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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CLINICAL SIGNIFICANCE OF CYTOKINE PROFILE IN SURGICAL TREATMENT OF LIVER ECHINOCOCCOSIS

Specialty: 3213.01-Surgery

Field of science: Medicine

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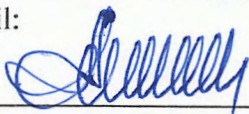
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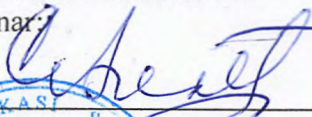
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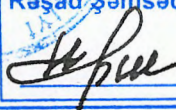
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GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the topic: Echinococcosis is a severe parasitic disease characterized by cyst formation. The majority of parasite eggs are retained in the sinusoids of the liver, leading to the development of hydatid cysts in the liver in 54–84% of cases. However, a small number of eggs can bypass the liver sinusoids, entering the heart, lungs, and systemic circulation. Combined forms of the disease are observed in 10–18% of cases¹.

The cyst of *Echinococcus granulosus* has a very complex structure, consisting of both parasitic (hydatid) and host (adventitial) components². Despite advancements in modern diagnostic and treatment methods for echinococcosis, the incidence of complicated forms of the disease remains high, reaching 57.3%, with no observed tendency to decline³.

Because large areas of the world are endemic for echinococcosis, and the disease affects the liver in 70% of cases, it results in \$3 billion in healthcare costs annually⁴.

Due to the improvement in surgical techniques and technologies, the frequency of relapses of the disease varies from 3% to 22%. Some authors explain the development of relapses by the association of cysts developing from the germinal elements of the main cyst, while others note that cysts missed during the initial operation cause relapses.

¹ Ветшев, П.С. Мини-инвазивные технологии в лечении эхинококкоза печени (клиническая лекция) / П.С. Ветшев, Г.Х. Мусаев, Р.Х. Шарипов // – Москва: Анналы хирургической гепатологии, – 2021. № 4, – с. 77-86.

² Atmaca, H.T. Determination of macrophage types by immunohistochemical methods in the local immune response to liver hydatid cysts in sheep // *Acta Tropica*, – 2022. 229, – p. 106364.

³ Рахматуллаев, Р. Эффективности применение современной технологии в лечение эхинококкоза органов брюшной полости / Р. Рахматуллаев, С. Хасанов // – Душанбе: Здравоохранение Таджикистана, – 2019. № 3, – с. 36-41.

⁴ Magistri, P.] Not just minor resections: robotic approach for cystic echinococcosis of the liver / Magistri P, Pecchi A, Franceschini E. [et al.] // *Infection*, – 2019. 47 (6), – p. 973-979.

Postoperative mortality in hepatic echinococcosis varies across countries, ranging from 13.4% to over 23%⁵.

Early cysts in intermediate organisms stimulate a Th1-type immune response, which is the product of most infectious parasites, providing a high level of immunity against subsequent infection⁶. Hydatid cysts can persist in the body for a long time in the absence of clinical symptoms and mild to moderate inflammation. IL-4, IL-5, IL-10, and IL-13 and cytokines have been shown to play a key role in the cystic phase in human and animal models of echinococcosis⁷.

In recent years, modern aspects of the diagnosis and treatment of complications of hepatic echinococcosis, as well as the study of factors affecting the outcome of the disease, have changed views on the pathogenesis and principles of treatment of this disease⁸. The pathogenesis of hepatic echinococcosis is associated with the development of inflammatory reactions, accompanied by the activation of a number of immunopathological defense mechanisms. The process of liver regeneration is specifically regulated by cytokines produced by inflammatory cells⁹.

A lack of cytokine synthesis in the pre-treatment period suggests a severe course of hepatic echinococcosis and a high

⁵ Амонов, Ш.Ш. Современные аспекты диагностики и хирургического лечения эхинококкоза печени / Ш.Ш. Амонов, Д.А. Рахмонов, З.Ш. Файзиев [и др.] // – Душанбе: Вестник Авиценны, – 2019. № 3, – с. 480-488.

⁶Tamarozzi, F. The intermediate host immune response in cystic echinococcosis / F. Tamarozzi, M. Mariconti, A. Neumayr [et al.] // *Parasite Immunology*, – 2016. 38, – p. 170-181.

⁷ De Biase, D. Evaluation of the Local Immune Response to Hydatid Cysts in Sheep Liver / D. De Biase, F. Prisco, P. Pepe [et al.] // *Veterinary Sciences*, – 2023. 10 (5), – p. 315.

⁸Вишневский, В.А. Эхинококкоз печени. Хирургическое лечение / В.А. Вишневский, М.Г. Ефанов, Р.З. Икрамов [и др.] // – Москва: Доказательная гастроэнтерология, – 2013. № 2, – с. 18-25.

⁹Grubor, N.M. Liver cystic echinococcosis and human host immune and autoimmune follow-up: A review / N.M. Grubor, K.D. Jovanova-Nesic, Y. Shoenfeld // *World Journal of Hepatology*, – 2017. 9 (30), – p. 1176-1189.

recurrence rate¹⁰. Considering this, targeted immune modulation is deemed effective when significant changes in inflammatory mediators are observed. We found it appropriate to prescribe Immunofan, a drug that affects phagocyte activity in exudative pathologies. Currently, Immunofan is regarded as a promising approach to immunocorrection.^{11,12}

In this regard, studying the body's immune responses and cytokine regulation at different stages of treatment of patients with hepatic echinococcosis and improving treatment outcomes through the use of Immunofan could represent a promising approach.

Object of the study. The objects of the study were 100 patients in the main group and 40 patients in the comparison group who were treated for hepatic echinococcosis at the Educational-Surgical Clinic of the Azerbaijan Medical University during 2016-2020 and 14 practically healthy individuals. After echinococcectomy, the Immunofan preparation was administered to the patients of the main group in complex treatment.

Purpose of the study. Investigation of cytokine profile dynamics and improvement of disease outcomes in patients diagnosed with hepatic echinococcosis after surgery, against the background of the addition of an immunomodulator to complex treatment.

Tasks of the research.

1. Analysis of biochemical laboratory parameters, cytokine profiles, and immunoglobulin levels in patients with and without

¹⁰ Mihmanli, M. Current status of diagnosis and treatment of hepatic echinococcosis / M. Mihmanli, U.O. Idiz, C. Kaya [et al.] // World Journal of Hepatology, – 2016. 8(28), – p. 1169-1181.

¹¹ Кологривова, Е.Н. Влияние интраназального применения Имунофана на активность фагоцитов при комплексной терапии экссудативного среднего отита у детей» / Е.Н. Кологривова, Р.И. Плешко, Н.В. Щербик [и др.] // Медицинская иммунология, – 2020. № 4. – с. 741-750.

¹² Лысенко, О.В. Влияние имунофана на некоторые показатели синдрома эндогенной интоксикации и иммунитета у больных раком молочной железы на фоне специального лечения / Лысенко О.В., Коробкова Т.Н., Пинегин А.А. [и др.] // Главный Врач Юга России, –Ростов-на-Дону: – 2018, №3, – с. 27-30.

complications in the main and comparison groups before surgery.

2. Analysis of biochemical parameter dynamics in patients with and without complications in the main and comparison groups after surgery.
3. Analysis of cytokine profile parameter dynamics in patients with and without complications in the main and comparison groups after surgery.
4. Analysis of immunoglobulin fraction parameter dynamics in patients with and without complications in the main and comparison groups after surgery.

The main provisions of the dissertation presented for the defense.

- During hepatic echinococcal cysts, biochemical markers such as CRP and cytokines (IL-1, IL-4, IL-6, IL-10, and TNF- α), along with immunoglobulin fractions (IgA, IgG, and IgM), undergo changes in the blood. To correct these alterations, combining Immunofan with traditional postoperative medical treatment is a more effective approach.
- In addition to the above-mentioned cytokine profile and immunoglobulin fraction indicators, the Immunofan preparation has similar effects on the quantitative indicators of enzymes such as ALT, AST, and GGT in the blood.

Scientific novelty of the research. Based on the cytokine profile examination in patients diagnosed with hepatic echinococcosis, the use of an immunomodulator after surgery in complex treatment is justified.

