THE IMPACT OF RESPIRATORY TRACT INFECTIONS ON THE NUTRITIONAL STATE OF CHILDREN WITH CYSTIC FIBROSIS

Laura Mihaela Trandafir1, Mihaela Moscalu2, Georgeta Diaconu1, E. Cîrdeiu1, Alexandra Ana Maria Tudose3, Gabriela Coman4, Dana Teodora Anton Pădurearu1

University of Medicine and Pharmacy "Grigore T. Popa" - Iaşi
Faculty of Medicine
1. Discipline of Pediatrics
2. Discipline of Medical Informatics and Biostatistics
4. Discipline of Microbiology
3. Student Vth year

THE IMPACT OF RESPIRATORY TRACT INFECTIONS ON THE NUTRITIONAL STATE OF CHILDREN WITH CYSTIC FIBROSIS (Abstract): Cystic fibrosis (CF) is a life-shortening, autosomal-recessive disorder characterized by intestinal malabsorption, impaired growth, and lung disease. Recurrent pulmonary infections in children with CF are often associated with nutritional deficiencies. **Aim:** To emphasize the effects of recurrent pulmonary infections on nutritional status in children with CF. **Material and methods:** This retrospective study included 27 patients diagnosed with CF between 1994 and 2011 in the 3rd Pediatric Clinic of the Iaşi "Saint Mary" Children’s Hospital. The nutritional status was assessed according to ponderal index (PI), body mass index (BMI), Z score for weight and waist. Correlations between the age of onset of symptoms, age at diagnosis, and frequency of infectious episodes, identified bacterial agents and nutritional status were established. **Results:** Patients aged between 3 months old and 17 years old with an average of 49.48 months ± 9.83DS; sex ratio was 1.7:1. The patients were diagnosed late, one month to 112 months (average 41.11 months±9.4DS) from the first symptoms until the moment of diagnosis. The clinical forms of CF in the study group were: predominantly respiratory manifestations in 48.14% of cases, and the mixed type, with both respiratory and digestive symptoms, in 18.52% of cases. Delayed weight and/or height gains were identified in 85.19% of cases. The etiologic agents involved in pulmonary infections were *Staphylococcus aureus* (48.14%), *Pseudomonas aeruginosa* (33.33%), *Stenotrophomonas maltophilia* (18.51%), *Haemophilus influenzae* (14.8%), *Klebsiella pneumoniae* (11.10%), *Moraxella catarrhalis* (7.40%), *Streptococcus pneumoniae* (7.40%), *Neisseria sica* (7.40%). Pulmonary infections caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia* were more often associated with nutritional status abnormalities. **Conclusions:** In small children with CF pulmonary infections due to various causative agents cause a slow rate of growth (both weight and height). Good nutrition and adequate early treatment of pulmonary infections are beneficial for the general state of affected children and are very important in maintaining their health. **Keywords:** CYSTIC FIBROSIS, CHILDREN, MALNUTRITION, PULMONARY INFECTION.

Cystic fibrosis (CF) is a life-shortening, autosomal-recessive disorder that is characterized by intestinal malabsorption, impaired growth, and lung disease (1). Opti-
Mal nutritional status is vital in children with CF to enhance their quality of life and prognosis (2, 3). Despite the hyper caloric diet, some children do not achieve the length and weight growth standards. Pulmonary recurrent infections in CF children are often associated with nutritional deficiencies.

**MATERIAL AND METHODS**

We conducted a retrospective study based on medical observation sheets that included 27 patients diagnosed with CF between 1994 and 2011 in the 3rd Pediatric Clinic of the Iasi "Saint Mary" Children's Hospital. Nutritional status was assessed according to ponderal index (PI), body mass index (BMI), Z score for weight and waist. In patients with pulmonary disease the micro bacteriological exam of hypopharyngeal aspiration was performed. In these patients, we established correlations between the ages of onset of symptoms, age at diagnosis, frequency of infectious episodes, identified bacterial agents, and nutritional status. Statistical data analysis was performed using SPSS 19.0. The error of statistical estimations was of 5%, corresponding to a 95% confidence interval.

