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**RHEUMATIC MANIFESTATIONS IN PARASITIC
INFECTIONS**

321.04 – RHEUMATOLOGY

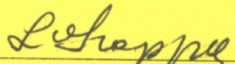
Summary of PhD thesis in medical sciences

Chişinău, 2024

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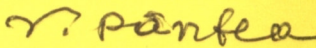
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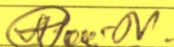


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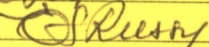
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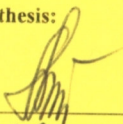


PhD thesis defense will take place on 4 December 2024, at the premises of SUMPh "Nicolae Testemițanu", 165 Ștefan cel Mare și Sfânt blvd., office 205, at 14.00 at the meeting of the Commission for public defence of the doctoral thesis, approved by the decision of the Scientific Council of the Consortium on 26 June 2024, no. 41.

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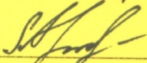
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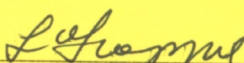
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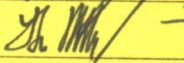


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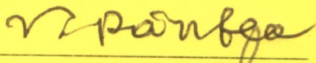


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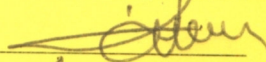


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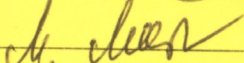
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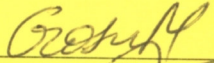
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ESSENTIAL ASPECTS OF RESEARCH

The current information and importance of the topic. Parasites are a current global problem with an increased prevalence in underdeveloped countries. According to a study carried out by the World Health Organization, in 2010, 48,4 million cases of parasitic diseases were estimated, of which 59,724 died [4, 9].

In the Republic of Moldova, parasitic diseases have a high incidence among infectious diseases, following acute respiratory infections and acute diarrheal diseases. During 2021, 7,483 cases of infestations with various helminth species were reported, compared to 11,781 in 2019. The comparative evaluation with the year 2019 is more representative, because in the year 2020, on the background of the outbreak of the SARS-COV-2 pandemic and the suspension of many medical services including prophylactic examinations, the cases of detected invasions, were also essentially reduced. Of the total number of cases, 69,5% were registered among the rural population. The major share, 87,9%, belongs to children up to 17 years old (in 2020, it was 89,3%) [5, 17, 22].

In addition to the gastrointestinal, visceral, encephalic, skin manifestations, in parasitosis, the musculoskeletal system is also affected [3, 9, 11].

The main pathogen agents involved are: *cestodes* (*teniosis*, *echinococcosis*); *trematodes* (*schistosomiasis*, *opisthorchosis*); *nematodes* (*toxocarosis*, *hookworm*, *strongyloidosis*, *filariasis*, *dranculosis*); *protozoa* (*giardiasis*, *toxoplasmosis*) [24, 28].

In the last 10 years, remarkable progress has been achieved in researching the field of parasitology. Discoveries of new interleukins and their cellular networks have reorganized information about how parasites and the human immune system work together to produce protection against infection/reinfection or how parasites manage to survive in the human body for long periods of time. But all these discoveries are insufficient to solve the existing problems due to gaps in the control system of many infections, which reduces the quality of daily life [8, 10, 13].

Impairment of the musculoskeletal system from parasitic infections are rare diseases, with an endemic tendency, more common in tropical countries. Of course, the Republic of Moldova is not considered an endemic area for parasitic pathologies with serious musculoskeletal disorders, but, with the migration and seasonal travels of the population, many diseases considered exotic are more and more common in our country. In the Republic of Moldova, the most common parasites, in which alterations of the musculoskeletal system have been observed, are infections caused by *Echinococcus granulosus* (the average morbidity index for the republic in the last decade is 4,3%) [15, 18], *Giardia lamblia* (4,86%) [5, 22], *Toxocara canis* (24,6%) [12, 26].

Although in the specialized literature many clinical cases of locomotor system damage in parasitic infections are described, there is a lack of systematic research capable of providing valuable summaries (both nationally and internationally) for the development of early management tactics in diagnosis and treatment musculoskeletal conditions in parasitosis.

Purpose of the paper: was to research the clinical-evolutionary and paraclinical particularities of cases of parasitic infections, associated with locomotor system disorders, for the proposal of early diagnostic principles of osteo-articular disorders in parasitic pathologies.

To meet the requirements of the theme, we have achieved the following **research objectives:** research of the clinical and evolutionary peculiarities of arthritis in parasitosis; evaluation of immuno-inflammatory indices of arthritis in parasitosis; comparative characterization of locomotor system impairments in various parasitic infections through imaging investigations; characteristic of early diagnostic features of arthritis in parasitosis, determining the impact on quality of life in parasitic reactive arthritis.

The methodology of scientific research. The type of study was clinical and analytical. Inclusion and exclusion criteria were used to select patients for the study. The patient groups studied were homogeneous and comparable. Data accumulation was of the "case-control" type. From an ethical point of view, the study did not include elements of human experimentation, and the evaluation criteria did not change throughout the study. The analysis of the obtained data was performed at the end of the study. Considering the presence, in the statistical examination, of groups with several types of variants (nominal and scaling), they were processed separately. The obtained data were statistically processed through variational, regression, clusterian, multiple scanning, factorial correlation ANOVA (ANalysis Of VAriance) analyses, calculating the arithmetic mean (M), standard error (ES) and mean standard deviation (SD), coefficients of parametric correlation (r) and nonparametric Spearman, Kendall Tau, gamma (Rr). Differences in arithmetic means (P) were compared using Student's test (t). Methodological support was provided by using the methods presented in the works of well-known specialists in the field.

Scientific novelty and originality. This study represents a landmark in the research of parasitic reactive arthritis, because for the first time a comparative evaluation was made between the clinical manifestations of different forms of invasive agents responsible for these conditions. The research made a significant contribution by investigating the relationship between laboratory and instrumental manifestations and how they influence the clinical course of parasitic reactive arthritis. The impact of reactive parasitic arthritis on the patients' quality of life was also evaluated, analyzing not only the physical but also the social, mental and emotional aspects. The pain, both chronic and acute, generated by the inflammatory process, was a central aspect in this analysis, providing a deeper understanding of how this condition influences different areas of daily life.

The scientific problem solved in the thesis: The study brought new opportunities for the differential diagnosis of parasitic reactive arthritis, both clinically and paraclinically. In this way, a specific pattern of reactive arthritis manifestations was identified in the context of parasitosis, contributing to a better understanding of the clinical and etiological diversity of this pathology. This discovery allows a more precise differentiation between the etiological forms of the disease, facilitating the choice of a more personalized and effective therapeutic approach.

The theoretical significance: The results obtained from this study constitute a significant scientific foundation for the development of diagnostic algorithms aimed for the early identification of musculoskeletal disorders associated with parasitosis. These algorithms are essential for rapid and accurate diagnosis, which can greatly improve patient prognosis and reduce long-term complications. The theoretical contribution of the study provides solid support for future research in the field of parasitic reactive arthritis, being of major importance to clinicians in the appropriate management of these complex conditions.

Application value of the study: The obtained data according to the different expressions of the clinical-paraclinical manifestations in parasitic reactive arthritis will allow establishing the diagnosis and launching an appropriate treatment. The results of the conducted study will contribute to predicting the effect of antiparasitic drugs, indicated for different forms of parasitic reactive arthritis, operating on the basis of the incriminated pathogen.

Implementation of the scientific results: The results of the study were included in the clinical activity of the rheumatology and arthrology sections of "Timofei Moşneaga" Republican Clinical Hospital, the rheumatology section of "Sfânta Treime" Clinical Hospital and in the didactic activity of the Department of Internal Medicine, Discipline of Rheumatology and Nephrology.

Approval of scientific results: The results of the thesis were discussed, approved and recommended for presentation at the meeting of the Discipline of Rheumatology and Nephrology of

"Nicolae Testemitanu" State University of Medicine and Pharmacy (meeting no. 4 of 03.04.2024), at the Scientific Seminar of Profile 321, specialty 321.04 - Rheumatology (meeting no. 10 of 15.04.2024). The results of the study were reported at 18 national and international forums. The materials of the study were reflected in 16 scientific publications, including 4 articles, - all in peer-reviewed journals, in presentations and summary communications at 14 international and 4 national scientific conferences.

Key words: parasitic reactive arthritis, manifestations, particular clinical forms, giardiasis, toxocarosis, echinococcosis.

Summary of the thesis. The work is presented on 163 pages in electronic text, 124 pages in basic text and is divided as follows: introduction, 5 chapters of own research, conclusions and practical recommendations; the bibliography cites 216 literary sources. The thesis is illustrated with 23 tables, 24 figures and 11 appendices. The study received the favorable approval of the Research Ethics Committee (No. 83 of 19. 06. 2018) of the "Nicolae Testemițanu" State University of Medicine and Pharmacy. The research subjects signed the informed consent to participate in the study.

1. UPDATES IN THE CLINICAL-PARACLINICAL EVOLUTION OF REACTIVE PARASITIC ARTHRITIS

Reactive parasitic arthritis is associated with the infestation of the patient's body by parasitic species of worms and protozoan microorganisms. It has been established that parasitic reactive arthritis can be caused by almost any species of these agents. In most situations, they accompany such parasitic diseases as echinococcosis, taeniasis, schistosomiasis, filariasis, dracunculosis [9, 11].

There are two main mechanisms by which arthritis in parasitosis can develop. The simplest of them is when the parasite itself or its eggs are in the joint cavity or in the surrounding tissues. There may also be joint damage with antibodies produced against the invading parasite, located in the body, but in a completely different organ.[6, 14, 24].

Parasites stimulate the release of cytokines, which promote Th2 polarization and the production of specific Th2 cytokines, which mediate the humoral immune response and the type 2 inflammatory response, thus resembling the immunopathological mechanisms in seronegative spondyloarthritis. The development of regulatory T cells (Treg) is also stimulated during parasitic infection, which enhances the costimulatory effect through the release of regulatory cytokines. In addition, IL 4-specific cytokines induce parasite-specific immunoglobulin E (IgE) activation and mobilization of innate immune systems, including mast cells, eosinophils, and basophils [7, 8, 20, 27].

Most authors attest that reactive parasitic arthritis is manifested by arthralgias, hyperemia, joint swelling and dysregulation of their function, including morning stiffness. The clinical picture includes signs characteristic of seronegative spondylarthropathy, which includes reactive arthritis and psoriatic arthritis. Among the distinctive features of parasitic reactive arthritis, also found in spondylarthropathies, we find enthesitis which is the inflammation of the insertion sites of the tendon, ligament and joint capsule on the bone, dactylitis – swelling and true inflammation of the fingers, associated by an asymmetric involvement of the joints in the inflammatory process, and sometimes with oligoarthritis and iritis presentation. It is not associated with oral ulcers, urethritis, but has a multitude of intestinal symptoms. Fibrosis and ankylosis of small joints are rarely determined. Early ankylosis of the proximal interphalangeal joints can manifest only in the severe evolution of the disease. Arthritis in parasitosis has a gradual onset, usually affects the lower extremities, and is less associated with periartthritis [1, 2, 4, 7, 15, 29].

