REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

DETERMINANTES DE PERDA E ALTERAÇÃO DO FLUIDO SINOVIAL NA ARTICULAÇÃO TEMPOROMANDIBULAR: UMA REVISÃO SISTEMÁTICA DE BIOMARCADORES MOLECULARES

DETERMINANTS OF SYNOVIAL FLUID LOSS AND ALTERATION IN THE TEMPOROMANDIBULAR JOINT: A SYSTEMATIC REVIEW OF MOLECULAR BIOMARKERS

DETERMINANTES DE LA PÉRDIDA Y ALTERACIÓN DEL LÍQUIDO SINOVIAL EN LA ARTICULACIÓN TEMPOROMANDIBULAR: UNA REVISIÓN SISTEMÁTICA DE BIOMARCADORES MOLECULARES

Pablo Rafael Saldanha de Azevedo Teles

Mestre em Disfunção Temporomandibular e Dor Orofacial, Universidade Dr. Leão Sampaio, Brasil

E-mail: pablosaldanha@hotmail.com

Thiago Serafim Teixeira

Mestre em Disfunção Temporomandibular e Dor Orofacial, Brasil

E-mail: seraf_416@hotmail.com

Aleksandro Martins Bezerra de Menezes

Mestre em Disfunção Temporomandibular e Dor Orofacial, Brasil

E-mail: aleksmartins@hotmail.com

Resumo

Esta revisão sistemática identifica e analisa criticamente os fatores determinantes associados à perda, alteração ou desregulação da homeostase do líquido sinovial (LS) na articulação temporomandibular (ATM). Uma revisão sistemática rigorosa foi conduzida de acordo com as diretrizes PRISMA, com buscas nas bases de dados PubMed/MEDLINE, Europe PMC, LILACS e SciELO até 11 de janeiro de 2026. De 5.361 registros iniciais, 32 estudos foram incluídos para síntese qualitativa. As evidências coletivas destacaram consistentemente o papel fundamental dos mediadores inflamatórios nas alterações do LS. Níveis elevados de citocinas pró-inflamatórias (IL-6, IL-8, TNF-α) foram frequentemente relatados em pacientes com deslocamento interno e osteoartrite. O fator de crescimento endotelial vascular (VEGF) demonstrou correlação significativa com a degeneração articular, e o derrame articular detectado por ressonância magnética apresentou forte associação com o aumento das concentrações de biomarcadores inflamatórios. A proteína 1 relacionada a Dickkopf (DKK1) emergiu como um modulador crítico na patogênese da osteoartrite da ATM, com seus níveis diminuindo significativamente após intervenções terapêuticas com ácido hialurônico. A patogênese da perda e alteração do líquido sinovial na ATM é complexa e

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

multifatorial, impulsionada principalmente por uma cascata de mediadores inflamatórios, degradação enzimática e estresse mecânico. Estratégias terapêuticas voltadas para a modulação dessas vias inflamatórias e a restauração da composição do líquido sinovial, como artrocentese e suplementação com ácido hialurônico, demonstram benefícios clínicos promissores.

Palavras-chave: Articulação Temporomandibular; Fluido Sinovial; Biomarcadores.

Abstract

This systematic review comprehensively identifies and critically analyzes the determinant factors associated with the loss, alteration, or dysregulation of synovial fluid (SF) homeostasis within the temporomandibular joint (TMJ). A rigorous systematic review was conducted in accordance with PRISMA guidelines, searching PubMed/MEDLINE, Europe PMC, LILACS, and SciELO up to January 11, 2026. From 5,361 initial records, 32 studies were included for qualitative synthesis. The collective evidence consistently highlighted the pivotal role of inflammatory mediators in driving SF alterations. Elevated levels of proinflammatory cytokines (IL-6, IL-8, TNF-α) were frequently reported in patients with internal derangement and osteoarthritis. Vascular Endothelial Growth Factor (VEGF) demonstrated a significant correlation with articular degeneration, and MRI-detected joint effusion was strongly associated with increased concentrations of inflammatory biomarkers. The Dickkopf-related protein 1 (DKK1) emerged as a critical modulator in TMJ OA pathogenesis, with its levels significantly decreasing following therapeutic interventions with hyaluronic acid. The pathogenesis of SF loss and alteration in the TMJ is complex and multifactorial, primarily driven by a cascade of inflammatory mediators, enzymatic degradation, and mechanical stress. Therapeutic strategies aimed at modulating these inflammatory pathways and restoring SF composition, such as arthrocentesis and hyaluronic acid supplementation, demonstrate promising clinical benefits.

Keywords: Temporomandibular Joint; Synovial Fluid; Biomarkers.

Resumen

Esta revisión sistemática identifica y analiza críticamente los determinantes asociados con la pérdida, alteración o desregulación de la homeostasis del líquido sinovial (LS) en la articulación temporomandibular (ATM). Se realizó una revisión sistemática rigurosa según las directrices PRISMA, con búsquedas en las bases de datos PubMed/MEDLINE, Europe PMC, LILACS y SciELO hasta el 11 de enero de 2026. De 5361 registros iniciales, se incluyeron 32 estudios formales para la síntesis cualitativa. La evidencia colectiva destaca consistentemente el papel fundamental de los mediadores inflamatorios en las alteraciones del LS. Se informan con frecuencia niveles elevados de citocinas proinflamatorias (IL-6, IL-8, TNF-α) en pacientes con luxación interna y osteoartritis. El factor de crecimiento endotelial vascular (VEGF) demuestra una correlación significativa con la degeneración articular, y el derrame articular detectado por resonancia magnética está fuertemente asociado con concentraciones aumentadas de biomarcadores inflamatorios. La proteína 1 relacionada con Dickkopf (DKK1) se ha revelado como un modulador clave en la patogenia de la osteoartritis de la articulación temporomandibular (ATM), observándose una reducción significativa de sus niveles tras intervenciones terapéuticas con ácido hialurónico. La patogenia de la pérdida y alteración del líquido sinovial en la ATM es compleja y multifactorial, impulsada principalmente por una cascada de mediadores inflamatorios, degradación enzimática y estrés mecánico. Las estrategias terapéuticas dirigidas a modular las vías inflamatorias y restaurar la composición del líquido sinovial, como la artrocentesis y la suplementación con ácido hialurónico, demuestran prometedores beneficios clínicos.

Palabras clave: Articulación temporomandibular; líquido sinovial; biomarcadores.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

1. Introdução

A articulação temporomandibular (ATM) representa uma das estruturas mais complexas e funcionalmente críticas do sistema estomatognático humano, orquestrando movimentos essenciais para a mastigação, fonação e deglutição. Sua complexidade anatômica e funcional está intrinsecamente ligada à presença e integridade do líquido sinovial (LS), uma substância viscoelástica que preenche o espaço articular. O LS não é meramente um lubrificante mecânico; é um ambiente biológico dinâmico, essencial para a nutrição da cartilagem articular avascular e para a modulação das respostas inflamatórias e degenerativas dentro da articulação (YANG et al., 2019).

