Analysis of clinical and paraclinical findings in children with community-acquired pneumonia and comorbid chronic tonsillitis

Abstract. Background. Respiratory morbidity is the most frequent cause for children consulting a doctor, accounting for about one-quarter of primary care consultations. The current research aimed to analyze the clinical and paraclinical features of community-acquired pneumonia (CAP) with comorbid chronic tonsillitis in children and to assess the prognostic value of the proposed diagnostic procedures to optimize the management of patients. Materials and methods. The study was conducted at the Pulmonology and Allergology and Infectious Department of the Municipal Medical Establishment “Chernivtsi Regional Children’s Clinical Hospital”, Ukraine. Clinical group I included 20 children (mean age 9.40 ± 1.56 years) with uncomplicated community-acquired pneumonia and concomitant chronic tonsillitis, and the clinical group II consisted of 16 patients (mean age 9.60 ± 1.13 years) with CAP without concomitant pathology of the upper respiratory tract. Results. Community-acquired pneumonia in children with comorbid chronic tonsillitis is characterized by an intense proinflammatory response in the airways, which manifests itself in fever (odds ratio (OR) 6.0), malaise and fatigue (OR 14.3), persistent cough and dyspnea (OR 3.7), leucocytosis (OR 2.0), high levels of acute phase proteins (OR 4.5), activation of the oxidative protein modification according to the exhaled breath condensate examination (OR 6.0–30.0), and more frequent fungal-bacterial association according to the microbiological examination of sputum and oropharyngeal swab (OR 11.1). The obtained data suggest that parenteral antibiotic therapy was used in 20 % of patients from group I and 12.5 % from group II, while 6.3 % of children from group II received only oral antibiotics. In children with CAP and chronic tonsillitis versus comparison group, the OR of receiving parenteral antibiotic therapy for longer than 7 days reached 10.0, and the OR of oral antibiotic therapy for longer than 5 days reached 4.0. Conclusions. The results obtained from the study show that children with CAP and comorbid chronic tonsillitis have more pronounced clinical symptoms, accompanied by paraclinical signs of inflammation that last longer during hospital treatment and require comprehensive therapy (OR 3.3) of longer duration (OR 4.0–10.0).

Keywords: community-acquired pneumonia; chronic tonsillitis; inflammatory markers
some authors, on the contrary, emphasize the milder course of asthma when combined with allergic rhinitis [7, 8]. Thus, there are unresolved issues in the management of children with comorbid respiratory diseases that require a deeper understanding of the pathophysiology of inflammation and optimization of the individualized treatment depending on the nature and severity of inflammation in the airways.

The objective of the current research was to analyze the clinical and paraclinical features of community-acquired pneumonia (CAP) with comorbid chronic tonsillitis in children and to assess the prognostic value of the proposed diagnostic procedures to optimize the management of patients.

**Materials and methods**

The study was conducted at the Pulmonology and Allergology and Infectious Department of the Municipal Medical Establishment “Chernivtsi Regional Children’s Clinical Hospital” (Ukraine). Informed consent was obtained from all the study subjects. The study was approved by the Bioethics Committee of the Bukovinian State Medical University.

Thirty-six school-aged children with combined inflammatory pathology of the upper and lower respiratory tract in the form of uncomplicated CAP and chronic tonsillitis were examined. Some data were extracted from patients’ clinical records. The treatment of children with community-acquired pneumonia and chronic tonsillitis was carried out following regulatory documents and international protocols for the diagnosis and treatment of these nosologies. Clinical group I included 20 patients (8 boys, 12 girls, mean age 9.40 ± 1.56 years) with uncomplicated community-acquired pneumonia and concomitant chronic tonsillitis, and the clinical group II included 16 patients (7 boys, 9 girls; mean age 9.60 ± 1.13 years) with CAP without concomitant pathology of the upper respiratory tract.

To obtain sputum, a procedure was performed to induce its discharge by inhalation of serial hypertonic solutions of sodium chloride according to the method of Pavord and Pizzichini [9]. Exhaled breath condensate was sampled using a self-designed and patented device, following the recommendations of Horváth et al. [10]. In the exhaled breath condensate, the total protein content, products of protein oxidation, and proteolytic activity were measured. Biochemical studies were carried out in the accredited laboratory of the Chernivtsi Regional Children’s Clinical Hospital.