Methods of the research:

- Clinical examinations
- Biochemical examinations
- Immunological examinations
- Instrumental examinations
- Mathematical and statistical analysis methods

In the healthy individuals included in the study, enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and amylase, protein metabolism parameters such as albumin and creatinine, lipid metabolism products such as cholesterol, bile metabolism products such as total bilirubin, conjugated bilirubin and free bilirubin, interleukin fractions such as IL-1, IL-4, IL-6, IL-10 and TNF α , and antibody fractions such as IgA, IgG and IgM were quantified in blood samples. The same examinations were performed on the main and comparison group patients included in the study, but the examinations were repeated before the operation and 1 day, 5 days, and 10 days after the operation.

Immunoenzyme analysis (IEA) methods are applied based on 2 principles. In the first method, the functional activity of the enzyme-antibody complex bound to a solid phase by a covalent or non-covalent bond (cleavage of the enzyme, substrate, binding of the antibody to the antigen) is used, while in the second method, the biological activity of the antibody-enzyme complex in the form of a conjugate in solution is mainly used. IEA has several forms, such as ELISA (enzyme-linked immunoadsorbent assay), EIA (enzyme immunoassay), and EMIT (enzyme multiplied immunoassay technique). The first two methods (ELISA and EIA) are considered heterogeneous or solid-phase, and the third is considered homogeneous IEA. IEA is used to determine hormones, proteins, tumor markers, antibodies to bacteria and viruses, types and specificity of immunoglobulins, drugs, and pharmaceuticals.

The levels of IL-1, IL-4, IL-6, IL-10 and TNF- α cytokines, IgA, IgM, and IgG immunoglobulins in the blood of healthy persons and those requiring surgical treatment for pathological conditions included in the study contingent were analyzed using the immunoenzymatic method.

Practical significance.

- The results of this research can contribute to understanding the complications that arise in the regulation of cytokines and immune responses during echinococcal cysts of the liver.

- The study of complications allows for a more precise assessment of the effectiveness of complex treatment and helps evaluate their potential role in the treatment process.
- The inclusion of medications, such as Immunofan, which affect the regulation of immune responses and cytokines, in the traditional treatment regimen for the diagnosis and management of hepatic echinococcosis has led to more satisfactory treatment outcomes.
- By examining the relationship between cytokines and the body's immune reactivity in blood samples of patients with hepatic echinococcosis before and after surgical intervention (echinococcectomy), it is possible to optimize diagnostic and treatment outcomes in complex patient management by considering this interaction.

Approbation of the research. The results of the research were reported at the following conferences:

1. "Issues of Education and Science". Tambov, October 30, 2021;
2. III Karabakh International Conference "Year of Shusha -2022". Baku, June 7-10, 2022.

The dissertation was initially discussed on September 28, 2023 (Protocol No2) and extensively discussed at the meeting of the Approval Council under the ED 2.05 Dissertation Council on October 04, 2024 (Protocol No7).

Publications. 19 scientific works were published on the results and fragments of the dissertation. Of these, 14 were articles (2 articles abroad) and five theses.

Application of the dissertation results.

The results of the dissertation work have been included in the scientific research, practical, and experimental work plan of the Educational-Surgical Clinic of the Azerbaijan Medical University and Republican Clinical Hospital named after Academician Mirgasimov, The public legal entity Management Union of Medical Territorial Units.

Organization where the dissertation was conducted. The research work was carried out at the Educational-Surgical Clinic of Azerbaijan Medical University.

The structure and volume of the dissertation. The dissertation work is presented on 160 pages of typewritten text (204290 characters) and consists of an introduction (7897 characters), Chapter I (74683 characters), Chapter II (22515 characters), Chapter III (16617 characters), Chapter IV (50349 characters), Results (29814 characters), Conclusions (1903 characters), and Practical recommendations (512 characters). The results of the dissertation are displayed in 35 tables, 22 graphs, and 6 images. The bibliography includes 146 sources.

MATERIALS AND METHODS

The objects of the study were 100 patients in the main group and 40 patients in the comparison group who were treated for hepatic echinococcosis at the Educational-Surgical Clinic of the Azerbaijan Medical University during 2016-2020 and 14 practically healthy individuals. The amounts of various enzymes, cytokine profiles and immunoglobulin fractions were determined in blood samples. Of the patients with echinococcosis, 89 were female and 51 were male, which accounts for 63.5% and 36.5% of the contingent, respectively.

We performed echinococcectomy on the liver of patients diagnosed with echinococcosis. Open laparoscopic surgery was performed in 102 patients (72.8%), while closed laparoscopic surgery was performed in 38 patients (27.2%). The study included 89 female and 51 male patients. Patients were grouped by age into the following categories: 14–25, 26–40, 41–60, 61–75, and 75 and older. Besides, patients with echinococcosis (n=140) were grouped based on whether they had single or multiple echinococcal cysts in the liver, the presence or absence of various concomitant diseases, the occurrence of various echinococcosis-related complications, cyst size, and the presence of cysts in the liver and other organs.

The main changes in the results of biochemical and immunological examinations in the preoperative blood samples of 140 patients with hepatic echinococcosis included in the study were detected in the biochemical CRP indicator and immune-inflammatory indicators.

Of the 140 patients in whom we performed echinococcectomy, 98 had uncomplicated and 42 had complicated forms, accounting for 70.0% and 30.0%, respectively.

Based on clinical and instrumental indicators and the level of biochemical indicators, such as CRP and immune-inflammatory indicators (IL-1, IL-4, IL-6, IL-10, and TNF- α), within these two groups, patients were divided into two subgroups: severe and non-severe.

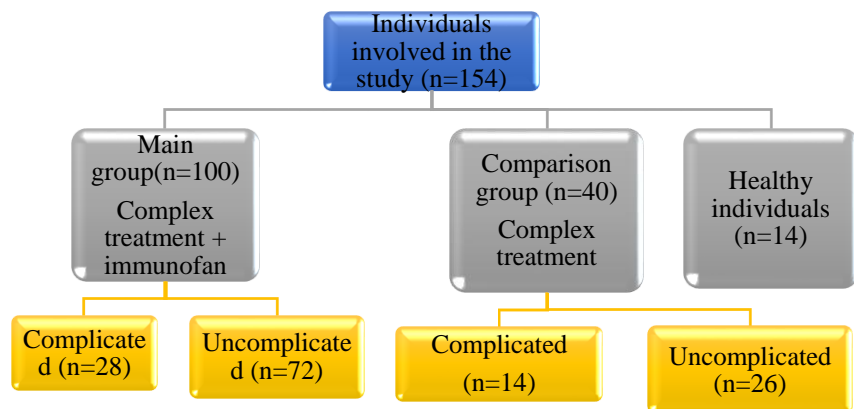


Figure 1. Research design

Then, in healthy individuals and patients with echinococcosis, enzymes, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and amylase, protein metabolism parameters such as albumin and creatinine, lipid metabolism products such as cholesterol, bile metabolism products such as total bilirubin, conjugated bilirubin and unconjugated bilirubin, interleukin fractions

such as IL-1, IL-4, IL-6, IL-10 and TNF- α , and antibody fractions such as IgA, IgG and IgM were studied in blood samples taken before the respective operation and 1 day, 5 days, and 10 days after the operation. In our study, patients who underwent echinococcectomy were administered an immunomodulator (Immunofan) for 7 days, including the day of surgery.

The obtained data were processed using statistical methods and taking into account modern requirements. For group indicators, the mean values (M), their standard error (m), the minimal (min) and maximal (max) values of the ranks, as well as the frequency of occurrence of qualitative indicators in the groups were determined. In the research, non-parametric criteria were used, including the Wilcoxon (Mann-Whitney) U-test and Pearson's χ^2 test. The results were processed using the Statistics 7.0 software application.

RESULTS OF PERSONAL RESEARCH

We analyzed the patients who would undergo echinococcectomy by age group (Table 1).

Table 1
Distribution of patients (n=140) who underwent echinococcectomy by age group

Age groups	14-25 years	26-40 years	41-60 years	61-75 years	>75 years
Number	17	47	55	18	3
%	12.1	33.6	39.2	13	2.1

In the study, among 140 patients, 52 (37.1%) had one and 88 (62.9%) had two or more echinococcal cysts. Of these, 32 (22.8%) had small cysts (up to 5 cm), 72 (51.4%) had medium-sized cysts (5-10 cm), and 36 (25.8%) had large cysts (larger than 10 cm).

Before the surgery, biochemical markers such as ALT, AST, ALP, QTT, and amylase were determined in the main group, the comparison group, and the group of healthy individuals.