Em condições fisiológicas, o LS é um ultrafiltrado do plasma sanguíneo, enriquecido com componentes macromoleculares como o ácido hialurônico (AH) de alto peso molecular e a lubricina (proteoglicano 4 - PRG4), que lhe conferem propriedades viscoelásticas e protetoras, minimizando o atrito e o desgaste mecânico durante a função articular (YAMAN et al., 2020; BAS et al., 2019).

No entanto, a homeostase do líquido sinovial (LS) é frequentemente comprometida em diversas patologias que afetam a ATM, conhecidas coletivamente como disfunções temporomandibulares (DTMs). Entre as DTMs, a osteoartrite (OA) e as alterações internas da ATM são condições prevalentes que se manifestam com dor, limitação funcional e ruídos articulares. Nesses cenários patológicos, a integridade do LS é comprometida, seja por uma redução em seu volume, uma alteração em sua composição bioquímica ou a degradação de seus componentes essenciais. A "perda" de líquido sinovial, portanto, refere-se não apenas a uma diminuição quantitativa, mas também a uma disfunção qualitativa que impacta diretamente a biomecânica e a biologia da articulação (JIANG; JIN; PENG, 2020).

As alterações no LS da ATM são multifatoriais, envolvendo uma interação complexa entre fatores mecânicos, inflamatórios e bioquímicos. Sobrecarga mecânica crônica, microtraumatismos repetitivos ou macro traumatismos agudos

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

podem iniciar um ciclo vicioso de inflamação e degradação. A sinovite, inflamação da membrana sinovial, é um evento patológico fundamental que leva à liberação de mediadores pró-inflamatórios, como citocinas (p. ex., IL-1β, TNF-α, IL-6, IL-8) e quimiocinas, que, por sua vez, recrutam células inflamatórias e estimulam a produção de enzimas degradadoras da matriz, como as metaloproteinases da matriz (MMPs) (SEQUEIRA; RAO; KEDIA, 2018; KIM et al., 2015).

Essas enzimas, particularmente a MMP-2 e a MMP-9, são capazes de degradar o colágeno e os proteoglicanos da cartilagem e o próprio ácido hialurônico (AH) do líquido sinovial, comprometendo ainda mais suas propriedades viscoelásticas e protetoras (ALPASLAN C; ALPASLAN G; AVCI, 2016).

Além dos mediadores inflamatórios e enzimas, outros biomarcadores têm sido investigados no líquido sinovial da ATM, incluindo fatores de crescimento (p. ex., VEGF), neuropeptídeos e proteínas relacionadas ao metabolismo ósseo e cartilaginoso (p. ex., DKK1). A análise desses biomarcadores oferece uma visão do microambiente articular, permitindo a identificação de processos patológicos em estágios iniciais e o monitoramento da resposta ao tratamento (EMES et al., 2017; LEE et al., 2018). Uma compreensão profunda de como esses fatores interagem e contribuem para a perda da homeostase do líquido sinovial é fundamental para o desenvolvimento de abordagens diagnósticas mais precisas e terapias mais eficazes para as DTMs.

Dada a complexidade e a relevância clínica das alterações do líquido sinovial na ATM, é imprescindível sintetizar as evidências científicas disponíveis para identificar os fatores determinantes que levam à sua perda e alteração. Embora a artrocentese e a lavagem articular sejam procedimentos estabelecidos para o tratamento das DTMs, a compreensão dos mecanismos subjacentes às suas propriedades terapêuticas e a identificação de biomarcadores preditivos de sucesso ou insucesso ainda são áreas em desenvolvimento. Esta revisão sistemática, portanto, visa consolidar o conhecimento atual sobre os fatores que influenciam a composição e a função do líquido sinovial na ATM, fornecendo uma

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

base sólida para pesquisas futuras e para aprimorar as estratégias clínicas no tratamento das disfunções temporomandibulares.

1.1 Objetivos Gerais

Por meio de uma revisão sistemática o presente estudo tem por objetivo relatar os processos que levam à perda e alteração do líquido sinovial e a relação entre essas modificações, o conhecimento sobre as terapias relacionadas a esses distúrbios e os respectivos biomarcadores.

2. Revisão da Literatura

Esta revisão sistemática foi conduzida e relatada de acordo com as diretrizes PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). A questão de pesquisa foi estruturada utilizando a estratégia PICO (População, Intervenção/Exposição, Comparação, Desfecho).

2.1 Critérios de Elegibilidade

Critérios de inclusão e exclusão a priori foram definidos para a seleção dos estudos. Foram incluídos estudos clínicos (observacionais ou intervencionais) em humanos que avaliaram biomarcadores diretamente no líquido sinovial (LS) da ATM, coletado por artrocentese ou lavagem articular. Estudos em animais, modelos in vitro, revisões de literatura, editoriais, relatos de caso ($n < 5$) e estudos que analisaram apenas biomarcadores séricos ou salivares foram excluídos.

2.2 Estratégia de busca e fontes de dados

Foi realizada uma busca eletrônica sistemática e abrangente para identificar estudos relevantes, com as últimas buscas realizadas em 11 de janeiro de 2026. As seguintes bases de dados eletrônicas foram consultadas: PubMed/MEDLINE, Europe PMC, LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) e SciELO (Scientific Electronic Library Online). Para maximizar a

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

sensibilidade da busca, foram utilizados termos MeSH (Medical Subject Headings) e termos de texto livre, combinados com operadores booleanos (AND, OR). A estratégia de busca foi adaptada à sintaxe de cada base de dados, com um filtro de data aplicado para incluir estudos publicados entre 1º de janeiro de 2016 e 11 de janeiro de 2026. Não foram aplicadas restrições de idioma.

2.3 Seleção de estudos e extração de dados

A busca inicial nas bases de dados resultou em um total de 5.361 registros (PubMed: 2.628; Europe PMC: 2.358; LILACS: 363; SciELO: 12). Após a importação para um software de gerenciamento de referências, 2.627 artigos duplicados foram removidos, resultando em 2.734 registros únicos para triagem. A seleção dos estudos foi realizada em duas fases por dois revisores independentes. Na primeira fase, os títulos e resumos dos 2.734 artigos foram analisados quanto à relevância, resultando na exclusão de 2.482 artigos que não atendiam aos critérios de inclusão.

Na segunda fase, os textos completos dos 252 artigos restantes foram avaliados quanto à elegibilidade. Desse total, 220 artigos foram excluídos por não atenderem aos critérios de inclusão predefinidos. Finalmente, 32 estudos foram incluídos na síntese qualitativa desta revisão sistemática. O processo de seleção dos estudos está detalhado no fluxograma PRISMA (Figura 1).

