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COMPARATIVE RELATIONSHIP OF MARKERS OF INFLAMMATORY CHANGES IN PERIPHERAL BLOOD IN PERSONS SUFFERING WITH CHRONIC PAIN SYNDROME IN DORSOPATHIES


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ДОРСОПАТИЯЛАРДА СУРУНКАЛИ ОҒРИҚ СИНДРОМИ БИЛАН ОҒРИГАН БЕМОРЛАРДА ПЕРИФЕРИК ҚОНДАГИ ЯЛЛИҒЛАНИШ ЎЗГАРИШЛАРИ БЕЛГИЛАРИНИНГ ҚИЁСИЙ АЛОҚАСИ

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СРАВНИТЕЛЬНАЯ ВЗАИМОСВЯЗЬ МАРКЕРОВ ВОСПАЛИТЕЛЬНЫХ ИЗМЕНЕНИЙ ПЕРИФЕРИЧЕСКОЙ КРОВИ У ЛИЦ, СТРАДАЮЩИХ ХРОНИЧЕСКИМ БОЛЕВЫМ СИНДРОМОМ ПРИ ДОРСОПАТИЯХ

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Резюме. *Дорсопатия, умуртқа поғонасининг асептик яллиғланиши билан тавсифланган кенг тарқалган касаллик, яллиғланиш белгилари бўйича яхшилаб ўрганилмаган. Шу билан бирга, ўткир фазали оқсилларни ва яллиғланиш белгиларини ўлчаш учун қон тестини ўрганиш танадаги яллиғланиш жараёнларида даражаси ошиб борадиган турли хил оқсилларни ҳар томонлама таҳлил қилишни таъминлайди. Шунинг учун кўрсаткичларни ўрганиш ва дорсопатияда сурункали оғриқ синдроми билан оғриган беморларнинг периферик қонида яллиғланиш белгилари ўртасида қиёсий корреляцияни ўргатиш долзарбдир. Ушбу тадқиқот учун 320 йилдан 2018 йилгача Самарқанд шаҳар тиббиёт бирлашмасининг неврология бўлимида даволанган турли келиб чиқиши дорсопатияли сурункали оғриқ синдроми билан оғриган 2021 киши синчковлик билан танлаб олинди. Уларнинг ҳолатини баҳолаш учун биз ўткир фазали оқсилларни ва фибриноген, С-реактив оқсил ва интерлейкин-1 каби яллиғланиш белгиларини ўлчаш учун қон тестларидан фойдаландик. Сиқиш-ишемик, бруцеллёз, ревматик ва герпетик каби турли хил дорсопатиялар билан оғриган беморларни ўрганиш натижалари шуни кўрсатадики, фибриноген, С-реактив оқсил ва интерлейкин-1 турли хил келиб чиқадиган дорсопатияларда сурункали оғриқ синдроми бўлган беморларни фарқлаш учун қимматли биокимёвий кўрсаткичлар бўлиб хизмат қилиши мумкин. Сиқилиш-ишемик дорсопатиялар, бруцеллёз, ревматик ва герпетик генезис натижасида келиб чиққан сурункали оғриқ синдроми бўлган беморларда сурункали оғриқни қўзғатадиган яллиғланиш жараёнининг турли кўрсаткичлари кузатилди. Бундай кўрсаткичларга қон зардобидаги фибриноген, С-реактив оқсил ва интерлейкин-1нинг концентрацияси киради. Ушбу маълумотлар оғриқнинг яллиғланиш хусусиятини тасдиқлайди ва унинг сурункали ва доимий йўналишини тушунтиради.*

Калит сўзлар*: яллиғланиш белгилари, фибриноген, С-реактив оқсил, интерлейкин-1, дорсопатия.*

Abstract. *Dorsopathy, a frequently occurring condition characterized by aseptic inflammation in the spine, has not been thoroughly examined in terms of inflammatory markers. However, conducting a blood test to measure acute phase proteins and inflammatory markers can provide a comprehensive analysis of various proteins that tend to increase during inflammatory processes in the body. Therefore, it is essential to investigate the indicators and establish a comparative correlation between inflammatory markers in the peripheral blood of patients suffering from chronic pain syndrome in dorsopathy. A total of 320 individuals suffering from chronic pain syndrome with dorsopathies of different origins, who are currently undergoing treatment at the neurology department of the City Medical Association of Samarkand from 2018 to 2021, were carefully chosen for this study. In order to assess their condition, we employed blood tests to measure acute phase proteins and inflammatory markers such as fibrinogen, C-reactive protein, and interleukin-1β. The study findings from patients with different types of dorsopathies, such as compression-ischemic, brucellosis, rheumatic, and herpetic, indicate that fibrinogen, C-reactive protein, and interleukin-1β could serve as valuable biochemical indicators for distin-*

guishing patients with chronic pain syndrome in dorsopathies of different origins. Various indicators of an inflammatory process, which provoke chronic pain, were observed in patients with chronic pain syndrome caused by compression-ischemic dorsopathies, brucellosis, rheumatic and herpetic origins. These indicators include the concentrations of fibrinogen, C-reactive protein, and interleukin-1β in the blood serum. These findings confirm the inflammatory nature of the pain and explain its chronic and persistent course.

