

## **An Analysis of Different Types of Arthritis with Joint Effusions among Kashmiri Population in a Tertiary Care Hospital**

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### **Abstract**

**Introduction:** Arthritis is the initial manifestation of many joint disorders. Synovial fluid analysis helps in this aspect. An analysis of synovial fluid has long been recommended as a routine procedure to assist in the diagnosis of arthritis.

**Objective:** To analyse the gross, microscopic and biochemical variations in the synovial fluid in various causes of joint effusions and to assess the synovial fluid cytology with biochemical parameters in various types of arthritis to increase the accuracy of diagnosis.

**Materials and Methods:** In the present cross sectional study, the synovial fluid of 477 cases was analysed in the Department of Biochemistry in collaboration with the Department of Pathology at SKIMS Medical College & Hospital, Bemina, Srinagar, India. Gross examination was done to find total volume, clarity, viscosity of the synovial fluid and it was equally divided into two halves. One half of synovial fluid was sent for biochemical analysis and the other half for microscopic examination.

**Results:** Out of 477 synovial fluid samples analysed, joint involvement was seen in patients between the age of 16 and 75 years which included 182 males and 295 females. Total leucocyte count was found to be highest in septic arthritis and lowest in osteoarthritis. Neutrophils were highest in septic arthritis (95%) and lowest in osteoarthritis (24%). Sugar level in synovial fluid was highest in osteoarthritis and gouty arthritis (70-90 mg/dL each) and lowest in septic arthritis. Proteins were highest in rheumatoid arthritis and traumatic arthritis (4.1-6.5 gm/dL and 4.2-6.4 gm/dL respectively) and lowest in osteoarthritis (1.2-2.4 gm/dL). Out of 290 positive cases in synovial C-reactive protein levels, the highest were found in rheumatoid arthritis (130), rheumatoid factor was found positive in 143 cases while it was negative in 127 cases of osteoarthritis.

**Conclusion:** Biochemical analysis of synovial fluid for proteins and sugar contributes in diagnosis of different types of arthritis. RF in synovial fluid proves to be of value in diagnosis of monoarticular arthritis. C-reactive protein levels in synovial fluid were elevated in rheumatoid arthritis and can be used for the diagnosis of this disease in addition to other tests available.

**Keywords:** Synovial fluid, Arthritis, Osteoarthritis, Rheumatoid arthritis, Rheumatoid factor, C-reactive protein

### **1.Introduction**

Arthritis and other rheumatic conditions are among the most prevalent chronic conditions in India and other parts of the world. They include many types of arthritis and autoimmune diseases that affect the bones and joints causing morbidity, disability with resultant health care utilization. Arthritis is perceived as a disease of the aged and poses a major economic and health burden to society.[1] Arthritis is the initial manifestation of many joint disorders. Synovial fluid analysis helps in this aspect. Analysis

of synovial fluid has long been recommended as a routine procedure to assist in the diagnosis of arthritis.[2]

Joints are constructed to provide both movement and mechanical support. Their anatomy is complex and directly related to their function.[3] Synovial fluid fills the spaces in the joint cavities and its function is to moisturize and lubricate the joints. Synovial fluid analysis has been widely recommended as an important aspect of diagnostic

examination of patients with arthritis and joint effusions.[4,5] Rheumatologists say that synovial fluid analysis is the most important laboratory test in arthritis so much so that it is considered as the 'liquid biopsy of the joint'. Analysis of synovial fluid may provide an easier non-invasive option and a vital step in the diagnosis and management of arthritis. Also, it helps to distinguish between various inflammatory, non-inflammatory, traumatic, septic and crystal induced arthritis.[6,7] The present study was conducted to analyse the gross, microscopic and biochemical variations in the synovial fluid in various causes of joint effusions and to assess the synovial fluid cytology with biochemical parameters in various types of arthritis to increase the accuracy of diagnosis.

## 2. Materials and Methods

This cross sectional study was undertaken on patients attending OPD and on those admitted in the Orthopaedic wards. The synovial fluid of 477 cases were analysed in the Department of Biochemistry in collaboration with the Department of Pathology. The study was approved by the ethics committee of the Institute. Informed and written consent was obtained from all the patients. Joint fluid was obtained by arthrocentesis from knee joint effusion cases. All the knee aspirations were done by orthopedic surgeons after taking all aseptic precautions. Gross examination was done to find total volume, clarity, viscosity of the synovial fluid and it was equally divided into two halves. One half of synovial fluid was send for biochemical analysis like sugar, proteins, C-reactive protein and rheumatoid factor and the other half was send for microscopic examination for total and differential leucocyte counts. All the patients with one or more joint effusions were included in the study. Patients with septicemia or with cutaneous soft tissue infection mimicking acute arthritis were excluded from the study.

