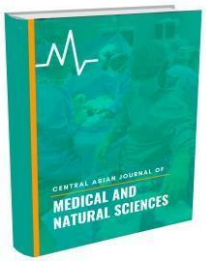

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Article

Clinical and Immunological Characteristics of The Course of Community-Acquired Pneumonia in Children

U.R. Fayziyeva[*1]

1. Termez branch of Tashkent Medical Academy
* Correspondence: ugilbibi@mail.ru

Abstract: Community-acquired pneumonia (CAP) continues to be a major health challenge and a leading cause of child mortality globally, particularly in ecologically unfavorable regions. In Uzbekistan, environmental, socio-cultural, and infrastructural disparities exacerbate CAP prevalence among children, while viral-bacterial shifts post-COVID-19 complicate its clinical course. Despite advancements in diagnosis and treatment, limited regional studies have explored cytokine profiles in young children with CAP, particularly in the Uzbek population of the Surkhandarya region, where genotyping and immune response data remain insufficient. This study aims to characterize the clinical features of CAP in children and investigate serum levels of IL-1β, IL-4, TNF-α, and interferons (α, β, γ), identifying their diagnostic and prognostic value.The study of 50 children revealed a predominance of acute clinical symptoms such as hyperthermia, dyspnea, and severe intoxication, accompanied by distinct cytokine imbalances, notably elevated IL-1β and IL-4 levels and significant shifts in interferon profiles, indicating a strong inflammatory response. This is the first immunogenetic investigation of pediatric CAP in the Surkhandarya region, highlighting the relationship between cytokine levels and disease severity, and offering a molecular perspective on the pathogenesis of CAP. Findings suggest cytokine profiling can inform early diagnostics, prognostics, and individualized immunomodulatory therapies, supporting improved clinical outcomes and rational antibiotic use in pediatric CAP.

Keywords: Children, Community-Acquired Pneumonia, Interleukins, Cytokines, Interferons, Immunology, Uzbekistan, Inflammation

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1. Introduction

Community-acquired pneumonia (CAP) remains a complex clinical and diagnostic task for pediatricians. A number of studies devoted to COVID-19 indicate a change in modern seasonal circulation patterns of many endemic respiratory pathogens (viruses, bacteria) in children over the past 5 years. Perhaps this is associated with the sharp increase in cases of CAP in children noted in many countries in 2023 [1].

Pneumonia is a common and quite serious respiratory disease. According to official statistics, childhood respiratory diseases, including pneumonia, are the third leading cause of death in our country. Pneumonia is the most important cause of death in children worldwide. At the same time, there is a steady increase in community-acquired pneumonia in children worldwide [2]. Streptococcus pneumoniae is the main causative agent of pneumonia, more than 95% of pneumococcal pneumonias are community-acquired . In addition, pneumococcal infection is a common cause of morbidity and

mortality in many countries around the world. According to WHO, about 1 million children die from various forms of pneumococcal infection every year . Currently, mortality from diseases caused by pneumococcal infection can be prevented by vaccination . Nasopharyngeal colonization and carriage are considered the main factor and stage in the pathogenesis of diseases of pneumococcal etiology. The use of pneumococcal vaccine in different countries of the world has shown high clinical efficacy in the prevention of pneumonia, otitis and carriage of pneumococcus bacteria in the nasopharynx [3].

One of the most important scientific and practical areas of social pediatrics and health care organization is the regional approach to studying the health status of children. Its formation is influenced by climatic, geographical, ecological and economic conditions of residence, the degree of population migration, ethnic and socio -cultural features, as well as significant differences in the material and technical base of medical and preventive institutions by region. It is believed that diseases of the bronchopulmonary system are among the diseases whose prevalence in ecologically unfavorable regions is one of the first[4]. Harmful environmental factors can cause the development of chronic pathology of all organs and systems, in particular: the immune system, respiratory organs, gastrointestinal tract, biliary tract and liver, endocrine and a number of other systems. Unfavorable environmental factors can act directly as allergens. Pneumonia occupies a significant place in the structure of bronchopulmonary diseases in childhood. The prevalence of pneumonia and the number of hospitalizations associated with it in children are increasing worldwide[5]. In recent years, the course of pneumonia has changed, the severity and protracted course of the disease is increasing. The main etiologic factor causing the disease may be a viral-bacterial or atypical pathogen, the effectiveness of antibacterial therapy is decreasing . The main problem of modern pulmonology is CAP. The incidence and prevalence of the disease remains one of the main problems, despite the successes achieved in recent years, CAP is a type of controlled infection, but mortality is recorded annually. Data from around the world show that the irrational use of antibiotics continues. Irrational use of ABT entails not only medical, but also social, deontological, economic and other consequences. Antibiotic resistance of hospital pathogens remains[6].