Key words: *inflammation markers, fibrinogen, C-reactive protein, interleukin-1β, dorsopathy.*

Introduction. The analysis of acute phase proteins and inflammation markers in a blood test involves the comprehensive study of multiple proteins, which are found to increase during various inflammatory processes in the body. Most commonly associated with aseptic inflammation in the back is drooping pathology, but none [2, 3] has been studied for markers of this type of inflammation.

An increase in the quantity of fibrinogen is not only a part of the blood coagulation system, but also serves as an indicator of acute and chronic inflammatory, immune, and tumor-related phenomena. The current understanding of inflammation and radiculopathies is grounded on the fact that the process was restricted to one or more spinal segments, with a local character [6, 7]. In these diseases, an increase in fibrinogen concentration beyond the physiological norm is moderately significant and can be effectively stopped by NSAIDs [8, 9].

Objective of the study: examination of factors and comparative relationship of markers of inflammatory changes in the peripheral blood of individuals suffering from chronic pain syndrome in various types of back disorders.

The aim of the research was to investigate the levels of fibrinogen, C-reactive protein, and interleukin-1β in the plasma of patients with chronic pain syndrome caused by compressive-ischemic dorsopathies, brucellosis, rheumatism, and herpes.

Materials and research methodology. A total of 320 patients with chronic pain syndrome associated with different types of back disorders were chosen from the neurology department of the city medical association in Samarkand from 2018 to 2021**.**

For further scientific research, the patients were divided into the following groups:

- 1st group: chronic dorsopathy of compression-ischemic genesis (DCIG) - 82 patients;

- 2nd group - dorsopathy in chronic brucellosis (CBR) - 84 patients;

- 3rd group - dorsopathy of rheumatic genesis (DRheuG) - 76 patients;

- 4th group - dorsopathy in chronic herpes (DHerH) - 78 patients;

- the control group consisted of 40 conditionally healthy people with signs of dorsopathies, commensurate in sex and age with the above groups (employees of the city medical association were selected).

The research was conducted in accordance with the provisions of the Helsinki Declaration of the World Association "Ethical guidelines for scientific and medical research involving human subjects", as revised in 2000. All data pertaining to the participants was gathered, examined, and documented in written form with the participants' informed consent. The scholarly investigation was sanctioned by the institute's ethics board as per the agreements regarding collaborative scientific endeavors.

All patients with CPS were in the age range of persons from 16 to 75 years, with predominantly 30-39 years old - 96 (30%), and also 50-59 years old - 67 (20.9%).

Gender gradation of 320 patients: women - 205 (64.1%), men - 113 (35.4%) (Table 1).

Dorsopathies of different origins have sparked significant interest: compression-ischemic dorsopathy, chronic brucellosis-induced dorsopathy, rheumatic dorsopathy, and TORCH infection-induced dorsopathy, specifically herpes.The objective of this article was to highlight the laboratory findings. We have analyzed the clinical and biochemical blood tests, as well as urinalysis.

For rheumatic tests: a) rheumatic factor (RF) - venous blood was examined using immunoturbidimetry, with a result of over 8 IU/ml considered positive; b) C-reactive protein (CRP) - venous blood was examined after fasting for 12 hours, with no physical or emotional overexertion 30 minutes before the study, and no smoking for 30 minutes before the study.

Table 1. Gradation by sex and age

Age (years)	Women (abs/%)	Men (abs/%)	Total (abs/%)
Under 19	13 (4,1%)	11 (3,4%)	24 (7,5%)
20-29	44 (13,7%)	13 (4,1%)	57 (17,8%)
30-39	59 (18,4%)	37 (11,6%)	96 (30%)
40-49	30 (9,4%)	23 (7,2%)	53 (16,6%)
50-59	44 (13,7%)	23 (7,2%)	67 (20,9%)
60 and older	17 (5,3%)	6 (1,9%)	23 (7,2%)
Total	207 (64,7%)	113 (35,3%)	320 (100%)

Readings greater than 10 mg/l indicate acute inflammation or chronic disease; c) antistreptolysin (ASLO) - venous blood was examined after fasting, with no eating the night before the study to exclude any interference from food.alcohol, intense physical activity and medication. Readings above 200 IU/mL are considered positive [10].