Statistical processing of the obtained data was performed using the Statistica 8.0 software (StatSoft Inc., USA). All data are represented as a mean ± standard error of the mean (M ± m). The estimation of the differences between the samples was conducted using a parametric Student’s t-test and a nonparametric Mann-Whitney U test. P < 0.05 was accepted as statistically significant. The population analysis assessed the attributable risk (AR), relative risk (RR), and odds ratio (OR) with determination of confidence interval (95% CI).

**Results**

Before the hospitalization, an increase in body temperature was reported in all children from clinical group I and 62.5 % of patients from clinical group II (p < 0.05). At the time of admission to the hospital, fever was found in 80 and 62.5 % of patients, respectively; and on the 7th day of the inpatient treatment — only in 10 % of patients from group I (p > 0.05). The RR of fever during the outpatient care in children with pneumonia and comorbid chronic tonsillitis reached 23.1 (95% CI: 19.88–26.94), the OR 6.0 (95% CI: 1.20–29.9), and the AR 61.3 %. At the same time, the RR of fever on the 7th day of inpatient treatment in children from clinical group I versus patients from group II was 5.3 (95% CI: 4.98–5.68), the OR 11.1 (95% CI: 0.22–56.7), the AR 51.6 %.

On admission to the hospital, all children with community-acquired pneumonia and concomitant chronic tonsillitis (clinical group I) and 87.5 % (p > 0.05) of patients from clinical group II had complaints of malaise and fatigue. Thus, the OR of malaise and fatigue on admission to hospital in case of combined inflammatory pathology of the upper and lower airways was 14.3 (95% CI: 0.28–72.42), the RR 67.2, the AR 52.5 %.

At the beginning of hospital treatment, the severe cough was observed in 80 % of patients from clinical group I and 75 % from group II. On the 7th day of hospital stay, the severe cough persisted in 40 % of children from group I and in 18.8 % from group II (p > 0.05), on the 10th day — in 20 and 6.3 % of patients, respectively (p > 0.05). At the same time, the risk of persistent cough on the 10th day was characterized by the OR of 3.7 (95% CI: 1.45–9.56), the RR of 1.65, and the AR of 30 %.

On admission to the hospital, tachypnea was found in 50 % of children from group I and 56.3 % from group II (p > 0.05), dyspnea — in 80 and 68.8 %, respectively (p > 0.05).

According to the results of the chest X-ray, segmental pneumonia was found in 60 % of cases in clinical group I and 50 % in group II (p > 0.05), focal pneumonia — in 30 and 37.5 %, respectively (p > 0.05). Most children had right-sided pneumonia (70 % from clinical group I and 56.3 % from group II; p > 0.05), left-sided pneumonia was found in 20 and 37.5 % of cases, respectively (p > 0.05), and bilateral pneumonia — in 10 % of patients from group I and 6.2 % in group II (p > 0.05).

The leukogram of patients at the beginning of hospital treatment is given in Table 1. According to obtained results, despite the absence of significant differences in the leukogram between groups, the patients from the group II showed more intense inflammatory response. Thus, the total leukocyte count over 12 · 10³/μL was found in 40 % of patients from clinical group I, and in 25 % from the group II (p > 0.05).

At the end of the hospital treatment, there was a tendency towards a more active inflammatory response in patients from clinical group I compared to those from group II (Table 2). A total white blood cell count over 9 · 10³/μL was found in 20 % of children from group I and 12.5 % from group II (p > 0.05). It should be noted that the risk of the severe inflammatory response in the case of a combined pathology of CAP and chronic tonsillitis was characterized by the OR of 2.0 (95% CI: 1.09–3.66), the RR of 1.38, and the AR of 17.1 %.

The plasma level of C-reactive protein in patients from the clinical group I reached 8.00 ± 0.55 mg/L, in group II —
6.00 ± 0.25 mg/L (p > 0.05). With a C-reactive protein level over 6 mg/L, the OR of the severe inflammation in patients with pneumonia and comorbid chronic tonsillitis versus comparison group was 4.5 (95% CI: 2.45–8.23), the RR 2.2 (95% CI: 1.70–2.89), and the absolute risk 35.8 %.