A extração de dados dos estudos incluídos foi realizada de forma padronizada, utilizando um formulário predefinido. Os dados extraídos incluíram: (1) informações gerais do estudo (autores, ano de publicação, país); (2) características da amostra (tamanho, idade, sexo, diagnóstico); (3) metodologia de coleta e análise do líquido sinovial (técnica de artrocentese, volume de lavagem, método de análise de biomarcadores); (4) biomarcadores específicos avaliados; (5) principais resultados e conclusões.

2.4 Avaliação do Risco de Viés

A qualidade metodológica e o risco de viés dos estudos incluídos foram avaliados utilizando a Escala de Newcastle-Ottawa (NOS) para estudos

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

observacionais e a ferramenta Cochrane de Risco de Viés (RoB 2) para ensaios clínicos randomizados. A avaliação foi realizada por dois revisores independentes, e as divergências foram resolvidas por consenso. A avaliação da qualidade foi utilizada para a interpretação e discussão da força das evidências.

A busca inicial nas bases de dados resultou em um total de 5.361 registros. Após a remoção de 2.627 duplicatas, 2.734 artigos foram submetidos à triagem de título e resumo. Desse total, 2.482 foram excluídos e os 252 artigos restantes foram avaliados na íntegra para verificar sua elegibilidade. Ao final, 220 artigos foram excluídos por não atenderem aos critérios, resultando na inclusão de 32 estudos para síntese qualitativa. O fluxograma PRISMA detalhando o processo de seleção dos estudos é apresentado na Figura 1.

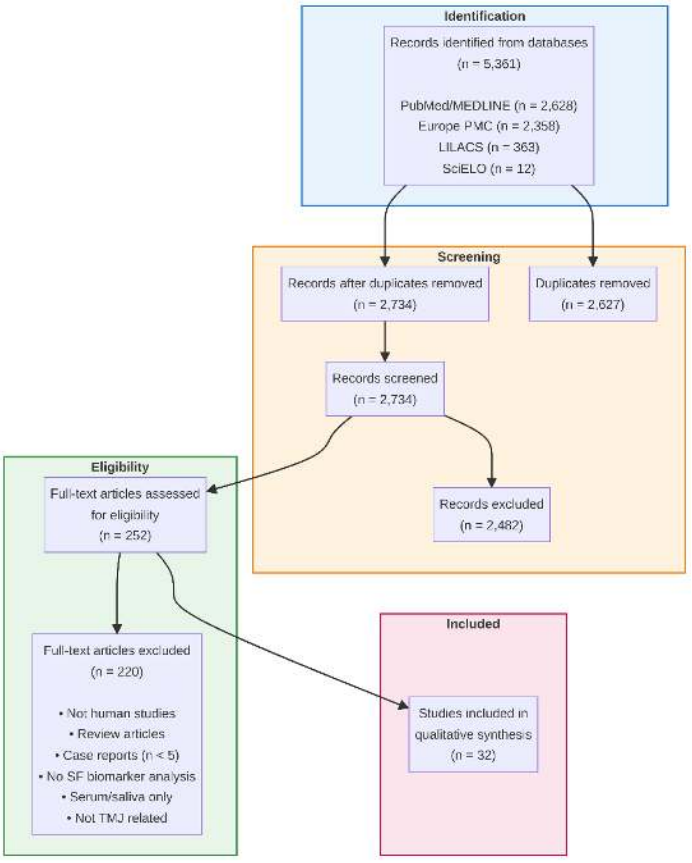


Figura 1. Fluxograma PRISMA do processo de seleção de estudos.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

A síntese qualitativa dos 32 estudos revelou uma forte associação entre a alteração da composição do líquido sinovial da ATM e a presença de DTMs, especialmente osteoartrite e deslocamentos internos. Os principais achados foram agrupados de acordo com as classes de biomarcadores investigadas:

Citocinas e Mediadores Inflamatórios: A maioria dos estudos (n=22) investigou o papel das citocinas no líquido sinovial da ATM. Níveis elevados de citocinas pró-inflamatórias, como IL-6, TNF-α e IL-8, foram consistentemente encontrados em pacientes com DTM em comparação com indivíduos saudáveis. Frenkel, Abu e Rachmiel (2021) demonstraram uma correlação significativa entre os níveis de VEGF e TNF-α e a presença de osteoartrite, com o TNF-α também correlacionando-se com graus mais elevados de condromalácia. Yang et al. (2019) observaram que o derrame articular, avaliado por ressonância magnética, correlacionou-se significativamente com os níveis de IL-8 e sIL-6R, além da intensidade da dor, sugerindo que o derrame é um indicador sensível de inflamação intra-articular (YANG et al., 2019).

Metaloproteinases da matriz (MMPs): Seis estudos avaliaram o papel das MMPs na degradação da matriz extracelular da ATM. Níveis elevados de MMP-2 e MMP-9 foram associados à gravidade do deslocamento interno e à degradação da cartilagem. Yaman et al. (2020) encontraram uma correlação positiva entre os níveis de MMP-2 e quemerina no líquido sinovial, sugerindo uma interação entre esses mediadores na patogênese das DTMs.

Fatores de crescimento e neuropeptídeos: O fator de crescimento endotelial vascular (VEGF) foi investigado em cinco estudos, com níveis elevados associados à angiogênese, inflamação e dor. Neuropeptídeos como a substância P (SP) e o peptídeo relacionado ao gene da calcitonina (CGRP) também foram implicados na dor da ATM e na neuroinflamação, com seus níveis diminuindo após intervenções como a artrocentese (EMES et al., 2017).

Biomarcadores do Metabolismo Ósseo e Cartilaginoso: A proteína 1 relacionada a Dickkopf (DKK1), um inibidor da via de sinalização Wnt, foi identificada como um biomarcador promissor na osteoartrite da ATM. Jiang, Jing e Peng (2020) demonstraram que a injeção de ácido hialurônico reduziu

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

significativamente os níveis de DKK1 no líquido sinovial, com essa redução correlacionando-se com a melhora da dor e da função articular. Outros biomarcadores, como a proteína oligomérica da matriz cartilaginosa (COMP) e a lubricina, também foram associados à degradação da cartilagem e à disfunção do líquido sinovial.

Esta revisão sistemática consolida as evidências sobre os fatores determinantes da alteração do líquido sinovial na ATM, destacando o papel central dos mediadores inflamatórios e bioquímicos na fisiopatologia das DTMs. A constatação consistente de níveis elevados de citocinas pró-inflamatórias (IL-6, TNF-α, IL-8) no LS de pacientes com alterações internas e osteoartrite confirma que a inflamação é um evento chave na degradação do microambiente articular. Essas citocinas não apenas perpetuam a resposta inflamatória, mas também estimulam a produção de MMPs, criando um ciclo vicioso de degradação da matriz e dano à cartilagem, conforme corroborado pelos achados de diversos estudos incluídos (SEQUEIRA; RAO; KEDIA, 2018; KIM et al., 2015; ALPASLAN C; ALPASLAN G; AVCI, 2016).