At the present time, according to the data of the world literature, the diagnosis of parasitic reactive arthritis is a clinical one, since there are no paraclinical or instrumental tests with pathognomonic value, but the damage must be suspected in any patient with arthritis or inflammatory,

asymmetric tendinitis. The scientists note that the evaluation of such a patient should include a careful investigation for the existence of a precipitating episode in the history: for example, a diarrhea or abdominal disturbances. On physical examination, the distribution of joint and tendinous lesions should be carefully noted, as well as possible extra-articular lesions: eyes, mucous membranes, skin, nails, lungs and liver [11, 16, 19, 25].

The study of laboratory data according to specialized literature data can show the following relevance: the values of acute phase reactants, including ESR and PCR (C-reactive protein), are usually increased, but, after the inflammation subsides, they return at the normal level; other laboratory examinations can distinguish a normochromic anemia with normocytosis, leukocytosis and mild thrombocytosis in the acute phase [9, 12, 20, 30]. Urinalysis may reveal an aseptic pyuria; immunological markers: total Ig E, ELISA - *Giardia lamblia* antigen in faeces, anti-*G. lamblia* IgM, IgG, IgA, ELISA – IgG antibody to *Echinococcus granulosus*, *E. granulosus* antibodies, ELISA – IgG antibody to *Toxocara canis*, *T. canis* antibodies and of other parasitic infections; complex coproparasitological examination; coprocytogram; rheumatoid factor, anti-citrullinated protein antibodies and antinuclear antibodies are negative. Currently, the world medical community is guided in establishing the diagnosis of reactive parasitic arthritis by two sets of criteria. One of these includes the general clinical criteria of seronegative spondyloarthritis, and the second – serological confirmation of parasitic infestations [3, 11, 21, 23, 30].

2. MATERIALS AND RESEARCH METHODS

2.1. Clinical and status characteristics of the study group

To achieve the objectives in the described study, we selected a group of 161 patients with the definite diagnosis of reactive parasitic arthritis, established in two stages of correspondence according to specific and serological criteria. The first stage included the correspondence of the diagnosis according to the criteria of inflammatory osteoarticular damage. The second stage of defining the diagnosis aimed at the correspondence according to the positive results of the serological or parasitological diagnosis, definitively positive. The type of study was of a clinical and analytical observational case-control type.

The patients were treated in the rheumatology and arthrology departments of "Timofei Moşneaga" Republican Clinical Hospital and rheumatology of "Sfânta Treime" Clinical Hospital in Chisinau (Discipline of rheumatology and nephrology) during 2017-2022. All patients were divided into three observation groups, differentiated according to the pathogen of infestation and the clinical variant of parasitic reactive arthritis. The first group (97 patients) it consisted of patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* infestation, the second (31 patients) – patients with parasitic reactive arthritis on the background of *Toxocara canis* and the third (33 patients) included patients with parasitic reactive arthritis on the background of *Giardia lamblia* infestation (Figure 1).

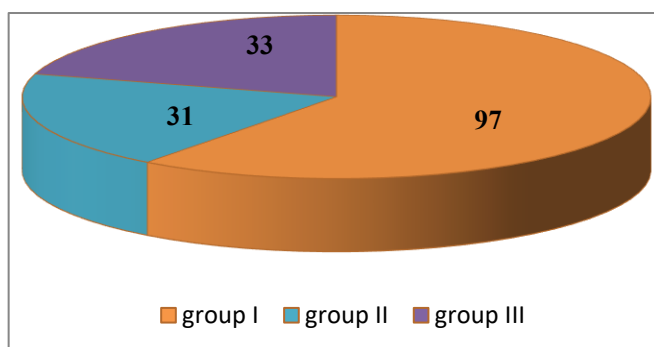


Figure 1. Distribution of patients according to study groups

The patients in the studied groups were thoroughly evaluated clinically and paraclinically, according to an extensive examination program, presented and described in the study design (Figure 2), which would quantify the level of presentation and clinical-paraclinical progression of parasitic reactive arthritis.

The diagnosis of parasitic reactive arthritis is made in two stages. The first stage consisted in the definition of an inflammatory (clinical-paraclinical) articular process, unclassifiable according to the diagnostic and classification criteria for seropositive (RA) and seronegative (AS, ReA, PsA) arthritis. The second stage – clinical and laboratory confirmation of the specific parasitic invasion and the existence of the correlation with the joint syndrome.

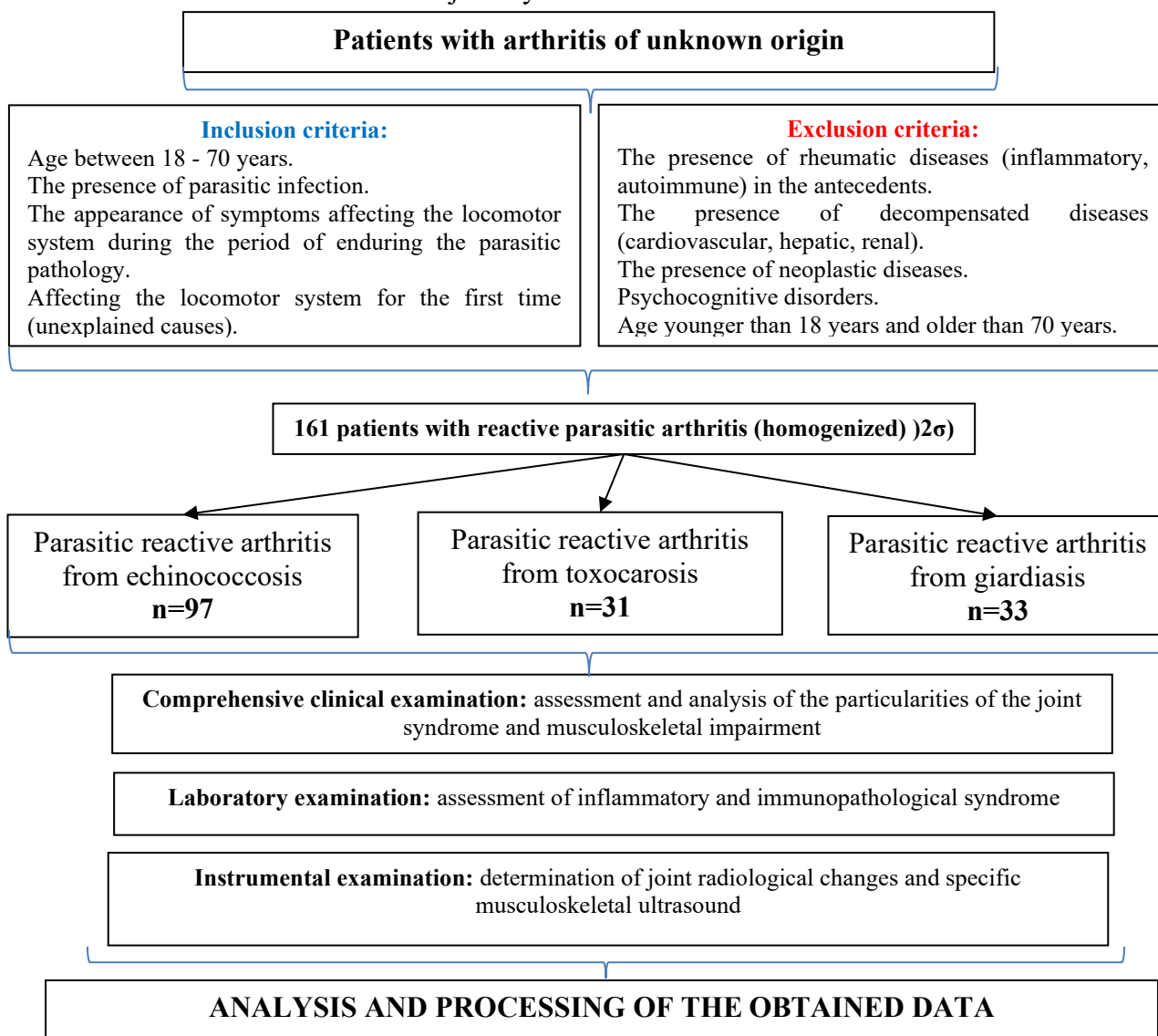


Figure 2. Study design

2.2. Statistical analysis of the results

We determined the required number of patients for the research group using the following formula:

$$n = (Z)^2 \frac{P(1-P)}{e^2} \quad (1)$$

Where: the prevalence of musculoskeletal pathologies, found in parasitosis, is up to 3,0% (P=0,03); Z = 1,96 for the 95,0% confidence interval; e – the accepted error of 5,0% (e=0,05); $n=0,03 \times 0,97 (1,96/0,05)^2=43,79$, design effect = $44,72 \times 1,5 = 67$ and with a 10,0% non-response

rate, the representative group will constitute $(67/0,90) = 74$ respondents with locomotor pathology of parasitic etiology.

The data obtained as a result of program investigations were processed computerized by methods of variational, correlational and discriminant analysis [29, 38, 115, 149], using the STATISTICA StatSoft 9,0 software for Windows.

2.3. The general characteristic of the studied parameters

The impairment of the functional capacity of the joints of patients with reactive parasitic arthritis was determined by the gradation developed by Steinbrocker O (1949). To determine the functional impairment of the spinal joints, the BASFI (Bath Ankylosing Spondylitis Functional Index) index was used.

As can be seen from table 1, the average age of the patients was $47,0 \pm 2,1$ years, they had a history of the disease of $4,2 \pm 1,3$ years, so were included only patients with chronic parasitic reactive arthritis (evolution approximately over 1 year). The insufficiency of joint function is presented in table 1.

Table 1. **General characteristics of the study group**

Evaluated indices		Total patients (n=161)
Age, years (M±ES)		47,0±2,1
Gender M/F		4/1
Age of the disease, years (M±ES)		4,2±1,3
Insufficiency of joint function (%)	FC I	34,78±0,23
	FC II	49,62±0,35
	FC III	10,02±0,16
	FC IV	5,59±0,09
Activity by DAREA score (%)	Grade I	11,8±0,08
	Grade II	49,06±0,64
	Grade III	39,13±0,71
Unilateral sacroiliitis (%)	Stage I	27,32±0,21
	Stage II	59,46±0,39
	Stage III	10,1±0,07
	Stage IV	3,1±0,09

Note: FC – functional class, M – male, F – female, M – median, ES

All patients were divided into three groups, according to the type of infectious agents. Parasitic reactive arthritis is certain if the onset or exacerbation of arthritis was preceded by phenomena of parasitic invasion at least one month before.

The determination of the degree of activity of the arthritic process was carried out based on the DAREA and ASDAS-CRP activity score, because parasitic reactive arthritis, clinically and paraclinically, is close to seronegative arthritis and presents an arthropathy of reaction to parasites.

Degranulation of eosinophils was determined by the immunoenzymatic method with fluorimetric detection (FEIA), and **immunoglobulin E** by the immunochemical method or detection by electrochemiluminescence (ECLIA).

Determination of the infesting agent Through the coproparasitological examination, the presence of parasites in the intestine was determined, within the biological cycle of each parasite.

Examination of the Giardia antigen in faeces was performed by the ELISA test. The confirmation was carried out by the Westernblot Test.

Clinical-immunological laboratory examinations

Blood count and evaluation of ESR; general analysis of urine; bilirubin and its fractions; serum urea and creatinine, blood glucose, C-reactive protein, fibrinogen, prothrombin, uric acid, ionogram were assessed using routine techniques. The detection of RF in the patients' serum was carried out by the latex-test method, authorized by Refa-Dac. Anti-citrullinated protein antibodies are determined by methods using, as an antigenic substrate, synthetic cyclic citrullinated peptides. Antinuclear antibodies (ANA) were determined by the classical serological method. The quantitative determination of immunoglobulins A, M and G was performed according to the Mancini method.