The patients included in the study were divided into two subgroups based on the presence or absence of complications. The comparison group consisted of patients with complicated form (conditionally, n=14) in subgroup C1 and patients with uncomplicated form (n=26) in subgroup C2. In the main group, patients with complicated form (n=28) were in subgroup M1, and patients with uncomplicated form (n=72) were in subgroup M2.

Based on these data, we analyzed the differences between various biochemical parameters of the C1 and M1 groups before surgery.

It was found that the ALT level in group C1 was statistically non-significantly lower compared to group M1 ($t=1.65$, $p>0.05$). The AST level in group C1 was statistically non-significantly lower than in group M1 ($t=2.18$, $p<0.05$). The ALP level in group C1 was lower than in group M1, but the difference (240.0 ± 4.8) was not statistically significant ($t=1.39$, $p>0.05$). The GGT level in group C1 was also lower than in group M1, but the difference was not statistically significant ($t = 1.09$, $p > 0.05$). Similarly, the amylase level in group C1 was lower than in group M1 without statistical significance ($t=1.05$, $p>0.05$).

Thus, in patients with preoperatively complicated echinococcosis, only the AST parameter was found to be statistically significantly higher in group M1 compared to group C1.

We analyzed biochemical parameters between patient groups with preoperatively complicated echinococcosis. Among these groups, only the level of ALP was statistically significantly lower in the C2 group compared to the M2 group. The levels of ALT ($t=0.80$, $p>0.05$), AST ($t=0.51$, $p>0.05$), GGT ($t=0.38$, $p>0.05$), and amylase ($t=0.58$, $p>0.05$) were statistically insignificantly lower in the C2 group compared to the M2 group.

In addition, protein metabolism indicators and bilirubin fraction levels were also determined before operation in the study groups and healthy individuals (Table 2).

Table 2

Preoperative quantitative parameters of protein metabolism and bilirubin fractions in patients with complicated and uncomplicated echinococcosis

Parameters	C1 (n=14)	M1 (n=28)	C2 (n=26)	M2 (n=72)
Albumin	29.0±1.1	28.0±0.6	40.0±1.5	40.5±0.8
Creatinine	150.0±5.5	155.0±3.1	100.0±3.7	100.5±2.0
Cholesterol	270.0±9.9	280.0±5.6	180.0±6.6	200.0±4.0
CRP	31.0±1.1	34.0±0.7	14.0±0.5	15.0±0.3
TB	22.0±0.8	24.0±0.5	14.0±0.5	14.5±0.3
CB	7.5±0.3	7.6±0.1	6.0±0.2	6.5±0.1
UCB	12.6±0.5	13.5±0.3	10.0±0.4	10.5±0.2

We also compared the statistical accuracy coefficients for protein metabolism indicators and bilirubin fractions across groups.

After surgery, the differences in albumin ($t=0.80$, $p>0.05$), creatinine ($t=0.79$, $p>0.05$), cholesterol ($t=0.88$, $p>0.05$), CB ($t=1.38$, $p>0.05$) and UCB ($t=1.38$, $p>0.05$) in the C1 and M1 groups were statistically non-significant. The differences in CRP ($t=2.31$, $p<0.05$) and TB ($t=2.06$, $p<0.05$) before surgery in these groups were statistically significant.

We also determined preoperative parameters among patients with uncomplicated echinococcosis. There were no statistically significant differences between the C2 group and the M2 group in the preoperative albumin ($t=0.29$, $p>0.05$), creatinine ($t=0.12$, $p>0.05$), CRP ($t=1.72$, $p>0.05$), TB ($t=0.86$, $p>0.05$), CB ($t=1.67$, $p>0.05$) and UCB ($t=1.11$, $p>0.05$). However, cholesterol was statistically significantly lower in the C2 group than in the M2 group ($t=2.60$, $p<0.05$).

Immune parameters in patients with complicated and uncomplicated echinococcosis were also analyzed in the main and comparison groups before surgery (Table 3).

Table 3

Preoperative quantitative indicators of essential immune parameters in patients with complicated (C1, M1) and uncomplicated (C2, M2) forms of echinococcosis

Immune parameters	C1 group (n=14)	M1 group (n=28)	C2 group (n=26)	M2 group (n=72)
IL-1	21.0±0.8	24.0±0.5	15.5±0.5	15.0±0.3
IL-4	11.0±0.4	12.0±0.2	10.5±0.4	10.0±0.2
IL-6	31.0±1.1	32.0±0.6	16.0±0.6	16.5±0.3
IL-10	26.0±0.9	28.0±0.6	15.0±0.5	15.5±0.3
TNF- α	22.0±0.8	24.0±0.5	16.0±0.6	19.0±0.3
IgA	7.0±0.3	8.0±0.2	6.4±0.2	6.5±0.1
IgG	18.0±0.7	20.0±0.4	14.0±0.5	14.5±0.3
IgM	4.0±0.1	4.2±0.1	4.2±0.1	4.0±0.1

Table 3 presents the mean values of immune parameters in patients with complicated and uncomplicated echinococcosis. As seen, the IL-1 level in patients with complicated echinococcosis in the comparison group was 21.0±0.8 pg/mL and in the main group, it was 24.0±0.5 pg/mL, while in patients with uncomplicated echinococcosis in the comparison group, this parameter was 15.5±0.5 pg/mL, and in the main group it was 15.0±0.3 pg/mL. The preoperative IL-4 level was 11.0±0.4 pg/mL in patients with complicated echinococcosis in the comparison group and 12.0±0.2 pg/mL in the main group, while in patients with uncomplicated echinococcosis, it was 10.5±0.4 pg/mL in the comparison group, and 10.0±0.2 pg/mL in the main group. The level of IL-6 was found to be 31.0±1.1pg/mL in patients with complicated echinococcosis in the comparison group and 32.0±0.6pg/mL in the main group, while in patients with uncomplicated echinococcosis, it was 16.0±0.6pg/mL in the comparison group, and 16.5±0.3 pg/mL in the main group.

The preoperative IL-10 level was 26.0 ± 0.9 pg/mL in patients with complicated echinococcosis in the comparison group and 28.0 ± 0.6 pg/mL in the main group, while in patients with uncomplicated echinococcosis, it was 15.0 ± 0.5 pg/mL in the comparison group and 15.5 ± 0.3 pg/mL in the main group.

Before the surgery, the IL-10 level was recorded as 26.0 ± 0.9 pg/mL in patients with complicated echinococcosis in the comparison group and 28.0 ± 0.6 pg/mL in patients with complicated echinococcosis in the main group, 15.0 ± 0.5 pg/mL in patients with uncomplicated echinococcosis in the comparison group, and 15.5 ± 0.3 pg/mL in patients with uncomplicated echinococcosis in the main group.

The TNF- α level also differed in patients with complicated and uncomplicated echinococcosis. It was recorded as 22.0 ± 0.8 pg/mL in patients with complicated echinococcosis in the comparison group, 24.0 ± 0.5 pg/mL in patients with complicated echinococcosis in the main group, 16.0 ± 0.6 pg/mL in patients with uncomplicated echinococcosis in the comparison group, and 19.0 ± 0.3 pg/mL in patients with uncomplicated echinococcosis in the main group.

Before the surgery, we conducted comparative analyses of immunoglobulins IgA, IgG, and IgM between patients with complicated and uncomplicated echinococcosis. As seen, the IgA level was 7.0 ± 0.3 g/L in patients with complicated echinococcosis in the comparison group, 8.0 ± 0.2 g/L in patients with complicated echinococcosis in the main group, 6.4 ± 0.2 g/L in patients with uncomplicated echinococcosis in the comparison group, and 6.5 ± 0.1 g/L in patients with uncomplicated echinococcosis in the main group (Table 3).

The IgG level was recorded as 18.0 ± 0.7 g/L in patients with complicated echinococcosis in the comparison group, 20.0 ± 0.4 g/L in patients with complicated echinococcosis in the main group, 14.0 ± 0.5 g/L in patients with uncomplicated echinococcosis in the comparison group, and 14.5 ± 0.3 g/L in patients with uncomplicated echinococcosis in the main group.

The IgM level was recorded as 4.0 ± 0.1 g/L in patients with complicated echinococcosis in the comparison group, 4.2 ± 0.1 g/L in patients with complicated echinococcosis in the main group, 4.2 ± 0.1 g/L in patients with uncomplicated echinococcosis in the comparison group, and 4.0 ± 0.1 g/L in patients with uncomplicated echinococcosis in the main group.

