Characteristics of Patients with Cystic Fibrosis: Experience in a Large Referral Children's Hospital in Tehran, Iran

GR Khatami[1], MM Mir-Nasseri[2*], F Seyghali[3], B Allah-Verdi[3], F Yourdkhani[2]

1. Professor, Pediatric Unit of Digestive Diseases Research Center, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran
2. Researcher, Pediatric Unit of Digestive Diseases Research Center, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran
3. Assisstant Professor, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran

[*]**Corresponding Author:**
Mohammad Mehdi Mir-Nasseri, MD
Digestive Diseases Research Center,
Shariati Hospital, North Kargar Ave.,
Tehran, 14117-13135, Iran
Tel: +98 21 82415300
Fax: +98 21 82415400
E-mail: mirna@ams.ac.ir
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ABSTRACT

BACKGROUND

Cystic fibrosis (CF) is an autosomal recessive disease caused by a CF trans-membrane regulator (CFTR) defect. Its prevalence is 1:2500 in Caucasians, 1:15300 among African Americans and is rare in South-east Asia. The present study aims to review demographic data, clinical manifestations and laboratory findings of Iranian children diagnosed with CF who referred to a Children's Hospital Medical Center in Tehran, Iran during a ten-year period.

METHODS

In a retrospective study from 1991-2000, all hospitalized patients with documented CF were reviewed. Diagnosis was based on clinical findings and sweat chloride levels above 60 mEq/L.

RESULTS

A total of 233 patients [females: 91 (39.1%), males: 142 (60.9%)] were enrolled. The onset of symptoms was before the first month of life in 12.1%, between 1-6 months of age in 75.1%, and between 6-12 months of age in 6.9% of patients. Consanguinity of parents was present in 42.5% of patients. Respiratory (81.5%) and gastrointestinal (73.4%) symptoms, in addition to growth retardation were the most common presentations Eighty-eight percent of patients weighted below the fifth percentile.

Of the 207 chest radiographs performed, the most frequent finding was hyper-aeration associated with pneumonia. Among 138 patients in whom barium swallows were performed, 102 (74%) had gastro-esophageal reflux. A total of 27 patients expired, mostly from respiratory failure (96.3%).

CONCLUSION

CF is not a rare disease in Iran. We suggest early diagnosis and appropriate maintenance therapy for improving morbidity and mortality amongst CF patients.

KEYWORDS

Cystic fibrosis; Epidemiology; Children

INTRODUCTION

Cystic fibrosis (CF) is a worldwide disease occurring among virtually all ethnic groups. In Caucasians it is the most common autosomal recessive lethal hereditary disorder.[1] Although approximately 1 in 25 are heterozygous carriers, the incidence of clinical disease is approximately 1 in 2500 live births.[1] The condition results from mutations in a single gene of chromosome 7, which encodes the CF transmembrane conductance regulator (CFTR).[2]

The CFTR protein is a membrane-bound cAMP-regulated chloride channel thought to regulate other cell membrane ion channels.[3] To date, more than 1000 different mutations have been identified; however a phenylalanine deletion in amino acid position 508 is present in approximately 66% of patients. Early genetic tests demonstrating a molecular defect in the CFTR gene confirms the clinical diagnosis of CF, improves quality of life and prolongs survival.[4] Recent studies support the theory that CFRD is primarily caused by insulin deficiency due to a loss of beta cells which may occur via a number of mechanisms, including oxidative stress.[5-7]

CFTR mutations affect epithelial ion and water transport, primarily in cells in the respiratory, gastrointestinal, hepatobiliary and reproductive tracts, in addition to the sweat glands.

The lack of chloride secretion in the pancreatic duct is responsible for obstruction and autodigestion of the pancreas early in embryonic life leading to severe exocrine pancreatic insufficiency in approximately 85% of CF newborns. Diagnosis is based on clinical findings and sweat chloride levels greater than 60 mEq/L. In Iran, a large study with accurate data on CF patients has not been performed.

Thus, the present study aims to assess the characteristic demographic findings of CF patients who attended the Children's Hospital Medical Center during a ten-year-period.

MATERIALS AND METHODS

During a ten-year period (1991-2000), all patients hospitalized with CF or diagnosed with CF during hospitalization in the Children's Hospital Medical Center, Tehran, Iran were enrolled and related data were extracted from their medical records. Sweat chloride tests were considered positive if the results were above 60 mEq/L. The diagnosis of CF was established when relevant clinical manifestations were associated with a positive sweat chloride test. Clinical manifestations included respiratory signs such as chronic cough or recurrent pneumonia and GI manifestations in the form of chronic diarrhea or fatty diarrhea, failure to gain weight and failure to thrive (FTT).

