



## Letter to Editor

# Interleukin-6 in Synovial Fluid as a Tool for Differentiation of Inflammation and Degeneration in Chronic Synovitis and Treatment Selection

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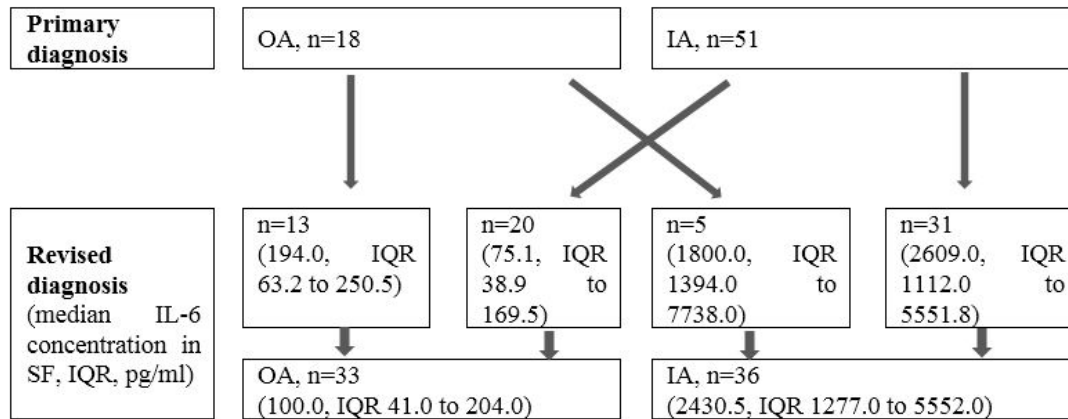
Although Osteoarthritis (OA) is a widespread type of arthritis, no cure or medication can halt its natural progression. Only weight loss and physiotherapy can help to relieve pain and preserve function. Chronic un-inflammatory synovitis is not uncommon in OA; however, Inflammatory Arthritis (IA) can also start in middle-aged adults affected by OA. Pain and swelling of the joints, especially in the knee joints, are usual complaints in rheumatological practice where the primary treatment for chronic inflammatory arthritis is disease-modifying antirheumatic drugs (DMARDs). At the same time, persistent chronic synovitis leads to secondary OA due to inflammation, aging, and other factors. Discrimination between chronic synovitis due to inflammation or degeneration poses a significant challenge, especially when specific markers for IA are negative. Interleukin-6 (IL-6) has been a research topic for many scientific publications over the past several years. Although IL-6 production and signaling have been observed in OA, a recently published article shows much more elevated IL-6 concentration in synovial fluid (SF) of symptomatic joints in different types of IA [1]. We decided to clarify the importance of IL-6 concentration in synovial fluid (SF) for diagnostic and treatment purposes.

We analyzed data from 69 consented patients with known types of arthritis with symptomatic chronic synovitis mostly of the knee joint who underwent joint arthrocentesis for therapeutic reasons. Depending on the concentration of IL-6 in the SF, we revised and changed the patient's primary diagnosis to either IA or secondary OA. Patients with low IL-6 concentration (below 1000.0 pg/ml) continued therapy as OA or secondary OA patients

with physiotherapy, without DMARDs escalation in case they previously were diagnosed with IA. Only for patients with high IL-6 concentration (above 1000.0 pg/ml) - DMARD treatment was prescribed or adjusted. 51 patients with a primary diagnosis of IA (Rheumatoid Arthritis (RA)-6; Psoriatic Arthritis (PsA-7); Reactive Arthritis (ReA)-32; Ankylosing Spondylitis (AS)-1; Undifferentiated IA (UIA)-2; juvenile idiopathic arthritis (JIA)-2) and 18 patients with OA were included in the study. After analysis of IL-6 concentration, 36 patients were re-classified as having IA (RA-6; PsA-4; ReA-24; UIA-1; JIA-1) and 33 patients were re-classified as having OA. Out of these 33 patients with low IL-6 concentration in SF, 20 patients previously had a diagnosis of IA. Of 36 patients with high IL-6 concentration in SF, 5 patients had a primary diagnosis of OA (Table 1). In 33 patients re-classified as OA, the median IL-6 concentration was 100 pg/ml, and in 36 patients who were re-classified as IA – the median IL-6 was 2430.5 pg/ml. The Mann-Whitney U test showed a statistically significant difference ( $p < 0.001$ ) between these two groups. In the 20 patients with primary diagnosis IA and then re-classified as OA, the median IL-6 concentration was 75.1 pg/ml. In the five patients with primary diagnosis OA, mean age  $58.2 \pm 3.6$  years, and then re-classified as IA, the median IL-6 concentration was 1800.0 pg/ml. In this group, three patients were without any serological and genetic markers for IA such as rheumatoid factor, anti-cyclic citrullinated peptides antibodies, and HLA-B27.

As we know cell count measuring in the SF is another option for differentiating inflammatory and non-inflammatory processes. It is helpful in acute situations but must be performed shortly after sampling, which is not always possible in clinical practice. On the other hand, no correlation was found between cell count and IL-6 concentration in SF of RA patients [2]. IL-6 is not the only marker

of inflammation and increases in the different types of IA. It elevates in case of acute traumatic joint injuries [3] and infections [4], but with critical clinical assessment, it becomes a valuable tool in IA diagnostic. Our experience shows that IL-6 concentration in SF may be helpful as an additional factor to laboratory testing (inflammatory, immunological, and genetic markers) and radiological studies in decision-making regarding patients with synovitis and selecting treatment options.



IA- inflammatory arthritis, IL-6- interleukin 6, IQR- interquartile range, OA- osteoarthritis, n- patient number, SF- synovial fluid

**Table 1:** Primary diagnosis and final diagnosis cross-tabulation.

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## References

- Mihailova A (2022) Interleukin 6 Concentration in Synovial Fluid of Patients with Inflammatory and Degenerative Arthritis. *Curr Rheumatol Rev* 18: 230-233.
- Meehan RT, Regan EA, Hoffman ED, et al. (2021) Synovial Fluid Cytokines, Chemokines and MMP Levels in Osteoarthritis Patients with Knee Pain Display a Profile Similar to Many Rheumatoid Arthritis Patients. *J Clin Med Res* 10: 5027.
- Watt FE, Paterson E, Freidin A, et al. (2016) Acute Molecular Changes in Synovial Fluid Following Human Knee Injury: Association with Early Clinical Outcomes. *Arthritis Rheumatol* 68: 2129–40.
- Gonzalez-Chapa JA, Peña-Martinez VM, Vilchez-Cavazos JF, Salinas-Carmona MC, Rosas-Taraco AG (2022) Systemic and Local Cytokines Profile Determine Severity and Prognosis in Human Septic Arthritis. *Arch Med Res* 53: 170–178.