Analysis: The IgM level is similar in the C1 and M1 groups (4.0 and 4.2) as well as in the C2 and M2 groups (4.2 and 4.0). The IgM levels are comparable across all groups, which probably indicates that the initial immune response is at a similar level. The similarity in immunoglobulin IgM levels suggests that the initial immune response is comparable in both groups. The obtained results indicate that complicated echinococcosis has a deeper impact on the immune system and triggers a more active immune response.

Before the surgery, the levels of IL-1 ($t=3.09$, $p<0.01$), IL-4 ($t=2.22$, $p<0.05$), TNF- α ($t=2.13$, $p<0.05$), IgA ($t=2.78$, $p<0.05$), and IgG ($t=2.44$, $p<0.05$) were statistically significantly lower in the C1 group compared to the M1 group. However, no statistically significant differences were observed between the C1 and M1 groups in terms of IL-6 ($t=0.80$, $p>0.05$), IL-10 ($t=1.82$, $p>0.05$), and IgM ($t=1.43$, $p>0.05$) (Table 3). In the C2 group (patients with uncomplicated echinococcosis), the concentration parameters of IL-1 ($t=1.02$, $p>0.05$), IL-4 ($t=0.98$, $p>0.05$), IL-6 ($t=1.02$, $p>0.05$), and IL-10 ($t=1.02$, $p>0.05$) showed no statistically significant differences compared to the M2 group.

A comparative analysis of the functional activity markers of the liver, pancreas, and bile ducts was conducted among patients with complicated (M1, C1 groups) and uncomplicated (M2, C2 groups) echinococcosis on days 1, 5, and 10 after surgery.

On the first day after surgery, the mean ALT level in the C1 group was statistically significantly higher compared to the M1 group ($t=7.87$, $p<0.001$). Similarly, the AST level in the C1 group was also statistically significantly higher than in the M1 group ($t=8.01$, $p<0.001$). No statistically significant differences were found among other parameters. Although the levels of ALP ($t=0.44$, $p>0.05$), GGT

($t=0.40$, $p>0.05$), and amylase ($t=0.23$, $p>0.05$) were lower in the M1 group compared to the C1 group, the differences were minimal and not considered statistically significant.

On the first day after surgery, although some differences were observed between the groups of patients with uncomplicated echinococcosis (M2, C2), no statistically significant differences were found in ALT ($t=0.82$, $p>0.05$), AST ($t=0.12$, $p>0.05$), ALP ($t=0.78$, $p>0.05$), GGT ($t=0.67$, $p>0.05$), and amylase ($t=0.13$, $p>0.05$) levels.

On the first day after surgery, certain differences were observed in the protein metabolism indicators and bilirubin fractions. These differences were statistically analyzed between patients with complicated and uncomplicated echinococcosis.

Statistically significant differences were observed between the M1 and C1 groups of patients with complicated echinococcosis. One day before surgery, the albumin level in the C1 group was lower than in the M1 group ($t=0.80$, $p>0.05$), while the creatinine level in the C1 group was higher than in the M1 group ($t=0.35$, $p>0.05$), and the cholesterol level in the C1 group was also higher than in the M1 group ($t=0.45$, $p>0.05$). The CRP level was higher in the C1 group than in the M1 group ($t=0.43$, $p>0.05$), the TB level was higher in the C1 group than in the M1 group ($t=0.71$, $p>0.05$), the UCB level was higher in the C1 group than in the M1 group ($t=0.67$, $p>0.05$), the CB level was higher in the C1 group compared to the M1 group ($t=0.36$, $p>0.05$), however, no statistic significance was detected.

No significant differences were found between the C2 and M2 groups in protein metabolism indicators and bilirubin fractions among the groups of patients with uncomplicated echinococcosis 1 day after surgery. Thus, the albumin level was lower in the C2 group than in the M2 group ($t=0.29$, $p>0.05$), the creatinine level was higher in the C2 group than in the M2 group ($t=1.05$, $p>0.05$), the cholesterol level was lower in the C2 group than in the M2 group ($t=0.23$, $p>0.05$). The CRP level was lower in the C2 group than in the M2 group ($t=1.04$, $p>0.05$), the TB level was lower in the C2 group than in the M2 group ($t=1.14$, $p>0.05$), the UCB level was lower in the C2 group than in the M2 group ($t=0.67$, $p>0.05$), the CB level was lower in the C2 group than

in the M2 group ($t=1.25$, $p>0.05$), however, no statistic significance was detected.

On the first day after surgery, the concentration parameters of cytokines were also comparatively analyzed between the groups of patients with complicated and uncomplicated echinococcosis.

Slight differences between the groups with complicated echinococcosis were detected. Thus, the IL-1 level was lower in the C1 group compared to the M1 group ($t=3.35$, $p<0.01$), IL-6 was higher in the C1 group compared to the M1 group ($t=1.78$, $p>0.05$), IL-10 was lower in the C1 group compared to the M1 group ($t=0.56$, $p>0.05$), and the TNF- α level was lower in the C1 group compared to the M1 group ($t=0.48$, $p>0.05$). However, no statistically significant differences were found between the groups in terms of the cytokine concentration parameters. As for the IL-4 level, a statistically significant lower level was observed in the C1 group compared to the M1 group ($t=3.26$, $p<0.01$).

In patients with uncomplicated echinococcosis, we also determined the cytokine concentrations and found statistically significant differences in some parameters. The levels of IL-1 ($t=1.00$, $p>0.05$) and TNF- α ($t=0.98$, $p>0.05$) were higher in the C2 group compared to the M2 group, but the differences were not statistically significant. Statistically significant differences were observed in the other three parameters. Thus, the IL-4 level was statistically significantly higher in the C2 group compared to the M2 group ($t=2.50$, $p<0.05$), the IL-6 level was statistically significantly higher in the C2 group compared to the M2 group ($t=3.33$, $p<0.01$), and the IL-10 level was also statistically significantly higher in the C2 group than in the M2 group ($t=3.33$, $p<0.01$).

One day after surgery, certain differences in the levels of immunoglobulins were observed between the comparison and main groups of patients with complicated echinococcosis. Thus, the levels of IgA ($t=1.25$, $p>0.05$), IgG ($t=0.34$, $p>0.05$), and IgM ($t=1.43$, $p>0.05$) were higher in the C1 group compared to the M1 group, but no statistically significant differences were found.

One day after surgery, the levels of immunoglobulins were analyzed between the comparison and main groups of patients with uncomplicated echinococcosis. In this period, the IgA level was lower in the C2 group compared to the M2 group ($t=1.33$, $p>0.05$), but the difference was not statistically significant. On the other hand, the IgG level was statistically significantly higher in the C2 group compared to the M2 group ($t=2.22$, $p<0.05$), and the IgM level was also statistically significantly higher in the C2 group compared to the M2 group ($t=2.86$, $p<0.05$).

To monitor the dynamics of changes in the parameters we determined during the study, we repeated the examinations five days after the surgery. The differences in the biochemical parameters we analyzed became more pronounced. Thus, in patients with complicated echinococcosis, statistically significant differences were observed in most parameters five days after surgery. In the C2 group, the levels of ALT ($t=12.8$, $p<0.001$), AST ($t=11.9$, $p<0.001$), ALP ($t=10.4$, $p<0.001$), and GGT ($t=5.02$, $p<0.001$) were statistically significantly higher compared to the M2 group, which was the group treated with Immunofan. The level of amylase ($t=1.34$, $p>0.05$) was also lower in the C1 group compared to the M1 group, but the difference was not statistically significant. Thus, by the fifth day after surgery, a positive dynamic shift towards normalization of biochemical parameters was observed in the main group receiving Immunofan.

We also determined the same biochemical parameters in patients with uncomplicated echinococcosis. In the C2 group, the levels of ALT ($t=0.61$, $p>0.05$), ALP ($t=1.75$, $p>0.05$), and GGT ($t=0.80$, $p>0.05$) were slightly higher compared to the M2 group, but the differences were not statistically significant. The levels of AST ($t=0.29$, $p>0.05$) and amylase ($t=0.16$, $p>0.05$) in the C2 group were slightly lower compared to the M2 group, but these differences were also not statistically significant. As observed, five days after surgery, patients treated with Immunofan showed only slight positive changes in ALT, ALP, and GGT parameters.

Five days after the surgery, we also compared the protein metabolism indicators and bilirubin fractions between the complicated (C1, M1) and uncomplicated (C2, M2) groups.

