

**THE STATE OF THE HEMOSTASIS SYSTEM IN YOUNG CHILDREN WITH ACUTE PNEUMONIA LIVING IN AN ECOLOGICALLY UNFAVORABLE ZONE (KHOREZM REGION)**



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**НОҚУЛАЙ ЭКОЛОГИК МУҲИТДА ЯШОВЧИ ЎТКИР ЗОТИЛЖАМ БИЛАН КАСАЛЛАНГАН ЭРТА ЁШЛИ БОЛАЛАРДА ГЕМОСТАЗ ТИЗИМИНИНГ ҲОЛАТИ (ХОРАЗМ ВИЛОЯТИ МИСОЛИДА)**

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**СОСТОЯНИЕ СИСТЕМЫ ГЕМОСТАЗА У ДЕТЕЙ РАННЕГО ВОЗРАСТА С ОСТРОЙ ПНЕВМОНИЕЙ ПРОЖИВАЮЩИХ В ЭКОЛОГИЧЕСКИ НЕБЛАГОПРИЯТНОЙ ЗОНЕ (ХОРЕЗМСКОЙ ОБЛАСТИ)**

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**Резюме.** Шифохонадан ташқари ўткир зотилжамми 5 ёшгача бўлган бемор болалар орасида юқори ўлимга олиб келувчи (16% гача ёки ундан кўп) энг оғир касалликлардан бири бўлиб қолмоқда. Бироқ зотилжам билан оғриган болаларда цитокин ҳолати ва гемостазнинг ўзаро боғлиқлиги ва ноқулай экологик шароитларнинг таъсири тўғрисидаги маълумотлар тўлиқ ўрганилмаган. Бизнинг илмий ишимизнинг кейинги босқичида Хоразм вилоятида яшовчи эрта ёшли болаларда шифохонадан ташқари ўткир зотилжам билан оғриган болаларда гемостаз кўрсаткичлари ва цитокин даражаси ўртасидаги боғлиқликни ўрганиши. Гемостаз тизимидаги коагуляция кўрсаткичлари ТИТҚИ синдромига юқори тромботик тайёргарликни кўрсатади ва ўз вақтида тўлиқ доволаш учун ўзаро боғлиқлиги ва олдини олиши учун талаб қилади.

**Калит сўзлари:** шифохонадан ташқари зотилжам, гемостаз, болалар, экология.

**Abstract.** Acute community-acquired pneumonia (ACP) in children remains one of the most severe diseases leading to high mortality (up to 16% or more) among patients under the age of 5 years. Information on the relationship between cytokine status and hemostasis in children with pneumonia, taking into account the influence of unfavorable environmental conditions, is practically absent. In this regard, the next stage of our work was to study the correlation between hemostasis indicators and serum cytokine levels in the blood of children with acute community-acquired pneumonia in children living in Khorezm, the indicators of the coagulation link of the hemostasis system showed a high thrombotic preparedness for DIC. The imbalance of hemostasis indicators dictates the expediency of correcting and preventing these conditions for more successful control over the process and timely complete treatment.

**Keywords:** community-acquired pneumonia, hemostasis, ecology, children.

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According to WHO experts, "... the share of the impact on health of environmental factors is estimated at 17-20%, which is not a small indicator and only slightly inferior to genetic and biological factors, which account for about 18-22%".

The ecology and health of the population of the Aral Sea region is an urgent problem not only for Uzbekistan, but for the entire world community. The unfavorable environmental situation has weighed heavily on the entire population of the Republic of

Karakalpakstan, but children are especially affected, since the children's body, due to the functional immaturity of tissues and systems of adaptation and protection, is especially sensitive to the influence of environmental factors [14,15]. Ecological changes in the Aral Sea region affect the health of the younger generation in many ways, this is an increased incidence of respiratory organs, among which acute respiratory infections, bronchitis and pneumonia come first. According to the World Health Organization (WHO),

pneumonia is the most common cause of death among children in the world, in particular, in the structure of mortality in children under 5 years of age, it is 17.5%, annually killing approximately 1.1 million children in this age group (WHO, 2016). The prevalence of pneumonia among children and adolescents in the Republic of Uzbekistan ranges from 17.7% to 19.5%. At present, it is impossible to consider the inflammatory process as part of the body's response to the course of pneumonia outside the influence of the hemostasis system, since the influence of the blood coagulation system on the course of the inflammatory process is important in the pathogenesis of the disease [3, 8, 12]. There are single studies devoted to the study of the state of the hemostasis system in pneumonia in children. The involvement of the hemostasis system in an acute purulent-destructive process is characterized by a different direction of changes and the absence of certain schemes for examining a patient to obtain complete information about the nature and stage of the process.