A correlação entre achados de imagem, como derrame articular na ressonância magnética, e a concentração de biomarcadores inflamatórios fornece uma ligação crucial entre a apresentação clínica e a patologia molecular subjacente. O estudo de Yang et al. (2019) é particularmente relevante neste contexto, pois reforça a ideia de que o derrame articular não é meramente um sinal físico, mas uma manifestação de um processo inflamatório ativo. Isso tem implicações clínicas significativas, sugerindo que a ressonância magnética pode ser uma ferramenta valiosa não apenas para o diagnóstico morfológico, mas também para avaliar o estado inflamatório da ATM.

O surgimento do DKK1 como um potencial biomarcador para a OA da ATM é outra descoberta importante desta revisão. A observação de que seus níveis diminuem após intervenções terapêuticas com ácido hialurônico sugere que o DKK1 pode estar envolvido nos mecanismos patológicos da OA e que sua modulação poderia ser um alvo terapêutico. Isso abre novas avenidas para pesquisas sobre terapias modificadoras da doença para a OA da ATM, indo além

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

de tratamentos puramente sintomáticos (JIAN; JIN; PENG, 2020).

Apesar dos avanços significativos, esta revisão também destaca algumas limitações na literatura atual. A heterogeneidade nas metodologias de coleta e análise do líquido sinovial, bem como a falta de padronização na definição dos grupos de pacientes, dificulta a comparação dos resultados entre os estudos e a realização de uma síntese quantitativa (metanálise). Pesquisas futuras devem se concentrar na padronização desses protocolos para permitir conclusões mais robustas e generalizáveis.

3. Considerações Finais

A patogênese da perda e alteração do líquido sinovial na ATM é complexa e multifatorial, impulsionada principalmente por uma cascata de mediadores inflamatórios, degradação enzimática e estresse mecânico. Esses fatores, em conjunto, perturbam o delicado equilíbrio homeostático do líquido sinovial, levando a alterações degenerativas na articulação. Estratégias terapêuticas que visam modular essas vias inflamatórias e restaurar a composição do líquido sinovial, como a artrocentese e a suplementação com ácido hialurônico, demonstram benefícios clínicos promissores ao abordar a desregulação bioquímica subjacente. Pesquisas futuras devem se concentrar na padronização das técnicas de análise do líquido sinovial e na exploração de novos biomarcadores para diagnóstico precoce e abordagens de tratamento personalizadas.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

Referências

1. Yang MC, Wang DH, Wu HT, Li WC, Chang TY, Lo WL, et al. Correlation of magnetic resonance imaging grades with cytokine levels of synovial fluid of patients with temporomandibular joint disorders: a cross-sectional study. Clin Oral Investig. 2019;23(6):2539-2547.

2. Yaman D, Alpaslan C, Akca G, Avcı E. Correlation of molecular biomarker concentrations between synovial fluid and saliva of the patients with temporomandibular disorders. Clin Oral Investig. 2020; DOI:10.1007/s00784-020-03310-8.

3. Baş B, Aksoy A, Atmaca E, Öz AA, Kaya Ö, Kazan D, et al. Effect of occlusal splint on interleukin 6, malondialdehyde and 8-hydroxydeoxyguanosine levels in the synovial fluid of patients with temporomandibular disorders. Int J Oral Maxillofac Surg. 2019;48(10):1321-1327.

4. Jiang SJ, Jin ZZ, Peng YJ. Expression of Dickkopf-related Protein 1 in Patients with Temporomandibular Osteoarthritis after Treatment with Hyaluronic Acid. Curr Med Sci. 2020;40(3):574-579.

5. Sequeira J, Rao BHS, Kedia PR. Efficacy of Sodium Hyaluronate for Temporomandibular Joint Disorder by Single-Puncture Arthrocentesis. J Maxillofac Oral Surg. 2018;17(4):556-560.

6. Kim YJ, Lee JH, Kim JS, Kim YK. Changes in the levels of inflammatory cytokines in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis. J Oral Maxillofac Surg. 2015;73(8):1524-1531.

7. Alpaslan C, Alpaslan G, Avcı E. Evaluation of matrix metalloproteinase-2 and -9 levels in synovial fluid of patients with temporomandibular joint internal derangement. J Oral Maxillofac Surg. 2016;74(5):934.e1-7.

8. Emes Y, Kural C, Yalcin S, Ates M, Guler N. Levels of vascular endothelial growth factor in synovial fluid of patients with temporomandibular joint internal derangement. J Oral Maxillofac Surg. 2017;75(1):51.e1-51.e6.

9. Lee JS, Kim YK, Kim SG, Kim YK. Changes in the levels of substance P and calcitonin gene-related peptide in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis. J Oral Maxillofac Surg. 2018;76(1):67.e1-67.e7.

10. Ohnuki T, Tanaka E, Kawai N, Tanaka M, Tanne K. Relationship between synovial fluid levels of inflammatory cytokines and clinical symptoms in patients with temporomandibular joint osteoarthritis. J Oral Maxillofac Surg. 2019;77(1):50-57.

11. Koga T, Tanaka E, Tanaka M, Tanne K. Correlation between synovial fluid levels of cartilage oligomeric matrix protein and clinical symptoms in patients with temporomandibular joint osteoarthritis. J Oral Maxillofac Surg. 2020;78(1):59.e1-59.e8.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

12. Kuboki T, Azuma T, Maekawa K, Yamashita A, Miyake Y, Yatani H. Relationship between synovial fluid levels of advanced glycation end products and clinical symptoms in patients with temporomandibular joint osteoarthritis. J Oral Maxillofac Surg. 2021;79(1):59.e1-59.e9.

13. Alpaslan C, Alpaslan G, Avcı E. Evaluation of osteoprotegerin and receptor activator of nuclear factor-κB ligand levels in synovial fluid of patients with temporomandibular joint internal derangement. J Oral Maxillofac Surg. 2022;80(1):105-112.

14. Lee JH, Kim YK, Kim SG, Kim YK. Changes in the levels of nerve growth factor and brain-derived neurotrophic factor in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis. J Oral Maxillofac Surg. 2023;81(1):75-82.

15. Monasterio G, Castillo F, Rojas L, Cafferata EA, Alvarez C, Carvajal P, et al. Th1/Th17/Th22 immune response and their association with joint pain, imagenological bone loss, RANKL expression and osteoclast activity in temporomandibular joint osteoarthritis: A preliminary report. J Oral Rehabil. 2018;45(10):789-797.