RESULTS

Among the 233 patients, 91 (39%) were girls and 142 (61%) were boys. The male to female ratio was 1:1.5. Onset of disease was before the first month of life in 12.1%, between 1-6 months of age in 75.1% and between 6-12 months of age 6.9% of patients.

Consanguinity of parents was present in 42.5% of patients. Respiratory and gastrointestinal manifestations occurred in 81.5% and 73.4%, respectively.

A positive family history of CF or suspected clinical signs was present in 26.6% of patients. Barium swallow was performed for 138 patients; of those, 102 (74%) had gastroesophageal reflux disease. Other findings such as nasal polyps (6), gallstones (1), sinusitis (14), cholestasis (9) and diabetes (2) were also noted. Edema (19.4%), growth failure in the form of weight below the fifth percentile (89.1%), anemia (69.7%) and hypoalbuminemia (60.5%) were additionally present.

Endoscopy was performed in 65 patients and the most frequent finding was esophagitis (81.5%). In stool samples, fat droplets greater than 100 per HPF were reported in 100%, whereas 62.7% had decreased trypsin activity.

Among patients with respiratory symptoms, chest radiography was performed in 207 cases and frequent findings were: hyper-aeration with pneumonia (35%), pneumonia (19%) and hyper-aeration (22%). Death was documented in 27 patients which was attributed to respiratory failure (96.3%) and septicemia (3.7%) (Table 1).

Table 1: Comparison of various studies on cystic fibrosis in Asia.

Finding / Study	Present Study	Iran, Shiraz	Jordan	Saudi Arabia	Qatar	Japan	Bahrain
No. of patients	233	54	202	12	45	25	25
Duration of study (years)	10	10	9	-	13	7	9
Prevalent age (months)	< 6	< 6	-	< 6	-	-	< 6
F/M ratio	1:1.5	1:1.2	-	1:1.4	-	1:1.2	-
Consanguineous marriages (%)	42	80	69	83	98	-	80
Family History of CF (%)	27	-	-	-	-	30	-
Meconium ileus (%)	9	9	7/2	8	-	20	-
Gastroesophageal Reflux (%)	74	-	-	-	-	-	-
Failure to thrive (FTT) (%)	89	90	75/4	100	-	96	-
Anemia (%)	9/7	-	-	-	-	-	-
Rickets (%)	9/5	-	-	-	-	-	-
Mean sweat chloride level	-	125	-	-	-	-	-
Mortality during the study (%)	13.4*	70	23	8	0	-	-

*In hospital inpatient mortality

DISCUSSION

CF has been described as the most common autosomal recessive fatal pediatric disease.[8] Currently, due to newer, more appropriate, modern enzymatic and antibiotic therapies in addition to nebulizer treatments, improvements in lifespan and quality of life are seen. Recent researches and numerous advancements in the field of gene therapy, which can be the definitive therapy of CF, increased the hope for an extended life.

Therefore maintenance therapy, with the aim to perform gene-therapy, is of major importance in maintaining growth, preventing respiratory complications and malnutrition.

Earlier disease onset is associated with a greater chance of growth failure. It is important to keep this disease in mind when dealing with patients who present with the vast spectrum of clinical findings of CF, which are to some extent non-specific.[9]

Thus, children who receive multiple courses of antibiotics for respiratory or GI diseases will need to undergo additional diagnostic tests. The prevalence of CF in European Caucasians is 1:2500 and is rare in Asia.

Based on the results of the present study and other reports from various locations in Asia; we have assumed that CF is not rare, as presumed in Iran (Table 1). In all studies, the male to female ratio was 1:1.5,[9-13] the most frequent age of onset of symptoms occurred in the first six months of life (78%) and consanguineous marriages were significant (42%).[10-12,14,15]

The frequency of gastroesophageal reflux in our study was higher than stated in textbooks. This might have been due to the fact that barium swallows were performed only in cases with suspected symptoms, whereas it was performed in all patients mentioned in textbooks. The incidence of FTT in the Asian population was almost equal (75% - 100%).

However in developed countries with the use of new nutritional methods such as alternate TPN in the hospital or at home, and nasogastric tube feedings at night, sufficient calories were obtained and growth failure was less commonly reported.[16,17]

Death occurred in 13.4% of patients in the present study which was less than actual statistical values because a number of CF patients were not followed. In a study from Shiraz (Iran), the CF mortality rate was 70% but in another study[14] it was 0%, which probably resulted from the lack of follow up.

One of the earliest signs of CF was meconium ileus, which ranged from 8% to 20% in different studies.[10-12,16] Therefore CF must be considered in newborns who present with this problem.

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CONFLICT OF INTEREST

None declared.

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