Radiological and ultrasonographic evaluation

The joints involved in the pathological process were radiologically examined: predominantly palmar and plantar (in 100% of patients), knee, shoulder and spine joints (in the lumbar region 100%) in all 161 patients included in the study to determine the radiological signs of joint damage. Ultrasonographic examinations were performed on high-class devices: HDI 3500 (ATL-Philips) and Power Vision (Toshiba).

Assessing the impact on the quality of life

The Short Form 36 (SF-36) questionnaire is a broad but generic method of assessing the impact of the underlying disease on the patient's quality of life, developed and tested by the New England Medical Center within the Medical Outcomes Study. This questionnaire uses eight scales: physical capacity, social component, limitation of activity and social role (due to physical and emotional causes), mental health, activity capacity or energy, integral or general somatic pain, general state of health.

3. ASSESSMENT OF THE CLINICAL, PARACLINICAL AND IMAGING MANIFESTATIONS OF THE IMMUNE-INFLAMMATORY STATUS IN PATIENTS WITH REACTIVE PARASITIC ARTHRITIS

3.1. Clinical characteristics of patients according to the clinical forms of reactive parasitic arthritis

In order to carry out a broad analysis of the clinical manifestations in parasitic reactive arthritis of diverse origin of the infestation agents, the study focused, firstly, on the causative pathogens (table 2), according to which parasitic reactive arthritis by *Echinococcus granulosus* was diagnosed in 97 (60,24%) of patients, that of *Toxocara canis* - in 31 (19,25%) and *Giardia lamblia* infestation - in 33 (20,49%) cases.

Table 2. **Forms of parasitic reactive arthritis (n=161)**

Form of parasitic reactive arthritis	%
<i>Echinococcus granulosus</i>	60,24
<i>Toxocara canis</i>	19,25
<i>Giardia lamblia</i>	20,49

With the aim of detailed differentiation of the general status of patients depending on the clinical-evolutionary variant of parasitic reactive arthritis, the separation was carried out according to each etiological category of the infecting agent, as presented in table 3.

Tabelul 3. **Clinical and status parameters of the general study group, n=161**

The clinical variant	Examined indexes		
ECHINOCOCCIC FORM OF PARASITIC REACTIVE ARTHRITIS (n=97 patients)	Median age, years (M±ES)	39,0±1,1	
	Gender M/F	6/1	
	Age of the disease, years (M±ES)	3,3±0,98	
	Insufficiency of joint function (%)	FC I	21,6
		FC II	51,2
		FC III	17,5
		FC IV	9,7
	Activity by DAREA score (%)	Grade I	15,9
		Grade II	63,8
		Grade III	20,3
	Activity by ASDAS-CRP score (%)	< 1,3	9,27
		>1,3 < 2,1	36,08
		>2,1 < 3,5	38,14
		> 3,5	16,49
	Unilateral sacroiliitis (%)	Stage I	23,2
		Stage II	65,4
Stage III		7,9	
Stage IV		3,5	
TOXOCARA FORM OF PARASITIC REACTIVE ARTHRITIS (n=31 patients)	Median age, years (M±ES)	53,0±3,4	
	Gender M/F	½	
	Age of the disease, years (M±ES)	2,4±0,56	
	Insufficiency of joint function (%)	FC I	27,9
		FC II	59,6
		FC III	10,2
		FC IV	2,3
	Activity by DAREA score (%)	Grade I	28,9
		Grade II	66,4
		Grade III	4,7
	Activity by ASDAS-CRP Score (%)	< 1,3	22,58
		>1,3 < 2,1	61,29
		>2,1 < 3,5	16,12
		> 3,5	0
	Unilateral sacroiliitis (%)	Stage I	38,4
		Stage II	51,6
Stage III		7,1	
Stage IV		1,93	
GIARDIA FORM OF PARASITIC REACTIVE ARTHRITIS (n=33 patients)	Median age, years (M±ES)	48,5±2,7	
	Gender B/F	3/1	
	Age of the disease, years (M±ES)	5,3±0,41	
	Insufficiency of joint function (%)	FC I	10,5
		FC II	51,2
		FC III	28,7
		FC IV	9,6
	Activity by DAREA score (%)	Grade I	8,7
		Grade II	59,8
		Grade III	31,5
	Activity by ASDAS-CRP score (%)	< 1,3	0
		>1,3 < 2,1	54,54
>2,1 < 3,5		36,36	

		> 3,5	9,09
Unilateral sacroiliitis (%)	Stage I		14,5
	Stage II		48,9
	Stage III		31,6
	Stage IV		5,0

Note: FC – functional class, ASDAS – ankylosing spondylitis disease activity score, DAREA – disease activity index for the assessment of reactive arthritis, CRP – C reactive protein, M – male, F – female, M – median, ES – standard error

Parasitic reactive arthritis is characterized by a diversity of articular clinical manifestations, expressing itself through different inhomogeneous clinical variants, which often do not clearly correlate with each other. The spectrum of agents identified with the clinical expression is presented in table 4.

Table 4. Frequency of identification of different parasitic forms in patients with parasitic reactive arthritis

Pathogen and expression	n=161	%
Pulmonary echinococcosis	67	41,61
Hepatic echinococcosis	30	18,63
<i>Toxocara canis</i>	31	19,25
<i>Giardia lamblia</i> extended form	19	11,8
<i>Giardia lamblia</i> limited form (only joint syndrome)	14	8,69

Pathogenic agents of the infestation were diagnosed coprologically and serologically in accordance with the Guide of the National Agency for Public Health "Coproparasitological diagnosis in intestinal invasions" [22], and the diagnosis was established on the basis of the clinical picture, which is possible when using the main clinical-paraclinical criteria of inflammatory arthritis and confirmation of parasitosis, in the absence other possible rheumatic diseases.

When analyzing the frequency of detection of parasitic agents depending on the type of clinical expression of the joint syndrome, we had the data presented in figure 3.

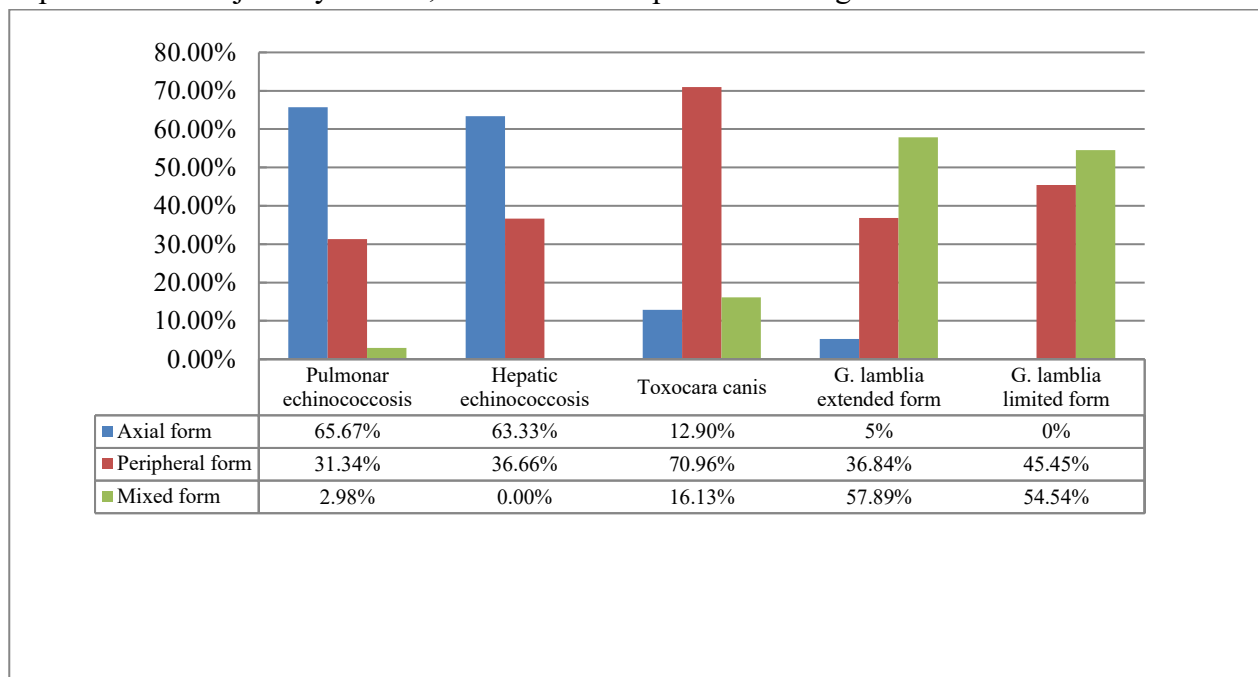


Figure 3. The frequency of parasitic species presented according to the clinical variant of the joint syndrome.

3.2. Non-specific cellular immune-inflammatory status of patients with parasitic reactive arthritis, analyzed depending on the infecting pathogen

The research of the body's non-specific and specific protection systems is important because their changes are responsible for the initiation, persistence and progression of the articular and systemic inflammatory process. A vital role in the functioning of the immune system belongs to leukocytes, which represent the main defense mechanism against nonself antigens. The studies carried out by us under this aspect demonstrated an increased proportion of leukocytes in the peripheral blood, especially in patients with parasitic arthritis with *Giardia lamblia*.

As shown in table 5, the number of leukocytes in the blood of patients with parasitic reactive arthritis in all clinical forms is increased, reaching values between 9,0 – 12,0x10⁹/l and even higher. The number of patients with normal indices is relatively small and prevails, especially in the toxocariasis variant of reactive parasitic arthritis (45,16%, p<0,01). Slightly elevated indices (9,0-12,0x10⁹/l) were found significantly more frequently in parasitic reactive arthritis due to echinococcosis (74,23%, p<0,001) than in patients with *Giardia lamblia* of parasitic reactive arthritis (33,33%). The marked increase in the leukocyte count was detected only in 6,45% of patients with toxocarosis and in 19,28% of those with parasitic reactive arthritis from echinococcosis. In the case of *Giardia lamblia*, the analyzed index was significantly increased in more than half of the patients (57,58%, p<0,001).

Table 5. Quantitative index of leukocytes in the blood of patients with parasitic reactive arthritis depending on the etiological agent of the disease (absolute indices, x10⁹/l)

The number of leukocytes	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
< 9,0	16 (6,49%)	14 (45,16%)* ¹	3 (9,09%)
9,0-12,0	72 (74,23%)* ²	15 (48,39%)* ³	11 (33,33%)
>12,0	9 (19,28%)	2 (6,45%)	19 (57,58%)* ⁴
Average index (M±ES)	10,1±0,02	9,2±0,01	12,5±0,03* ⁵

Note: *1p<0,01 – parasitic reactive arthritis by toxocariasis vs echinococcal and giardiasis; *2p<0,001 – reactive echinococcal parasitic arthritis vs toxocariasis and giardiasis; *3p<0,05 – parasitic reactive arthritis due to toxocariasis vs giardiasis; *4p<0,001 – parasitic reactive arthritis due to giardiasis vs echinococcosis and toxocariasis; *5p<0,01 – parasitic reactive arthritis due to giardiasis vs echinococcosis and toxocariasis; M – median, ES – standard error, Pre-A - parasitic reactive arthritis.