2 - tests for the identification of brucellosis: a) Heddelson's test - a blood sample was taken on an empty stomach from a finger on a glass slide, brucellosis diagnosticum was added to it. The presence of an agglutination reaction was considered as a positive result; b) Wright's test - venous blood was examined to detect antibodies to the brucellosis antigen. Titer values of 100-200 indicated a positive result, which could indicate a transition from an acute to a chronic process.

3 - blood test for TORCH infection, which included tests for antibodies to 4 infections: herpes, toxoplasmosis, cytomegalovirus, and rubella virus. We specifically focused on patients with antibodies to herpes, as it is commonly reported that this condition mainly affects the sensory ganglia and peripheral nerves. Antibodies to herpes 1 and 2 types IgG and IgM were analyzed. A positive IgG response indicated chronic carriage [11].

To investigate endothelin-1, blood collected from the cubital vein on an empty stomach (14 hours post-meal) was utilized. The blood was analyzed twice, upon admission and at the conclusion of the treatment. Within 2 hours of blood sampling, the serum was separated through centrifugation (3000 rpm) and the examination was promptly conducted.

Measurement of fibrinogen levels. Fibrinogen concentration in blood plasma was determined using a standard, modified laboratory-clinical technique developed by A. Glauss [11], employing a novel test system called "Multi Tech-Fibrinogen". This approach enabled the determination of fibrinogen concentration across a broad range, without the need for any dilution steps that might impact accuracy, precision, and dilution. The main idea of the method was to measure the time it takes for citrate platelet-poor plasma to form a clot when excess thrombin is present. To carry out the experiment, venous blood was mixed with sodium citrate in a plastic tube and left to incubate for two minutes at 37°C. After that, 50 ml of thrombin solution was added. The clotting time of the plasma ranged from 5 to 100 seconds. The test system was calibrated using coagulograms with different methods of recording the time it takes for a clot to form. The calibration curve showed a linear relationship between 0.5 - 6 g/l [12]

CRP is a type of protein that is produced during the inflammatory process and its production is stimulated by anti-inflammatory substances such as interleukin-1, interleukin-6, and tumor necrosis factor. It is considered a marker of the body's response to inflammation and plays a role in both humoral and cellular immunity. Elevated levels of CRP can indicate a viral or bacterial infection, tissue damage, autoimmune disorders, or exacerbation of chronic diseases. Blood samples are typically taken after a 4-hour fast and precautions are taken to avoid factors that could affect the results, such as intense physical activity, smoking, and alcohol consumption. The level of CRP is measured by the amount of precipitation that occurs, and a linear calibration curve is used to determine the concentration of CRP in the sample [14].

Interleukin-1β is a type of cytokine that causes inflammation and is involved in both general and specific immune responses. It is produced and released by certain types of white blood cells and is a key part of the body's defense against harmful substances. In our research, we measured interleukin-1β levels using ELISA

Discussion. The amount of fibrinogen found in the blood plasma of patients with compression-ischemic dorsopathies (group I) did not exceed 4.3 g/l, which is within the normal range. In patients with chronic pain caused by brucellosis-related dorsopathies (group II), the levels of fibrinogen ranged from 1.7 to 3.2 g/l, with an average of 2.45 g/l, also within the normal range. However, in the third group of patients with rheumatic radiculopathies, the levels of fibrinogen were significantly higher, ranging from 12 to 18 g/l, with an average of 15 g/l

Fibrinogen levels in blood plasma in patients with herpetic radiculopathies were slightly increased and amounted to 4.8-5.8 g/l, which averaged an average of 5.3 g/l.

Thus, based on the data obtained, the presence of native fibrinogen in the blood plasma can be chosen as an additional biochemical criterion for the differential diagnosis of patients with chronic pain syndrome in dorsopathies of various origins.

CRP is a protein that is part of the body's response to inflammation and can be measured through various biochemical and immunochemical markers. In cases of compression-ischemic radiculopathy, chronic pain syndrome can be caused by degenerative-dystrophic changes in the spine and intervertebral discs. This pain is triggered by mechanical, biochemical, and immunological factors that affect the spinal roots, leading to aseptic autoimmune inflammation

We examined C-reactive protein in our research to evaluate the level of inflammation. In healthy individuals, CRP is present in small amounts in the blood serum and is less than 3 mg/l.

