Clinical Profile and Growth Status in Patients with Cystic Fibrosis: A 2-year Follow up Study

Kianifar H[1], Fazeli F[2], Mehdizadeh A[2]

[1]Assistant Professor, Cystic Fibrosis Clinic, Sarvar Pediatric Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Researcher, Cystic Fibrosis Clinic, Sarvar Pediatric Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Background: Cystic fibrosis (CF) is a common genetic disorder chiefly characterized by respiratory and gastrointestinal symptoms. The purpose of this study was to evaluate the clinical presentation and growth status in CF patients at the time of diagnosis and following conventional treatment.

Materials and Methods: A cross-sectional study was conducted on 67 CF patients who enrolled for at least a two-year follow up period in the CF Clinic of Sarvar Pediatric Hospital. Disease diagnosis was based on a positive sweat test. Growth indicators and initial clinical presentations of patients were registered at the time of diagnosis. Weight and height was measured at each clinical visit during follow up. All patients were treated with enzyme replacement, vitamin and mineral supplements. Other medications were prescribed as clinically indicated. Statistical analyses were performed by SPSS 16.0 for MS Windows.

Results: The mean age of patients was 24.9 ± 37.7 months at the time of diagnosis, whereas it was 3.1 ± 2.1 months at the onset of CF symptoms. At diagnosis, the majority of CF patients suffered from malnutrition, growth failure, and presented with pulmonary and gastrointestinal symptoms. After conventional and nutritional treatments, significant improvements were seen in weight and height.

Conclusion: A delay in the diagnosis of CF as seen in our country causes patients to further suffer from malnutrition and growth failure in comparison to developed countries. This emphasizes the necessity of neonatal screening. The results of this study show the dramatic effects of nutritional treatment on growth status.

Keywords: **Cystic fibrosis, Growth status, Conventional treatment**
Govaresh/ Vol.15, No.1, Spring 2010: 73-76

INTRODUCTION

Cystic fibrosis (CF) is a life-limiting autosomal recessive disorder with highly variable clinical presentations that include respiratory and gastrointestinal symptoms. Approximately 85% of CF patients develop exocrine pancreatic insufficiency, which may lead to malabsorption, malnutrition and growth failure if untreated (1). In developed countries, newborn screening is routine due to the high prevalence of CF and importance of early diagnosis. According to previous studies, treatment plans have provided several advantages, such as improving clinical, nutritional and growth status as well as increasing the quality of life and survival rate among CF patients (2-7).

Corresponding author:
Cystic Fibrosis Clinic, Sarvar Pediatric Hospital
Mashhad University of Medial Sciences, Mashhad, Iran
Telefax: +98 511 8679713
E-mail: aty_mehdizadeh@yahoo.com

A review of reports in our country suggests that CF is under-diagnosed or missed in many cases due to the absence of neonatal screening as well as unavailable initial clinical presentations. This may lead to improper treatment, particularly for malnutrition, pulmonary problems and growth failure (8-10). Therefore it seems necessary to diagnose, treat and follow up CF patients appropriately in our country. This study was conducted to identify common initial clinical symptoms and growth status of patients at the time of diagnosis and to evaluate the effects of conventional treatments on growth status and clinical presentations.

MATERIALS AND METHODS

This was a cross-sectional study of 67 CF patients followed in the CF Clinic of Sarvar Pediatric Hospital for a minimum of two years. The majority of patients who were referred by their physicians presented with common clinical symptoms of CF, such as chronic diarrhea, recurrent pneumonia and failure to thrive or positive CF family history. CF diagnostic criteria included the existence of clinical features related to CF accompanied by a repeat positive sweat test (sweat chloride level greater than 60 meq/L). The sweat test procedure involves stimulation of sweating on the arm or upper back with an iontophoresis device for five minutes. Sweat is collected on filter paper and analyzed for sodium and chloride levels with a flame system.