The rapid development of medicine, ensuring early diagnosis of CP, reducing the rate of its development and improving the quality of life of sick children with the help of timely measures, is accompanied by the emergence of an increasing number of scientific publications devoted to the study of the etiology of CP, pathogenetic mechanisms of development, new methods of diagnosis and treatment. Despite significant advances in the study of CP, the introduction of new diagnostic and treatment regimens and the expansion of indications for existing drugs, the use of immunomodulators and other problems of treatment for CP, as well as rehabilitation, follow-up studies remain the most complex area of pulmonology [7]. The last decade has been marked by an increase in research devoted to the study of cytokine status disorders in the respiratory organs, in particular CP. However, to date, there is insufficient scientific research devoted to a detailed analysis of the immunogenetic mechanisms of cytokine interaction in the development of inflammatory changes, the relationship between the levels of various groups of interleukins in assessing the clinical and immunogenetic status of patients. Scientific research devoted to a comprehensive study of the immune system and gene polymorphisms in VP has been studied sufficiently , but this is a problem given the regional characteristics of young children has not been fully studied. To date, polymorphisms and methods of genotyping of IL1β and IL4 genes in children of the Uzbek population of the Surkhandarya region have not been studied . Immunological studies in this scientific research are the most modern research methods [8].

An analysis of foreign and domestic literature has shown that insufficient research has been conducted to take into account risk factors for the occurrence of CP in young

children . In -depth study and improvement of methods for early diagnosis of CP is relevant and important from a practical point of view[9].

Based on the data, the following objective is set in this paper:

1. To study the clinical and immunological features of the course of community-acquired pneumonia at children.

Research objectives:

1. To characterize the clinical characteristics of community-acquired pneumonia in children, taking into account regional features.
2. To study the levels of cytokines IL 1β and IL 4, TNFα and the interferon profile α, β, γ in the blood serum of children with community-acquired pneumonia.

2. Materials and Methods

The study was conducted in the regional children 's multidisciplinary medical center of the city. Termez since 2021 years of age at 22 years in the pulmonology department . The study is based on the examination data of 50 children with pneumonia, the age of the children ranged from 6 months to 10 years . A total of 50 children were examined, in particular, children from 6 months to 12 months - 15 children, from 1 year to 2 years - 18 children, from 3 to 6 years - 10 patients, from 6 to 10 years - 7 children. The diagnosis was established on the basis of patient complaints, life and disease history, laboratory tests, pulse oximetry data, chest X-ray results . The control group consisted of practical health children, in the amount of 30 children.

3. Results

Based on the first objectives of the study , the following results were obtained: patients were admitted to inpatient treatment at different times from the onset of the disease: 3-6 (72 %) - on the 1st-2nd day, 1-2 (24 %) - on the 3rd-5th day, 2 (4 %) - on the 6th-7th day. In severe condition were 2-1 (42 %), moderate - 29 (58 %) patients. In all patients, the onset of the disease was acute 5-0 (100%)[10], see Figure 1.