The cellular composition of sputum in patients from the clinical comparison groups is given in Table 3. With relatively higher viability of sputum cells (76 vs 68 %, respectively; p > 0.05), a higher count of eosinophils and macrophages and lower lymphocytes count was found in children from the clinical group I compared with those from group II.

According to the bacteriological examination of sputum, bacterial flora predominated in patients from both groups (30 % in clinical group I and 50 % in group II; p > 0.05). On the other hand, in 10 % of children from group I versus none in group II (p > 0.05), a fungal-bacterial association was found in both sputum and oropharyngeal swab (OR 11.1).

Catalase activity in the exhaled breath condensate was decreased in patients with CAP and chronic tonsillitis and reached 52.9 ± 21.1 in group I and 81.0 ± 14.9 μmol/min × mg protein in group II (p > 0.05), which indicates the exhaustion of antioxidant defense mechanisms in conditions of the active inflammation of the upper and lower respiratory tract. Table 4 shows the indicators of the oxidative modification of proteins in the exhaled breath condensate of children from the clinical comparison groups.

Increased activity of the protein oxidation induced by inflammation and oxidative stress was found in children from clinical group I. The risk of severe inflammation of the respiratory tract at the level of protein oxidation products in the exhaled breath condensate over 80 mmol/g protein was characterized by the OR of 30 (95% CI: 5.98–150), the RR of 6.0 (95% CI: 4.27–8.44), and the AR of 79.9 % with a likelihood ratio of 4.0. A similar tendency towards a higher activity of inflammation of the upper and lower respiratory tract was confirmed by some indicators of the proteolytic activity in the exhaled breath condensate of children from the observation groups (Table 5).

The obtained results show higher proteolytic activity in the exhaled breath condensate in children from clinical

### Table 1. Leukogram of patients from the clinical observation groups at the beginning of the inpatient treatment

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Total WBC (× 10^3/μL)</th>
<th>Leukogram, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Eosinophils</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>9.80 ± 1.51</td>
<td>3.10 ± 0.66</td>
</tr>
<tr>
<td>II</td>
<td>9.70 ± 1.25</td>
<td>3.30 ± 0.96</td>
</tr>
</tbody>
</table>

p > 0.05

### Table 2. Leukogram of patients from the clinical observation groups at the end of the inpatient treatment

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Total WBC (× 10^3/μL)</th>
<th>Leukogram, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Eosinophils</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>7.60 ± 0.71</td>
<td>4.80 ± 0.98</td>
</tr>
<tr>
<td>II</td>
<td>6.90 ± 0.40</td>
<td>3.70 ± 0.64</td>
</tr>
</tbody>
</table>

p > 0.05 p < 0.05

### Table 3. Cellular composition of sputum in patients from the clinical comparison groups, %

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Eosinophils</th>
<th>Neutrophils</th>
<th>Lymphocytes</th>
<th>Macrophages</th>
<th>Epitheliocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4.00 ± 1.40</td>
<td>65.50 ± 5.50</td>
<td>2.00 ± 0.62</td>
<td>23.50 ± 4.50</td>
<td>22.50 ± 5.50</td>
</tr>
<tr>
<td>II</td>
<td>0.10 ± 0.17</td>
<td>75.70 ± 11.33</td>
<td>7.30 ± 1.85</td>
<td>17.00 ± 2.77</td>
<td>33.70 ± 5.84</td>
</tr>
</tbody>
</table>

p < 0.05 p > 0.05 p < 0.05 p > 0.05

### Table 4. Indicators of oxidative protein modification in the exhaled breath condensate of children from the comparison groups