We analyzed both the overall quantitative proportion of leukocytes and their distribution by cellular subcategories for each nosological form of parasitic reactive arthritis separately. Thus, in the echinococcal etiology, these values mostly fell within the limits of the norm – 83,51% (p<0,001), in the toxocarcic form – 67,74% (p<0,001). In giardiasis, there was an even smaller number of patients with normal values (33,33%). In arthritis from toxocarosis, and especially in that from giardiasis, unsegmented leukocytes appear clearly increased (0,3x10⁹/l, and over 6%).

In patients with the etiological form of *Toxocara canis*, the relative values are twice higher than in patients with parasitic reactive arthritis from echinococcosis (38,71% - relative index), and in the one with *Giardia lamblia*, twice the values of the toxocarcic variant (69,70% - relative index). These values were presented with different degrees of statistical significance (table 6).

Table 6. The population of unsegmented leukocytes, estimated in the blood of patients with reactive parasitic arthritis depending on the etiological agent of the disease (ind. rel, %)

No. unsegmented leukocytes	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
< 6,0	83 (85,57%)* ¹	19 (61,29%)* ²	10 (30,30%)
>6,0	14 (14,43%)	12 (38,71%)* ⁴	23 (69,70%)* ³
Average index (M±ES)	4,1±0,02	5,3±0,04* ⁶	6,9±0,04* ⁵

Note: *1p<0,001 – echinococcal parasitic reactive arthritis vs toxocariasis and giardiasis; *2p<0,001 – parasitic reactive arthritis from toxocara vs giardiasis; *3p<0,01 – arthritis from giardiasis vs echinococcosis and toxocariasis; *4p<0,001 – parasitic reactive arthritis by toxocariasis vs echinococcosis; *5p<0,05 – arthritis from giardiasis vs toxocarosis; *6p<0,01 – arthritis from giardiasis vs echinococcosis; M – median, ES – standard error, Pre-A - parasitic reactive arthritis.

The relative indices were higher in patients with parasitic reactive arthritis from echinococcosis and giardiasis (table 7), but it should be noted the lack of statistically valid differences when examining group mean values, except for an insignificant prevalence in the group of patients with *Giardia* reactive arthritis, despite some average values, within the range of the physiological norm.

Table 7. Quantitative proportion of segmented leukocytes in the blood of patients with different etiological variants of parasitic reactive arthritis (relative indices, %)

No. segmented leukocytes	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
< 47%	2 (2,06%)	0	2 (6,06%) * ¹
47 - 72%	86 (88,66%)	30 (96,77%)	27 (81,82%) * ²
>72%	9 (9,28%)	1 (3,23%) * ³	4 (12,12%)
Average index (M±ES)	64±0,07%	59,5±0,09%	69±0,18%

Note: *1p<0,05 – arthritis from giardiasis vs echinococcosis and toxocariasis; *2p<0,05 – arthritis from giardiasis vs toxocariasis; *3p<0,05 – toxocara parasitic reactive arthritis vs echinococcosis and giardiasis; M – mean, ES – standard error, Pre-A - parasitic reactive arthritis.

3.3. Cellular immunoinflammatory status in patients with parasitic reactive arthritis according to etiologic factor

Another important marker for immune system activity is the lymphocyte. Our research demonstrated that the average percentage indices of lymphocyte content in the peripheral blood of patients with parasitic reactive arthritis (21,5±0,4) were within the normal range and did not undergo changes, having average values without differences statistics between the studied groups (table 8).

Table 8. Relative (%) and absolute (10⁹/l) indices of lymphocytes in patients included in the study (%)

Lymphocyte content, %	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
Relative indices,% (M±ES)	37,5±0,4	37,9±0,3	37,1,3±0,5
Absolute indices,10 ⁹ /l (M±ES)	2341±22,1	2344±21,6	2337±25,1

Note: M – median, ES – standard error, Pre-A - parasitic reactive arthritis.

3.4. Humoral immunoinflammatory status in patients with parasitic reactive arthritis depending on the etiologic factor

Taking into account the increase in the number of leukocytes, it was of interest to research the level of immunoglobulins in these patients. The evaluation of the level of immunoglobulins in the blood revealed the increase of the average values of IgA well above the normal physiological values

in all patients with reactive parasitic arthritis (table 9), with the index of significance very high (Kendall-Tau $0,99 \pm 0,001$; $p < 0,001$).

Table 9. Level of IgA, IgG and IgM in peripheral blood

Average index (M±ES)	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33	Normal value
IgA level, g/l	4,5±0,17	4,07±0,21	4,39±0,12	0,9-3,5 g/l
IgG level, g/l	1,25±0,3	1,23±0,4	1,19±0,7	0,8-2 g/l
IgM level, g/l	1,99±0,017	1,64±0,032	2,09±0,011	0,6-2,1 g/l

Note: M – median, ES – standard error, Ig – immunoglobulin, Pre-A - parasitic reactive arthritis.

The average indices of the IgG level were within the normal range in all the studied groups, but they were at the upper limit of the normal range and showed no differences between the studied groups ($p < 0,05$). However, a slight decrease in IgG concentration was observed in patients with *Giardia lamblia* parasitic reactive arthritis compared to the other studied groups, but these differences were not statistically significant ($p < 0,05$).

The average indices of the level of IgM in the blood did not show significant changes (Table 11). Like in the case of IgG, patients with physiological levels of immunoglobulins M predominate (91%), except for a tendency of their increase in the groups of patients with *E. granulosus* parasitic reactive arthritis and *G. lamblia* parasitic reactive arthritis compared to group of *T. canis*. However, the differences were not statistically significant.

Most visible increase in the course of all three parasitosis, were high levels of IgE. Its quantity exceeds the control by more than 10 times – with *Echinococcus granulosus* (38,40 ng/ml), 9 times – with *Toxocara canis* (34,16 ng/ml), 11 times – with *Giardia lamblia* (45,06 ng/ml) (table 10).

Table 10. IgE level in peripheral blood

	ARe-P <i>E. granulosus</i> n=97	ARe-P <i>T. canis</i> n=31	ARe-P <i>G. lamblia</i> n=33
Ig E (ng/ml) (Normal < 4) M±ES	38,40 ± 0,16*	34,16 ± 0,23,	45,06 ± 0,12**
Ig E (UI/mL) (Normal < 100) M±ES	1612,7 ± 0,76*	1434,1 ± 1,16	1892,5 ± 1,2**

Note: * $p < 0,05$; ** $p < 0,01$, M – median, ES – standard error, Pre-A - parasitic reactive arthritis.

A significant increase (compared to the normal) in the content of leukocytes from the eosinophilic series in the blood of the examined patients was observed (up to $45,43 \pm 8,71\%$, $p = 0,001$ – in patients with *E. granulosus*; in patients with *G. lamblia*, eosinophilia it was determined in 60% of cases and was recorded at the level of $39,51 \pm 1,76\%$, $p = 0,019$, $p = 0,001$) (table 11).

Table 11. Relative indices (%) and degranulation capacity (% , abs) of eosinophils

Eosinophil content, %	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
Relative indices, % (M±ES)	45,43±8,71, $p < 0,001$	33,5±0,3, $p < 0,05$	39,51 ± 1,76, $p < 0,01$
Degranulation capacity (M±ES) ECP	7,79±2,04%, $p < 0,001$ 21,0±0,01 µg/l, $p < 0,05$	6,05±1,13%, $p < 0,05$ 27,0±0,03 µg/l, $p < 0,05$	6,37±0,83%, $p < 0,05$ 7,0±0,00 µg/l, $p < 0,01$

Note: M – median, ES – standard error ($p < 0,05$), Pre-A - parasitic reactive arthritis, ECP- Eosinophilic cationic protein

Eosinophils perform different functions in parasitosis and differ from other cells by the presence of granules intensely stained by acid dyes, especially eosinophilic cationic protein. The significant increase in the cytotoxic function of eosinophils may be due to the intensification of their capacity for degranulation and cytolysis [12, 16]. This position is confirmed by the results of our study, which revealed a significant increase in relation to the norm (table 11).

3.5. Assessment of joint syndrome

The presence of acute phase markers (ESR, CRP, Fibrinogen) in increased amounts both in the serum of patients with *G. lamblia* parasitic reactive arthritis, as well as in those with *E. granulosus* and *T. canis* indicates a high activity of the inflammatory process at the joint synovial level and determines the progression joint destruction. The values of these indices are presented in table 12.

Table 12. Acute phase marker values according to the nosological forms of parasitic reactive arthritis, M±ES

Evaluated index	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33	Normal values
ESR	27,9±0,15* ²	20,3±0,17	31,5±0,22* ¹	2-10 mm/h
C reactive proteine	52,14±0,24* ⁴	40,16±0,12	64,71±0,16* ³	0-50 mg/l
Fibrinogen	3,17±0,09	2,52±0,03	4,11±0,07* ⁵	240-290 mg/dl

Note: *1p<0.01 – parasitic reactive arthritis by giardiasis vs toxocarosis and p<0.05 for echinococcosis; *2p<0.05 – parasitic reactive arthritis due to echinococcosis vs toxocarosis; *3p<0.01 – parasitic reactive arthritis due to giardiasis vs parasitic reactive arthritis due to toxocarosis and p<0.05 for echinococcosis; *4p<0.05 – parasitic reactive arthritis due to echinococcosis vs toxocarosis; *5p<0.05 – parasitic reactive arthritis due to giardiasis vs echinococcosis and toxocarosis, M – median, ES – standard error, ESR – erythrocyte sedimentation rate, Pre-A - parasitic reactive arthritis.

Research of C-reactive protein titers (CRP) found normal values in only 16,49% of patients with parasitic reactive arthritis due to echinococcosis, and for those with parasitic reactive arthritis due to giardiasis, there were 3,0% (1 patient), respectively, for patients with arthritis due to toxocarosis – 16,3% cases. The remaining patients had elevated C-reactive protein titers.

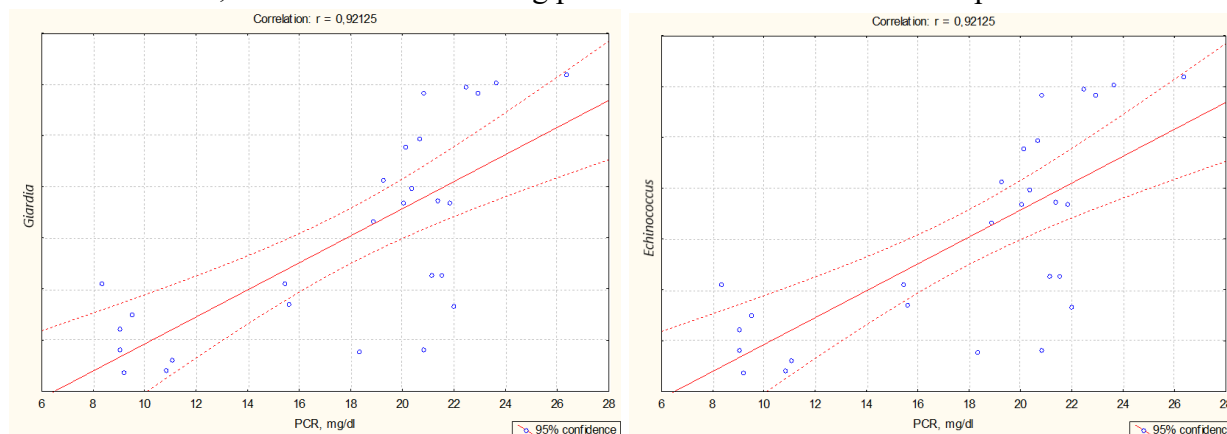


Figure 4. Correlative interdependence between the PCR value (mg/dl) and the clinical-nosological form of reactive parasitic arthritis

In patients with parasitic reactive arthritis due to echinococcosis, the CRP was estimated at an average of 52,14±0,24, in the group with parasitic reactive arthritis due to giardiasis – 64,71±0,16, and in the form of toxocarosis – 40,16±0,12 (table 12), with statistically significant differences being deduced between the compared groups: parasitic reactive arthritis due to echinococcosis vs toxocarosis – p<0,05; parasitic reactive arthritis due to giardiasis vs toxocarosis – p<0,01; parasitic reactive arthritis due to giardiasis vs echinococcosis – p<0,05.

