CHANGES IN THE CELLULAR COMPOSITION AND BIOCHEMICAL INDICATORS OF SYNOVIAL FLUID IN CHRONIC SYNOVITIS

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Abstract. *The article presents the results of a study of the cellular composition and physicochemical properties of synovial fluid (SF) in patients with acute and chronic synovitis of the knee joint. It was found that chronic synovitis is accompanied by more pronounced changes in cellularity and inflammatory markers in the SF compared to the acute process. An analysis of cytological parameters was performed, including the number of leukocytes, erythrocytes, the presence of polynuclear cells, rhagocytes, histiocytes, macrophages and crystals, using a modified formula for the inflammatory activity index. A direct relationship was found between the degree of turbidity of the SF, the number of leukocytes and the severity of degenerative changes in the joint. The data obtained confirm the diagnostic significance of a comprehensive analysis of the SF in assessing the severity of the inflammatory process and predicting the course of chronic synovitis of the knee joint.*

Keywords: *Chronic synovitis, synovial fluid cellularity, biochemical changes in synovial fluid.*

In 2020, there were approximately 654.1 million people worldwide aged 40 and older with knee osteoarthritis (Aiyong Cui, Huizi Li. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine. 2930 (2020) 100587). By 2024, the burden of osteoarthritis continued to grow globally, affecting about 7.6% of the world's population, with projections indicating an increase of 60% to 100% by 2050 (Osteoarthritis year in review 2024: Epidemiology and therapy. Alice Courties, Inès Kouki, Nadine Soliman, Sylvain Mathieu, Jérémie Sellam. Osteoarthritis and Cartilage, Vol. 32, Issue 11, Nov 2024, pp. 1397–1404). Notably, osteoarthritis ranks seventh among leading causes of disability worldwide after age 70, primarily affecting the knee joints.

The overall annual incidence of soft tissue knee injuries was 718 per 100,000 people (672 per 100,000 in women and 766 per 100,000 in men) (Charlotte Bergknut, George Peat. Population incidence of soft tissue knee injury: estimates from a Swedish healthcare register. Abstract #916. American College of Rheumatology, 2012 Annual Meeting, November 9–14, 2012, Washington). The most common injuries diagnosed were knee contusions (31.3%), followed by ligament sprains (27.7%), damage to various knee structures (22.3%), meniscal tears (11.3%), collateral ligament injuries (10.7%), and cruciate ligament injuries (9.9%).

Among the various manifestations of chronic joint diseases, synovitis holds a leading position. The inflammatory process developing in the synovial membrane determines the key clinical features and drives disease progression. It represents the body's response to a pathogenic stimulus, manifested either as primary synovial inflammation in chronic arthritis or secondary synovitis in osteoarthritis. According to current understanding, a critical step in chronic arthritis development is the recognition of an unidentified pathogenic factor by an antigen-presenting cell.

Since the progression of joint pathology through arthritis and synovitis involves inflammation—and the nature of the disease depends on the ratio of specific cellular elements in the synovial fluid—we attempted to develop a method for objectively evaluating the course of the pathological process and predicting chronic synovitis.

Synovial fluid (SF) originates from three main sources:1. Blood transudate containing water, electrolytes, and proteins;2. Secretions from synovial lining cells—hyaluronic acid and proteolytic enzymes;3. Waste products from cell turnover and matrix components—mainly proteoglycans and glycoproteins—continuously entering the joint cavity during its normal functioning.

The primary functions of SF include: - Metabolic: exchange between the joint cavity and the bloodstream, and elimination of foreign and certain autoantigens; - Locomotor: production of biological joint "lubrication" to ensure smooth movement of joint surfaces; - Trophic: transportation of key energy substances to cartilage tissue.

SF reflects processes occurring in the cartilage and synovial membrane, responding sensitively to even minor disruptions with changes in physicochemical characteristics and cellular composition. Thus, laboratory analysis of SF is of fundamental importance in diagnosing joint diseases and chronic synovitis. It is especially important to emphasize that typical changes in SF often appear before clinical signs develop. Therefore, comprehensive laboratory analysis of SF—the synovial environment of the joint—is essential to understanding the nature of intra-articular changes. Cytosis is one of the most sensitive criteria in differential diagnosis. In addition to the total number of cellular elements, their qualitative composition is also significant for diagnosing joint pathology. While the cellular composition of SF is well studied under normal and autoimmune inflammatory conditions, research on acute and chronic synovitis is limited and inconsistent.