## 3. Results

Out of 477 synovial fluid samples analysed, joint involvement was seen in patients between the age of 16 and 75 years which included 182 males and 295 females. 405 patients had single knee joint involvement and the rest i.e., 72 had both knees involved. Duration of disease was from one week to thirty years. As far as deformity among such cases was concerned, it was found that 47 patients had deformity while among the rest, it was not present (Table-1) but the swelling was present in all cases. Also, out of all cases 172 (36%) had osteoarthritis (OA), 145 (31%) were suffering from rheumatoid arthritis (RA), 79 (16%) had traumatic arthritis (TA) whereas, only 25 (5%) had septic arthritis (SA). 15 (3%) were suffering from tuberculous arthritis (TbA), 27 (6%) had gouty arthritis (GA) and 14 cases (3%) were undiagnosed-Non Diagnostic Aspirate (NDA) (Table-2). Gross analysis of synovial fluid revealed that the volume was larger in osteoarthritis and rheumatoid arthritis as compared to its other types. On the aspects of clarity 204 cases were found to be clear while as in case of 273 patients it was opaque. Examining viscosity, 256 cases were found to be normal while as in 221 cases it was low. Total leucocyte count was found to be highest in septic arthritis and lowest in osteoarthritis. Neutrophils were highest in septic arthritis (95%) and lowest in osteoarthritis (24%). Lymphocyte count was highest in osteoarthritis (68%) and lowest in septic arthritis (5%) while as macrophages were higher in traumatic and gouty arthritis (10% each). Sugar level in synovial fluid was highest in osteoarthritis and gouty arthritis (70-90 mg/dL each) and lowest in septic arthritis. Proteins were highest in rheumatoid arthritis and traumatic arthritis (4.1-6.5 gm/dL and 4.2-6.4 gm/dL respectively) and lowest in osteoarthritis (1.2-2.4 gm/dL). Out of 290 positive cases in synovial C-reactive protein levels, the highest were found in rheumatoid arthritis (130). Rheumatoid factor (RF) was found positive in 143 cases and among these the highest number i.e. 87 had rheumatoid arthritis while it was found negative in 127 cases of osteoarthritis (Table-3).

**Table-1: General description of the cases with joint effusions**

| Parameters          |                         | OA            | RA            | TA                 | SA       | TbA       | GA       | NDA              |
|---------------------|-------------------------|---------------|---------------|--------------------|----------|-----------|----------|------------------|
| Mean Age (in years) |                         | 40-75         | 20-65         | 16-70              | 30-50    | 45-70     | 42-60    | 30-70            |
| Sex                 | Males (182)             | 60            | 10            | 61                 | 10       | 12        | 21       | 08               |
|                     | Females (295)           | 112           | 135           | 18                 | 15       | 03        | 06       | 06               |
|                     | Total (477)             | 172           | 145           | 79                 | 25       | 15        | 27       | 14               |
| Joint Involvement   | Single Knee joint (405) | 154           | 113           | 79                 | 25       | 15        | 05       | 14               |
|                     | Both Knee joint (72)    | 18            | 32            | 0                  | 0        | 0         | 0        | 0                |
| Duration of Disease |                         | 5 to 20 (yrs) | 1 to 30 (yrs) | 2 (wks) to 2 (yrs) | 1-2(wks) | 2-12(yrs) | 1-2(yrs) | 2(wks) to 5(yrs) |
| Deformity           | Present(47)             | 24            | 17            | 02                 | 00       | 02        | 01       | 01               |
|                     | Absent(430)             | 148           | 128           | 77                 | 25       | 13        | 26       | 13               |