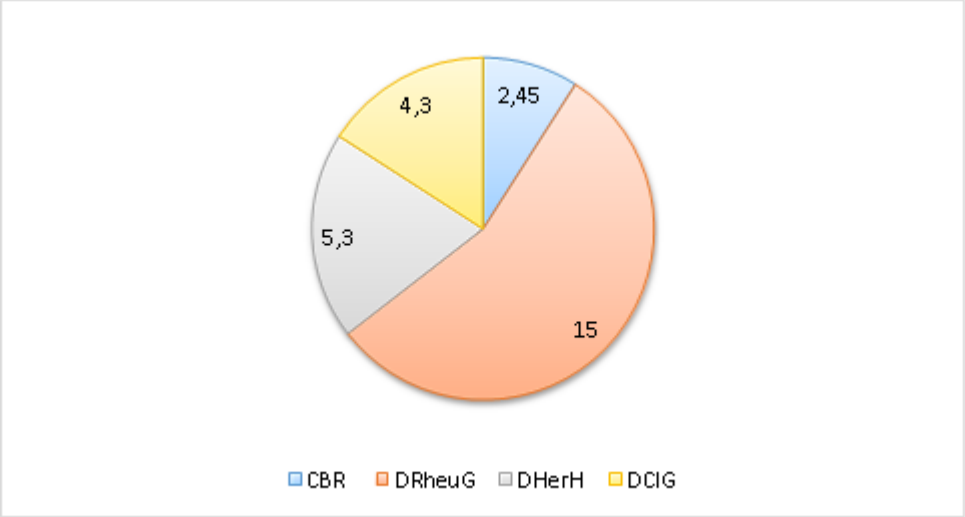

Fig.1. Fibrinogen concentration in patients with radiculopathies of various origins

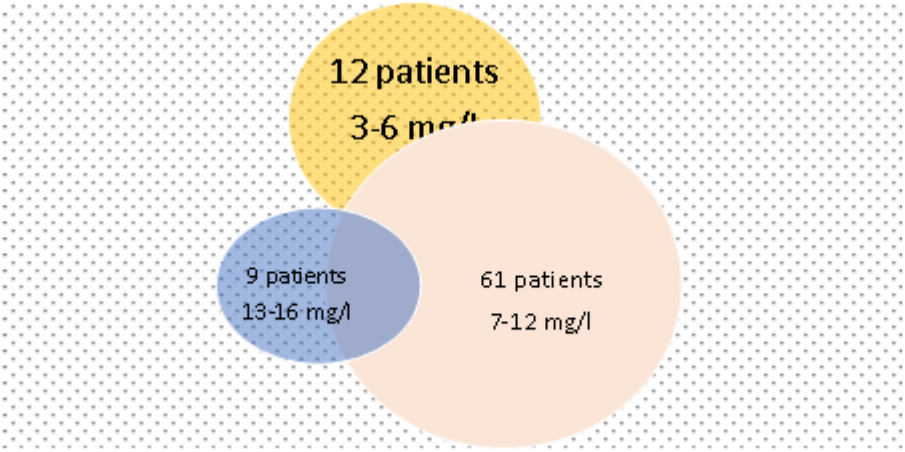

Fig.2. Indicators of C-reactive protein in group I

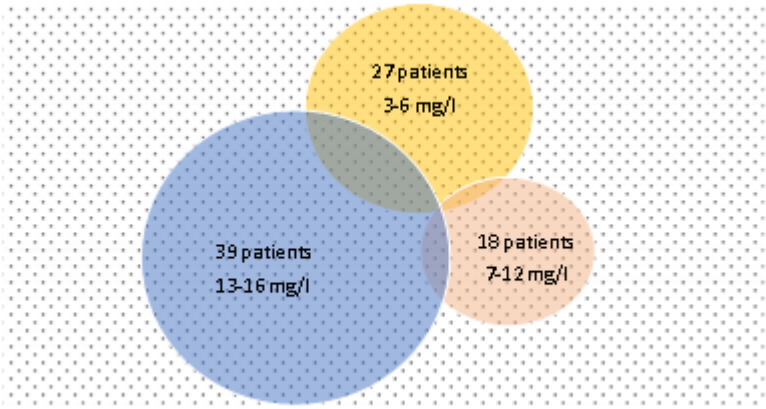

Fig.3. Indicators of C-reactive protein in group II

In cases of mild inflammation, CRP in the blood serum can reach up to 7 mg/l. A range of 7.1 to 50 mg/l indicates a moderate level of inflammation. In serious inflammatory and autoimmune disorders, CRP levels are higher than 50 mg/l

The day prior to donating blood, individuals were instructed to avoid strenuous exercise, smoking, and alcohol consumption. Blood was collected from a vein in the morning while fasting. The research was carried out on a total of 82 participants. The level of CRP was measured using a precise quantitative technique with a kit from "Thermo scientific".