Objective: to investigate the cellular composition of synovial fluid in acute and chronic synovitis of the knee joint.

Materials and Methods

The study included 50 patients with knee synovitis admitted to the trauma department of the 2nd clinic of TMA. Of these, 24 (48%) had acute synovitis and 26 (52%) had chronic synovitis.

Among all patients, 28 (56%) were men and 22 (44%) were women. Patient ages ranged from 25 to 69 years. The average age in the acute group was 42.42±2.15 years, and in the chronic group, 49.46±2.60 years. Distribution by age and sex was conducted following WHO (2018) guidelines. Most were of young and middle age. In the acute group, there were 14 (58.3%) men (41.7% young and 16.7% middle-aged) and 10 (41.7%) women (middle-aged). In the chronic group, 14 (53.8%) were men (15.4% young, 23.1% middle-aged, and 15.4% elderly) and 12 (46.2%) women (7.7% young, 23.1% middle-aged, and 15.4% elderly). Acute synovitis was more common in middle-aged men, while chronic synovitis occurred in men of all age groups and in middle-aged and elderly women.

The study recorded the duration of chronic synovitis, previous joint trauma, and genetic predisposition to osteoarthritis. Diagnoses were established jointly with traumatologists based on clinical history, MRI, and arthroscopy, assessing intra-articular pathology. The Bauer-Jackson classification was used for cartilage condition; ISAKOS classification for meniscal damage.

Synovial fluid collected during arthroscopy was used as the material for research. Physicochemical properties and cellular composition were determined via microscopy. Both native and stained samples were examined. Native preparations provided an estimate of cell content, while stained samples allowed cell type differentiation. CRP levels were determined using a biochemical analyzer and LAHEM biotests. As synovial fluid cannot be collected from healthy individuals, literature data was used for comparison. Statistical analysis was conducted using Statistica software.

The conducted research revealed certain differences in the studied indicators depending on the course of synovitis. For instance, a change in the color of synovial fluid (SF) to red in cases of acute synovitis of the knee joint was observed in 50% of the subjects and was associated with mechanical trauma and the development of hemosynovitis. In contrast, during the chronic course, the SF was red in 30.8% of cases, milky in 7.7%, and straw-yellow in 61.5%. Furthermore, while in acute synovitis the SF was cloudy in 33.3% of cases, during the chronic course this figure increased to 46.2%. Normally, SF should be light yellow and transparent.

It should be noted that the observed changes in the physical properties of synovial fluid (SF) in cases of acute knee synovitis were mainly associated with mechanical trauma, which led to varying degrees of hemorrhage. In chronic synovitis of the knee joint, cloudiness of SF samples was more frequently observed, along with the presence of lipid droplets and a creamy consistency. This was likely related to the presence of knee osteoarthritis in most patients with chronic synovitis. In this group, arthroscopy more often revealed old meniscal injuries, patellofemoral osteoarthritis, increasing pain syndrome, and degenerative changes. Duplex scanning also revealed varicose veins of the lower limbs, inguinal lymphadenopathy, and secondary lymphedema of the lower limbs.

The creamy appearance of SF in two female patients was associated with disability despite their young age, as well as high cholesterol levels. Charcot-Leyden crystals and elevated cellularity were also found.

Cellularity of the synovial fluid plays an important role in evaluating the degree of inflammation in the knee joint. Normally, SF should not contain red blood cells. In patients with acute knee synovitis, the number of erythrocytes in the SF ranged from 3 to 364 per μL, with an average of 84.33 ± 25.37 per μL. In 58.3% of cases, the count did not exceed 20 per μL, in 16.7% it reached up to 100, and in 25.0% it exceeded that, indicating the presence of hemosynovitis. In patients with chronic synovitis, the erythrocyte count ranged from 4 to 3200 per μL, with an average of 376.23 ± 181.07 per μL. In 69.2% of cases, the count did not exceed 20 per μL; in 15.4% it reached up to 100, and in 15.4% it exceeded that.

Counting cellular elements and determining their ratios is one of the most important components of laboratory examination in joint pathology. In addition to the total number of cellular elements, the qualitative composition of SF is critically important in diagnosing joint disorders. It is known that an increased presence of polymorphonuclear cells, ragocytes, histiocytes, macrophages, and crystals indicates an inflammatory nature of joint changes.