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Total protein, g/L</th>
<th>Protein oxidation products, mmol/mg protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Basic hydrazones</td>
</tr>
<tr>
<td>I</td>
<td>3.00 ± 0.35</td>
<td>80.00 ± 1.84</td>
</tr>
<tr>
<td>II</td>
<td>3.20 ± 0.28</td>
<td>65.80 ± 5.60</td>
</tr>
</tbody>
</table>

p > 0.05 p < 0.05 p > 0.05
group I versus group II. The OR of severe inflammation in the airways at the activity of high-molecular weight protein lysis in the exhaled breath condensate over 1.35 ml/h in patients from group I versus group II reached 20.0, the RR 4.0, the AR 74.9 % at the accuracy of 63.6 % and a likelihood ratio of 67.0. The risk of the chronic inflammation and the conformation of cell collagen in patients with pneumonia and comorbid chronic tonsillitis was confirmed by indicators of collagen lysis activity in the exhaled breath condensate over 0.24 ml/h in patients from group I versus group II with an OR of 6.0 (95% CI: 3.25–11.11), the RR of 2.4, the AR of 42 %. It was found that children from the clinical group I required inpatient treatment for 15.10 ± 1.43 days, and those from group II — for 14.80 ± 1.10 days (p > 0.05). Intravenous (IV) fluid therapy (normal saline solution) was received by 90 % of patients from clinical group I and 62.5 % from group II (p > 0.05). Parenteral antibiotic therapy was used in 20 % of cases in group I and in 12.5 % in group II, while 63.6 % of children from group II received only oral antibiotics. A combination of oral and parenteral antimicrobial therapy was administered to 80 % of children from group I and 81.2 % from group II (p > 0.05). The average duration of IV fluid and antibiotic therapy in children from the clinical comparison groups is shown in Fig. 1.

The obtained data suggest that the patients from the clinical group I required somewhat longer IV fluid and antibiotic therapy during the hospital treatment. Thus, the RR of IV fluid therapy for longer than 5 days in patients from group I compared with those from group II was 3.9 (95% CI: 3.14–4.74), the OR 9.0 (95% CI: 4.20–19.28), and the AR 47.6 %. In children with CAP and chronic tonsillitis versus comparison group, the RR of receiving parenteral antibiotic therapy for longer than 7 days reached 33.4 (95% CI: 27.45–40.64), the OR was 10.0 (95% CI: 2.00–49.94), the AR 66.5 %. The RR of oral antibiotic therapy for longer than 5 days reached 2.2 (95% CI: 1.73–2.68), the OR 4.0 (95% CI: 2.14–7.49), and the AR 33.0 %.

The parenteral antibiotic therapy included cephalosporins (40 % of cases in group I and 43.8 % in group II; p > 0.05), aminoglycosides (10 and 12.5 % of cases, respectively; p > 0.05), or their combination (50 and 31.2 %; p > 0.05). Oral antibiotic therapy included penicillins (30 % of cases in group I and 25 % in group II; p > 0.05), macrolides (30 and 25 %, respectively; p > 0.05), or cephalosporins (20 and 43.7 %; p > 0.05).

In patients with CAP and chronic tonsillitis, the risk of receiving three or more antibiotics during hospital treatment was characterized by the OR of 3.3 (95% CI: 1.84–5.91), the RR of 1.8 (95% CI: 1.28–2.49), and the AR of 29 %. It should be noted that 20 % of patients from group I had recommendations to continue antibacterial therapy after discharge from the hospital. Thus, children with CAP and comorbid chronic tonsillitis compared with patients with CAP more often require combination antibiotic therapy (OR 3.3) of longer duration (OR 4.0–10.0) during hospital treatment and its continuation during outpatient treatment (OR 25.0).

**Discussion**

The inflammatory biomarkers of sputum and exhaled breath condensate have been analyzed in a wide range of pathologies, including respiratory diseases. These diagnostic methods are actively used to determine the activity and nature of the inflammatory process and contribute to expanding the collection of available non-invasive technics to study pathological mechanisms underlying respiratory disorders [11–14]. The obtained data on the inflammatory biomarkers of sputum and exhaled breath condensate in comorbid conditions used to determine the severity of the inflammatory process are confirmed in other research on pneumonia. Some findings indicate an increase in the protein level in sputum or exhaled breath condensate in patients with chronic obstructive pulmonary disease [15–18].