The initial group of patients had 12 (14.6%) individuals with CRP levels of 3-6 mg/l, 61 (74.4%) with levels of 7-12 mg/l, and 9 (11%) with levels of 13-16 mg/l. Based on current understanding, this rise in CRP concentration in the blood plasma of the patients suggested the presence of a subclinical inflam-

matory process. It demonstrated the presence of systemic inflammation and immunopathological processes in the bodies of patients with chronic pain syndrome caused by compression-ischemic radiculopathy.

The second group of patients had unique features in the examination of C-reactive protein. It is understood that the cause of brucellosis is found within cells, which leads to the identification of loose connective tissue cells and their attachment to receptors. These signals then activate the innate immune system. Foreign pathogens within the cell also stimulate the production and release of pro-inflammatory cytokines into the bloodstream from loose connective tissue [14]. Hepatocytes produce C-reactive protein in reaction to cytokine production. All 84 patients in group II were tested for C-reactive protein, with the following results: 28 (33.3%) had levels of 3-6 mg/l, 39 (46.4%) had levels of 7-12 mg/l, and 17 (20.3%) had levels of 13-19 mg/l

The characteristics of C-reactive protein in patients belonging to group III were specific and revealing. This type of study is typically performed for all patients with rheumatic conditions. In response to the presence of toxins in the bloodstream, the body produces C-reactive protein, which binds to them and neutralizes their harmful effects. In certain cases, the levels of C-reactive protein may increase more rapidly than the symptoms, serving as an indicator of both the progression and regression of the disease. The parameters of C-reactive protein were examined in all 76 patients in group III. Out of these, 8 (10.5%) had levels between 3-6 mg/l, 12 (15.8%) had levels between 7-12 mg/l, and 56 (73.7%) had levels between 13-19 mg/l.

Every patient in group IV had their blood drawn to test for C-reactive protein, which is not a specific indicator according to research. This protein is associated with inflammation and can aid in diagnosing bacterial infections. Out of the 78 patients in group IV, 27 (34.6%) had levels of 3-6 mg/l, 50 (64.1%) had levels of 7-12 mg/l, and 1 (1.3%) had levels of 13-19 mg/l.

Summing up the results of the study of C-reactive protein in patients with chronic pain syndrome, we obtained the following results.

Therefore, the examination of CRP levels in the blood serum of patients with chronic pain syndrome caused by various dorsopathies is a highly accurate quantitative method that can serve as an additional diagnostic indicator in the development of this condition.