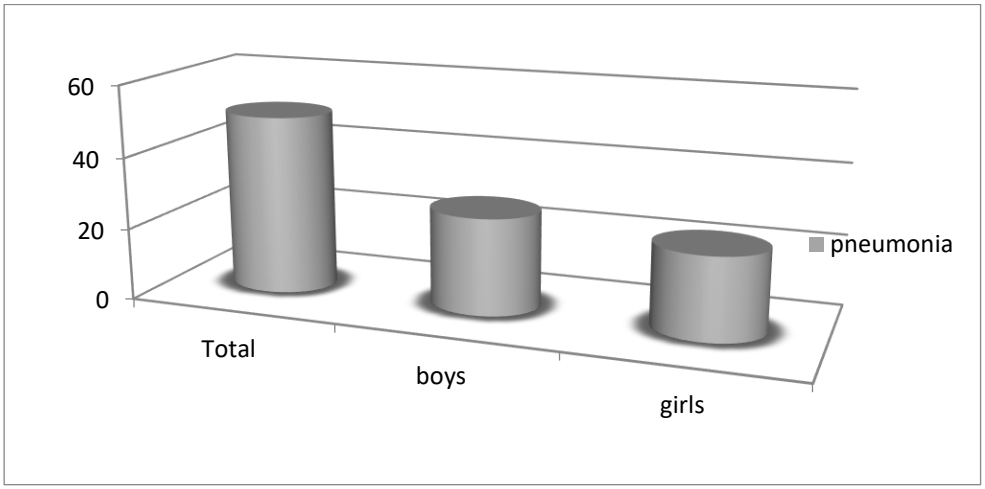

Figure 1. Distribution of patients by gender.

The main clinical manifestation of pneumonia was a wet cough. Wet cough was observed in 4-6 (92 %) children, dry cough - in 4 (8 %). Severe intoxication, hyperthermia was observed up to 38.4 - 38.8 ˚C in all patients 50 (100%) patients), inspiratory dyspnea 2-6 (52 %), dyspnea of mixed genesis - 24 (48 %), refusal to breastfeed 11 (22 %), lethargy and anxiety 42 (84 %), pale skin 3-2 (64 %), moderate cyanosis of the nasolabial triangle 2-4 (48 %), increased respiratory rate with retraction of the intercostal spaces and swelling of the wings of the nose 27 (5-4 %). Chest percussion revealed shortening of the pulmonary sound

over the affected foci. Auscultation revealed persistent local fine-bubble rales and crepitations against the background of harsh breathing. All examined patients underwent chest X-ray, which revealed homogeneous infiltrative shadows in the form of foci of varying size. In the peripheral blood of sick children from 6 months to 12 months 15 (30 %) and from 1 year to 2 years, hypochromic anemia 18 (36 %), as well as leukocytosis, were determined. Some patients had leukopenia with a shift in the formula to the left 2 (4 %). Also, an acceleration of ESR 38 (76 %) was detected. When studying the biochemical blood analysis, hypoproteinemia (up to 65 g/l of protein) was determined in 6 1.2 %), the enzymes alanine transaminase, aspartate transaminase were normal. In 47 (94 %) children, a decrease in diuresis was noted in the first days of the disease against the background of intoxication and fever[11].

Study of the dynamics of pneumonia incidence in children different areas of the region will allow us to obtain new statistical data on the characteristics growth of pneumonia and a significant excess of the regional level[12].

4. Discussion

From the second task, the immunological study was carried out in the laboratory of the Scientific and Diagnostic Center at the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan. The content of interleukin -1 (IL-1β), interleukin - 4 (IL-4), interferon status were studied: - and interferon-alpha, interferon -beta, interferon-gamma in the blood serum were determined by the method of solid-phase enzyme immunoassay. The principle of operation of the IFA-4IL kit is based on the "sandwich" - a version of solid-phase enzyme immunoassay. In order to identify the dependence of local cytokine production on the activity and severity of the disease, in this work, cytokines were measured in the serum of peripheral blood in sick children with community-acquired pneumonia[13].

Considering that the children under observation had uncomplicated focal and focal confluent, segmental forms of pneumonia, it is likely that interleukin - IL-1β acted locally, without spreading beyond the boundaries of the inflammation focus. The level of IL-1β in the blood serum of children with community-acquired pneumonia, apparently, reflects the depth of local inflammation in the lung tissue. This may be evidenced by the relationship between the content of IL-1β in the blood serum and the duration of physical changes in the lungs of a pneumonic nature, such as (shortened percussion sound, weakened breathing, local moist fine bubbling rales, crepitation). Thus, according to the results of the study suggest that IL - 1β is produced and acts on immunocompetent cells, initiating an inflammatory response, and a high level of the latter is a reflection of the activity and severity of the pathological process[14].