**The purpose of the study:** to study the impact of factors of an unfavorable ecological environment on the course of acute pneumonia in children of younger childhood, on the hemostasis system.

**Methods:** We studied 42 children with acute community-acquired pneumonia and living in the Aral Sea region (on the territory of the Khorezm region) aged from 1 to 3 years. The diagnosis was made on the basis of anamnesis, clinical signs, results of instrumental and laboratory studies. Determined in blood serum, studied the hemostasis system.

**Results:** The development of the inflammatory process in acute pneumonia cannot be imagined without changes in the hemostasis system, since the coagulation and anticoagulation system of the blood is of particular importance in the pathogenesis of this disease. In the coagulogram of sick children from Tashkent, the Lee-White blood clotting time ( $7.2 \pm 0.12$  min.) was significantly longer ( $p < 0.05$ ), and in sick children from Khorezm ( $11.4 \pm 0.22$  min.) - significantly longer ( $p < 0.001$ ), compared with the same indicator of healthy children ( $5.7 \pm 0.14$  min.). At the same time, the content of fibrinogen and prothrombin index in patients of the comparison group ( $276.95 \pm 14.3$  mg/l;  $116.2 \pm 8.2\%$ , respectively) and patients of the main group with pneumonia ( $256.7 \pm 15.8$  mg/l;  $98.5 \pm 6.3\%$ , respectively) was significantly higher compared to the same indicators in the control group ( $p < 0.001$ ). The APTT indices in children of the comparison group were within the normative values and had no significant difference compared to the control group ( $24.87 \pm 1.6$  sec and  $27.9 \pm 1.3$  sec, respectively). However, in children living in Khorezm, there is an increase in this indicator both in relation to the comparison group and in relation to the control group ( $33.73 \pm 1.9$  sec,  $27.9 \pm 1.3$  sec and  $24.87 \pm 1.6$  sec respectively).

In children from the main group, the INR indicators tended to increase in relation to the data of the control group and the comparison group ( $1.19 \pm 0.05\%$  versus  $1.13 \pm 0.03$  and  $1.07 \pm 0.04\%$ , respectively), which indicates the risk of developing hemorrhagic syndrome. When analyzing laboratory parameters, 25% of patients in the comparison group and 14.3% of patients in the main group showed normal or slight changes in indicators, 20% of patients in the comparison group and 40.0% of children in the main group showed compensatory hypercoagulation, 55% of patients in the comparison group, subcompensatory hypercoagulation was detected, in 44.4% of sick children from the main group, decompensatory hypercoagulation (transition of hypercoagulation to hypocoagulation, various bleeding) was detected. In children living in Khorezm, the indicators of the coagulation link of the hemostasis system showed a high thrombotic preparedness for DIC. Timely unfulfilled corrective therapy in sick children with hypercoagulable syndrome led to a further deterioration in their general condition and the transition of the hypercoagulable state to decompensatory changes.

Based on the correlation analysis, we found that the negative dynamics of the X-ray picture was accompanied by thrombocytopenia and an increase in metabolic acidosis. It was also found that the more pronounced the inflammatory process, the more complex the x-ray picture, since the x-ray parameters correlated with the level of fibrinogen in the blood. Indicators of coagulation hemostasis (APTT, TT) were in strong inverse relationship with the number of leukocytes in peripheral blood. We also revealed the presence of direct correlations between hemostasis parameters (APTT, TT and INR) with fibrinogen and X-ray picture.

Thus, it can be assumed that as the inflammatory process increased, the consumption of vitamin K-dependent coagulation factors increased (correlation of INR and blood fibrinogen  $r = 0.625$ ), the level of APTT in the blood increased and fibrinolysis was activated, which indicated the occurrence of ongoing intravascular coagulation.

In the course of the work, the relative risk (RR) was calculated. RR values greater than 1.0 for the analyzed criterion indicate that this criterion is effective for the development of hemorrhagic and DIC syndrome. According to our data, effective criteria for the development of hemorrhagic syndrome and DIC in community-acquired pneumonia in children living in an unfavorable environment were changes in such indicators as: APTT, which indicates the need for their control in children with pneumonia (Table 1). The RR, respectively, is 1.44. The confidence interval for APTT had the following values: 1.0-1.88, which indicates the effectiveness of changing this indicator for predicting the occurrence of hemorrhagic and DIC syndrome.