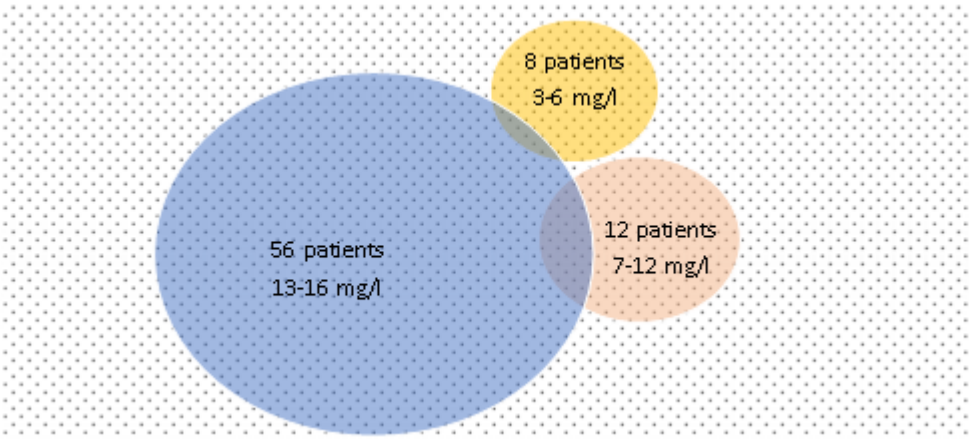

Fig.4. Indicators of C-reactive protein in group III

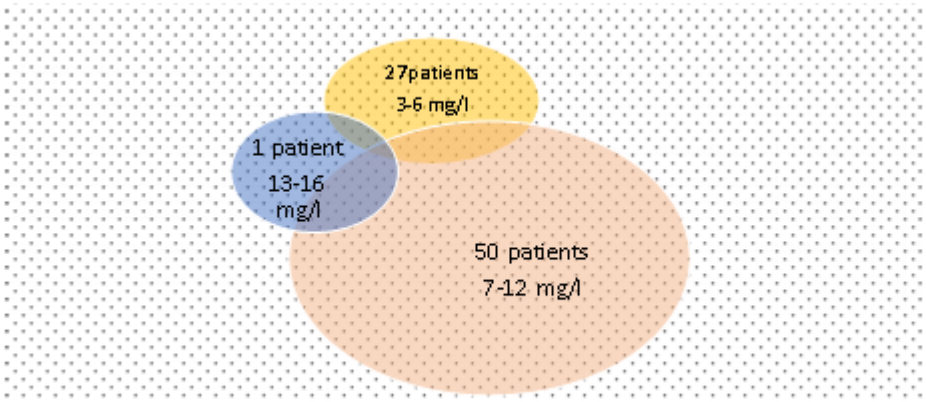

Fig.5. Indicators of C-reactive protein in group IV

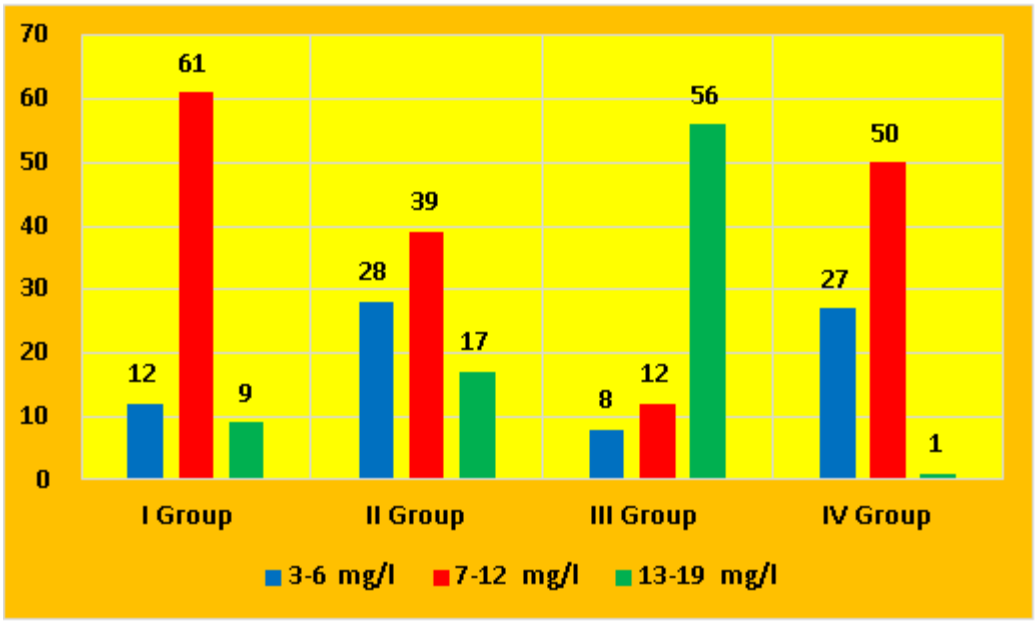

Fig.6. Parameters of C-reactive protein in the blood plasma of patients with chronic pain syndrome in dorsopathies of various origins

Table 2. The content of interleukin-1β in blood serum in patients of group I

Examined patients	11 (44%)	5 (20%)	9 (36%)	10 people in the control group
interleukin-1β pg/ml	4,51 (4,47-4,55)	1,35 (1,29-1,41)	0,56 (0,54-0,58)	0,58 (0,55-0,61)

Table 3. The content of interleukin-1β in blood serum in patients of group II

Examined patients	2 (8%)	15 (60%)	9 (36%)	10 people in the control group
interleukin-1β pg/ml	5,61 (5,60 – 5,62)	2,35 (2,29-2,41)	1,56 (1,54-1,58)	0,58 (0,55-0,61)

Table 4. The content of interleukin-1β in blood serum in patients of group III

Examined patients	17 (68%)	5 (20%)	3(12%)	10 people in the control group
interleukin-1β pg/ml	7,65 (7,59 – 7,71)	5,32 (5,26-5,38)	3,75 (3,72-3,78)	0,58 (0,55-0,61)

Table 5. The content of interleukin-1β in blood serum in patients of group IV

Examined patients	17 (68%)	4 (16%)	4 (16%)	10 people in the control group
interleukin-1β pg/ml	1,55 (1,49-1,61)	0,75 (0,69-0,81)	0,58 (0,56-0,60)	0,58 (0,55-0,61)

CRP may contribute to the inflammatory process that leads to pain, and also stimulate the production of pro-inflammatory cytokines. Interleukin-1β, a cytokine found in the blood serum, is produced by mononuclear cells and plays a role in both specific and nonspecific protective responses in the body, and can affect cells involved in dorsopathies.