Slight and significant differences were found between the groups of patients with complicated echinococcosis. Thus, albumin in the C1 group ($t=0.32$, $p>0.05$) was lower than in the M1 group, cholesterol ($t=0.22$, $p>0.05$) and CRP ($t=1.43$, $p>0.05$) were higher in the C1 group than in the M1 group. However, the differences were not statistically significant. The creatinine level was statistically significantly higher in the C1 group than in the M1 group ($t=2.23$, $p<0.05$). There were also certain differences detected in the bilirubin fraction. It was found that in the C1 group, the TB ($t=4.48$, $p<0.001$) and CB ($t=3.10$, $p<0.01$) were statistically significantly higher compared to the M1 group. However, the level of UCB in the C1 group ($t=1.61$, $p>0.05$) was statistically non-significantly higher compared to the M1 group.

Five days after surgery, we compared the protein metabolism indicators between the patient groups with uncomplicated echinococcosis. In the C2 group, the levels of albumin ($t=0.29$, $p>0.05$), creatinine ($t=1.40$, $p>0.05$), cholesterol ($t=0.18$, $p>0.05$), and CRP ($t=0.79$, $p>0.05$) were statistically non-significantly lower compared to the M2 group.

In patients with uncomplicated echinococcosis, the level of TB ($t=2.52$, $p<0.05$) in the C2 group was statistically significantly lower compared to the M2 group. However, the levels of CB ($t=0.34$, $p>0.05$) and UCB ($t=0.51$, $p>0.05$) were not statistically significantly higher in group C2 compared to group M2.

Five days after surgery, we also determined cytokine concentrations in patients with complicated and uncomplicated echinococcosis. Various changes in cytokine levels were detected in patients with complicated echinococcosis. Thus, only the level of IL-1 in group C1 was not statistically significantly lower compared to group M1 ($t=1.14$, $p>0.05$). However, the levels of IL-4 ($t=3.75$, $p<0.001$), IL-6 ($t=7.50$, $p<0.001$), IL-10 ($t=2.86$, $p<0.01$), and TNF- α

($t=4.6$, $p<0.001$) in group C1 were statistically significantly higher compared to group M1 (Table 4).

Table 4

Quantitative indicators of cytokine concentration and immunoglobulin parameters in patients with complicated (C1, M1) and uncomplicated (C2, M2) echinococcosis five days after surgery.

Parameters	C1 group (n=14)	M1 group (n=28)	C2 group (n=26)	M2 group (n=76)
IL-1	12.0±0.4	12.5±0.2	9.4±0.3	8.4±0.2
IL-4	9.0±0.3	7.5±0.2	7.5±0.3	6.2±0.1
IL-6	19.0±0.7	13.0±0.3	10.0±0.4	8.0±0.2
IL-10	16.0±0.6	14.0±0.3	10.0±0.4	8.5±0.2
TNF- α	14.0±0.5	11.0±0.2	11.0±0.4	7.5±0.2
IgA	6.5±0.2	5.2±0.1	5.8±0.2	5.3±0.1
IgG	11.0±0.4	11.1±0.2	10.0±0.4	9.0±0.2
IgM	3.1±0.1	2.2±0.1	3.0±0.1	2.8±0.1

We determined cytokine concentration parameters in patients with uncomplicated echinococcosis five days after surgery. Statistically significant differences were observed in all assessed cytokine parameters. Thus, the levels of IL-1 ($t=2.78$, $p<0.01$), IL-4 ($t=3.25$, $p<0.01$), IL-6 ($t=4.17$, $p<0.001$), IL-10 ($t=3.12$, $p<0.01$), and TNF- α ($t=7.12$, $p<0.001$) in group C2 were statistically significantly higher compared to group M2. However, in group C2, the levels of immunoglobulins IgA ($t=1.67$, $p>0.05$) and IgG ($t=1.43$, $p>0.05$) were not statistically significantly higher compared to group M2.

As can be seen, 5 days after surgery, positive trend differences in cytokine concentration parameters were prominent in the group of patients with uncomplicated echinococcosis against the background of Immunofan administration.

The studied parameters were analyzed comparatively between the groups of patients with complicated and uncomplicated echinococcosis ten days after surgery.

Ten days after surgery, the biochemical parameters of patients with uncomplicated and complicated echinococcosis were analyzed (Table 5).

Table 5
Quantitative indicators of biochemical parameters, protein metabolism parameters, and bilirubin fractions in patients with complicated (C1, M1) and uncomplicated (C2, M2) echinococcosis ten days after surgery

Parameters	C1 group (n=14)	M1 group (n=28)	C2 group (n=26)	M2 group (n=72)	Healthy indv. (n=14)
ALT	48.0±1.8	20.4±0.4	29.0±1.1	28.2±0.6	22.9±0.9
AST	45.0±1.6	18.4±0.4	28.0±1.0	27.4±0.6	21.6±1.2
ALP	124.0±4.5	81.0±1.6	100.0±3.7	100.5±2.0	176.6±1.4
GGT	42.0±1.5	26.0±0.5	27.0±1.0	26.5±0.5	21.4±1.4
Amylase	78.0±2.9	52.0±1.0	58.0±2.1	61.0±1.2	60.8±2.5
Albumin	38.0±1.4	45.0±0.9	45.0±1.6	44.0±0.9	42.6±0.6
Creatine	100.0±3.7	75.0±1.5	75.0±2.7	80.0±1.6	84.5±2.1
Cholesterol	210.0±7.7	180.0±3.6	158.0±5.9	160.0±3.2	184.6±4.2
CRP	12.0±0.4	5.0±0.1	8.0±0.3	6.0±0.1	3.6±0.2
TB	11.0±0.4	6.0±0.1	6.0±0.2	6.2±0.1	12.6±0.2
CB	5.0±0.2	2.5±0.1	3.2±0.1	3.0±0.1	2.71±0.07
UCB	9.0±0.3	7.1±0.2	7.6±0.3	8.0±0.2	10.54±0.2

As seen in the table, differences in all biochemical parameters, protein metabolism indicators, and bilirubin fractions between the main and comparison groups of patients with complicated echinococcosis were statistically significant. In group C1, the levels of ALT ($t=15.0$, $p<0.001$), AST ($t=16.1$, $p<0.001$), ALP ($t=8.77$, $p<0.001$), GGT ($t=10.1$, $p<0.001$), and amylase ($t=8.39$, $p<0.001$) remained statistically significantly higher compared to group M1. The fact that the biochemical parameters in the main group of patients with complicated echinococcosis were even lower compared to those observed in healthy individuals demonstrates the high effectiveness of the Immunofan preparation.

Ten days after surgery, the albumin level in the C1 group was statistically significantly lower than in the M2 group ($t=4.22$, $p<0.001$). Notably, the albumin level in the M2 group was also higher compared to healthy individuals ($t=4.22$, $p<0.001$). Additionally, in the C1 group, the levels of creatinine ($t=6.26$, $p<0.001$), cholesterol ($t=3.53$, $p<0.001$), C-reactive protein (CRP) ($t=14.1$, $p<0.001$), total bilirubin (TB) ($t=10.1$, $p<0.001$), conjugated bilirubin (CB) ($t=11.7$, $p<0.001$), and unconjugated bilirubin (UCB) ($t=4.75$, $p<0.001$) were statistically significantly lower compared to the M1 group. As seen in Table 5, certain differences were also observed when compared to healthy individuals. Thus, in the healthy group, the levels of creatinine (84.5 ± 2.1), cholesterol (184.6 ± 4.2), TB (12.6 ± 0.2), CB (2.71 ± 0.07), and UCB (10.54 ± 0.2) were higher than in the M1 group. However, the CRP level (3.6 ± 0.2) in the healthy group was found to be lower compared to the M1 group.

Biochemical parameters, protein metabolism parameters, and bilirubin fractions were also assessed in patients with uncomplicated echinococcosis. Ten days after surgery, all differences in biochemical parameters were statistically non-significant. In the C2 group, ALT ($t=0.64$, $p>0.05$), AST ($t=0.51$, $p>0.05$), ALP ($t=0.12$, $p>0.05$), GGT ($t=0.45$, $p>0.05$), and amylase ($t=1.25$, $p>0.05$) were statistically insignificantly higher compared to the M2 group. The albumin level in the C2 group was statistically insignificantly lower than in the M2 group ($t=0.55$, $p>0.05$). Additionally, creatinine ($t=1.59$, $p>0.05$) and cholesterol ($t=0.33$, $p>0.05$) levels in the C2 group were also insignificantly lower. However, it is noteworthy that the CRP level in the C2 group remained statistically significantly higher compared to the M2 group ($t=5.12$, $p<0.001$).