The predominance of the immunoinflammatory syndrome was demonstrated in patients with reactive parasitic arthritis due to echinococcosis and giardiasis, and in parasitic reactive arthritis due to toxocarosis, the inflammation was less expressive, so it is of interest to compare the status of the disease activity in accordance with the inflammation indices, expressed by the DAREA score and ASDAS-PCR.

To complete the DAREA score, the analysis of the damage to the various joints was carried out depending on the clinical-nosological form of reactive parasitic arthritis, where the damage to the metatarsophalangeal joints (79%), talocrural (77%), radiocarpal (52%) and knees (56%) predominates. In parasitic reactive arthritis due to giardiasis, the coxofemoral (72%), talocrural (66%) and knee joints (51%) are more often involved in the process; in toxocarosis arthritis – palmar (71%), plantar (68%) and talocrural (51%) joints.

Table 13. Inflammatory joint syndrome values and DAREA score data in patients with parasitic reactive arthritis

Average index (M±ES)	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33
NPJ (M±ES)	6,5±0,09	5,4±0,01	7,1±0,08* ¹
NSJ (M±ES)	7,75±0,07	6,05±0,09	8,75±0,02* ²
VAS (M±ES)	45,15±0,13	37,04±0,19	55,07±0,14* ⁴
DAREA (M±ES)	69,28±0,29	59,55±0,51	84,29±0,47* ³
DAREA Grade I (%)	15,9	28,9	8,7
DAREA Grade II (%)	63,8* ¹	66,4* ¹	59,8* ¹
DAREA Grade III (%)	20,3* ⁴	4,7	31,5* ¹
ASDAS-CRP < 1,3 (%)	9,27	22,58	0
ASDAS-CRP >1,3 < 2,1 (%)	36,08* ³	61,29* ²	54,54* ¹
ASDAS-CRP >2,1 < 3,5 (%)	38,14* ³	16,12	36,36* ¹
ASDAS-CRP > 3,5 (%)	16,49	0	9,09* ¹

Note: *1p<0.01 – parasitic reactive arthritis by giardiasis vs toxocarosis and p<0.05 for echinococcosis; *2p<0.01 – parasitic reactive arthritis due to giardiasis vs toxocarosis and p<0.05 for toxocarosis; *3p<0.01 – parasitic reactive arthritis due to giardiasis vs toxocarosis and p<0.05 for toxocarosis; *4p<0.05 – parasitic reactive arthritis due to giardiasis vs toxocarosis and toxocarosis, M – median, ES – standard error, CRP – C reactive proteine, ASDAS – ankylosing spondylitis disease activity score, DAREA – disease activity index for the assessment of reactive arthritis, NSJ - number of swollen joint, NPJ – number of painfull joint, Pre-A - parasitic reactive arthritis.

As shown in table 13, parasitic reactive arthritis manifests a severe clinical picture with the involvement of a large number of joints in the inflammatory process and is characterized by high values of the disease activity score - DAREA. Thus, the NPJ for parasitic reactive arthritis due to giardiasis is 7,1±0,08, which is a significantly higher value compared to echinococcosis 6,5±0,09 (p<0,05) and toxocarosis 5,4± 0,01 (p<0.01). For NSJ, the same dynamics of indices were revealed, which, in giardiasis, were valued at 8,75±0,02, which denotes statistically significant differences with echinococcosis 7,75±0,07 (p<0,05) and toxocarosis 6,05±0,09 (p<0,01).

3.6. Instrumental analysis by conventional radiography of parasitic reactive arthritis with extension to clinical questionnaires

Considering the existence of various forms of spinal damage in parasitic reactive arthritis, we considered it necessary to examine, separately, the values of the BASDAI, BASFI and BASRI spinal damage indices depending on the study group and the clinical form of parasitic reactive arthritis. When analyzing these indices (table 14), within the values of the group of patients with parasitic reactive arthritis from echinococcosis and the groups of giardiasis and toxocariasis, a statistically significant difference was determined only between the values of the BASDAI index ($4,23 \pm 0,33$; $5,07 \pm 0,28$ vs $3,4 \pm 0,45$; $p < 0,005$).

Table 14. Summary of the analysis of BASDAI, BASFI and BASRI index values between study groups I and II

Clinical indices	Pre-A <i>E. granulosus</i> n=97	Pre-A <i>T. canis</i> n=31	Pre-A <i>G. lamblia</i> n=33	P
BASDAI (M±ES)	4,23±0,33	3,40±0,45	5,07±0,28	p<0,005
BASFI (M±ES)	4,3±0,38	4,0±0,47	4,61±0,34	p>0,05
BASRI (M±ES)	4,6±0,41	4,29±0,71	5,0±0,33	p>0,05

Notă: BASDAI - Bath Ankylosing Spondylitis Disease Activity Index, BASFI - Bath Ankylosing Spondylitis Functional Index, BASRI - Bath Ankylosing Spondylitis Radiology Index, M – median, ES – standart error, Pre-A - parasitic reactive arthritis.

3.7. Ultrasonography as an important method in the diagnosis of musculoskeletal pathology in patients with reactive parasitic arthritis and the correlation of the obtained ultrasonographic data with the MRI results

Ultrasonographic examination was the main method in the complex diagnosis of parasitic reactive arthritis. The results of the study demonstrated that, in patients with parasitic reactive arthritis, damage to all anatomical structures of the joint with polymorphism of the ultrasound pattern is detected. Due to the small number of patients and the impossibility of appreciating sensitive signs for separate clinical-nosological categories, we decided to examine the entire batch of 161 patients with parasitic reactive arthritis as an integral group.

The most common changes in the joints in patients with reactive parasitic arthritis were the increase in the amount of intra-articular fluid and the proliferation of the synovial membrane. The presence of fluid in the joints occurred in an overwhelming number of patients ($n = 102$) and in only 36,6% ($n = 59$) of the observations there was no fluid. In total, fluid was detected in 293 of (9,1%) 3,232 joints. In the affected knee joints (68 joints), a small increase in the amount of intra-articular fluid was recorded in 32.35% of observations (grade 1), a moderate amount of fluid was in 17.65% (grade 2), and in 14.7% was a manifest fluid effusion (grade 3). In the radiocarpal joints, the maximum thickness of the liquid in the joints was 6 mm, in the ankle joints - 8 mm. The maximum fluid thickness in the small joints was 2 mm. In our study, homogeneous effusion in the joint cavity predominated (68,6%).

Synovial proliferation was detected in 296 (9,16%) joints. In the majority of observations ($n = 286$; 96,6%), diffuse thickening of the synovial membrane was determined. The echogenicity of the synovial membrane was different: decreased ($n = 200$; 67.6%) and increased ($n = 96$; 32.4%). Cartilage thickening was detected in 4 joints (2,9%). In 58 (97,1%) cases, there was a thinning of the cartilage, which, in a number of observations, was accompanied by a change in contours in the form of blurring, and in a number of cases - a change in the normal ecostructure. In some patients with cartilage thinning (22%), an increase in its echogenicity was observed.

In some patients (10%), there was a significant decrease in echogenicity of the patellar ligament at the bony insertion site, also with loss of typical structure. These were patients with marked disease activity, and the visible clinical picture was considered by us to be enthesitis.

Tenosynovitis of the flexors of the fingers, flexors and extensors of the hands was detected in 30 locations. In the majority of observations (93,3%), the appearance of fluid in the synovial sheath of the tendon was combined with the preservation of the normal ecostructure of the tendon itself. And only in 2 cases (6,7%), there was thickening of the tendon with loss of typical tendon ecostructure.

According to the ultrasound data, bone erosions were detected in only two people (1,4%) in the ends of the metacarpal bones, while, on radiography and magnetic resonance imaging, the frequency and severity of this symptom was higher.

Magnetic resonance imaging was the second investigation method in the complex diagnosis of reactive parasitic arthritis (performed in 39 patients) and was used as a reference method. In the study group, synovial fluid constituted the predominant symptom in terms of frequency (92,86%), including in the small joints of the hands (100%) and plants (100%). Synovial proliferation was the second most common sign of knee joint involvement (71,43%) and was detected in 3,6% of plantar joints and 7,1% of hand joints.

Since MRI was chosen as the reference method for the correct evaluation of the diagnostic effectiveness of ultrasonography in detecting existing changes, MRI results, obtained in 39 patients from 256 joints, were compared with ultrasound data of the same patients (table 15).

In our study, MRI data were generally in agreement with ultrasound results in the diagnosis of the presence of intra-articular fluid, synovial proliferation, cartilage changes, as well as the evaluation of tenosynovitis, syndesmophytes, and enthesopathies.

Table 15. Comparison of signs visualized at USG and MRI, in 39 patients (256 joints)

Symptom	The number of joints with detected changes	
	Ultrasound with PD	MRI
Liquid effusion	28,6%	28,6%
Proliferation of the synovial membrane	19,6%	24,1%*
Cartilage modification	7,1%	7,1%
Bone erosion	3,5%	7,1%*
Syndesmophytes	12,5%	12,5%
Enthesitis	42,9%	50,5%
Tenosynovitis	5,4%	5,4%

Note: *p<0,05, PD – Power Dopple, MRI – magnetic resonance imaging

To evaluate the possibilities of energy Doppler mapping in reflecting the activity of reactive parasitic arthritis, the results of ultrasound studies and clinical and laboratory data of 68 patients's knees in the study were compared. Indicators that reflect the general activity of the disease (ESR and number of leukocytes) and indicators that directly reflect the presence and activity of the inflammatory process in the investigated joints were studied: pain, inflammation and hyperemia, the severity of the main ultrasound symptoms of synovitis in the knee joints and small joints of hands and feet, depending on the clinical manifestations of inflammation (table 16).