**Table-2: Depicting distribution of cases with joint effusion**

| Serial. No   | Nature of Disease             | Cases      | Percentage  |
|--------------|-------------------------------|------------|-------------|
| 1            | Osteoarthritis (OA)           | 172        | 36%         |
| 2            | Rheumatoid Arthritis (RA)     | 145        | 31%         |
| 3            | Traumatic Arthritis (TA)      | 79         | 16%         |
| 4            | Septic Arthritis (SA)         | 25         | 5%          |
| 5            | Tuberculous Arthritis (TbA)   | 15         | 3%          |
| 6            | Gout Arthritis (GA)           | 27         | 6%          |
| 7            | Non Diagnostic Aspirate (NDA) | 14         | 3%          |
| <b>Total</b> |                               | <b>477</b> | <b>100%</b> |

**Table-3: Biochemical and microscopic analysis of synovial fluid**

| Synovial Fluid                              |                 | OA              | RA                | TA                | SA                 | TbA                | GA                | NDA               |
|---|-----------------|-----------------|-------------------|-------------------|--------------------|--------------------|-------------------|-------------------|
| Volume (2-10 ml)                            |                 | 4-10            | 2-10              | 4-8               | 4-5                | 4-6                | 4-5               | 2-3               |
| Clarity                                     | Clear (204)     | 161             | 21                | 0                 | 0                  | 0                  | 22                | 0                 |
|   | Opaque (273)    | 11              | 124               | 79                | 25                 | 15                 | 05                | 14                |
| Viscosity                                   | Normal (256)    | 163             | 10                | 79                | 0                  | 0                  | 04                | 00                |
|   | Low (221)       | 09              | 135               | 0                 | 25                 | 15                 | 23                | 14                |
| Total Leucocyte count (TLC)<br>(cells/cumm) |                 | 150 to<br>1,800 | 3000 to<br>20,000 | 1,500 to<br>4,500 | 60,000to<br>90,000 | 7,000 to<br>11,000 | 2,000 to<br>4,000 | 1,000 to<br>3,000 |
| Differential Leucocyte<br>count (DLC)       | Neutrophils(%)  | 24              | 86                | 70                | 95                 | 77                 | 70                | 60                |
|   | Lymphocytes(%)  | 68              | 11                | 20                | 05                 | 16                 | 20                | 35                |
|   | Macrophages (%) | 08              | 03                | 10                | 0                  | 07                 | 10                | 05                |
| Sugar (mg/dL)                               |                 | 70-90           | 15-60             | 20-40             | 18-35              | 30-40              | 70-90             | 60-100            |
| Protein (gm/dL)                             |                 | 1.2-2.4         | 4.1-6.5           | 4.2-6.4           | 4.5-5.5            | 4.2-4.5            | 1.2-2.4           | 2.0-3.5           |
| C-reactive protein                          | Positive (290)  | 101             | 130               | 08                | 25                 | 01                 | 25                | 00                |
|   | Negative (187)  | 71              | 15                | 71                | 00                 | 14                 | 02                | 14                |
| Rheumatoid factor (RF)                      | Positive (143)  | 45              | 87                | 04                | 00                 | 03                 | 00                | 04                |
|   | Negative (334)  | 127             | 58                | 75                | 25                 | 12                 | 27                | 10                |

#### 4. Discussion

The abnormal accumulation of fluid inside the joint has been recognized as the proximal cause of joint diseases. Osteoarthritis prevalence increases with age and is more common in women than in men. Risk factor includes obesity, knee injury, previous knee surgery and occupational bending and lifting and is the leading cause of impaired mobility in elderly. [8,9] In a study by Partik *et al* of 178 patients where mean age was 72, range 33 to 96 years compared to the present study where mean age is 60 years, range 40-75.[10] Gross examination of synovial fluid in the present study showed yellow colour. Viscosity was found normal and the fluid was clear. It also showed normal sugar and low protein levels. Saase *et al* concluded that osteoarthritis is a worldwide disease and that no population investigated so far has been spared. Synovial fluid white cell count below 1000/cubic millimeter is consistent with osteoarthritis.[9] In contrast to the present study where the mean synovial fluid white blood cells count was 350 cells/cubic millimeter. Percy *et al* in his study showed that the synovial fluid is a degenerative disease with clear yellow fluid, high viscosity and with total leukocyte count less than 2000 cells/cumm.[11] The level of synovial C-reactive protein was increased in 101/172 cases, same was seen in a study by Pearle *et al*. [12]