The TB fraction in the C2 group was statistically insignificantly lower compared to the M2 group ($t=0.67$, $p>0.05$). Similarly, the levels of CB ($t=1.43$, $p>0.05$) and UCB ($t=0.91$, $p>0.05$) in the C2 group were statistically insignificant compared to the M2 group.

When comparing the biochemical parameters in the C2 and M2 groups with those of healthy individuals, it was found that the values

in the main group (patients with uncomplicated echinococcosis) were closer to those of healthy individuals.

Protein metabolism parameters in the M2 group were also closer to those of the healthy group compared to the C2 group. The same trend was observed in the mean values of bilirubin fractions. In the main group, TB, CB, and UCB levels of the patients with uncomplicated echinococcosis were closer to those of healthy individuals.

Table 6

Quantitative indicators of immune parameters in patients with complicated (C1, M1) and uncomplicated (C2, M2) echinococcosis 10 days after surgery

Indicators	C1 group (n=14)	M1 group (n=28)	C2 group (n=26)	M2 group (n=72)	Healthy individuals (n=14)
IL-1	10.0±0.4	4.2±0.1	6.9±0.3	5.2±0.1	3.35±0.2
IL-4	8.6±0.3	3.5±0.1	6.9±0.3	4.0±0.1	3.8±0.2
IL-6	11.0±0.4	4.5±0.1	7.8±0.3	5.0±0.1	3.27±0.2
IL-10	10.0±0.4	5.0±0.1	7.7±0.3	5.5±0.1	13.2±0.6
TNF-α	9.6±0.4	4.2±0.1	6.8±0.2	4.6±0.1	4.2±0.2
IqA	6.1±0.2	2.2±0.1	4.3±0.2	3.2±0.1	1.6±0.1
IgG	8.5±0.3	5.2±0.1	8.0±0.3	6.0±0.1	11.5±0.7
IqM	2.5±0.1	1.1±0.1	2.7±0.1	1.4±0.1	1.08±0.1

Ten days after surgery, we also compared immune parameters. The results revealed significant differences in immune parameters between patients with complicated and uncomplicated echinococcosis. In the comparison group of patients with complicated echinococcosis, the IL-1 level was 10.0±0.4 pg/mL, while in the main group of patients with complicated echinococcosis, it was 4.2±0.1 pg/mL. In the comparison group of patients with uncomplicated echinococcosis, the IL-1 level was 6.9±0.3 pg/mL, whereas in the main group of patients with uncomplicated echinococcosis, it was 5.2±0.1 pg/mL. Among healthy individuals, the IL-1 level was recorded as 3.35±0.2 pg/mL. Notably, in the main group of patients with complicated echinococcosis, the IL-1 level was closer to that of healthy individuals.

Ten days after the surgery, the IL-4 level was 8.6 ± 0.3 pg/mL in the comparison group of patients with complicated echinococcosis, 3.5 ± 0.1 pg/mL in the main group of patients with complicated echinococcosis, 6.9 ± 0.3 pg/mL in the comparison group of patients with uncomplicated echinococcosis, 4.0 ± 0.1 pg/mL in the main group of patients with uncomplicated echinococcosis, and 3.8 ± 0.2 pg/mL in healthy individuals. Significant differences in IL-6 levels were also observed during this period. Thus, the IL-6 level was 11.0 ± 0.4 pg/mL in the comparison group of patients with complicated echinococcosis, 4.5 ± 0.1 pg/mL in the main group of patients with complicated echinococcosis, 7.8 ± 0.3 pg/mL in the comparison group of patients with uncomplicated echinococcosis, 5.0 ± 0.1 pg/mL in the main group of patients with uncomplicated echinococcosis, and 3.27 ± 0.2 pg/mL in healthy individuals.

The level of IL-10 was found to be 10.0 ± 0.4 pg/mL in the comparison group of patients with complicated echinococcosis, 5.0 ± 0.1 pg/mL in the main group of patients with complicated echinococcosis, 7.7 ± 0.3 pg/mL in the comparison group of patients with uncomplicated echinococcosis, 5.5 ± 0.1 pg/mL in the main group of patients with uncomplicated echinococcosis, and 13.2 ± 0.6 pg/mL in healthy individuals.

The level of TNF- α changed significantly across the groups 10 days after surgery. Thus, it was found to be 9.6 ± 0.4 pg/mL in the comparison group of patients with complicated echinococcosis, 4.2 ± 0.1 pg/mL in the main group of patients with complicated echinococcosis, 6.8 ± 0.2 pg/mL in the comparison group of patients with uncomplicated echinococcosis, 4.6 ± 0.1 pg/mL in the main group of patients with uncomplicated echinococcosis, and 4.2 ± 0.2 pg/mL in healthy individuals.

When comparing cytokine concentrations in patients with complicated echinococcosis, statistically significant differences were found between the C1 and M1 groups. It was found that in the C1 group, IL-1 ($t=9.67$, $p<0.001$), IL-4 ($t=11.6$, $p<0.001$), IL-6 ($t=13.1$, $p<0.001$), IL-10 ($t=10.1$, $p<0.001$), and TNF- α ($t=10.6$, $p<0.001$) were statistically significantly higher than in the M1 group.

Statistically significant differences were also found in the average levels of immunoglobulins between the main and comparison groups of patients with complicated echinococcosis. Thus, the levels of IgA ($t=13.1$, $p<0.001$), IgG ($t=6.87$, $p<0.001$), and IgM ($t=10.1$, $p<0.001$) were statistically significantly higher in the C2 group compared to the M2 group.

All differences between the main and comparison groups of patients with uncomplicated echinococcosis were also statistically significant. Thus, in the C2 group, cytokine concentration parameters IL-1 ($t=3.51$, $p<0.001$), IL-4 ($t=7.25$, $p<0.001$), IL-6 ($t=7.02$, $p<0.001$), IL-10 ($t=5.50$, $p<0.001$), and TNF- α ($t=7.33$, $p<0.001$) remained statistically significantly higher than in the M2 group. Similarly, in the C2 group of patients with uncomplicated echinococcosis, the mean levels of immunoglobulins IgA ($t=3.67$, $p<0.01$), IgG ($t=5.10$, $p<0.001$), and IgM ($t=9.28$, $p<0.001$) remained statistically significantly higher in the M2 group (Table 6).

As seen in the table, the immune indicators in both complicated and uncomplicated echinococcosis patients from the main group were closer to the mean values observed in healthy individuals compared to the corresponding parameters in the comparison group.

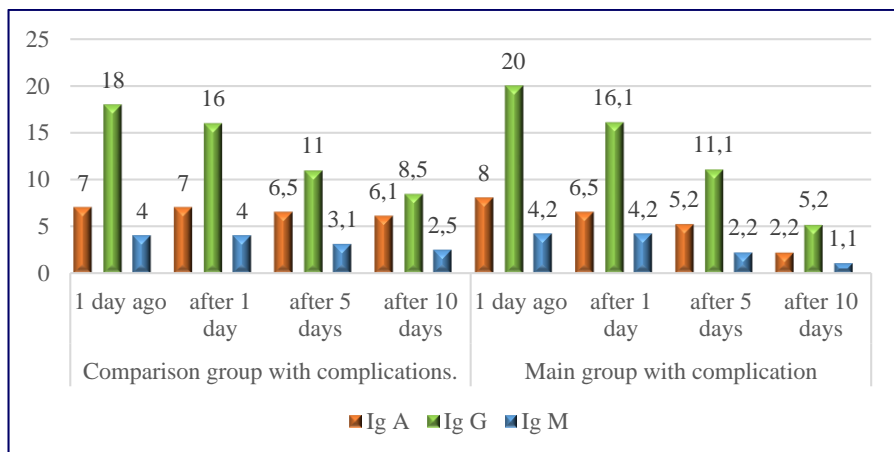


Figure 1. Description of the dynamics of immunoglobulin level changes in patients with complicated echinococcosis in the main and comparison groups before surgery and on the 1st, 5th, and 10th days after surgery

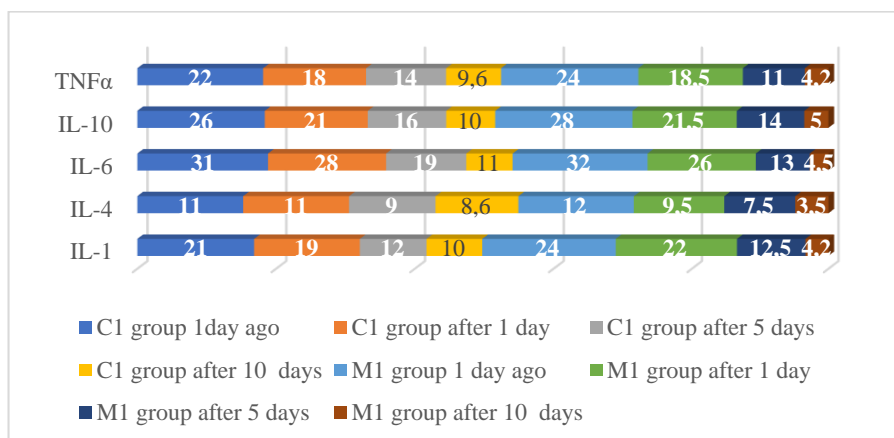


Figure 2. Description of the dynamics of cytokine level changes in patients with complicated echinococcosis in the main and comparison groups before surgery and on the 1st, 5th, and 10th days after surgery

Statistically significant differences were found in all immunoglobulin levels examined 10 days after surgery.