Pro- and anti-inflammatory cytokine levels in blood serum of patients with CAP. Table 1 shows that the amount of IL- 4 in sick children aged 7-12 months ranges from 1,3 to 2.1,54 ⊚pg/ml, $p<0.001$, INF α concentrations 15.8±3.5 pg/ml 7-12 months. in children aged 1-2 years, the amount of IL -4 was 12.3±0.63 pg/ml (in the control group - 4.7±0.32 pg/ml). In the group of practically healthy children, the average IL-1/ IL-4 ratio was 5.50 ± 0.28 pg /ml. In the group of children with nosocomial pneumonia in the acute phase of the disease, the average IL1/IL 4 ratio was 1.4,8±2,5 pg/m , which is 3,8 times higher than the control values ($p<0.01$). The following indicators of the composition of interferons: the amount of interferon is 2.5 times higher than the norm, INF β amount 11,6 ±1,2 pg/ml, In patients aged 7-12 months it was 14,9±0,77 pg/ml. INF γ–10,8±0,61 pg/ml, $p<0,01$. Changes in the cytokine index thus indicate an acute inflammatory process in the body. At the onset of the disease, a natural increase in the concentration of anti-inflammatory cytokine IL - 4 was observed in almost all patients, statistically significant $p< 0,001$.

Table 1. Age-Dependent Changes in Cytokine and Interferon Levels in Children with Nosocomial Pneumonia Compared to the Control Group.

		Cytokine levels				
	groups	**control group**	**3-6 months (n=13)**	**7-12 months (n=15)**	**1 – 2 years (n=78)**	**2-3 years (n=44)**
1.	IL-1 pg/ml	5,8±0,45	7,8±1,2	9,6 ±2,1*	10,3±1,5*	9,5 ±1,0***
2.	IL-4 pg/ml	4,7±0,32	4,4±0,74	13,2±1,54 ***	12,3±0,63 ***	11,7±0,24 ***
3.	IL1/IL4	5,50±0,28	9,8±1,2	14,8 ± 2, 5	15 ,8 ± 3,5	14,2 ±1,24
4.	INF α pg/ml	4,8±0,40	11,6±1,2 ***	14,9 ±0.77 ***	13,1±0,5 0***	12,4±0,60 ***
5.	INF β pg/ml	1,9±0,08	0,32±0,0 5 **	0.26±0,09 ***	0,23±0,01 0***	0,27±0,009 ***
6.	INF γ pg/ml	8,5±0,6	7,3±2,0	9 ,8±0,6 1*	8,2±1,3	8,6± 1,2

Note:* - significant compared to the control group (* - p<0,05;** - p<0,01;*** - p <0.001).

Statistical processing of the research results was performed using the statistica 10.0 software package. The data are presented as arithmetic mean values with the error of the mean. The difference in values was considered significant at p<0.05[15].

5. Conclusion

Thus, in conclusion, it can be said that VP in children remains a common and life - threatening pathology of the respiratory system. The main role in the prevention of VP is played by vaccination, primarily against pneumococcal infection. The course of pneumonia also depends on living conditions, nutrition, the presence of bad habits in parents, as well as on the environment and background diseases in the anamnesis. Based on the obtained results, the goals and objectives of the study of the role of proinflammatory and anti-inflammatory cytokines in community-acquired pneumonia in children allow us to look at the ongoing pathological processes not at the tissue level, but at the cellular and molecular levels. With timely diagnosis and treatment, pneumonia in children occurs without complications.

1. In blood serum, IL-1 β and IL-4 Children with community-acquired pneumonia have an increased incidence of IL-1β, interferon-gamma–γ, the content of interferon-alpha - α and interferon beta-β increases slightly.
2. Level proinflammatory (IL-1β) and anti-inflammatory (IL-4) and interferon-alpha - α, interferon-beta - β and interferon-gamma - γ) cytokines can serve as an informative indicator for predicting the further course of pneumonia in children.
3. In sick children with community-acquired pneumonia, upon detection of a secondary immunodeficiency state, immunomodulators can be recommended in addition to basic therapy, taking into account the weight and age of the children.
4. The obtained results of the study of cytokine production can serve as a basis for individual selection of therapy.

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