THE PREDICTIVE VALUE OF SOME SERUM PROINFLAMMATORY BIOMARKERS IN RESPIRATORY INFECTIONS IN CHILDREN – CLINICAL THERAPEUTIC CORRELATIONS

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The premises of the study and the working hypothesis

Pediatric patients hospitalized with bacterial or mixed pneumonia (viral and bacterial) have an increased risk of severe complications or death. These complications are more serious the younger the patient (in terms of age or body weight) and the more biologically uncalibrated they are. The prognosis of these patients is influenced by the responsiveness of initiating appropriate therapy and supporting vital functions. Early initiation of antibiotic therapy decisively influences the healing.

The purpose and objectives of the thesis

This thesis aimed to establish whether there are proinflammatory biomarkers with predictive value in respiratory infections in children and whether independent risk factors can be identified in this group of patients. The first main objective was to determine morbidity and mortality from diseases of the lower respiratory tract, in newborns and young children, by analyzing the causes of death. The second main objective was to analyze the incidence of respiratory infections in premature and mature newborns. The third main objective was to establish a histopathological and immunohistochemical model (a tissue model) of lung lesions detected postmortem in pediatric patients. The fourth main objective was to assess the proinflammatory status in children with bacterial or mixed pneumonia (viral and bacterial) treated with antibiotics. The present study aimed to conduct four independent studies on lower respiratory tract infections in children.

In study no. 1, the causes of death in newborns and children from the Târgu Mureș area were analyzed through a retrospective study using data from the necropsy protocols. The study included 226 pediatric patients who died over three years (2016–2018) on which pathological autopsy was performed.

The conclusions of study no. 1: 1. The highest number of deaths was recorded in newborns (first 28 days of life) and infants (first year of life). 2. The leading cause of death was primary lung disease. 3. Male gender, as an unchangeable risk factor, was a negative, significant prognostic factor in the short- and medium-term evolution of newborns. 4. The environment of origin and socio-economic status is an important risk factor in the evolution of these patients.

In study no. 2, a retrospective study was performed on the incidence of infections in premature and full-term infants by analyzing the general clinical observation sheets of patients from the Neonatology and Premature Clinics. Two groups of patients were established: a group of premature newborns (n = 115) from 2017–2020 called group 1 PM, and a group of mature newborns (n = 120) from 2017–2019 called group 2 M.

The conclusions of study no. 2: 1. The most common pathology found among newborns had an infectious nature. 2. The APGAR score at one and five minutes was the most accurate indicator for the risk of neonatal infection. 3. The number of hospitalization days was correlated with the APGAR score at one and five minutes and with the parity. 4. The mother's advanced age was a major risk factor for prematurity. 5. The treatment of most patients with infectious syndromes included betalactamine monotherapy or a combination of betalactamine and aminoglycosides.

In study no. 3, a detailed post-mortem histopathological and immunohistochemical analysis was performed regarding the changes from the lung parenchyma in the case of lower respiratory tract infections. A morphological study of lung samples grossed from the lungs during the pathological autopsy was performed. For the immunohistochemical study, an automatic method was used.

The conclusions of study no. 3: 1. In premature infants, deaths occurred intrapartum or immediately postpartum (first days after birth) due to pulmonary anectasis. 2. Premature babies who died in the first month of life had hyaline membrane pneumopathy. 3. In full-term infants that had normal weights (between 2500–4000g), most deaths occurred in the first month of life, and amniotic fluid and meconium aspiration pneumonia were highlighted. 4. Most deaths between one and three years of age associated with congenital heart malformation were due to cardiac decompensation due to pulmonary hypertension and pulmonary vascular disease.

5. In children without congenital heart defects, the main causes of death after the first year of life were pneumonia and bronchopneumonia. 6. CD3, CD20, CD68, and CD14 markers were used for immunohistochemical evidence of inflammatory cells in pneumonia. 6. CD34 and CD31 markers were used to highlight endothelial cells in the pulmonary vessels when examining lung vascular diseases in the context of congenital malformations.

In study no. 4, a prospective study was performed in which proinflammatory status was evaluated in children with antibiotic-treated pneumonia. The study included patients admitted to the Pediatric Clinic with diseases of the lower respiratory tract, between September 2018 and December 2019. We included 95 patients, aged from one month (30 days) to 16 years.

The clinical methods used included the following: complete clinical examination, daily monitoring of the patients' condition, and monitoring body temperature, diuresis, diet, etc. Paraclinical methods were represented by lung radiographies and laboratory tests: blood count, acute-phase protein, biomarkers for inflammation, biological samples for liver and kidney function, microbiological tests, and antibiograms. Blood samples for routine tests required at hospitalization were processed at the Central Laboratory of the Târgu Mureș County Emergency Clinical Hospital. Blood samples for the analysis of modern inflammatory markers (TNF-α, IL-1β, and IL-6) were processed at the Center for Advanced Medical-Pharmaceutical Research (CAMPR) of UMFST "George Emil Palade" in Târgu Mureș.

The conclusions of study no. 4: 1. Pneumonia (infections of the lung parenchyma) that occur in pediatric patients are associated with different proinflammatory statuses, their degree being variable in relation to the severity of pneumonia. 2. Statistically significant correlations were established for TNF-α, although three cytokines (TNF-α, IL-1β, and IL-6) were monitored. 3. Early proinflammatory status in childhood pneumonia has been demonstrated by correlations between TNF-α, C-reactive protein, highly sensitive variant (hsCRP), and blood count values (absolute leukocyte values: neutrophils, lymphocytes, monocytes and platelets or ratio values of blood cells: NLR and PLR). 4. Pneumonia in children associated with early proinflammatory status requires urgent diagnosis and appropriate treatment to prevent possible serious complications, including death. 5. The most commonly administered antibiotics in the patients in our study were first Ceftriaxone, then, in descending order, Ampicillin and Clindamycin.