To carry out this research, we chose 25 participants from each group and included 10 individuals in the control group for comparison.

We chose 25 individuals from Group I to measure interleukin-1β levels using ELISA and standard reagent kits (Bender MedSystem 224/2, Austria) following the provided instructions. Among patients with chronic pain caused by compression-ischemic radiculopathy, the following findings were observed: 11 (44%) patients showed a significant expression of interleukin-1β, with levels reaching 4.51 (4.47-4.55) pg/ml, 5 (20%) had levels of 1.35 (1.29-1.41) pg/ml, indicating a mild degree of inflammatory reaction, and 9 (36%) had levels of 0.56 (0.54-0.58) pg/ml, suggesting the absence of inflammatory processes (Table 2).

To make it easier to compare the collected data on the levels of interleukin-1β (IL-1β) in the blood serum of patients in group II, 25 patients were also chosen. As a result, the following values were obtained: 5.61 (5.60 - 5.62) pg/ml in 2 (8%) patients, 2.35 (2.29-2.41) pg/ml in 15 (60%) patients, indicating a mild level of inflammation, and 1.56 (1.54-1.58) pg/ml in 8 (32%) patients, indicating a weak level of inflammatory processes.

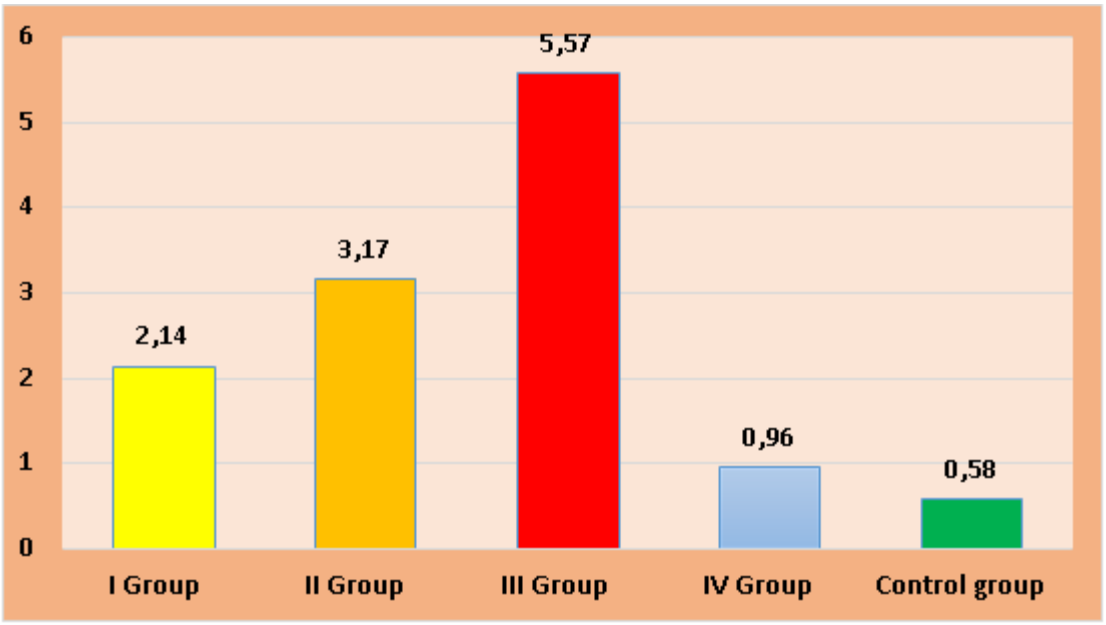

Fig.7. The content of interleukin-1β in blood serum in patients with chronic pain syndrome in dorsopathies

The content of IL-1β in the blood serum of patients of group III was as follows: in 17 (68%) patients 7.65 (7.59 - 7.71) pg / ml indicated a fairly high degree of inflammation, in 5 (20%) - 5 .32 (5.26-5.38) pg / ml, which indicated a pronounced degree of inflammatory reaction and in 3 (12%) in 75 (3.72-3.78) patients, the results indicated a moderate degree of inflammatory processes.