After the diagnosis was confirmed, necessary data such as personal and medical histories, symptoms and physical examination results, which included growth indicators, were gathered and recorded in separate files. Patients were recalled monthly for routine evaluations for two years.

Measurements of height and weight were charted at each clinical visit during the follow up period. Patients younger than two years were weighed without clothes on an infant scale and height was measured in the supine position. Patients over the age of two years were weighed in their underclothes with an adult scale to the nearest 0.1 kg. Height was measured without shoes, with a meter accurate to 0.1 m. Weight and height were expressed as Z scores. Patients under the 3rd percentile or -2 standard deviation (SD) according to the World Health Organization (WHO) recommendation were considered malnourished.

Patients continued to ingest pancreatic enzyme replacement (Creon® 25000, primary ingredient: pancreatic lipase, 2000-5000 units/kg/day), vitamins (A, D, E, K) and mineral supplements (Ca, Zn) for an average period of 30.59 months (including the study period). Antibiotic courses, nebulizers, H_2 blockers and medium change triglyceride oil (MCT oil) were prescribed as needed. Statistical analyses were performed with SPSS 16.0, MS Windows. Results for weight and height measures before and after conventional treatment were compared using the paired and non-paired two-tailed t-test when the distribution was normal and Wilcoxon test when the distribution was not normal. $P <0.05$ was considered to be statistically significant.

RESULTS

There were 67 CF patients (28 females, 39 males) aged 1 month to 15 years in this study. Baseline clinical and demographic characteristics of patients were registered (Table 1). Details of first clinical symptoms and signs indicated that 31.81% of the patients predominantly suffered from respiratory problems and 34.85% had both respiratory and gastrointestinal involvement.

Mean age of the patients was 24.91 ± 37.7 months at the time of CF diagnosis while it was 3.14 ± 2.1 months at initial CF clinical presentation. There was no significant difference between the two sexes for mean age (t-test, $P = 0.38$).

Table 1: Baseline clinical and demographic characteristics of patients.

Age (years)	<2	49 (73.1)*
	2-5	10 (14.9)
	>5	8 (11.9)
Sex (female)		28 (41.7)
Growth < 3rd percentile		52 (77.7)

*(%)

Growth indicators (weight and height) of patients were registered before treatment intervention based on age and sex (Tables 2 and 3).

The mean weight and height Z scores for both males and

Table 2: Growth indicators of patients before treatment, based on age.

|	Age (years)	Mean (SD)*
Weight (Z score)	< 1	-2.62 (1.0)
	1-2	-1.35 (0.9)
	2-5	-1.37 (0.8)
	> 5	-2.25 (1.1)
	Total	-2.30 (0.1)
Height (Z score)	< 1	-2.34 (1.1)
	1-2	-1.74 (0.7)
	2-5	-0.47 (1.1)
	> 5	-2.49 (1.5)
	Total	-2.04 (0.3)

*(Standard Deviation)

Table 3: Growth indicators of patients before treatment, based on sex.

