is concluded that the frequency of CF is quite high even in the Asian population like Pakistan in children. A further mass screening program is necessary to find out the prevalence of CF in the community. Early diagnosis of CF will not only reduce the mortality or morbidity associated with it but it will also improve the quality of life of patients.

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