

## **Changes in the level of TNF- $\alpha$ depending on severity in children with community-acquired pneumonia.**

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### **Abstract**

**Introduction:** Community-acquired pneumonia refers to one of the most relevant infectious diseases, due to the high prevalence among the pediatric population. In last years, interest has been growing in the study of the cytokine status of the child.

**Materials and methods:** In a prospective cohort study under the supervision of 110 children at the age of 5 to 14 y, of them 90 children with community-acquired pneumonia and 20 children from the control group, undergoing treatment in the respiratory department of Children's Hospital of Karaganda, in which 43.64% were girls (95% CI 31.51%-56.33%) and boys 57.27% (95% CI 34.91%-59.88%). The diagnosis of pneumonia was verified on the basis of standards ICD-10 (10<sup>th</sup> revision of the International Statistical Classification of Diseases) for diagnosis and treatment of pneumonia in children. General clinical examination was carried out in accordance with the protocols of examination of children with this pathology approved in the Republic of Kazakhstan, with the inclusion of: a bacteriological method of investigation, studies of TNF- $\alpha$  in serum by enzyme immunoassay.

**Results:** Statistical processing of the obtained results of the difference in quantitative traits marker concentrations was carried out using a nonparametric Mann-Whitney's U test.

**Conclusion:** The results of our study indicate that as the severity of pneumonia increases, the titers of TNF- $\alpha$  in the blood serum and in urine of patients increase. The results of the study in patients with bacterial pneumonia TNF- $\alpha$  can be used as predictors to predict the severity of pneumonia.

**Keywords:** Community-acquired pneumonia, Children, Cytokine, TNF- $\alpha$ .

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### **Introduction**

Community-acquired pneumonia refers to one of the most relevant infectious diseases, due to the high prevalence among the pediatric population [1,2]. In recent years, significantly increasing the number of patients with severe and complicated of community-acquired pneumonia [3,4]. The main focus in the assessment of pneumonia is a complex approach assessment of the severity of the patient's condition to the prediction of the disease, especially in the early stages of its development. Community-acquired pneumonia is accompanied by a systemic response of the organism to inflammation in the lung tissue. In recent years, much attention is given to study proinflammatory cytokine of infection, but in these studies analyse data trends cytokine profile reflected pneumonia insufficient depending on the form and severity of the disease [5]. Therefore, to study the possibility of using the complex quantitative inflammatory markers, particularly TNF $\alpha$  in the blood serum and in urine is of great practical importance for assessing prognosis of community-acquired pneumonia in children.

### **Objective**

To explore the use of quantitative content of markers of inflammation, in particular TNF $\alpha$  in blood serum and in urine to predict the severity of the process of community-acquired pneumonia in children.

### **Materials and Methods**

In a prospective cohort study were under the supervision of 90 children with community-acquired pneumonia at the age of 5 to 14 y, undergoing treatment in the respiratory department of Children's Hospital, of which 45.45% were girls (95% CI 31.51%-56.33%) and boys 54.55% (95% CI 34.91%-59.88%) [3]. Depending on the severity of the patients were divided into three groups on 30 children per groups (I- III). The control group consisted of 20 healthy children.

Patients and healthy children were included in the study on the basis of informed consent. The criteria for inclusion in the group of subjects were:

- 1) Children from 5-14 y.
- 2) Voluntary participation of parents of children with registration of informed consent.
- 3) Elimination of the risk of harm (physical, psychological, social and economic).

**Exclusion criteria were:**

- 1) Failure of parents of children participating in the study,
- 2) Previously held antimicrobial therapy,
- 3) The presence of comorbidity: another chronic inflammatory disease, congenital heart disease, active tuberculosis, the presence of cancer, neurological and endocrine diseases.

The diagnosis of pneumonia was verified on the basis of standards ICD-10 (10<sup>th</sup> revision of the International Statistical Classification of Diseases) for diagnosis and treatment of pneumonia in children.

On admission to hospital in patients determined TNF $\alpha$  content in serum and urine. TNF $\alpha$  was determined by ELISA using a kit of reagents for immunoenzyme determination of the concentration of tumor necrosis factor-alpha in serum, "TNF-alpha ELISA- BEST" (0-300 pg/ml). Statistical processing of the obtained results of the difference in quantitative traits

marker concentrations was carried out using a nonparametric Mann-Whitney's U test. Differences were considered significant at  $p < 0.05$ .

**Results**

Analysis results of evaluation of serum TNF $\alpha$  quantitative characteristics presented in Table 1.