The results of our study showed that children with the combined course of CAP and chronic tonsillitis had a more intense proinflammatory response in the airways, which is confirmed by a leukocytosis (OR 2.0), higher levels of acute phase proteins (OR 4.5), activation of the oxidative protein modification according to the exhaled breath condensate examination (OR 6.0–30.0), and more frequent fungal-bacterial association according to the microbiological examination of sputum and oropharyngeal swab (OR 11.1). Apparently, this can be explained by the prolonged activation of the proinflammatory cytokines and blood granulocytes caused by chronic inflammation of the pharyngeal

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>LMW protein lysis</th>
<th>HMW protein lysis</th>
<th>Collagen lysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.49 ± 0.30</td>
<td>1.35 ± 0.03</td>
<td>0.23 ± 0.04</td>
</tr>
<tr>
<td>II</td>
<td>1.54 ± 0.12</td>
<td>1.20 ± 0.04</td>
<td>0.16 ± 0.03</td>
</tr>
<tr>
<td>p &gt; 0.05</td>
<td>p &lt; 0.05</td>
<td>p &gt; 0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5. Indicators of proteolytic activity in the exhaled breath condensate of children from the comparison groups, ml/h**

**Figure 1. The average duration of the IV fluid and antibacterial therapy in children from clinical comparison groups**
lymphoid ring. The research findings regarding the more frequent need for antimicrobial therapy and its longer duration in children with comorbid acute or chronic bacterial tonsillitis generally coincide with the literature data [19, 20].

Conclusions

The results obtained from the study show that children with CAP and comorbid chronic tonsillitis compared to those with CAP have more severe clinical symptoms like fever, malaise and fatigue, cough and dyspnea, accompanied by paraclinical signs of inflammation (leukocytosis, high levels of acute phase proteins, activation of the oxidative protein modification) that last longer during hospital treatment and require comprehensive therapy of longer duration.

References


Аналіз клінічної і параклінічної картини в дітей із позалікарняною пневмонією та коморбідним хронічним тонзилітом

Резюме. Актуальність. Найбільш частою причиною звернення дітей та їх батьків до лікаря є респіраторні захворювання, на які припадає значна частина звернень на амбулаторному етапі. Метою цього дослідження було проаналізувати клінічні й параклінічні особливості позалікарняної пневмонії (ПЛП) у дітей різного віку із коморбідним хронічним тонзилітом та оцінити прогностичну цінність запропонованих діагностичних заходів для оптимізації ведення пацієнтів. Матеріали та методи. Дослідження проводили на базі пульмонологічного, алергологічного та інфекційного відділень КНУ «Чернівецька обласна дитяча лікарня» (Україна). До I клінічної групи увійшли 20 пацієнтів (середній вік 9,40 ± 1,56 року) із неускладненою позалікарняною пневмонією та супутнім хронічним тонзилітом, до II клінічної групи — 16 осіб (середній вік 9,60 ± 1,13 року) із ПЛП без супутньої патології верхніх дихальних шляхів. Результати. Позалікарняна пневмонія в дітей із коморбідним хронічним тонзилітом характеризується інтенсивною запальною реакцією в дихальних шляхах, що проявляється лихоманкою (відношення шансів (ВШ) 6,0), загальною слабкістю (ВШ 14,3), постійним кашлем та задишкою (ВШ 3,7), лейкоцитозом (ВШ 2,0), високими рівнями протеїнів гострої фази (ВШ 4,5), активізацією окисної модифікації протеїнів за даними дослідження конденсату видихуваного повітря (ВШ 6,0–30,0), а також частішими грибко-бактеріальними асоціаціями за мікробіологічним дослідженням мокроти та мазка з ротовоглоху (ВШ 11,1). Отримані дані свідчать про те, що парентеральна антибіотикотерапія застосовувалася в 20 % хворих I групи та 12,5 % пацієнтів II групи, тоді як 6,3 % дітей II групи отримували тільки пероральні антибіотики. В осіб із ПЛП та хронічним тонзилітом на відміну від групи порівняння ВШ отримання парентеральної антибіотикотерапії довше 7 днів досягало 10,0, а пероральної антибіотикотерапії довше 5 днів — 4,0. Висновки. Отримані результати дослідження свідчать про те, що діти з ПЛП та коморбідним хронічним тонзилітом мають більш виражену клінічну симптоматику, що супроводжується параклінічними ознаками запалення, які зберігаються довше під час стаціонарного лікування та потребують комплексної терапії (ВШ 3,3) і більшої її тривалості (ВШ 4,0–10,0). Ключові слова: позалікарняна пневмонія; хронічний тонзиліт; маркери запалення.