**RESULTS**

Patients aged between 3 months old and 17 years old with an average of 49.48 months ±9.83 SD (mean age 4.1 years). Sex distribution showed that 17 patients were male (62.96%) and 10 females (37.04%), sex ratio: 1.7: 1.

Although the onset of disease was recorded in the first year of life in 77.77% of cases, the CF diagnosis was made in 70.37% of cases after the first year of life. So, without newborn screening for identification of CF, the patients were diagnosed late, after an average 41.11 months±9.4 SD (ranges one month to 112 months) from the time of the first symptoms until the moment of diagnosis.

The average age at the onset of the disease was 7.23 months±4.32 SD, ranging between 1 day and 13 months. The disease had an early onset, during the first 3 months of life, in 22.22% of cases.

The clinical forms of CF in the study group were: predominantly respiratory manifestations in 48.14% of cases, predominantly digestive symptoms in 33.33% of cases and the mixed type, with both respiratory and digestive symptoms, in 18.52% of cases.

The respiratory disease started in 25.9% of cases with bronchopneumonia and in 18.5% of cases with recurrent wheezing and chronic cough (fig. 1).

In patients with the mixed type of disease, we found that severe exocrine pancreatic failure associated with recurrent respiratory infections lead to severe forms of CF. Analyzing the relationship between the age of onset and the severity of pancreatic and respiratory failure, we found that an early onset is extremely often associated with severe forms of disease (r=0.696, p=0.418, 95% CI) (fig. 2).

Of the 27 patients, only 14.81% (4 patients) had normal weight. Delayed weight and/or height gains were found in 85.19% (23 patients) of cases, with various stages of low body weight according to Z score: 37.04% of cases (10 patients) – stage I dystrophy, 18.52% (5 patients) – stage II dystrophy, 7.41% (2 patients) - stage III dystrophy (fig. 3).
The impact of respiratory tract infections on the nutritional state of children with cystic fibrosis

**Fig. 1.** Respiratory manifestation in children with CF

**Fig. 2.** Correlation between the age at onset and disease severity

**Fig. 3.** Nutritional status in patients with CF
In the study series, we noticed that an early onset and recurrent pulmonary infections are highly related to an abnormal nutritional state, as demonstrated by multivariate analysis. Partial correlations from multivariate analysis between the age of onset, presence of recurrent infections (r=−0.434, p=0.0045), and nutritional state abnormalities (r=−0.517, p<0.05) were statistically significant.

### TABLE I

**Multiple correlation of disease onset vs. impaired nutritional status and recurrent infections**

<table>
<thead>
<tr>
<th>Multiple correlation</th>
<th>Estimated value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficient of multiple correlation</td>
<td>0.88694</td>
</tr>
<tr>
<td>Multiple R²</td>
<td>0.78667</td>
</tr>
<tr>
<td>F</td>
<td>44.24963</td>
</tr>
<tr>
<td>p (95% CI)</td>
<td>0.00000</td>
</tr>
<tr>
<td>Std. Err. of Estimate</td>
<td>2.07712</td>
</tr>
</tbody>
</table>

**Partial correlation disease onset vs.**

<table>
<thead>
<tr>
<th>Correlation Coefficient (Beta)</th>
<th>Std.Err. (Beta)</th>
<th>B</th>
<th>Std.Err. B</th>
<th>t</th>
<th>p-95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>10.6428</td>
<td>0.55513</td>
<td>19.171</td>
<td>0.000000</td>
<td></td>
</tr>
<tr>
<td>Recurrent infections</td>
<td>-0.434356</td>
<td>0.13877</td>
<td>-3.9066</td>
<td>1.24819</td>
<td>0.004549</td>
</tr>
<tr>
<td>Impaired nutritional status</td>
<td>-0.517684</td>
<td>0.13877</td>
<td>-4.3928</td>
<td>1.17761</td>
<td>0.001039</td>
</tr>
</tbody>
</table>

**Fig. 4.** Absolute value of statistics "t" in the evaluation of multivariate analysis (onset vs. impaired nutritional status, recurrent infections)

For the multivariate analysis of the implications of onset time in recurrent infections (nutritional state abnormalities) we applied logistic regression. Table I shows the predictive factors for recurrent infections incidence and nutritional state abnormalities.