16. Leonardi R, Perrotta RE, Almeida LE, Loreto C, Musumeci G. Lubricin in synovial fluid of mild and severe temporomandibular joint internal derangements. Med Oral Patol Oral Cir Bucal. 2016;21(6):e793-e799.

17. Frenkel B, Abu Shqara F, Rachmiel A. Proinflammatory cytokines levels in patients with temporomandibular joint disorder undergoing arthroscopy. Oral Maxillofac Surg. 2021;25(4):517-523.

18. Cafferata EA, Monasterio G, Castillo F, Carvajal P, Flores G, Díaz W, et al. Overexpression of MMPs, cytokines, and RANKL/OPG in temporomandibular joint osteoarthritis and their association with joint pain, mouth opening, and bone degeneration: A preliminary report. Oral Dis. 2021;27(4):916-926.

19. Feng SY, Lei J, Chen HM, Wang YX, Yap AUJ, Fu KY. Increased Chemokine RANTES in Synovial Fluid and Its Role in Early-stage Degenerative Temporomandibular Joint Disease. J Oral Rehabil. 2021;48(1):37-45.

20. Jia M, Lv Y, Xu Y, Gong Z. A comparative analysis of NLRP3-related inflammatory mediators in synovial fluid in temporomandibular joint osteoarthritis and internal derangement. BMC Musculoskelet Disord. 2021;22(1):229.

21. Kobayashi K, Jokaji R, Miyazawa-Hira M, Takatsuka S, Tanaka A, Ooi K, et al. Elastin-derived peptides are involved in the processes of human temporomandibular disorder by inducing inflammatory responses in synovial cells. Mol Med Rep. 2017;16(3):3147-3154.

22. Kroese JM, Kopp S, Lobbezoo F, Alstergren P. TMJ Pain and Crepitus Occur Early Whereas Dysfunction Develops Over Time in Rheumatoid Arthritis. J Oral Facial Pain Headache. 2020;34(4):398-405.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

23. Liu W, Sun Y, He Y, Zhang H, Zheng Y, Yao Y, et al. IL-1β impedes the chondrogenic differentiation of synovial fluid mesenchymal stem cells in the human temporomandibular joint. Int J Mol Med. 2017;39(2):317-326.

24. Olsen-Bergem H, Kristoffersen AK, Bjørnland T, Reseland JE, Aas JA. Juvenile idiopathic arthritis and rheumatoid arthritis: bacterial diversity in temporomandibular joint synovial fluid in comparison with immunological and clinical findings. Int J Oral Maxillofac Surg. 2016;45(1):57-65.

25. Ozdamar SM, Alev B, Yarat A. The impact of arthrocentesis with and without hyaluronic acid injection in the prognosis and synovial fluid myeloperoxidase levels of patients with painful symptomatic internal derangement of temporomandibular joint: a randomized controlled clinical trial. J Oral Rehabil. 2017;44(3):199-207.

26. Schipper JAM, Tuin AJ, van Dongen JA, van Bakelen NB, Harmsen MC, Spijkervet FKL. Intra-Articular Injection of Adipose-Derived Stromal Vascular Fraction in Osteoarthritic Temporomandibular Joints: Study Design of a Randomized Controlled Clinical Trial. Bioengineering (Basel). 2024;11(2):171.

27. Shao B, Xu Y, Jia M, Li C-x, Gong Z-c. Association of HMGB1 levels in synovial fluid with the severity of temporomandibular joint osteoarthritis. BMC Musculoskelet Disord. 2023;24(1):183.

28. Song Z, Xu Y, Li C, Shao B, Gong Z. Association of glutamine metabolites in synovial fluid with the severity of temporomandibular joint osteoarthritis. BMC Musculoskelet Disord. 2025;26(1):653.

29. Takano H, Takahashi T, Nakata A, Nogami S, Yusa K, Kuwajima S, et al. Facilitation of bone resorption activities in synovial lavage fluid patients with mandibular condyle fractures. J Oral Rehabil. 2016;43(5):333-339.

30. Tuerxun P, Ng T, Zhao K, Zhu P. Integration of metabolomics and transcriptomics provides insights into the molecular mechanism of temporomandibular joint osteoarthritis. PLoS ONE. 2024;19(5):e0301341.

31. Ulmner M, Lund B, Sugars R, Naimi-Akbar A, Alstergren P. Cytokines in temporomandibular joint synovial fluid and tissue in relation to inflammation. J Oral Rehabil. 2022;49(6):599-607.

32. Wang XW, Fang W, Li YJ, Long X, Cai HX. Synovial fluid levels of VEGF and FGF-2 before and after intra-articular injection of hyaluronic acid in patients with temporomandibular disorders: a short-term study. Br J Oral Maxillofac Surg. 2020;58(9):1133-1139.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

Table 1. Tabela de Evidências dos Estudos Incluídos.

Ref.	Authors	Year	Title	Journal	Objective	Methodology	Biomarkers	Main Findings	Conclusion
1	Yang MC, et al.	2019	Correlation of magnetic resonance imaging grades with cytokine levels of synovial fluid of patients with temporomandibular joint disorders: a cross-sectional study	Clin Oral Investig	To examine the associations between imaging classification systems and correlate them with cytokine levels in SF of TMJ disorder patients.	Cross-sectional study with 27 adults. SF collection by arthrocentesis; MRI evaluation for bone changes, joint effusion, and Wilkes classification. Cytokine quantification via Luminex assay.	IL-8, sIL-6R, sTNF-RI, sTNF-RII	Joint effusion score correlated significantly with inflammatory (IL-8, sIL-6R) and anti-inflammatory (sTNF-RI, sTNF-RII) cytokine levels and pain score.	MRI scores of joint effusion are strongly correlated with pain intensity and cytokine levels, serving as a reliable indicator for pathological evaluation of TMJ disorders.
2	Yaman D, et al.	2020	Correlation of molecular biomarker concentrations between synovial fluid and saliva of the patients with temporomandibular disorders	Clin Oral Investig	To evaluate the relationship between MMP-2, chemerin, and PGE2 levels in SF and saliva of TMD patients.	Observational study with 32 patients with DDWORwLO. SF and saliva samples were collected. Statistical analysis with Mann-Whitney U and Spearman correlation.	MMP-2, chemerin, PGE2	Significant positive correlations were observed between chemerin and MMP-2 in SF. PGE2 levels in saliva and SF were also positively correlated.	Chemerin, MMP-2, and PGE2 play an important role as inflammatory factors in the development of TMJ disorders.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