		Mean (SD)
Weight (Z score)	Male	-2.22 (1.3)
	Female	-2.41 (0.7)
	Total	-2.30 (0.1)
Height (Z score)	Male	-1.65 (1.2)
	Female	-1.77 (1.0)
	Total	-2.04 (0.3)
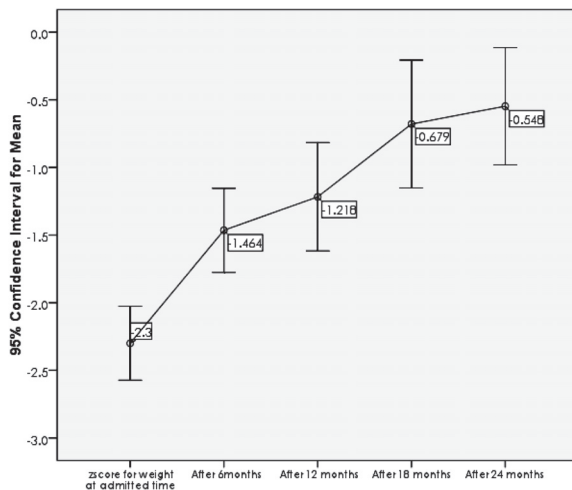
Fig1. Z scores for weight during follow up.
*Significant difference exists between Z scores for weights before and after 6, 12 and 18 months of treatment ($p < 0.001$, $p = 0.002$, $p = 0.01$, respectively).
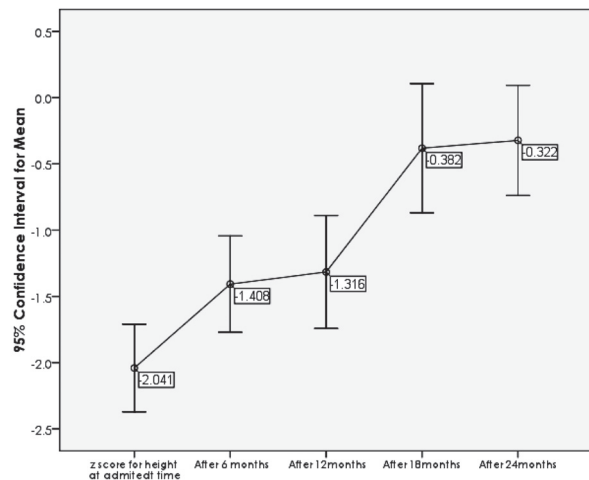
Fig 2. Z scores for height during follow up.
*Significant difference exists between Z scores for height before and after 6 and 18 months of treatment
($p = 0.04$, $p = 0.02$, respectively).

females were less than zero, indicating that they were shorter and weighed less for their age and sex than the reference population. Furthermore, the least Z scores for weight and height were particularly pronounced in patients younger than one year while patients who were two to five years of age had the highest Z scores.

After nutritional intervention and conventional therapy, there was a significant increase in weight and height Z scores (Figs. 1 and 2). All patients showed a great "catch-up" in growth status after six months of treatment.

DISCUSSION

The results of the current study indicate a time gap between initial presentations and clinical diagnosis of CF, both in our country and other underdeveloped countries which do not have neonatal screening programs, in comparison to developed countries (11-14). One probable reason for this delay in diagnosis is related to the

frequent perception that CF is primarily a respiratory condition rather than a multisystem genetic disorder (12,15). Kabra et al. have shown that delay in diagnosis in developing countries is associated with occurrence of severe malnutrition at the time of diagnosis, progressive lung disease and frequency of pneumonia (>4 episodes/year). However, all of these complications can be improved with early diagnosis and appropriate treatments (16). After conventional and nutritional treatments, significant improvement was noted in the growth indicators. Since significant association exists between the degree of malnutrition, rate of decline in pulmonary function and decreased survival, it is extremely important to optimize the nutritional status as a priority (2, 17, 18). Furthermore, many studies have been conducted to determine the benefits of nutritional intervention on slowing the decline in pulmonary function (19, 20).

Early diagnosis is important in CF and can be obtained by raising physicians' knowledge about its clinical features in order to achieve effective management of care. A limitation of the current study was due to the short follow up period, which should be longer in order to have more reliable results and evaluate treatment effects on linear growth, survival and quality of life in CF patients. Furthermore, the lung function test, as an important prognostic factor, is a necessary test as it seems to be strongly influenced by nutritional treatment. Further studies are required to assess the effects of long-term nutritional treatments on growth indicators, clinical presentations and pulmonary function in CF patients.

CONCLUSION

It is concluded that diagnosis of CF is delayed in our country and, as a result, patients further suffer from malnutrition and growth failure compared to developed countries. This emphasizes the necessity of neonatal screening which leads to early intervention and better therapeutic outcomes. The results of the current study indicate a significant improvement on growth indicators (weight and height) of CF patients after conventional treatment.

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