Under normal conditions, the leukocyte count in SF should not exceed 200 cells per μL. In our study, among patients with acute knee synovitis, the leukocyte count varied widely—from 120 to 16,840 per μL—with an average of 4006.58 ± 1244.10 per μL. In 8.3% of cases, the count did not exceed 200 per μL; in 58.4% of patients, it ranged from 200 to 2000 per μL, indicating a non-inflammatory origin; in 33.3%, it exceeded 2000 per μL, suggesting an inflammatory process.In chronic synovitis, the leukocyte count ranged from 320 to 21,200 per μL, with an average of 8346.92 ± 1574.61 cells per μL. In 42.2% of patients, the count ranged from 200 to 2000 per μL; in 53.8%, it exceeded 2000 per μL. It should be noted that a significant increase in leukocyte count coincided with high cloudiness of the SF and the presence of degenerative joint changes.

Table 1.

Indicators	Acute, n=24	Chronic, n=26
Total cellularity, cells in 1 μl	4095,42±1254,97	8727,15±1595,81
Leukocytes, cells in 1 μl	4006,58±1244,10	8346,92±1574,61
Erythrocytes, cells in 1 μl	84,33±25,37	376,23±181,07
Polynuclears, %	25,0	38,5
Rhagocytes, %	25,0	57,7
Histiocytes, %	33,3	46,1
Macrophages, %	16,7	38,5
Inflammatory activity index	2,45±0,66	4,75±0,80

In patients with acute knee synovitis, synovial fluid (SF) showed isolated occurrences of polymorphonuclear cells (25%), ragocytes (25%), histiocytes (33.3%), and macrophages (16.7%). In contrast, during the chronic course, these elements were detected more frequently—polymorphonuclear cells, ragocytes, histiocytes, and macrophages were observed in 38.5%, 57.7%, 46.1%, and 38.5% of cases, respectively—and in significantly higher quantities.

The total cellularity was 4095.42 ± 1254.97 cells per μL in the acute phase, and 8727.15 ± 1595.81 cells per μL during the chronic phase. To evaluate the activity level of the inflammatory process based on cytological data, a formula proposed by P. Stiehl (1981) was used, with modifications to include erythrocytes, polymorphonuclear cells, ragocytes, histiocytes, and macrophages. The calculated index of inflammatory activity (A) was interpreted as follows:

- A < 1.0 – no activity (Grade 0),
- A from 1.0 to 5.0 – low activity (Grade 1),
- A from 5 to 10 – moderate activity (Grade 2),
- A > 10 – high activity (Grade 3).

The results showed that 66.7% of patients with acute synovitis had an activity index of 0. Grade 1 inflammatory activity was identified in 12.5% of patients, and Grade 2 in 20.8%. Among patients with chronic synovitis, 46.1% had an activity index of 0, 7.7% showed Grade 1 activity, 30.8% Grade 2, and 15.4% Grade 3. These findings indicate that the inflammatory process was more pronounced in chronic synovitis.

Various types of crystals were also detected. In acute cases, crystals were found in 83.3% of patients—oxalates in 16.7% and uric acid crystals in 66.7%. In chronic cases, crystals were present in 100% of patients—oxalates in 7.7%, uric acid crystals in 84.6%, and Charcot-Leyden crystals in 7.7%.

According to several authors, in some cases, cytological examination of SF may be limited to the leukocyte formula (...). They recommend counting both viable and destroyed cells, as a significant number of destroyed cells is considered normal. These cells can be differentiated using supravital staining with neutral red.

Based on the conducted research, the following conclusions can be drawn:

1. In patients with acute knee synovitis, hemosynovitis was observed in 50% of cases. In chronic synovitis, the SF was red in 30.8% of cases, milky in 7.7%, straw-yellow in 61.5%, and cloudy in 46.2% of cases.

2. The leukocyte count varied widely: on average, it was 4006.58 ± 1244.10 per μL in acute cases and 8346.92 ± 1574.61 per μL in chronic synovitis, which correlated with increased cloudiness of the synovial fluid.

3. In patients with chronic synovitis, polymorphonuclear cells, ragocytes, histiocytes, macrophages, and various crystals were detected more frequently and in greater quantities than in acute synovitis.

An index for assessing inflammatory activity based on cytological data was proposed. Among patients with acute synovitis, Grade 1 and Grade 2 activity were found in 12.5% and 20.8% of cases, respectively. In chronic synovitis, Grade 1, 2, and 3 activity were found in 7.7%, 30.8%, and 15.4% of cases, respectively.

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