The same methods were used to measure the concentration of IL-1β in the blood serum of 25 patients in group IV. The results showed that 17 (68%) patients had a low level of interleukin-1β at 1.55 (1.49-1.61) pg/ml, 4 (16%) had a slightly higher level at 0.75 (0.69-0.81) pg/ml, indicating a mild inflammatory response, and 4 (16%) had a very low level at 0.58 (0.56-0.60) pg/ml, suggesting the absence of any inflammatory processes.

The recorded amount of IL-1β in patients diagnosed with Chronic Pain Syndrome (CPS) and Radiculopathy of Rheumatic Origin (RRO) was similar to the levels typically seen in both general and specific cases of infectious and non-infectious inflammation [1].

As evidenced by the tables presented, the IL-1β levels in the control group align with the standard values for healthy individuals and are in line with findings from other studies that utilized similar techniques [2, 4].

Based on the results of our research, we found that patients in the third group with CPS and RRO had a significantly higher expression of IL-1β (5.57 pg/ml) compared to the normal level. This was 10 times higher than normal. In the second group, patients with CPS and radiculopathy in chronic brucellosis (RCBr) had levels 5.5 times higher than normal, with an average of 3.17 pg/ml. The first group of patients with CPS in RCIG had values of 2.14 pg/ml, which were almost 4 times higher than normal. In the fourth group, patients with CPS in RG had an average level of 0.96 pg/ml, which was 2 times higher than normal. However, this still indicated a decrease in IL-1β production in herpes infection compared to the other groups

Conclusion. Studying the levels of inflammation markers in the blood serum of patients with chronic pain syndrome caused by various types of dorsopathies can help identify signs of inflammation. Measuring native fibrinogen in blood plasma can be used as an additional biochemical indicator for differentiating between patients with chronic pain from different types of dorsopathies. The concentration of CRP in the blood serum of patients with chronic pain syndrome and dorsopathies can be a highly sensitive quantitative method for diagnosing chronic pain. Additionally, CRP may act as a causative factor for inflammation and pain, as well as stimulate the production of pro-inflammatory cytokines. The levels of interleukin-1β in the blood serum can indicate the presence of an inflammatory process causing chronic pain. An increase in endothelin-1 levels in the blood serum of patients may indicate damage to the peripheral vascular endothelium in dorsopathies, which can also determine the nature of chronic pain depending on the etiology and pathogenesis.

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СРАВНИТЕЛЬНАЯ ВЗАИМОСВЯЗЬ МАРКЕРОВ ВОСПАЛИТЕЛЬНЫХ ИЗМЕНЕНИЙ ПЕРИФЕРИЧЕСКОЙ КРОВИ У ЛИЦ, СТРАДАЮЩИХ ХРОНИЧЕСКИМ БОЛЕВЫМ СИНДРОМОМ ПРИ ДОРСОПАТИЯХ

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Резюме. *Дорсопатия, часто встречающееся заболевание, характеризующееся асептическим воспалением позвоночника, не было тщательно изучено с точки зрения маркеров воспаления. Однако изучение анализа крови для измерения белков острой фазы и маркеров воспаления может обеспечить комплексный анализ различных белков, уровень которых имеет тенденцию повышаться при воспалительных процессах в организме. Поэтому актуальным является исследование показателей и установление сравнительной корреляции между маркерами воспаления в периферической крови пациентов, страдающих хроническим болевым синдромом при дорсопатии. Для данного исследования были тщательно отобраны 320 человек, страдающих хроническим болевым синдромом с дорсопатиями различного генеза, которые проходили лечение в отделении неврологии Городского медицинского объединения Самарканда с 2018 по 2021 годы. Чтобы оценить их состояние, мы использовали анализы крови для измерения белков острой фазы и маркеров воспаления, таких как фибриноген, С-реактивный белок и интерлейкин-1β. Результаты исследования пациентов с различными видами дорсопатий, такими как компрессионно-ишемическая, бруцеллезная, ревматическая и герпетическая, свидетельствуют о том, что фибриноген, С-реактивный белок и интерлейкин-1β могут служить ценными биохимическими индикаторами для дифференциации пациентов с хроническим болевым синдромом при дорсопатиях различного происхождения. У больных с хроническим болевым синдромом, обусловленным компрессионно-ишемическими дорсопатиями, бруцеллезом, ревматическим и герпетическим генезом, наблюдались различные показатели воспалительного процесса, провоцирующие хроническую боль. К таким показателям относятся концентрации фибриногена, С-реактивного белка и интерлейкина-1β в сыворотке крови. Эти данные подтверждают воспалительную природу боли и объясняют ее хроническое и упорное течение.*

Ключевые слова: *маркеры воспаления, фибриноген, С-реактивный белок, интерлейкин-1β, дорсопатия.*