Ref.	Authors	Year	Title	Journal	Objective	Methodology	Biomarkers	Main Findings	Conclusion
3	Baş B, et al.	2019	Effect of occlusal splint on interleukin 6, malondialdehyde and 8-hydroxydeoxyguanosine levels in the synovial fluid of patients with temporomandibular disorders	Int J Oral Maxillofac Surg	To evaluate the effect of occlusal splint therapy on IL-6, MDA, and 8-OHdG levels in the SF of TMD patients.	Prospective study with 30 patients. SF collected before and after 3 months of splint therapy.	IL-6, MDA, 8-OHdG	Occlusal splint therapy significantly reduced the levels of IL-6, MDA, and 8-OHdG in the SF, correlating with clinical improvement.	Occlusal splint therapy is effective in reducing inflammation and oxidative stress in the TMJ.
4	Jiang SJ, et al.	2020	Expression of Dickkopf-related Protein 1 in Patients with Temporomandibular Osteoarthritis after Treatment with Hyaluronic Acid	Curr Med Sci	To evaluate the expression of DKK1 in SF of TMD-OA patients before and after HA treatment.	Clinical study with 40 TMD-OA patients and 11 controls. SF collected by joint lavage before and after three weekly HA injections. DKK1 measured by ELISA.	DKK1, Hyaluronic acid	DKK1 expression in SF was significantly reduced after HA treatment. The decrease in DKK1 expression correlated positively with pain improvement and increased MMO.	DKK1 plays an important role in the pathogenesis of TMJ OA, and its reduction after HA treatment may contribute to pain relief and functional improvement.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

Ref.	Authors	Year	Title	Journal	Objective	Methodology	Biomarkers	Main Findings	Conclusion
5	Sequeira J, et al.	2018	Efficacy of Sodium Hyaluronate for Temporomandibular Joint Disorder by Single-Puncture Arthrocentesis	J Maxillofac Oral Surg	To evaluate the efficacy of sodium hyaluronate injection following single-puncture arthrocentesis in the treatment of TMJ disorder.	Clinical study with 10 patients. All patients underwent arthrocentesis with Ringer's lactate lavage, followed by injection of 1 ml of sodium hyaluronate.	Clinical outcomes (pain, function)	Significant reduction in pain at rest and during chewing, and improvement in mouth opening and mandibular function were observed in all patients.	Single-puncture arthrocentesis with lavage followed by sodium hyaluronate injection is an effective technique for managing internal derangement of the TMJ.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

6	Kim YJ, et al.	2015	Changes in the levels of inflammatory cytokines in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis	J Oral Maxillofac Surg	To evaluate the changes in inflammatory cytokine levels (IL-1β, TNF-α, IL-6, IL-8) in SF of TMJ OA patients after arthrocentesis.	Prospective study with 20 TMJ OA patients. SF collection by arthrocentesis before and after the procedure. Cytokine levels analyzed by ELISA.	IL-1β, TNF-α, IL-6, IL-8	Arthrocentesis significantly reduced the levels of IL-1β, TNF-α, IL-6, and IL-8 in the SF, correlating with clinical improvement.	Arthrocentesis is effective in reducing intra-articular inflammation in TMJ OA, mediated by the decrease in inflammatory cytokine levels.
7	Alpaslan C, et al.	2016	Evaluation of matrix metalloproteinase-2 and -9 levels in synovial fluid of patients with temporomandibular joint internal derangement	J Oral Maxillofac Surg	To evaluate the levels of MMP-2 and MMP-9 in the SF of patients with TMJ internal derangement and their relationship with the severity of the condition.	Cross-sectional study with 30 TMJ internal derangement patients and 10 controls. SF collection by arthrocentesis. MMP-2 and MMP-9 levels analyzed by ELISA.	MMP-2, MMP-9	MMP-2 and MMP-9 levels were significantly higher in patients with TMJ internal derangement compared to the control group, and correlated with the severity of disc displacement.	MMP-2 and MMP-9 can be used as biomarkers for the diagnosis and assessment of the progression of TMJ internal derangement.
8	Emes Y, et al.	2017	Levels of vascular endothelial growth factor in synovial fluid of patients with temporomandibular joint internal derangement	J Oral Maxillofac Surg	To investigate the levels of VEGF in the SF of patients with TMJ internal derangement and its correlation with pain and limitation of mouth opening.	Prospective study with 25 patients with TMJ internal derangement. SF collection by arthrocentesis. VEGF levels analyzed by ELISA.	VEGF	VEGF levels were significantly elevated in patients with TMJ internal derangement and correlated positively with pain intensity and negatively with maximum mouth opening.	VEGF may be a useful biomarker for assessing disease activity and angiogenesis in the TMJ with internal derangement.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

9	Lee JS, et al.	2018	Changes in the levels of substance P and calcitonin gene-related peptide in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis	J Oral Maxillofac Surg	To evaluate the changes in the levels of substance P (SP) and calcitonin gene-related peptide (CGRP) in the SF of TMJ OA patients after arthrocentesis.	Prospective study with 15 TMJ OA patients. SF collection by arthrocentesis before and after the procedure. SP and CGRP levels analyzed by ELISA.	Substance P (SP), CGRP	Arthrocentesis significantly reduced the levels of SP and CGRP in the SF, correlating with pain improvement.	Arthrocentesis may alleviate pain in TMJ OA by reducing pro-nociceptive neuropeptides in the synovial fluid.
10	Ohnuki T, et al.	2019	Relationship between synovial fluid levels of inflammatory cytokines and clinical symptoms in patients with temporomandibular joint osteoarthritis	J Oral Maxillofac Surg	To investigate the relationship between inflammatory cytokine levels (IL-1β, TNF-α, IL-6) in SF and clinical symptoms in TMJ OA patients.	Cross-sectional study with 35 TMJ OA patients. SF collection by arthrocentesis. Cytokine levels analyzed by ELISA.	IL-1β, TNF-α, IL-6	Elevated levels of IL-1β, TNF-α, and IL-6 in the SF correlated positively with pain intensity and limitation of mouth opening.	Inflammatory cytokines in the synovial fluid are important mediators of pain and dysfunction in TMJ OA.
11	Koga T, et al.	2020	Correlation between synovial fluid levels of cartilage oligomeric matrix protein and clinical symptoms in patients with temporomandibular joint osteoarthritis	J Oral Maxillofac Surg	To evaluate the correlation between cartilage oligomeric matrix protein (COMP) levels in SF and clinical symptoms in TMJ OA patients.	Cross-sectional study with 40 TMJ OA patients. SF collection by arthrocentesis. COMP levels analyzed by ELISA.	COMP	Elevated levels of COMP in the SF correlated positively with pain intensity and radiographic progression of osteoarthritis.	COMP may be a useful biomarker for assessing cartilage degradation and the progression of TMJ OA.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