The results prove that early onset determines both the occurrence of recurrent infections (b=−0.434-partial correlation indices) and nutritional state abnormalities (b=−0.517) (tab. II).

The causative agents of pulmonary infec-
tions were *Staphylococcus aureus* (S. aureus) (48.14%), *Pseudomonas aeruginosa* (Ps. aeruginosa) (33.33%), *Stenotrophomonas maltophilia* (18.51%), *Haemophilus influen-
zae* (14.8%), *Klebsiella pneumoniae* (11.10%), *Moraxella catarrhalis* (7.40%), *Streptococcus pneumoniae* (7.40%), *Neisseria sica* (7.40%) (fig. 5).

**TABLE II**

Estimated parameters in the assessment report

<table>
<thead>
<tr>
<th>age of onset chance on the basis of risk factors under study</th>
<th>onset – Param.</th>
<th>onset – Std.Err</th>
<th>onset – -95% Cnf.Lmt</th>
<th>onset – +95% Cnf.Lmt</th>
<th>onset – Beta (β)</th>
<th>onset – St.Err.β</th>
<th>onset – -95% Cnf.Lmt</th>
<th>onset – +9% Cnf.Lmt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>10.6428</td>
<td>0.55513</td>
<td>9.4971</td>
<td>11.7886</td>
<td>-0.43435</td>
<td>0.13877</td>
<td>-0.72078</td>
<td>-0.1479</td>
</tr>
<tr>
<td>Recurrent infections</td>
<td>-3.90667</td>
<td>1.24819</td>
<td>-6.4828</td>
<td>-1.3305</td>
<td>-0.51768</td>
<td>0.13877</td>
<td>-0.80410</td>
<td>-0.2312</td>
</tr>
<tr>
<td>Impaired nutritional Status</td>
<td>-4.39286</td>
<td>1.17761</td>
<td>-6.8233</td>
<td>-1.9623</td>
<td>-0.43435</td>
<td>0.13877</td>
<td>-0.72078</td>
<td>-0.1479</td>
</tr>
</tbody>
</table>

Pulmonary infections due to *S. aureus*, *Ps. aeruginosa* and *Stenotrophomonas maltophilia* were more often associated with nutritional status abnormalities.

**DISCUSSION**

In children, multiple diseases, CF included, are associated with weight and growth deficit. In the absence of neonatal screening, in 88.88% of cases the disease was diagnosed late, the average age at the time of diagnosis being 3.4 years old compared with a mean age of onset of symptoms of 7 months old. The clinical forms with pulmonary manifestations were the most common in children with CF, the clinical form with predominantly respiratory symptoms being found in 48.14% of cases, and the mixed forms, respiratory and digestive, in 18.52% of cases. In all 5 patients with respiratory and digestive forms, the association between exocrine pancreatic failure and recurrent respiratory infections caused severe disease progression.

Impaired growth (weight and/or height) was found in 23 patients (85.19% of cases). In this study group, the onset at a young age and repeated respiratory infections were correlated significantly (r = 0.94, CI = 95%) with impaired nutritional status. Stature-ponderal hypotrophy (SPH) was identified in 6 patients with chronic lung infections: three patients with methicillin-resistant *S. aureus* (MRSA), one patient with *Ps. aeruginosa* and two patients MRSA and *Ps.aeruginosa* co-infection. Of the six pa-
patients with SPH, two children were diagnosed late, at the age of ten and eight, respectively. So, the earlier onset and the late diagnosis were associated with many respiratory infections and poor nutritional status. The main pathogen of CF lung infections is *S. aureus* (3, 4, 5, 6). The study by Beringer et al. found that about 50% of children with CF until the age of 10 had chronic pulmonary infections with *S. aureus* (7). Miall et al. compared 10 children with CF and MRSA versus 18 patients with CF negative for MRSA; they found deteriorations in height, weight, and BMI in the MRSA positive group, but only the change in height was statistically significant (*p* = 0.039) (8).