In the C1 group, the IgG level was statistically significantly higher compared to the M1 group ($t=6.87$, $p<0.001$). The levels of IgA ($t=13.1$, $p<0.001$) and IgM ($t=10.1$, $p<0.001$) were also statistically significantly higher in the C1 group compared to the M1 group.

Thus, statistically significant differences were achieved between the indicators of cytokine concentration and immunoglobulin levels in patients with severe forms of hepatic echinococcosis. Thus, although there were no statistically significant differences between the indicators one day before the operation, statistically significant positive dynamics were observed in some indicators, for example, IL-1, IL-6, and TNF- α levels, one day after the operation. IgA and IgM were already statistically significantly lower in the main group in patients with severe hepatic echinococcosis than in the comparison group 1 day after surgery. On days 5 and 10 after surgery, statistically significant lower differences were observed in the main group for almost all immune parameters. On day 5 after surgery, only IgG indicators were statistically insignificantly lower in the main group than in the comparison group.

Thus, when comparing the effectiveness of Immunofan in immune correction in severe forms of hepatic echinococcosis, it was found that the immune parameters changed in positive dynamics, and differences were detected already on the first postoperative day, although statistically insignificant. On the 10th postoperative day, all differences became statistically significant, and an intensive decrease with positive dynamics was observed in the main group. It is of great importance to control the level of CRP and cytokines before surgery and to start treatment with Immunofan early.

When comparing two groups (n=14 and n=28) of patients with severe hepatic echinococcosis, biochemical parameters such as ALT, AST, GGT, CRP, and cytokines like IL-1, IL-6, TNF- α , and IgA levels were assessed. These parameters were analyzed against normal levels in patients from the C1 and M1 groups with severe hepatic echinococcosis. To conduct these analyses, the average values obtained before surgery and 10 days after the administration of the "Immunofan" preparation were used.

Table 7

Mean values of biochemical and immune parameters in patients with severe (C1, M1) echinococcosis and normal values of these parameters

Parameters	C1 group (n-14)		M1 group (n=28)		Normal parameters
	b/s,	a/s	b/s	a/s	
ALT, U/l	95.2	48	98.4	20.4	10-40
AST, U/l	96.4	45	98.4	18.4	15-45
GGT, IU/l	64	42	65	26	10-40
CRP, mg/dL	31	12	34	5	1-5
IL-1, pg/mL	21	10	24	4.2	1-6
IL-6, pg/mL	31	11	32	4.5	1-6
TNF- α , pg/mL	22	9.6	24	4.2	1-6
IgA, g/L	7	6.1	8	2.2	0.5-2.5

Note: b/s – before surgery, a/s – 10 days after surgery

As shown in Table 7, the ALT, AST, and GGT levels in the C1 and M1 groups were significantly different before surgery. However, 10 days after surgery, the levels in patients of the M1 group, who had received Immunofan, returned to normal. In the C1 group, the CRP level decreased by 52.5% compared to the pre-surgery levels, while in the M1 group, it decreased by 82.5%. The CRP level in the M1 group returned completely to the normal range 10 days after surgery.

In the C1 group, IL-1 decreased by 53.4% after surgery, while in the M1 group, it decreased by 82.5%. The average level of IL-6 decreased by 64.6% in the C1 group and by 86% in the M1 group, reaching normal levels in the M1 group. The average TNF- α level decreased by 56.4% in the C1 group and by 82.5% in the M1 group. In both groups, this parameter returned to normal 10 days after surgery. The IgA level decreased by 12.9% in the C1 group and by 72.5% in the M1 group. Contrary to the C1 group, the IgA level in the M1 group completely returned to normal.

Thus, in patients with severe echinococcosis, biochemical and immune parameters returned to normal more rapidly, significantly, and markedly against the background of treatment with Immunofan.

In patients with uncomplicated hepatic echinococcosis from the comparison (n=26) and main groups (n=72) (C2, M2 groups), the average levels of biochemical parameters such as ALT, AST, GGT, and CRP, as well as cytokines like IL-1, IL-6, TNF- α , and IgA, were compared with normal values.

In patients with uncomplicated echinococcosis, biochemical and immune parameters returned to normal with Immunofan treatment. In the C2 and M2 groups, ALT, AST, and GGT levels were significantly different before surgery. However, 10 days after surgery, these indicators returned to normal in the M2 group, which received Immunofan. The CRP level decreased by 42.9% in the C2 group and by 60% in the M2 group compared to pre-surgery values. The CRP level in the M2 group completely returned to normal 10 days after surgery. IL-1 decreased by 55.5% in the C2 group and by 69.7% in the M2 group after surgery. The mean IL-6 level decreased by 51.5% in the C2 group and by 69.7% in the M2 group, reaching normal levels

in the M2 group. The mean TNF- α level decreased by 57.5% in the C2 group and by 75.8% in the M2 group (Table 8).

Table 8

Average values of biochemical and immune parameters in patients with uncomplicated echinococcosis and normal values of these parameters

Parameters	C2 group (n=26)		M2 group (n=72)		Normal parameters
	b/s	a/s	b/s	a/s	
ALT, U/l	60	29	64.2	28.2	10-40
AST, U/l	60	29	64.2	27.4	15-45
GGT, IU/l	44	27	46	26.5	10-40
CRP, mg/dL	14	8	15	6	1-5
IL-1, pg/mL	15.5	6.9	15	5.2	1-6
IL-6, pg/mL	16	7.8	16.5	5	1-6
TNF, pg/mL	16	6.8	19	4.6	1-6
IgA, g/L	6.4	4.3	6.5	3.2	0.5-2.5

Note: b/s – before surgery, a/s – 10 days after surgery

The mean TNF- α level decreased by 57.5% in the C2 group and by 75.8% in the M2 group. In both groups, this parameter returned to normal levels 10 days after surgery. The IgA level decreased by 32.9% in the C2 group and by 50.8% in the M2 group. Unlike the M2 group, in the M2 group, it completely returned to normal levels.

Thus, in patients with complicated echinococcosis, biochemical and immune parameters returned to normal more rapidly and markedly with Immunofan treatment.

CONCLUSIONS

1. Based on the preoperative analysis results, the biochemical indicators in patients of the comparison group with uncomplicated echinococcosis, increased by 10-35%, CRP by 65%, cytokines by 60-65%, and IgA by 61%. In the patients of the main group with uncomplicated echinococcosis, biochemical indicators increased by 15-40%, CRP by 67%, cytokines by 60-70%, and IgA by 62%. In the patients of the comparison group with complicated echinococcosis, biochemical indicators increased by 35-60%, CRP by 84%, cytokines (IL-1, IL-6, TNF) by 70-85%, and IgA by 65%. In the patients of the main group with complicated echinococcosis, biochemical indicators increased by 37-60%, CRP by 85.3%, cytokines by 75-85%, and IgA by 68.8% (8,12,15).
2. Ten days after surgery, biochemical indicators in patients with uncomplicated echinococcosis in the comparison group decreased by 35-60%, and CRP by 43%. In patients with uncomplicated echinococcosis in the main group, biochemical indicators decreased by 40-60%, and CRP by 60%. In patients with complicated echinococcosis in the comparison group, biochemical indicators decreased by 30-55%, and CRP by 62%, while in the main group, biochemical indicators decreased by 60-85%, and CRP by 86%. As a result, in patients with uncomplicated echinococcosis in the main group, biochemical indicators improved by 3-5% and CRP by 17% compared to the comparison group. In patients with complicated echinococcosis in the main group, biochemical indicators improved by 25-30% and CRP by 24% compared to the comparison group (9,10,12,17,18).
3. Ten days after surgery, cytokine levels in patients with uncomplicated echinococcosis in the comparison group decreased by 50-60%, while in the main group, they decreased by 65-80%. In patients with complicated echinococcosis in the comparison group, cytokine levels decreased by 55-60%,

whereas in the main group, they decreased by 80-90%. As a result, cytokine levels in patients with uncomplicated echinococcosis in the main group showed a 15-20% improvement compared to the comparison group. In patients with complicated echinococcosis in the main group, a 25-30% improvement was observed in dynamics compared to the comparison group (2,3,5,6,16,19).