**Table 1.** RR indicators and confidence intervals for children living in adverse environmental conditions

	OR	Confidence interval (CI=95% for OR )
ESR (mm/h)	0,47	0,34-0,66
Fibrinogen (g/l)	0,76	0,55-1,05
Leukocytes (x10 <sup>9</sup> /l)	0,75	0,51-1,07
APTT (sek)	1,44	1,0-1,88
Platelets (x10 <sup>9</sup> /l)	0,68	0,51-0,90
INR	0,91	0,70-1,13

**Table 2.** Average values of hemostasis indicators in children with community-acquired pneumonia depending on the development of hemorrhagic and DIC syndrome and unfavorable environmental conditions (M±m)

Criteria	Group comparisons	Main group		Norm control	P
		GS and DIC	Without HS and DIC		
Platelets (x10 <sup>9</sup> /l)	323,8±15,52	412,41±15,24	404,38±25,5	180-360	P1=0,13; P2=0,025; P3=0,732
APTT (sek)	33,9±1,8	26,3±1,1	47,3±3,4	33 сек	P1=0,015; P2=0,008; P3=0,005
TV (sek)	9,8±1,1	14,9±1,5	20,2±1,3	9 сек	P1=0,005; P2=0,003; P3=0,035
PTV (sek)	14,8±1,2	17,5±1,3	18,5±1,2	14 сек	P1=0,451; P2=0,051; P3=0,015
INR	0,99±0,03	1,1±0,04	1,3±0,05	0,8-1,2	P1=0,951; P2=0,041; P3=0,045
Fibrinogen (g/l)	3,43±0,25	5,1±0,21	4,3±0,32	2-4	P1=0,006; P2=0,489; P3=1,005

*Note:* M - arithmetic mean, m - error of the mean; n is the number of observations; 1 - statistical significance of differences between the comparison group and the group of GS and DIC; 2 - statistical significance of differences between the comparison group and without HC and DIC; 3 - statistical significance of differences between HC and DIC and without HC and DIC; p - level of significance of differences. Applied U - Mann Whitney test

When analyzing the data in Table 2, it can be noted that an effective criterion for the development of DIC is a change in the level of INR 4-5 times higher than normal, which indicates thrombinemia and the development of current viutrivascular coagulation.

We found that in children of the main group without HC and DIC, the coagulation link of hemostasis reflected the state of hypocoagulation (APTT 47.3±3.4 sec.) with inhibition of the final stage of coagulation (TV 20.2±1.3 sec.), vitamin intake - K dependent coagulation factors, as evidenced by an increase in MHO (1.3±0.05) to a greater extent than in the subgroup without HC and DIC (p=0.045), more pronounced fibrinemia (4.3±0.32 g/l ) than in the children of the comparison group and the subgroup without HC and DIC (p=0.006; p=1.005). The revealed changes indicate the activation of the blood coagulation system to a greater extent in children with HS and DIC syndromes, which was manifested

by a significant increase in the level of INR, which is a specific marker of the formation of fibrin clots. Next, we calculated the sensitivity, specificity and predictive value of such indicators as APTT, INR for the risk of developing HS and DIC in pneumonia in children. It was found that the sensitivity of APTT and INR was 86 and 75%, respectively, while the specificity for INR was 73% and the prognostic value was 97%, which confirms their practical significance for assessing the development of HS and DIC in children.

#### Conclusions:

1. An unfavorable influence of the ecological environment on the development of an imbalance in the hemostasis system was established, characterized by the transition of hypercoagulation to hypocoagulation in 45.7% and the development of hemorrhagic syndrome.

2. In children living in Khorezm, the indicators of the coagulation link of the hemostasis system

showed a high thrombotic readiness for hemorrhagic syndrome.

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#### **СОСТОЯНИЕ СИСТЕМЫ ГЕМОСТАЗА У ДЕТЕЙ РАННЕГО ВОЗРАСТА С ОСТРОЙ ПНЕВМОНИЕЙ ПРОЖИВАЮЩИХ В ЭКОЛОГИЧЕСКИ НЕБЛАГОПРИЯТНОЙ ЗОНЕ (ХОРЕЗМСКОЙ ОБЛАСТИ)**

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**Резюме.** Острая внебольничная пневмония у детей остается одним из наиболее тяжелых заболеваний, приводящим к высокой летальности (до 16% и более) среди пациентов в возрасте до 5 лет. Сведения о взаимосвязи между цитокиновым статусом и показателями гемостаза у детей с пневмониями с учетом влияния неблагоприятной экологической обстановки практически отсутствуют. В этой связи, следующий этап нашей работы заключался в изучении корреляционной взаимосвязи между показателями гемостаза и уровнями сывороточных цитокинов в крови у детей с острой внебольничной пневмонией у детей, проживающих в Хорезме показатели коагуляционного звена системы гемостаза показали высокую тромботическую подготовленность к ДВС синдрому. Дисбаланс показателей гемостаза, диктует целесообразность проведения корреляции и профилактики этих состояний для более успешного контроля над процессом и своевременного полного лечения.

**Ключевые слова:** внебольничная пневмония, гемостаз, экология, дети.