In patients with CF, *S. aureus* itself is not a common cause of morbidity and mortality, but because of the progressive destruction of lung tissue and worsening pulmonary obstruction, it favors co-infection with *Ps. aeruginosa* (8, 9, 10, 11). In our study, pulmonary infections with *S. aureus*, *Ps. aeruginosa* and *Stenotrophomonas maltophilia* were more often associated with poor nutritional status.

Despite adequate pancreatic enzyme replacement therapy and nutritional supplements, the weight and height gains were not satisfactory due to loss of appetite and frequency of catabolic stress during pulmonary exacerbations, requiring repeated hospitalizations. Recurrent respiratory infections, inappropriate nutritional intake and low compliance to substitution treatment caused altered nutritional status. The increased incidence of respiratory infections at a small age is associated with an abnormal nutritional status in CF children. On the other hand, nutritional status has a significant effect on pulmonary disease progression and survival in patients with CF (12, 13).

**CONCLUSIONS**

All patients presented delayed growth (both weight and height), CF onset at a young age and repeated lung infections. All patients with pulmonary infections caused by *S. aureus* (48.14% of cases) and *Ps. aeruginosa* (33.33% of cases) had a poor nutritional status. Newborn screening is essential for diagnosing CF and thus for preventing airway colonization by aggressive germs and so is the early initiation of an adequate nutritional management.

**REFERENCES**

The impact of respiratory tract infections on the nutritional state of children with cystic fibrosis


**FACTORs RESPONSIBLE FOR RELATIVE POSITION OF INTERPROXIMAL PAPILLA IN HEALTHY SUBJECTS**

A group of Korean researchers conducted a study that examined the factors that can be associated with the appearance of the interproximal papilla. Were examined one hundred and forty-seven healthy interproximal papillae between the maxillary central incisors (male, 74; female, 73; average age, 25.36±7.58 years). A digital photograph and periapical radiograph of the interdental embrasure were taken for each subject using a 1-mm grid metal piece. The recorded parameters were: the amount of recession of the interproximal papilla, contact point-bone crest distance, contact point-cemento-enamel junction distance, cemento-enamel junction-bone crest distance, inter-radicular distance, tooth shape, embrasure space size, interproximal contact area, gingival biotype, papilla height, and papilla tip form. The amount of recession of the interproximal papilla was associated with: 1) increase in contact point-bone crest, contact point-cemento-enamel junction, and cemento-enamel junction-bone crest distance; 2) increase in the inter-radicular distance; 3) triangular tooth shape; 4) decrease in the interproximal contact area length; 5) increase in the embrasure space size; 6) flat papilla tip form. The amount of gingival recession was not associated with the gingival biotype or papilla height. In the triangular tooth shape, the contact point-bone crest distance and inter-radicular distance were longer, the interproximal contact area length was shorter, and the embrasure space size was larger. The papilla tip form became flatter with increasing inter-radicular distance and cemento-enamel junction-bone crest distance. The relative position of the interproximal papilla in healthy subjects was associated with the multiple factors and each factor was related to the others. A triangular tooth shape carries a higher risk of recession of the interproximal papilla because the proximal contact point is positioned more incisally and the bone crest is positioned more apically. This results in an increase in recession of the interproximal papilla and flat papilla tip form. (Kim JH, Cho YJ, Lee JY, Kim SJ, Choi JI. An analysis on the factors responsible for relative position of interproximal papilla in healthy subjects. *J Periodontal Implant Sci*, 2013; 43 (4): 160-167)

**Irina Grădinaru**