In our study, the analysis of serum TNF- $\alpha$  in children with community-acquired pneumonia (Table 2) showed that there were significant differences when comparing children in groups, depending on the severity of community-acquired pneumonia in children [6]. Thus, TNF- $\alpha$  in children of the 1st group was 1.23 pg/ml, and in the third group this index was 4.5 times higher and was 5.43 pg/ml with the indices of children in the control group 0.97 ( $p < 0.05$ ). The values obtained in children of 1-3 groups of children with community-acquired pneumonia had significant differences, depending on the severity of community-acquired pneumonia, the significance of confidence increased when comparing the level of markers of inflammation in children of the control group.

In patients with community- acquired pneumonia TNF $\alpha$  levels in the urine also increased with an increase in disease severity (Table 2).

**Table 1.** The content of TNF $\alpha$  in serum depending on the severity of community-acquired pneumonia in children.

Severity of pneumonia	Control group (n=20) Me (Q25; Q75)	group I (n=30) Me (Q25; Q75)	p-level	II (n=30) Me (Q25; Q75)	p-level	III (n=30) Me (Q25; Q75)	p-level
Community-acquired pneumonia	0.97 (0.40; 1.25)	1.23 (0.52; 1.82)	$P_{C-I} > 0.05$	1.44 (2.20; 1.69)	$P_{C-II} < 0.05^*$ $p_{I-II} < 0.05^*$	5.43 (3.69; 6.62)	$P_{C-III} < 0.05^*$ $p_{I-III} < 0.05^*$ $p_{II-III} < 0.05^*$

Note: pI-The level of significance, where a comparison group I-<sup>\*</sup>significance of differences in the two groups ( $p < 0.05$ )

**Table 2.** TNF- $\alpha$  content in the urine depending on the severity of community-acquired pneumonia in children.

Severity of pneumonia	Control group (n=20) Me (Q25; Q75)	group I (n=30) Me (Q25; Q75)	p-level	II (n=30) Me (Q25; Q75)	p-level	III (n=30) Me (Q25; Q75)	p-level
community-acquired pneumonia	0.89 (0.44; 1.51)	1.29	$p_{K-I} > 0.05$	2.00 (4.54; 3.00)	$p_{C-II} > 0.05^*$ $p_{I-II} > 0.05^*$	6.13 (3.85; 7.88)	$p_{C-III} < 0.05^*$ $p_{I-III} < 0.05^*$ $p_{II-III} < 0.05^*$

Note: pI-The level of significance, where a comparison group I-<sup>\*</sup>Significance of differences in the two groups ( $p < 0.05$ )

Comparable indices of TNF- $\alpha$  in urine had significant differences in the examined children depending on the degree of severity, and the values were determined within the limits of 1.29 pg/ml; 2.00 pg/ml and 6.13 pg/ml, respectively, in children with community-acquired pneumonia in children 1-3 groups. Statistically significant differences were obtained by comparing the TNF- $\alpha$  level of the control group with I group and I group with II group ( $p < 0.05$ ).

The level of TNF- $\alpha$  in patients with III severity was 5 times higher compared with group I ( $p < 0.05$ ) and 3 times compared with group II ( $p < 0.05$ ).

The results of our study of TNF- $\alpha$  depending on the severity of community-acquired pneumonia in children are certainly the possibility of their use in diagnosing the degree of severity of community-acquired pneumonia in children.

## Discussion

Increased TNF- $\alpha$  production may be the cause of inflammatory complications and septic shock and to identify the most informative of early markers of inflammation in children with community-acquired pneumonia could facilitate the timely development of the activities of the main complications of the disease. Cytokine levels increased during infection in various biological fluids (pleural, bronchoalveolar lavage, cerebrospinal, ascitic fluids), often exceeding their level in the blood. However, the literature until now this problem is still not fully illuminated.

Literature data on the level of cytokines in the urine of children with community-acquired pneumonia are rare and studies mainly carried out with urinary tract pathology [6-8]. Practically there is no comparative description of the diagnostic value of the level of TNF- $\alpha$  in the serum and urine of patients with community-acquired pneumonia, very little information about the possible use of TNF- $\alpha$  to assess the degree of activity of pneumonia, predicting its course and outcome.

Analysis of the data showed that children with community-acquired TNF- $\alpha$  concentration are increased in serum and urine as compared with the control group [9-11].

## Conclusion

In the course of our study on the basis of these data that as the worsening of the severity of community-acquired pneumonia increases TNF- $\alpha$  titers in serum and urine of sick children, justified the use of inflammatory markers for prognostic assessment of severity of community-acquired pneumonia in children. In this connection, the possibility of studying TNF- $\alpha$  level, not only in serum but also in the urine of children as a non-invasive and less traumatic pediatric method for predicting and preventing infectious complications of community-acquired pneumonia in children.

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