Table 16. Expression of ultrasonographic symptoms of synovitis depending on clinical activity of inflammation in knee joints (n=68)

Ultrasonographic sign	Group 1 (n=46) low activity	Group 2 (n=12) average activity	Group 3 (n=10) high activity
Thickness of the synovial membrane			
grade 1	44 (95,7%)	1 (8,3%)	-
grade 2	2 (4,3%)	10 (83,4%)	-
grade 3	-	1 (8,3%)	10 (100%)
Vascularization degree			
grade 0	26 (56,5%)	0	0
grade 1	20 (43,5%)	0	0
grade 2	0	12 (100%)	0
grade 3	0	0	10 (100%)
Liquid amount			
grade 0	24 (52,2%)	0	0
grade 1	22 (47,8%)	0	0
grade 2	0	10 (83,3%)	2 (20%)
grade 3	0	2 (16,7%)	8 (80%)
Cartilage changes			
thickening	0	0	4 (40%)
thinned	40 (87,0%)	12 (100%)	6 (60%)
contour modification	30 (65,2%)	8 (66,7%)	10 (100%)
modification of the ecostructure	30 (65,2%)	8 (66,7%)	10 (100%)
Decreased echogenicity of the ligament at the site of fixation (enthesis)	0	0	7 (70%)

During our study, ultrasonography and clinical and laboratory activity data were compared for all joints as a whole. The results of the correlation analysis indicate a positive correlation between the severity of sonographic symptoms of synovitis and the level of clinical signs and laboratory markers of inflammation. At the same time, the ultrasound symptom, which correlates the most with the level of local activity, is the degree of vascularization of the synovial membrane, which was both in large joints ($r = 0,508$) and in small joints ($r = 0,500$).

4. SPECIFICATIONS OF THE IMPACT OF REACTIVE PARASITIC ARTHRITIS ON QUALITY OF LIFE (SF-36 QUESTIONNAIRE)

An important objective in our study is to establish, using the SF 36 questionnaire approved in the rheumatology specialty, the interrelationships of the impact on the quality of life in reactive parasitic arthritis, analyzing the physical, social, mental and emotional capacities, combined with the chronic or acute pain syndrome, caused by the inflammatory process. Due to the small number of patients belonging to the giardiasis and toxocarosis groups, we considered it appropriate to examine the entire batch - to differentiate evolutionarily the echinococcosis group (group I) and the giardiasis - toxocarosis group (group II).

Analyzing the results from the quality of life questionnaire, it was determined that the average derivative of **physical functioning (PF)** in patients with parasitic reactive arthritis on the background

of *E. granulosus*, for example self-service, walking, obtained the value of $24,89 \pm 0,37$, but in the group with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia* – $28,11 \pm 0,14$, thus showing a statistically confirmatory difference ($p < 0,05$).

Continuing with the Pearson correlation analysis, it was demonstrated that, in group I, the possibility of self-service correlated significantly with the reduction of the emotional role through the RE scale ($r = 0,73$; $p < 0,05$) and showed an average correlation indicator with vitality (VT) ($r = 0,45$; $p < 0,05$) and concentration disturbance in the scale (RE) ($r = 0,45$; $p < 0,05$). In patients with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, the possibility of self-service and walking determined a direct correlation with the reduction of the emotional role through the RE scale ($r = 0,42$; $p < 0,05$), but with a lower level of the coefficient r compared to group I, which confirms the fact that, in patients with reactive parasitic arthritis on the background of *E. granulosus*, on the emotional sphere, it influences not only joint incapacity, but also polysomatic changes from echinococcosis. At the same time, in the patients of the group with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, there was also an indirect correlation between the reduction of the emotional role and fatigue according to the VT scale ($r = -0,34$; $p < 0,05$), nervousness according to the MH scale ($r = -0,31$; $p < 0,05$) and general pain syndrome according to the BP (Bodily Pain) scale ($r = -0,24$; $p < 0,01$).

The decrease in **physical role (RP scale)** and the disabilities determined by it were noted in patients with reactive parasitic arthritis on the background of *E. granulosus* with an average value of the indicator of $6,78 \pm 0,14$, but in patients with reactive parasitic arthritis on the background of *T. canis* and *G. lamblia* was $8,89 \pm 0,11$, with an imposing statistical significance ($p < 0,001$). Simultaneously, through the Pearson correlational analysis, it was determined that the decrease in the physical role correlated with the somatic pain BP ($r = 0,63$; $p < 0,05$) and with the decrease in the emotional role RE ($r = 0,44$; $p < 0,05$). However, in the group of patients with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, no correlations were determined.

Body pain (BP scale) in the group of patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* showed an average value of $3,71 \pm 0,17$, and in the group with parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia* of $3,03 \pm 0,02$, an impressive statistical difference was found ($p < 0,001$). The Pearson correlation test found that body pain in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* determined expected values through a significant direct correlation with worsening health ($r = 0,51$; $p < 0,05$) and an inverse correlation proportional to the possibility of self-service ($r = -0,59$; $p < 0,05$). So, parasitic reactive arthritis from echinococcosis directly influences the articular inflammatory process, confirmed not only by clinical and paraclinical data, but also by the influence on the level of quality of life by disrupting physical functioning. At the same time, in patients with parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia*, somatic pain showed a correlation with nervousness ($r = 0,47$; $p < 0,05$), which was expected, and fatigue ($r = 0,47$; $p < 0,05$), but also an indirect correlation with walking ($r = -0,24$; $p < 0,05$), by maintaining arthralgias during motor activity through the appearance of inflammatory pain.

The deterioration of the state of **general health (GH scale)** in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* showed averages of $16,11 \pm 0,31$, and in patients with reactive parasitic arthritis on the background of *Toxocara canis* and *Giardia lamblia*, there were determined averages of $22,88 \pm 1,15$ ($p < 0,001$). The correlative examination found that the deterioration of health in echinococcosis patients configured a correlation with the deterioration of the emotional role and depression ($r = 0,28$; $p < 0,05$); a correlation with the reduction of physical functioning ($r = 0,43$; $p < 0,05$) and the ability to climb stairs ($r = -0,34$; $p < 0,05$). And in patients with

parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia*, the damage to health did not detect any correlations, which confirms the severe evolution of musculoskeletal disorders in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus*.

Vitality - fatigability (VT scale) in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* showed averages of $14,16 \pm 0,11$, but in patients with parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia* it was $9,44 \pm 0,11$, a significant statistical difference was determined ($p < 0,001$). As it is difficult to attribute this situation only to the influence of the musculoskeletal status, because, according to data from the specialized literature, patients with echinococcosis show a high degree of fatigue, probably caused by the indirect influence of echinococcosis on the central and peripheral nervous system (through exotoxins).

Social functioning (SF scale) in patients with reactive parasitic arthritis on the background of *E. granulosus* presented mean values of $6,21 \pm 0,09$, and in patients with reactive parasitic arthritis on the background of *T. canis* and *G. lamblia* – values means of $7,56 \pm 0,07$, ($p < 0,001$). The correlative examination in patients with parasitic reactive arthritis on the background of *E. granulosus* demonstrated that social activity determined a weak significant correlation with the possibility of self-service ($r = 0,26$; $p < 0,05$); in patients with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, the correlation aimed at reducing physical functioning ($r = 0,42$; $p < 0,05$) and the feeling of MH anxiety ($r = 0,69$; $p < 0,05$).

The decrease in **emotional role (RE scale)** in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* determined averages of $5,31 \pm 0,12$, but in patients with parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia*, it was found averages of $5,91 \pm 0,16$, ($p < 0,001$), inducing the reduction of the emotional role in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* through the impact on the musculoskeletal system.

This fact can be explained by the patients' psychoemotional attention to echinococcal cysts, despite the presence of joint inflammatory pathology. Performing the correlational analysis, it was shown that, in patients with parasitic reactive arthritis on the background of *E. granulosus*, the reduction of activity and inattention determined a significant direct correlation with nervousness ($r = 0,52$; $p < 0,05$) and a inverse correlation with somatic pain ($r = 0,-34$; $p < 0,05$), but in the group with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, the reduction of activity determined an important correlation with social activity ($r = 0,42$; $p < 0,05$) and walking ($r = 0,42$; $p < 0,05$).

Mental health (MH scale) in patients with parasitic reactive arthritis on the background of *E. granulosus* showed averages of $19,41 \pm 0,17$, but in patients with parasitic reactive arthritis on the background of *T. canis* and *G. lamblia*, the average of was $25,6 \pm 0,19$ ($p < 0,001$). Therefore, the disruption of mental health (expressed predominantly by excessive nervousness and depressive-anxious syndrome) was more pronounced in patients with parasitic reactive arthritis on the background of *E. granulosus*, possibly due to a manifest syndrome of toxic-infectious impregnation.

The correlative examination in patients with parasitic reactive arthritis on the background of *Echinococcus granulosus* demonstrated that the deterioration of mental health had a significant correlation with the possibility of self-care ($r = 0,28$; $p < 0,05$) and the decrease in work capacity ($r = 0,28$; $p < 0,05$), but in patients with parasitic reactive arthritis on the background of *Toxocara canis* and *Giardia lamblia*, a significant correlation was detected with social activity ($r = 0,67$; $p < 0,05$) and fatigue ($r = 0,58$; $p < 0,05$).

5. EVOLUTIONARY CHARACTERISTICS OF PARASITIC REACTIVE ARTHRITIS DEPENDING ON PARASITIC GERMS (SYNTHESIS OF THE OBTAINED RESULTS)

The problem of parasitic infection in rheumatology is becoming more and more important to the attention of different specialists - rheumatologists, infectious disease specialists, microbiologists, immunologists, biochemists, etc. Their interest is supported by the importance of parasitic agents in the development of some rheumatic diseases by triggering inflammatory immunopathogenic processes in the "target" organs.

Following the systematization carried out, it was found that pulmonary Echinococcosis manifested more often through axial (65,67%) and peripheral (31,34%) clinical forms, the form of mixed clinical expression being extremely rare (2,98%) ($p < 0,001$). The strength of connection with the type of arthritis reached statistical significance (Kendall-Tau index = 0,92; $p < 0,001$).

Hepatic echinococcosis repeated the same principle as the pulmonary one with the predominance of the axial variant (63,33%), followed by the peripheral one (36,66%) in the absence of expressions of mixed variants (0%) ($p < 0,01$), with a major association for axial form of reactive parasitic arthritis (Kendall-Tau index = 0,96; $p < 0,001$).

Parasitic reactive arthritis, due to *Toxocara canis*, showed an overwhelming predominance of peripheral forms of clinical manifestations of the joint syndrome (70,96%), with an insignificant share of axial (12,9%) and mixed (16,13%) forms ($p < 0,01$), with a connection for the peripheral form of reactive parasitic arthritis (Kendall-Tau index = 0,93; $p < 0,01$).

The clinically developed form of parasitosis by *Giardia lamblia* showed a predominantly mixed joint syndrome (57,89%), confirming a predominantly peripheral (36,84%) rather than axial (5%) lesion, with a statistically significant significance ($p < 0,05$), but also a connection for the mixed-peripheral form of reactive parasitic arthritis (Kendall-Tau index = 0,81; $p < 0,05$).

During the evolution of parasitic reactive arthritis, significant changes occur in the immune status, especially in *Giardia lamblia* parasitic reactive arthritis, which were characterized by a marked increase in leukocytes and a decrease in the total number of lymphocytes. The changes that specify the immune deficiency status in *Giardia lamblia* parasitic reactive arthritis are probably due to the aggressiveness of the parasitic pathogens and the immune response through both prolonged hyperreactivity and parasite survival products.

Our investigations have shown that in the blood of people with parasitic reactive arthritis, there is an increased number of eosinophils, especially in patients with *G. lamblia* and *E. granulosus* ($p < 0,05$), compared to patients suffering of *T. canis* parasitic reactive arthritis, in which, their quantity was significantly increased above the physiological norm ($p < 0,01$). All those revealed denote the essential changes produced in the humoral immune status in patients with reactive parasitic arthritis, manifested by the marked quantitative increase of leukocytes.