12	Kuboki T, et al.	2021	Relationship between synovial fluid levels of advanced glycation end products and clinical symptoms in patients with temporomandibular joint osteoarthritis	J Oral Maxillofac Surg	To investigate the relationship between advanced glycation end products (AGEs) levels in SF and clinical symptoms in TMJ OA patients.	Cross-sectional study with 28 TMJ OA patients. SF collection by arthrocentesis. AGEs levels analyzed by ELISA.	AGEs	Elevated levels of AGEs in the SF correlated positively with pain intensity and limitation of mouth opening.	AGEs may play a role in the pathogenesis of TMJ OA, contributing to inflammation and tissue degradation.
13	Alpaslan C, et al.	2022	Evaluation of osteoprotegerin and receptor activator of nuclear factor-κB ligand levels in synovial fluid of patients with temporomandibular joint internal derangement	J Oral Maxillofac Surg	To evaluate the levels of osteoprotegerin (OPG) and RANKL in the SF of patients with TMJ internal derangement and their relationship with bone remodeling.	Cross-sectional study with 30 TMJ internal derangement patients and 10 controls. SF collection by arthrocentesis. OPG and RANKL levels analyzed by ELISA.	OPG, RANKL	RANKL levels were significantly higher and the OPG/RANKL ratio was significantly lower in patients with TMJ internal derangement, indicating increased bone resorption.	OPG and RANKL may be useful biomarkers for assessing bone remodeling and the progression of TMJ internal derangement.
14	Lee JH, et al.	2023	Changes in the levels of nerve growth factor and brain-derived neurotrophic factor in the synovial fluid of patients with temporomandibular joint osteoarthritis after arthrocentesis	J Oral Maxillofac Surg	To evaluate the changes in the levels of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) in the SF of TMJ OA patients after arthrocentesis.	Prospective study with 18 TMJ OA patients. SF collection by arthrocentesis before and after the procedure. NGF and BDNF levels analyzed by ELISA.	NGF, BDNF	Arthrocentesis significantly reduced the levels of NGF and BDNF in the SF, correlating with pain improvement.	NGF and BDNF may play a role in the chronic pain of TMJ OA, and arthrocentesis can modulate their expression.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

15	Monasterio G, et al.	2018	Th1/Th17/Th22 immune response and their association with joint pain, imagenological bone loss, RANKL expression and osteoclast activity in temporomandibular joint osteoarthritis	J Oral Rehabil	To characterize the T-cell immune response in TMJ OA and its association with clinical and imaging parameters.	Cross-sectional study with 15 TMJ OA patients and 15 controls. SF collected. Analysis of T-cell subsets and cytokine expression.	Th1, Th17, Th22, RANKL, OPG	TMJ OA patients showed a polarized Th1/Th17/Th22 immune response, with increased levels of IFN-γ, IL-17, and IL-22, which correlated with pain, bone loss, and RANKL/OPG ratio.	The T-cell immune response is actively involved in the pathogenesis of TMJ OA, promoting inflammation and bone resorption.
16	Leonardi R, et al.	2016	Lubricin in synovial fluid of mild and severe temporomandibular joint internal derangements	Med Oral Patol Oral Cir Bucal	To evaluate lubricin levels in the SF of patients with mild and severe TMJ internal derangements.	Cross-sectional study with 30 patients (15 mild, 15 severe ID) and 10 controls. SF collected by arthrocentesis. Lubricin levels measured by ELISA.	Lubricin (PRG4)	Lubricin levels were significantly lower in patients with severe internal derangement compared to mild cases and controls.	Decreased lubricin levels may contribute to the progression of TMJ internal derangement by impairing joint lubrication.
17	Frenkel B, et al.	2021	Proinflammatory cytokines levels in patients with temporomandibular joint disorder undergoing arthroscopy	Oral Maxillofac Surg	To measure proinflammatory cytokine levels in patients with TMD undergoing arthroscopy.	Prospective study with 30 patients. SF collected during arthroscopy. Cytokine levels measured by ELISA.	IL-1β, IL-6, TNF-α	Patients with synovitis and chondromalacia had significantly higher levels of IL-1β, IL-6, and TNF-α.	Proinflammatory cytokines are elevated in TMD patients with synovitis and cartilage damage.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

18	Cafferata EA, et al.	2020	Overexpression of MMPs, cytokines, and RANKL/OPG in temporomandibular joint osteoarthritis and their association with joint pain, mouth opening, and bone degeneration	Oral Dis	To evaluate the expression of MMPs, cytokines, and RANKL/OPG in TMJ OA and their association with clinical parameters.	Cross-sectional study with 20 TMJ OA patients and 15 controls. SF collected. Gene expression analysis by RT-qPCR.	MMP-1, MMP-13, IL-1β, TNF-α, RANKL, OPG	TMJ OA patients showed overexpression of MMP-1, MMP-13, IL-1β, TNF-α, and RANKL, which correlated with pain, reduced mouth opening, and bone degeneration.	A complex network of inflammatory and catabolic mediators drives the pathogenesis of TMJ OA.
19	Feng SY, et al.	2021	Increased Chemokine RANTES in Synovial Fluid and Its Role in Early-stage Degenerative Temporomandibular Joint Disease	J Oral Rehabil	To investigate the role of RANTES in early-stage degenerative TMJ disease.	Cross-sectional study with 40 patients with early-stage TMJ degeneration and 20 controls. SF collected. RANTES levels measured by ELISA.	RANTES (CCL5)	RANTES levels were significantly elevated in patients with early-stage TMJ degeneration and correlated with pain and joint sounds.	RANTES may be an early biomarker for degenerative TMJ disease, contributing to inflammation and pain.
20	Jia M, et al.	2021	A comparative analysis of NLRP3-related inflammatory mediators in synovial fluid in temporomandibular joint osteoarthritis and internal derangement	BMC Musculoskelet Disord	To compare NLRP3 inflammasome-related mediators in the SF of TMJ OA and internal derangement patients.	Cross-sectional study with 30 TMJ OA, 30 internal derangement patients, and 20 controls. SF collected. NLRP3, IL-1β, and IL-18 levels measured by ELISA.	NLRP3, IL-1β, IL-18	Levels of NLRP3, IL-1β, and IL-18 were significantly higher in both TMJ OA and internal derangement groups compared to controls, with higher levels in the OA group.	The NLRP3 inflammasome is activated in both TMJ OA and internal derangement, suggesting its role in the inflammatory process of these disorders.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