4. Ten days after surgery, IgA levels in patients with uncomplicated echinococcosis in the comparison group decreased by 32.9%, while in the main group, they decreased by 50.8%. In patients with complicated echinococcosis in the comparison group, IgA levels decreased by 12.9%, whereas in the main group, they decreased by 72.5%. As a result, IgA levels in patients with uncomplicated echinococcosis in the main group showed an 18% improvement compared to the comparison group. In patients with complicated echinococcosis in the main group, a 60% improvement in IgA levels was observed compared to the comparison group (4,7,10,16,19).

PRACTICAL RECOMMENDATIONS

1. The necessity of studying the cytokine profile in patients diagnosed with liver echinococcosis at both the diagnostic and treatment stages has been confirmed.
2. The use of the drug Immunofan in postoperative complex therapy is recommended to improve treatment outcomes in patients diagnosed with complicated liver echinococcosis.
3. In patients diagnosed with complicated liver echinococcosis, it is recommended to administer Immunofan (1 ml ampoule, 50 µg daily dose) intramuscularly for 7 days as part of postoperative complex therapy.

LIST OF PUBLISHED SCIENTIFIC WORKS ON THE TOPIC OF THE DISSERTATION

1. P.M. Abbasəliyeva, M.Y. Nəsirov Qaraciyər exinokokkozunun laparoskopik müalicə metodunun müasir vəziyyəti // – Bakı: Cərrahiyyə, – 2014. № 3 (39), – s.71-74.
2. P.M. Abbasəliyeva, M.Y. Nəsirov, R.B. Abbasaliyev, Nəbiyeva E.V. Qaraciyər exinokokkozunda əməliyyatdan sonrakı dövrdə sitokinlərin vəziyyəti // Tibb elmləri doktoru, Professor Əliağa Məmməd oğlu Əlizadənin anadan olmasının 100 illik yubileyinə həsr olunmuş elmi-praktik konfransın materialları, – Bakı, – 2015, – s.103.
3. P.M. Abbasəliyeva Qaraciyər exinokokkozunun cərrahi müalicəsinin effektivliyində sitokin profilinin və immunitetin rolu // – Bakı: Azərbaycan Tibb Jurnalı, – 2015. № 1, – s.152-157.
4. P.M. Abbasəliyeva, B.B. Abbasəliyev, B.N. Abbasəliyev Qaraciyər exinokokkozunun immundiagnostikasında və molekulyar diaqnostikasında yeni təkmilləşdirmələr // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, – 2017. № 3, – s.10-15.
5. P.M. Abbasəliyeva, R.B. Abbasəliyev, M.Y. Nəsirov Qaraciyər açıq exinokokkektomiya əməliyyatından sonra immün markerlərin dəyişməsi // Tibb elmləri doktoru, professor, Surxay Heydər oğlu Axundovun anadan olmasının 120 illiyinə həsr edilmiş elmi-praktik konfransın materialları. – Bakı, – 2017, – s. 130-131.
6. P.M. Abbasaliyeva, M.Y. Nasirov, R.B. Abbasaliyev The effectiveness of Immunofan during surgical treatment of liver echinococcus in the perioperative period // Abstracts of the XVIII international Euroasian congress of surgery and hepatogastroenterology, – Baku, –11-14 september – 2019. – s.199.
7. Abbasəliyeva P.M., Nəsirov M.Y., Abbasəliyev R.B., Qasımov A.Ş. Əməliyyatdan sonrakı dövrdə qaraciyər exinokokkozunun

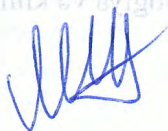
- cərrahi müalicəsi zamanı immunofanın tətbiqinin effektivliyi // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, – 2019. № 3, – s.48-52.
8. P.M. Abbasəliyeva Exinokokkoz sistləri olan pasiyentlərin, əməliyyat öncəsi bəzi fermentlərinin qanda miqdarı // – Bakı: Cərrahiyyə, 2019. № 2-3, – s.65-68.
 9. P.M. Abbasəliyeva Exinokokektomiya əməliyyatından sonrakı müxtəlif dövrlərdə, pasiyentlərin qan nümunələrində fermentlərin miqdarına immunomodulyatorların təsiri // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, 2021. № 4, – s.119-125.
 10. P.M. Abbasəliyeva, M.Y. Nəsirov Exinokokkoz sistləri olan pasiyentlərə əməliyyatdan sonrakı müxtəlif dövrlərdə immunomodulyatorların təsiri // – Bakı: Sağlamlıq, – 2021. № 3, – s. 58-63.
 11. П.М. Аббасалиева Современная оценка проблем диагностики и комплексного лечения эхинококкоза печени // – Полтава: Актуальні проблеми сучасної медицини, – 2021. Том 21, Випуск 4 (76), – с. 3-9.
 12. P.M. Abbasəliyeva, M.Y. Nəsirov Qaraciyərində exinokokkozu olan pasiyentlərin və sağlam şəxslərin qan nümunələrində mübadilə məhsullarının səviyyə göstəriciləri // – Bakı: Əziz Əliyev adına elmi-praktik jurnal “Tibb və Elm”, – 2021. № 4 (26), – s.60-65.
 13. П.М. Аббасалиева Диагностика и коррекция функциональных нарушений у больных с эхинококкозом печени // Вопросы образования и науки, – Част 2, – Тамбов, –30 октября 2021. – с.5-6.
 14. P.M. Abbasalievа Improvement of treatment and prevention of liver echinococcosis // – Миколаїв: Український журнал медицини, біології та спорту, – 2022, vol.7, Випуск 3, –с.18-26.
 15. P.M.Abbasəliyeva Exinokokkektomiya əməliyyatından əvvəl və sonra mübadilə məhsullarına immunomodulyatorların təsiri

// “Şuşa ili - 2022” III Qarabağ Beynəlxalq Konfransı. – Bakı, 7-10 iyun, – 2022. – s.

16. P.M. Abbasəliyeva Qaraciyər exinokokkozunun formalarından asılı olaraq, əməliyyatdan sonra immun parametrlərin dəyişməsinə İmmunofan preparatının təsiri // – Bakı: Azərbaycan təbabətinin müasir nailiyyətləri, – 2024. N1, – s.248-253
17. P.M. Abbasəliyeva Exinokokkozun müalicəsinin optimallaşdırılmasının biokimyəvi markerlərə təsirinin müqayisəli təhlili // - Bakı: Cərrahiyyə, – 2024. №1, – s.47-50
18. P.M. Abbasəliyeva, M.Y.Nəsirov, B.B.Abbasəliyev Qaraciyər exinokokkozunun formalarından asılı olaraq əməliyyatdan sonra biokimyəvi parametrlərin dəyişməsinə İmmunofan preparatının təsiri // Azərbaycan metabolizm jurnalı, – 2024, N 1, – s.24-31
19. P.M.Abbasəliyeva, M.Y. Nəsirov, R.B.Abbasəliyev Qaraciyər exinokokkozu zamanı əməliyyatdan sonrakı dövrlərdə İmmunofan preparatının sitokinlərin qatılığı və immunqlobulinlərin səviyyəsinə təsiri // – Bakı: Azərbaycan allergologiya və klinik immunologiya jurnalı, – 2024, №2, – s.

ABBREVIATIONS

ALP	– alkaline phosphatase
ALT	– alanine aminotransferase
AST	– aspartate aminotransferase
CB	– conjugated bilirubin
CRP	– C-reactive protein
IgA	– immunoglobulin A
IgG	– immunoglobulin G
IgM	– immunoglobulin M
IL-1	– interleukin 1
IL-10	– interleukin 10
IL-4	– interleukin 4
IL-6	– interleukin 6
GGT	–Gamma-glutamyl transferase
UB	–unconjugated bilirubin
TNF-α	– tumor necrosis factor
ÜB	–total bilirubin



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