Imbalances in the cellular immune status revealed the proliferation of the leukocyte and eosinophilic cell clone against the background of the lymphocyte decrease. Differences in immunohumoral status between groups were not determined, except for the increase in IgA concentration above physiological values. The increased microbicidal potential of eosinophils in patients with *E. granulosus*, *T. canis* and *G. lamblia* is due to the intensity of oxygen-independent lytic processes and their increased phagocytic activity. Morphological features of blood eosinophilic leukocytes in patients with *E. granulosus*, *T. canis* and *G. lamblia*, associated with eosinophilia, are characterized by degranulation, increased vacuolization of the nucleus and cytoplasm.

The evaluation of the joint syndrome was completed by the screening of the acute phase markers – ESR, CRP and fibrinogen. Their presence in increased amounts both in the serum of

patients with *G. lamblia* parasitic reactive arthritis and in those with *E. granulosus* and *T. canis* indicates a high activity of the inflammatory process at the joint synovial level and determines the advancement of joint destruction.

In the same way, the weight of the inflammatory process is also confirmed by significant values of the DAREA score. A fact also confirmed by the ASDAS-CRP score. Thus, the worst form of parasitic reactive arthritis from the point of view of the inflammatory syndrome was parasitic reactive arthritis from *G. lamblia*: it showed the highest score values, with the predominance of high disease activity (cumulative 100% patients the score is $> 1,3$), followed by parasitic reactive arthritis from *E. granulosus* (cumulative 90,73% patients the score is $> 1,3$, $p < 0,05$) and the mildest variant of parasitic reactive arthritis was that with *T. canis*.

The analysis of the BASDAI, BASFI and BASRI indices shows that the damage to the spine is much more pronounced in patients with reactive parasitic arthritis caused by *Giardia lamblia* and *Echinococcus granulosus*, than in those with reactive parasitic arthritis caused by *Toxocara canis*.

The imaging study of the subjects was carried out by Conventional Radiography (CR), Ultrasonography (USG) and Magnetic Resonance Imageing (MRI). USG has the potential to be the first-line method in detecting a wide range of morphological changes in the joints of patients with reactive parasitic arthritis. The highest sensitivity index was established in the detection of inflammatory fluid, cartilage changes, osteophytes and tenosynovitis. Less sensitivity was obtained in the detection of synovial membrane proliferation, enthesopathy, the lowest sensitivity was observed in the visualization of marginal bone erosions. At the same time, the specificity indicators were equally high. In large joints, proliferation of the synovial membrane was detected in half of the joints and had predominantly increased echogenicity, was accompanied by intra-articular effusion in all observations. In small joints, hypochoic synovial proliferation occurred very rarely, due to the rare lesion, and was combined with an increase in joint fluid volume in 92% of cases. Damage to the tendon-ligament apparatus in parasitic reactive arthritis included enthesopathy of the knee joints, tenosynovitis of the ankle, radiocarpal joints, and small joints of the hands and feet.

The ultrasound criteria for the validity of reactive parasitic arthritis are: the degree of severity of synovitis, the presence of tenosynovitis and enthesitis. The most relevant correlation was obtained between the activity of inflammation and the vascularization of the synovial membrane ($r = 0,591$) and tenosynovitis ($r = 0,547$), as well as between the levels of ESR and leukocytes, between the amount of inflammatory fluid ($r = 0,401$) and the degree of vascularization of the synovial membrane ($r = 0,508$).

An important aspect of the goals originally stipulated in our study was to determine the impact of reactive parasitic arthritis on the quality of life of the patients. Analyzing the results from the quality of life survey, it was determined that parasitic reactive arthritis significantly disperses the role of other risk factors for musculoskeletal pathology, occupying the leading role in the pathogenetic cascade of joint inflammatory destructions and also on the emotional sphere of these patients, influences not only joint incapacity, but also parasitic invasion.

Application of the results to the clinician's practice

The diagnosis of parasitic reactive arthritis is a clinical one, based on the thorough collection of the anamnesis and the specific manifestations of a seronegative arthritis. A high degree of caution is required because there are no specific investigations to confirm this diagnosis. The differential diagnosis is made with a large number of rheumatic pathologies, both seronegative (ReA, PsA) and autoimmune (RA, SLE), and clinical signs, specific to parasitic infections, and the presence of eosinophilia, high values of IgE and IgA are indicators- key to establishing the correct clinical diagnosis.

The pattern of arthralgias in parasitic reactive arthritis is frequently intermittent, migratory and nocturnal, with the predominant involvement of the joints of the lower limb, but also of the small joints of the hands.

Following the multiple regression analysis, we determined some specific clinical-evolutionary peculiarities, which we oriented in an algorithm way (Fig. 5).

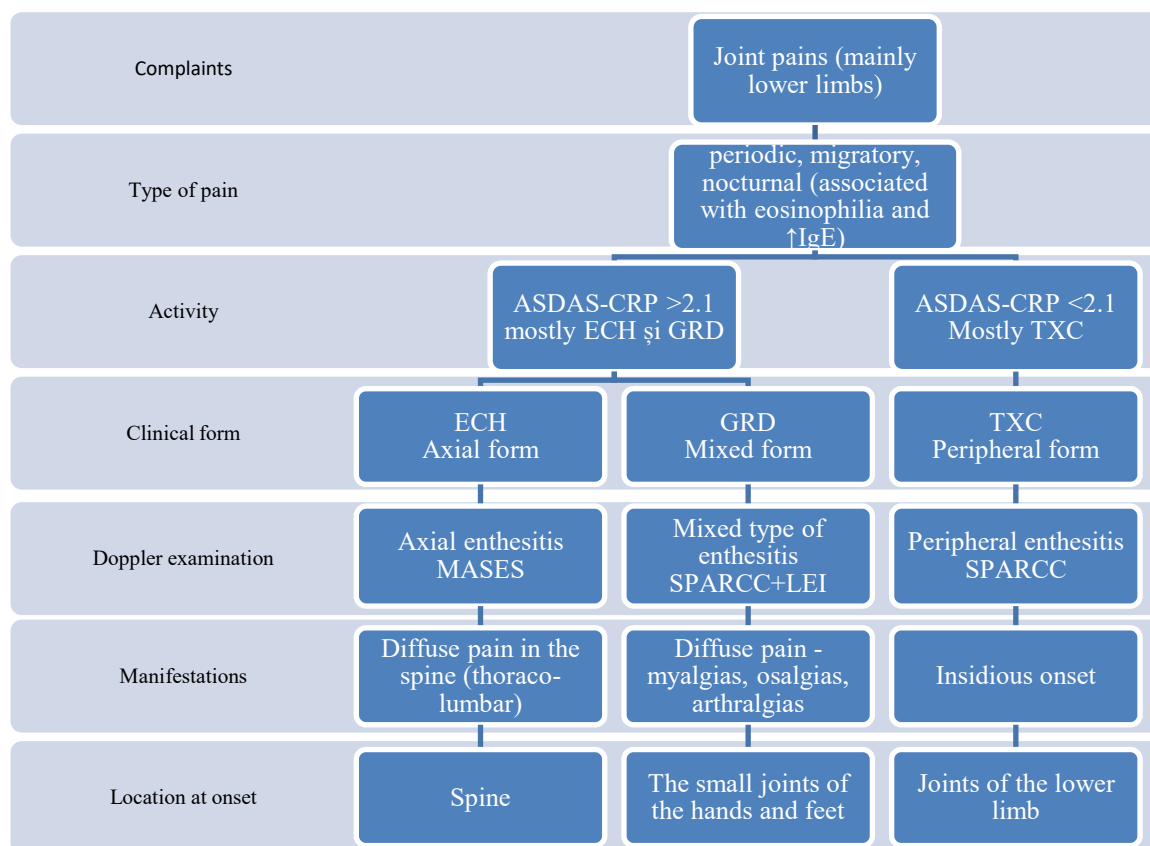


Figure 5. **Diagnosis algorithm of the joint impairment in parasitic infections**
 ECH – *Echinococcus*, GRD – *Giardia*, TXC – *Toxocara*

CONCLUSIONS

1. Parasitic reactive arthritis is characterized by the diversity of clinical joint manifestations, affecting any group of joints, but, with predilection, joints of low limb, which fall into three clinical variants: induced by infestation with *Echinococcus granulosus*, *Toxocara canis* and *Giardia lamblia*, of which giardiasis correlates with a more severe clinical evolution, followed by echinococcosis and toxocarosis.
2. The expression of the inflammatory syndrome was more relevant in patients with musculoskeletal disorders, associated with echinococcosis and giardiasis, compared to toxocarosis, demonstrating a significantly increased prevalence of acute phase reactants (NPJ, NSJ, ESR, CRP, fibrinogen). The immune status is characterized by a non-specific immunosuppression on the activity of neutrophils and lymphocytes (with optimal values of leukocytes), but with an increased activity of eosinophils, with their active degranulation and amplification of humoral immunity with the increase of IgA and IgE.
3. Despite a large number of painful and inflamed joints, which also associate an advanced radiological stage of joint damage, reactive parasitic arthritis is characterized by a comparatively attenuated joint pain syndrome. Thus, it was found that the damage to the spine and peripheral joints (imagistically confirmed) is much more pronounced in patients with parasitic reactive arthritis caused by *Giardia lamblia* and *Echinococcus granulosus*, than in those with parasitic reactive arthritis caused by *Toxocara canis*.
4. The special feature in the early stages of parasitic reactive arthritis is the damage to the enthesial apparatus and aponeuroses through enthesitis (41%) and tendinitis (24,2%). Damage to the tendon-ligament apparatus in parasitic reactive arthritis included enthesopathy of the knee joints, tenosynovitis of the ankle, radiocarpal joints, and small joints of the hands and feet.
5. Quality of life indices of patients with parasitic reactive arthritis from *Echinococcus granulosus* were shown, to a significant extent, to be defined by the patient's psychoemotional and physical status, the impact being reflected by physical-motor disturbances (expressed by the concepts of physical health, perceived by the SF-36 questionnaire – the PF, RP, BP, GH scales), clearly modified by the parasitic infestation, and by the psychological ones (VT, SF, RE, MH), predominantly influenced by it.

PRACTICAL RECOMMENDATIONS

1. In patients with hepatic or pulmonary echinococcosis, the presence of joint syndrome requires caution, because the arthritis has an early onset (not noticed), the patients being strongly influenced by the cystic damage to the internal organs, but, subsequently, the musculoskeletal damage progresses rapidly, with an aggressive character and polyerosive.
2. *Giardia lamblia* is the most common parasitosis and presents an increased degree of immune damage, including joint damage, so in infected patients it is advisable to carefully study possible immunological changes (cellular immune suppression and excessive eosinophilic activity, followed by increased IgA concentrations and IgE).
3. When detecting toxocarosis, it is recommended to initiate both an adequate treatment and a monitoring of the eradication of this pathogen, because the joint syndrome is more often erased, but, evolutionarily, it progresses to non-specific joint damage.
4. In patients with a non-specific inflammatory joint syndrome, similar to reactive arthritis, but in the absence of urogenital or enteral characteristic etiological agents, it is advisable to analyze the possible parasitic infestation, because the musculoskeletal disorders, although they may have a subclinical evolution, their evolution is progressive and disabling.