Rheumatoid arthritis is a multi-organ disease, the main target organs are the synovial lining of joints, bursae and tendon sheaths. Although the

diagnosis rests largely on the clinical criteria, a positive result for rheumatoid factor confirms the clinical impression.[13] According to various studies, the total leucocyte count varies between 2000-50,000 cell/cumm with the predominance of neutrophils. In the present study, the mean total leucocyte count was 15,000 cells/cumm. The mean differential leucocyte count showed 86% polymorphs and rheumatoid factor in synovial fluid was positive in 85/145 cases and synovial C-reactive protein was positive in 130/145 cases. Synovial fluid was yellow, cloudy, opaque fluid with low viscosity. Rheumatoid effusions may also show a low glucose. Synovial fluid protein rise proportional to the degree of synovial inflammation, our study showed low synovial sugar levels mean 25 mg/dL and raised protein levels.[14]

Traumatic arthritis is defined as the monoarticular arthritis occurring within 48 hours of overt trauma.[15] In the present study, synovial fluid was hemorrhagic, with normal viscosity. The amounts of inflammatory cells are mainly neutrophils-70%, lymphocytes-20%, monocytes-10% and the total leucocyte count varies from 1500 to 4500 cells per cubic millimetre, similar results were seen in a study by Naib on synovial fluids.[16] Septic arthritis is defined as the bacterial invasion of the synovial space. There are several routes by which it occurs. The most common causes are hematologic or direct invasion. The knee joint is most commonly affected joint in adults, the hip joint is most frequently affected in children.[17] In majority of

cases, septic arthritis is monoarticular and occurs most commonly in the large peripheral joints such as knee.[18] In the present study, patients presented with monoarticular arthritis affecting the knee joint. Traditionally, the cut off value for synovial fluid count for diagnosis of septic arthritis has been greater than 50000/mm<sup>3</sup> however, lower WBC counts can occur in early infectious arthritis or treated infection.[19] In the present study synovial fluid was white in colour, turbid with and reduced viscosity. Total leucocyte count ranged from 60,000 to 90,000 cell/cumm with a mean of 76,000 cells/cumm with neutrophil predominance i.e, 95%. According to Krey *et al* polymorpho nuclear neutrophils more than 90% had a sensitivity of 92% and specificity of 78% in diagnosing septic arthritis.[20] Synovial fluid glucose level was 18-40 mg/dL and proteins were 4.5 to 5.5 gm/dL. According to Shmerling *et al* protein more than 3gm /dl has a sensitivity of 50% and specificity of 46% in diagnosing septic arthritis.[21] All the cases were having synovial C reactive protein positive and all had negative rheumatoid factor.

Extra pulmonary tuberculosis manifestations are estimated to occur in approximately 20% of the patients with tuberculosis. As with most infectious disease, TB arthritis is characteristically monoarticular, however in approximately 10% of patients, multifocal joint disease does occur.[22] The synovial fluid from a patient with TB arthritis appeared yellow with reduced viscosity. The total nucleated cell count range from 10,000 to 20,000 cells/cumm but varies widely. In the present study the total leucocyte count mean 7,000-11,000 cells/cumm, with differential count of neutrophils (77%). [23] Most of the synovial C-reactive protein and rheumatoid factor were negative in this type of arthritis. Gout is more frequent in men and incidence increases with age. The gross appearance of gout is that of a chalk white deposit of paste like consistency. In the present study synovial fluid was yellow, opaque with low viscosity. Dai *et al* reported that the total WBC count ranges from 4500-10,000 cells/cumm. In the present study the total leukocyte count was 2,000 to 4,000 cells/cumm with the following distribution- polymorphs 70%, lymphocytes 20% and monocytes 10%. [24]

## 5. Conclusion

Synovial fluid analysis may help in the identification of patients with inflammatory arthritis that is at the risk of progressive destruction of particular joint. Examination of SF can be the only way in diagnosing conditions like septic arthritis, crystal arthritis and in other arthritis adds to the accuracy of diagnosis. Differences occur in cell

content of abnormal synovial fluid in different disease categories. Biochemical analysis of synovial fluid for proteins and sugar contributes in diagnosis of different types of arthritis. Rheumatoid factor in synovial fluid proves to be of value in diagnosis of monoarticular arthritis. C-reactive protein levels in synovial fluid were elevated in rheumatoid arthritis and can be used for the diagnosis of this disease in addition to other tests available.

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## Competing Interests

The authors declare that there were no competing interests associated with this study.

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