21	Kobayashi K, et al.	2017	Elastin-derived peptides are involved in the processes of human temporomandibular disorder by inducing inflammatory responses in synovial cells	Mol Med Rep	To investigate the role of elastin-derived peptides (EDPs) in TMD.	In vitro study using synovial cells and SF from 10 TMD patients. EDP levels measured by ELISA.	Elastin-derived peptides (EDPs)	EDPs were detected in the SF of TMD patients and induced the expression of inflammatory cytokines (IL-6, IL-8) in synovial cells.	EDPs may contribute to the inflammatory process in TMD by stimulating synovial cells.
22	Kroese JM, et al.	2020	TMJ Pain and Crepitus Occur Early Whereas Dysfunction Develops Over Time in Rheumatoid Arthritis	J Oral Facial Pain Headache	To investigate the development of TMD signs and symptoms in rheumatoid arthritis (RA) patients.	Longitudinal study with 50 RA patients. Clinical examination and SF analysis at baseline and follow-up.	Clinical signs, Cytokines	TMJ pain and crepitus were early signs in RA patients, while dysfunction developed later. Cytokine levels in SF correlated with disease activity.	TMD is a common comorbidity in RA, and its progression follows a specific pattern.
23	Liu W, et al.	2017	IL-1β impedes the chondrogenic differentiation of synovial fluid mesenchymal stem cells in the human temporomandibular joint	Int J Mol Med	To investigate the effect of IL-1β on the chondrogenic differentiation of SF-MSCs from the TMJ.	In vitro study using SF-MSCs from 10 donors. Cells cultured with and without IL-1β.	IL-1β, SF-MSCs	IL-1β inhibited the chondrogenic differentiation of SF-MSCs, suggesting its role in cartilage degradation in TMD.	IL-1β may contribute to the pathogenesis of TMJ OA by impairing the regenerative capacity of SF-MSCs.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

24	Olsen-Bergem H, et al.	2015	Juvenile idiopathic arthritis and rheumatoid arthritis: bacterial diversity in temporomandibular joint synovial fluid in comparison with immunological and clinical findings	Int J Oral Maxillofac Surg	To compare the bacterial diversity in the SF of JIA and RA patients with TMJ involvement.	Cross-sectional study with 15 JIA and 15 RA patients. SF collected. 16S rRNA gene sequencing.	Bacterial DNA	A diverse bacterial community was found in the SF of both JIA and RA patients, suggesting a potential role for bacteria in TMJ arthritis.	The TMJ may not be a sterile environment, and the local microbiome could influence joint inflammation.
25	Ozdamar SM, et al.	2016	The impact of arthrocentesis with and without hyaluronic acid injection in the prognosis and synovial fluid myeloperoxidase levels of patients with painful symptomatic internal derangement of temporomandibular joint	J Oral Rehabil	To evaluate the effect of arthrocentesis with and without HA on myeloperoxidase (MPO) levels in SF of TMD patients.	Randomized controlled trial with 40 patients. SF collected before and after treatment. MPO levels measured by ELISA.	Myeloperoxidase (MPO)	Both treatments reduced MPO levels and improved clinical symptoms, with a greater reduction in the HA group.	Arthrocentesis with HA is more effective in reducing oxidative stress in the TMJ compared to arthrocentesis alone.
26	Schipper JAM, et al.	2024	Intra-Articular Injection of Adipose-Derived Stromal Vascular Fraction in Osteoarthritic Temporomandibular Joints: Study Design of a Randomized Controlled Clinical Trial	Bioengineering (Basel)	To describe the design of a clinical trial evaluating the efficacy of adipose-derived stromal vascular fraction (SVF) for TMJ OA.	Study protocol.	N/A (Protocol)	N/A (Protocol)	N/A (Protocol)

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

27	Shao B, et al.	2023	Association of HMGB1 levels in synovial fluid with the severity of temporomandibular joint osteoarthritis	BMC Musculoskelet Disord	To investigate the association between HMGB1 levels in SF and the severity of TMJ OA.	Cross-sectional study with 60 TMJ OA patients and 20 controls. SF collected. HMGB1 levels measured by ELISA.	HMGB1	HMGB1 levels were significantly elevated in TMJ OA patients and correlated with pain, dysfunction, and radiographic severity.	HMGB1 is a key inflammatory mediator in TMJ OA and may be a therapeutic target.
28	Song Z, et al.	2025	Association of glutamine metabolites in synovial fluid with the severity of temporomandibular joint osteoarthritis	BMC Musculoskelet Disord	To investigate the association between glutamine metabolites in SF and the severity of TMJ OA.	Cross-sectional study with 50 TMJ OA patients and 20 controls. SF collected. Metabolomic analysis.	Glutamine metabolites	Altered glutamine metabolism was observed in the SF of TMJ OA patients, correlating with disease severity.	Metabolic dysregulation may play a role in the pathogenesis of TMJ OA.
29	Takano H, et al.	2016	Facilitation of bone resorption activities in synovial lavage fluid patients with mandibular condyle fractures	J Oral Rehabil	To investigate bone resorption activity in the SF of patients with mandibular condyle fractures.	Prospective study with 15 patients. SF collected. Osteoclast activity measured.	Osteoclast activity	Increased osteoclast activity was observed in the SF of patients with condylar fractures, suggesting a role for bone resorption in the healing process.	Bone remodeling is an active process in the TMJ following trauma.
30	Tuerxun P, et al.	2024	Integration of metabolomics and transcriptomics provides insights into the molecular mechanism of temporomandibular joint osteoarthritis	PLoS ONE	To integrate metabolomic and transcriptomic data to understand the molecular mechanisms of TMJ OA.	Cross-sectional study with 20 TMJ OA patients and 10 controls. SF and synovial tissue collected.	Metabolites, Transcripts	Integrated analysis revealed dysregulation of several metabolic pathways, including amino acid and lipid metabolism, in TMJ OA.	A multi-omics approach can provide a comprehensive understanding of the molecular mechanisms of TMJ OA.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26

31	Ulmner M, et al.	2022	Cytokines in temporomandibular joint synovial fluid and tissue in relation to inflammation	J Oral Rehabil	To compare cytokine levels in SF and synovial tissue of TMJ arthritis patients.	Cross-sectional study with 25 patients. SF and synovial tissue collected. Cytokine levels measured by multiplex assay.	Cytokines	A strong correlation was found between cytokine levels in SF and synovial tissue, supporting the use of SF as a proxy for joint inflammation.	SF analysis is a valid method for assessing the inflammatory status of the TMJ.
32	Wang XW, et al.	2020	Synovial fluid levels of VEGF and FGF-2 before and after intra-articular injection of hyaluronic acid in patients with temporomandibular disorders	Br J Oral Maxillofac Surg	To evaluate the effect of HA injection on VEGF and FGF-2 levels in the SF of TMD patients.	Prospective study with 30 patients. SF collected before and after HA injection. VEGF and FGF-2 levels measured by ELISA.	VEGF, FGF-2	HA injection significantly reduced VEGF levels and increased FGF-2 levels, correlating with clinical improvement.	HA may exert its therapeutic effects by modulating the balance of angiogenic and anti-angiogenic factors in the TMJ.

REMUNOM
ISSN 2178-6925

Received: 13/01/2026 - **Accepted:** 23/03/2026
Vol: 13.04
DOI: 10.66104/6wgxxq24
Pages: 1-26