Growth Status and Its Relationship with Serum Lipids and Albumin in Children with Cystic Fibrosis

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Abstract- Cystic fibrosis (CF) is an autosomal recessive disease, which affects many organs as it impairs chloride channel. This study was performed to evaluate growth status and its relationship with some laboratory indices such as Cholesterol (chol), Triglyceride (TG), albumin and total protein in children with CF referred to pediatrics center. This study was designed as a cross-sectional study in one year section. Demographic features were compared with standard percentiles curves. Chol, TG, albumin, total protein, prothrombin time, and hemoglobin were measured. Stool exams were also performed. A questionnaire was designed to obtain a history of the first presentation of disease, birth weight, type of labor and parent relativity. In 52% of patients, failure to thrive (FTT) was the first presentation. Steatorrhea and respiratory infections were the first presentations, which were seen in 13.7% and 33% of the cases, respectively. The weight of 88% of patients was below the 15th percentile while 82% had a height percentile below 15th. Head circumference in 53% of patients was below the 15th percentile. There was a significant association between weight percentile and serum albumin and total protein (P=0.03 and P=0.007, respectively). There was also a significant relationship between height percentile and serum albumin and total protein (P<0.001 and P<0.000, respectively). The relationships between head circumference and serum albumin and total protein were also significant (P=0.006 and P<0.000, respectively). There was also a significant association between height percentile and hemoglobin. The decrease in anthropometric percentiles leads to decreased serum albumin and total protein.

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Keywords: Cystic fibrosis; Growth; Failure to thrive

Introduction

Cystic fibrosis (CF) is an autosomal recessive disease, affects many organs as it impairs chloride channel due to CFTR defects. It can lead to frequent respiratory infections, malabsorption, failure to thrive (FTT), steatorrhea, meconium ileus, coagulopathy, infertility, pancreatitis, edema, hypoproteinemia, dehydration and metabolic alkalosis. According to previous studies, the most common manifestations of CF in Iran were gastrointestinal disorders and respiratory manifestations, while cough was the most common symptom (1-3). Mutations in the *CFTR* gene, located on chromosome 7, lead to CF, while its seems that there is an association between genotypes and phenotypes (4). Different studies showed that sufficient growth leads to better respiratory and immune function (5), and there is a linear association between respiratory function and growth parameters (6). Serum lipids in CF undergo some changes, which are secondary to lipid malabsorption and usually it is possible to normalize them with the replacement of pancreatic enzymes (7). It

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is important to evaluate growth status and plasma lipid concentrations as these factors are correctable and have noticeable effects on prognosis (8). Some children respond well to treatments and gain sufficient growth, but some others are non-responders to common treatment (9). It seems that suitable plasma free fatty acids condition cause some children to respond to treatments (10). The goal of this study was to evaluate growth status and its relationship with some laboratory indices, such as cholesterol (Chol), triglyceride (TG), albumin (Alb), total protein, hemoglobin (Hb), and prothrombin time (PT) in children with CF referred to a tertiary hospital in Iran.

Materials and Methods

This study was a cross-sectional study in the Children's Medical Center Hospital. All children with a definite diagnosis of CF referred to the hospital from September 2010 to September 2011 were enrolled in this study. Patients with liver diseases or other reasons of coagulopathy were excluded. Weight, height, head and arms circumferences were measured by standard tools and were compared with WHO standard percentiles curves and the related percentiles were obtained. Body mass index (BMI) was also measured and compared with standard curves. Blood samples were taken to measure Chol, TG, Alb, total protein, PT, and Hb. Stool exams were also performed. A questionnaire was designed to obtain a history of first presentation of disease, birth weight, type of labor and parent relativity, history of meconium ileus, steatorrhea, frequent respiratory infections or any other specific disorder. These data were analyzed by SPSS ver. 19.

Results

Fifty-one patients (68.6% male) with CF were enrolled in this study. Birth weight mean was 3043 grams which are obviously lower than normal curves of birth weight in healthy children. History of meconium ileus was detected in 31.4% of children while 60.8% had a history of steatorrhea, 55% had a history of respiratory infections, and 45.1% had a history of dehydration. In 52% of patients, failure to thrive (FTT) was the first presentation. Steatorrhea and respiratory infections were the most common first presentation, seen in 13.7% and 33%, respectively. Labor type in 29.4% was normal vaginal delivery and in 70.6% was caesarean section. Parents were consanguine in 68.6% of patients, in which 54.9% were first cousins and remaining 13.7% were far relativity. Weight in 88% of patients was below the 15th percentile while 82% had a height below 15th percentile; head circumference in 53% was below the 15th percentile. Anthropometric percentiles distributions are shown in Table 1.