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ADNOTARE

GROSU Maia, „Manifestări reumatice în infecțiile parazitare”, teză de doctor în științe medicale, Chișinău, 2024

Structura tezei : lucrarea este expusă pe 163 pagini de text electronic, 124 pagini de text de bază și include: introducerea, 5 capitole, concluzii și recomandări practice, bibliografia cu 216 surse literare. Teza este ilustrată cu 23 tabele, 24 figuri și 11 anexe. Rezultatele obținute au fost redată în 16 publicații științifice, 3 acte despre implementarea rezultatelor, 3 certificate de inovator.

Cuvinte-cheie: artrita parazitara, manifestări, forme clinice particulare, giardia, toxocara, echinococoza.

Domeniul de studiu: Reumatologie

Scopul lucrării: cercetarea particularităților clinico-evolutive și paraclinice ale cazurilor de infecții parazitare, asociate cu afectări ale aparatului locomotor, pentru propunerea unor principii de diagnostic precoce ale afectărilor osteo-articulare în patologiile parazitare.

Obiectivele cercetării: 1. Cercetarea particularităților clinice și evolutive ale artritelor în parazitoze. 2. Evaluarea indicilor imuno-inflamatori ale artritelor în parazitoze. 3. Caracterizarea comparativă a afectărilor aparatului locomotor în diverse infecții parazitare prin investigații imagistice. 4. Caracteristica particularităților de diagnostic precoce ale artritelor în parazitoze. 5. Determinarea impactului asupra calității vieții la artritele reactive parazitare.

Noutatea și originalitatea științifică: Acest studiu reprezintă un punct de referință în cercetarea artritelor reactive parazitare, deoarece pentru prima dată s-a realizat o evaluare comparativă între manifestările clinice ale diferitelor forme de agenți invazivi responsabili de aceste afecțiuni. Cercetarea a adus o contribuție semnificativă prin investigarea relației dintre manifestările paraclinice de laborator și cele instrumentale și modul în care acestea influențează evoluția clinică a artritei reactive parazitare. S-a evaluat și impactul artritei reactive parazitare asupra calității vieții pacienților, analizând nu doar aspectele fizice, dar și cele sociale, psihice și emoționale. Sindromul algic, atât cronic cât și acut, generat de procesul inflamator, a fost un aspect central în această analiză, oferind o înțelegere mai profundă a modului în care această afecțiune influențează diferite domenii ale vieții cotidiene.

Problema științifică importantă soluționată în teză: Studiul a adus noi oportunități pentru diagnosticarea diferențiată ale artritelor reactive parazitare, atât din punct de vedere clinic cât și paraclinic. În acest mod, s-a identificat un model specific al manifestărilor artritei reactive în contextul parazitozelor, contribuind la o mai bună înțelegere a diversității clinice și etiologice ale acestei patologii. Această descoperire permite o diferențiere mai precisă între formele etiologice ale bolii, facilitând alegerea unei abordări terapeutice mai personalizate și eficiente.

Semnificația teoretică a lucrării: Rezultatele obținute din acest studiu constituie un fundament științific significant pentru dezvoltarea unor algoritmi de diagnostic destinați identificării precoce ale afectărilor musculo-scheletale asociate cu parazitoze. Acești algoritmi sunt esențiali pentru o diagnosticare rapidă și precisă, ce poate îmbunătăți considerabil prognosticul pacienților și poate reduce complicațiile pe termen lung. Contribuția teoretică a studiului oferă un suport solid pentru cercetările viitoare în domeniul artritelor reactive parazitare, fiind de o importanță majoră pentru clinicieni în gestionarea adecvată ale acestor afecțiuni complexe.

Valoarea aplicativă: Datele obținute privind diferitele manifestări clinico-paraclinice ale artritei reactive parazitare vor facilita stabilirea unui diagnostic precis și inițierea unui tratament corespunzător. Rezultatele studiului realizat vor contribui la îmbunătățirea prognosticului tratamentului cu preparate antiparazitare, administrate în funcție de forma specifică a artritei reactive parazitare și de agentul patogen implicat.

Implementarea rezultatelor științifice: Rezultatele studiului au fost incluse în activitatea clinică a secțiilor de reumatologie și artrologie a IMSP SCR „Timofei Moșneaga”, secția reumatologie IMSP SCM „Sfânta Treime” și în activitatea didactică a Departamentului Medicină internă, Disciplina reumatologie și nefrologie.

ANNOTATION

GROSU Maia, "Rheumatic manifestations in parasitic infections", doctoral thesis in medical sciences, Chisinau, 2024

Thesis structure: the thesis is presented on 163 electronic text pages, 124 basic text pages and includes: introduction, 5 chapters, conclusions and practical recommendations, bibliography with 216 literary sources. The thesis is illustrated with 23 tables, 24 figures, 11 annexes. The obtained results were published in 16 scientific works, 3 acts on the implementation of the results, 3 innovator certificates.

Key words: parasitic arthritis, manifestations, particular clinical forms, giardia, toxocara, echinococcosis.

Domain of research: Rheumatology

Purpose of the paper: was to research the clinical-evolutionary and paraclinical particularities of cases of parasitic infections, associated with locomotor system disorders, for the proposal of early diagnostic principles of osteo-articular disorders in parasitic pathologies.

Research objectives: 1. Research of the clinical and evolutionary peculiarities of arthritis in parasitosis. 2. Evaluation of immuno-inflammatory indices of arthritis in parasitosis. 3. Comparative characterization of locomotor system impairments in various parasitic infections through imaging investigations. 4. Characteristic of early diagnostic features of arthritis in parasitosis. 5. Determining the impact on quality of life in parasitic reactive arthritis.

Scientific novelty and originality: This study represents a landmark in the research of parasitic reactive arthritis, because for the first time a comparative evaluation was made between the clinical manifestations of different forms of invasive agents responsible for these conditions. The research made a significant contribution by investigating the relationship between laboratory and instrumental manifestations and how they influence the clinical course of parasitic reactive arthritis. The impact of reactive parasitic arthritis on the patients' quality of life was also evaluated, analyzing not only the physical but also the social, mental and emotional aspects. The pain, both chronic and acute, generated by the inflammatory process, was a central aspect in this analysis, providing a deeper understanding of how this condition influences different areas of daily life.

The scientific problem solved in the thesis: The study brought new opportunities for the differential diagnosis of parasitic reactive arthritis, both clinically and paraclinically. In this way, a specific pattern of reactive arthritis manifestations was identified in the context of parasitosis, contributing to a better understanding of the clinical and etiological diversity of this pathology. This discovery allows a more precise differentiation between the etiological forms of the disease, facilitating the choice of a more personalized and effective therapeutic approach.

The theoretical significance: The results obtained from this study constitute a significant scientific foundation for the development of diagnostic algorithms aimed for the early identification of musculoskeletal disorders associated with parasitosis. These algorithms are essential for rapid and accurate diagnosis, which can greatly improve patient prognosis and reduce long-term complications. The theoretical contribution of the study provides solid support for future research in the field of parasitic reactive arthritis, being of major importance to clinicians in the appropriate management of these complex conditions.

Application value of the study: The obtained data according to the different expressions of the clinical-paraclinical manifestations in parasitic reactive arthritis will allow establishing the diagnosis and launching an appropriate treatment. The results of the conducted study will contribute to predicting the effect of antiparasitic drugs, indicated for different forms of parasitic reactive arthritis, operating on the basis of the incriminated pathogen.

Implementation of the scientific results: The results of the study were included in the clinical activity of the rheumatology and arthrology sections of "Timofei Moşneaga" Republican Clinical Hospital, the rheumatology section of "Sfânta Treime" Clinical Hospital and in the didactic activity of the Department of Internal Medicine, Discipline of Rheumatology and Nephrology.

АННОТАЦИЯ

ГРОСУ Майя, “Ревматические проявления при паразитарных инфекциях”, диссертация на соискание научной степени доктора медицинских наук, Кишинев, 2024

Структура диссертации: работа представлена на 163 страницах электронного текста, 124 страницах основного текста, состоит из введения, 5 глав, выводов, практических рекомендаций, библиографии из 216 источника, иллюстрирована 23 таблицами и 24 рисунками. Полученные результаты были опубликованы в 16 научных работах, 3 акта о внедрении результатов, 3 новаторских сертификатах.

Ключевые слова: паразитарные артриты, проявления, частные клинические формы, лямблии, токсокары, эхинококкоз.

Область исследования: Ревматология

Цель исследования: исследование клинико-эволюционных и параклинических особенностей случаев паразитарных инфекций, связанных с поражением опорно-двигательного аппарата, для предложения принципов ранней диагностики костно-суставных поражений при паразитарных патологиях.

Задачи исследования: 1. Изучение клинико-эволюционных особенностей артритов при паразитозах. 2. Оценка иммуновоспалительных показателей артритов при паразитозах. 3. Сравнительная характеристика нарушений опорно-двигательного аппарата при различных паразитарных инфекциях методами лучевых исследований. 4. Характеристика ранних диагностических признаков артритов при паразитозах. 5. Определение влияния на качество жизни при паразитарном реактивном артрите.

Научная новизна: Это исследование представляет собой точка отсчета в изучении паразитарного реактивного артрита, поскольку впервые проведена сравнительная оценка клинических проявлений различных форм инвазивных агентов, ответственных за эти состояния. Исследования внесли значительный вклад, изучив взаимосвязь параклинических лабораторных и инструментальных проявлений и их влияние на клиническое течение реактивного паразитарного артрита. Также оценивалось влияние реактивного паразитарного артрита на качество жизни пациентов, анализируя не только физические, но и социальные, психические и эмоциональные аспекты. Болевой синдром, как хронический, так и острый, вызванный воспалительным процессом, стал центральным аспектом в этом анализе, позволив более глубоко понять, как это состояние влияет на различные сферы повседневной жизни.

Важность решенной научной проблемы.: Исследование открыло новые возможности для дифференциальной диагностики паразитарного реактивного артрита как с клинической, так и с параклинической точки зрения. Таким образом, была выявлена конкретная модель проявлений реактивного артрита на фоне паразитозов, способствующая лучшему пониманию клинического и этиологического разнообразия этой патологии. Это открытие позволяет более точно дифференцировать этиологические формы заболевания, облегчая выбор более персонализированного и эффективного терапевтического подхода.

Теоретическая значимость: Результаты, полученные из данного исследования, составляют значимую научную основу для разработки диагностических алгоритмов, направленных на раннее выявление нарушений опорно-двигательного аппарата, связанных с паразитозами. Эти алгоритмы необходимы для быстрой и точной диагностики, что может значительно улучшить прогноз пациента и уменьшить долгосрочные осложнения. Теоретический вклад исследования обеспечивает надежную поддержку для будущих исследований в области паразитарного реактивного артрита, что имеет большое значение для клиницистов в правильном лечении этих сложных состояний.

Практическая значимость: Полученные данные о различных клинико-параклинических проявлениях реактивного паразитарного артрита будут способствовать установлению точного диагноза и началу соответствующего лечения. Результаты исследования будут способствовать улучшению прогноза лечения антипаразитарными препаратами, назначаемыми в зависимости от конкретной формы реактивного паразитарного артрита и возбудителя.

Внедрение в практику: Результаты исследования были включены в клиническую деятельность отделений ревматологии и артрологии Республиканской клинической больницы «Тимофей Мошняга», отделения ревматологии Муниципальной клинической больницы «Сфынта Трейме» и в дидактическую деятельность кафедр внутренних болезней, Ревматология и нефрология.

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✓ **international**

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