Table 1. Anthropometric percentiles distribution

Anthropometric index	Less than 3%	3-15%	15-50%	50-85%	85-97%	Higher than 97%
Weight/age	74.51%	13.73%	5.88%	1.96%	1.96 %	1.96%
Height/age	58.82%	23.53%	9.8%	3.92%	1.96%	1.96%
BMI	50.98%	23.53%	17.65%	1.96%	0 %	5.88%
Weight/height	29.41%	23.53%	27.45%	11.76%	1.96%	5.88%
Head circumference/age	45.1%	19.61%	17.65%	15.69%	1.96%	0%
Arm circumference/age	70.59%	19.41%	1.96%	3.92%	3.92%	0%

There was no significant association between weight percentile and serum TG and Chol, but a significant relationship between weight percentile and serum albumin, total protein and hemoglobin with a positive R (R-squared) and *P*-values of 0.036, 0.007, 0.006, respectively were detected.

There was also no significant relationship between height percentile and serum TG and Chol. There were also a significant relationship between height percentile and serum albumin, total protein and hemoglobin with a positive R (R-squared) and *P*-values of <0.001, <0.001, 0.05, respectively.

There was no significant relationship between BMI percentiles and serum TG, Chol, albumin, total protein, and hemoglobin. There was also no significant relationship between head circumference percentile and serum TG and cholesterol, but a significant relationship was detected between head circumference percentile and serum albumin, total protein and hemoglobin (*P* of 0.006, <0.001, 0.002, respectively). The R-squared indices were also positive which shows that these variables change in the same way.

There was a significant relationship between arm circumference percentiles and serum albumin, total protein and hemoglobin (*P*-value 0.025, 0.006, <0.001, respectively) with a positive R. There was no relationship between arms circumference percentile and serum TG and cholesterol.

The mean of PT was 13.57. We considered PT longer than 13 seconds as long PT. In 29.4% of patients, long PT was detected. Long PT demonstrates vitamin K deficiency in about 30% of patients. We also evaluated the prevalence of hypoalbuminemia and total protein deficiency in children with CF. We defined hypoalbuminemia as albumin below 3.5 and protein deficiency as total protein lower than 6.6. Hypoalbuminemia existed in 54.9% of patients, and 84.3% had a protein deficiency.

Discussion

Failure to thrive (FTT) was the most common manifestations of CF in the current study, which was seen in 88% of the patients. FTT was also the first presentation of disease in more than half cases. Another remarkable point is the high prevalence of dehydration in about 45% of patients. Parents' consanguinity was detected in 69%, which is expected considering high prevalence of relative marriages in the region, which leads to higher incidence of autosomal recessive disorders.

In 96% of the patients, the weight percentile was below 50th, which shows the extremely high prevalence of FTT and poor weight gain of patients. About 92% of patients had height percentile below the 50th curve and in 83% head circumference percentile was below the 50th curve. As the height and head circumference percentile decreases after weight percentile which shows severe FTT, high frequency of severe FTT in patients with CF are remarkable. Cystic fibrosis foundation revised the guidelines of CF classification and changed the definition of nutritional failure from BMI <10th to BMI <50th in 2005 (11). In this study, BMI was lower than the 50th percentile in 92% of patients, which shows a high frequency of nutritional failure. The decrease in anthropometric percentile leads to decreased serum albumin and total protein. It seems that growth status has no significant effect on serum TG and Chol. Thirty percent of patients had vitamin K deficiency which is shown by long PT. Almost all of these patients had a history of getting exogenous vitamin K, but still had coagulopathy which insists on more intense treatment in these patients to correct PT. Different protocols and supplement therapies have already been advised in patients with CF (12-17).

This study shows most children with CF in are suffering from severe FTT and common treatments do not seem to be enough for suitable weight gain. Hypoalbuminemia existed in 55% of patients while 84% had a protein deficiency. Therefore CF should be considered as a multidisciplinary field in which not only gastroenterologists and experts in respiratory diseases should care the patients, but also, nutritionist should help in the management of the patients.

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