

Evaluation of Osteopontin (OPN) as Diagnostic Marker of Osteoarthritis (OA)

Aatka Rauf¹, Wajeeha Imam², Hafiza Qurat Ul Ain³

^{1,2,3}Medical Officers , CMH Multan Institute Of Medical Sciences, Multan

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ABSTRACT

In osteoarthritis, a joint disease there is progressive loss of articular cartilage that leads to loss of function and chronic pain in affected joints. Clinically presents as pain, stiffness, decreased mobility, crepitus and deformity of joints. The patients with osteoarthritis exhibit a higher level of osteopontin (OPN) in serum, plasma and synovial fluids. A systemic review revealed that the OPN levels were markedly increased in plasma, serum and synovial fluids of patients with osteoarthritis. Therefore, OPN levels are directly related to advancements in joint damage as well as progression of disease. OPN is a matrix glycoprotein that is expressed in response to tissue trauma. It in turn increases the activity of nuclear factor kappa B and other inflammatory mediators and enhances the inflammatory cascade. Reduction in levels of OPN halts the apoptosis of chondrocytes and angiogenesis. It can also be used as a biomarker in grading the progression and severity of osteoarthritis.

Radiography are gold standard investigations but on radiography, the damage is visualized after a long time in terms of loss of joint space. Biomarkers are used now for diagnostic and prognostic purposes. A study revealed that OPN levels are also increased in idiopathic hip Osteoarthritis so it can be used as a biochemical marker for diagnosing and determining the severity of disease. Biomarkers like OPN help in diagnosing the disease in early stages leading to earlier intervention. However, further studies are still needed to establish a strong connection.

Keywords: Osteoarthritis, osteopontin, biomarker, progression of disease, severity, plasma

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease, in this there is progressive loss of articular cartilage that results in chronic pain and limitation of function in affected joints. The clinical symptoms of OA are pain, stiffness, decreased mobility, swelling, crepitus and deformity. The cause of this disease still remains poorly understood, despite substantial research. However there are many biochemical and biomechanical factors that are thought to be responsible for the disease pathogenesis.^[1] The daily activities are greatly affected by

the disease due to chronic pain and stiffness at joint that limits movement.^[2] The patients with Osteoarthritis (OA) have shown higher Osteopontin (OPN) levels in plasma, serum, and synovial fluid as compared to healthy individuals. In this review, our aim is to find out that can OPN be used as a diagnostic marker for OA symptoms and prognostic marker for disease severity.^[2]

Unveiling The Link Between Biomarkers and Osteoarthritis Severity

The most common type of arthritis is osteoarthritis. Osteoarthritis (OA) is a very

common condition, and its spread is expected to increase dramatically as most people reach the age of 60. These findings indicate a significant increase in the planned and local development of these biomarkers in early OA knee, as well as the link between disease severity and production, which means they may be involved in OA pathogenesis. Longitudinal studies with repetitive measurements of these biomarkers in plasma and synovial fluid and their interactions with knee pain OA are necessary to track or predict the clinical course of OA and, ultimately, determine their potential role in determining the best time participate.^[3]

In a systematic review and meta-analysis that consisted of 14 studies with a total of 776 cases and 530 controls. OPN levels were markedly increased in the plasma, serum and synovial fluid sample of patients with osteoarthritis. It has been revealed that OPN levels are directly related with advancement in joint damage in OA patients. Furthermore, increased levels of OPN is thought to be related with progression of disease (Figure 1)

In Figure 1 it is shown the increased levels of osteopontin in patients with osteoarthritis as compared to the controls

OPN, is the most explained biomarker in OA, OPN is an extracellular matrix glycoprotein and it shows high expression in patients having any trauma or injury to joint. Many studies have shown that the levels of OPN in plasma, serum and synovial fluid are higher in OA patients. It has been manifested by researches that OPN increase the activity of nuclear factor-kappa B (NF- κ B), which in turn increases the activity

of interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and many other inflammatory mediators that upregulate the inflammatory cascade. These results manifest that OPN and its levels in the synovial fluids and cartilage expression may lead to the development of OA. And many studies indicate that a reduction in levels of OPN may halt the joint cartilage destruction and joint swelling reducing the apoptosis of chondrocytes and angiogenesis in OA. OPN can be used as a biochemical marker in grading the progression and severity of OA and can also be used as a prognostic marker. The studies and meta-analysis has shown the association between the severity of OA and OPN levels, thus giving a useful diagnostic and prognostic tool for evaluation of OA patients.^[2]

Radiographs and OPN (Osteopontin) comparison : Key Players in Osteoarthritis Diagnosis and Progression

Although radiograph is gold standard investigation but by and large, biomarkers usually have early diagnostic potential, as on radiographs cartilage damage is documented and this damage is visualized after long time in form of loss of joint space. Biomarkers have been scrutinized for their use as diagnostic and prognostic tool. These biomarkers can either be substances released from cartilage injury like cartilage oligomeric matrix protein (COMP) and Osteopontin (OPN) or substances released during repair of cartilage like cartilage acidic protein 1, CRTAC1, which is a marker of chondrocyte development. Studies have shown robust usage of biomarkers for osteoarthritis severity and progression. The patients with primary knee OA had higher levels of synovial fluid OPN as compared to healthy individuals. OPN concentrations in synovial fluid and articular cartilage is greatly related with the severity of disease. Further studies are still under process to clarify the role of OPN in the pathogenesis of the degenerative process of OA.^[1]

OPN Levels: A Key Indicator of Osteoarthritis Progression

The use of Biochemical markers such as OPN can help in early diagnosis, as well as in observing the receptivity to treatments. According to Garner et al, by using and monitoring biomarkers it

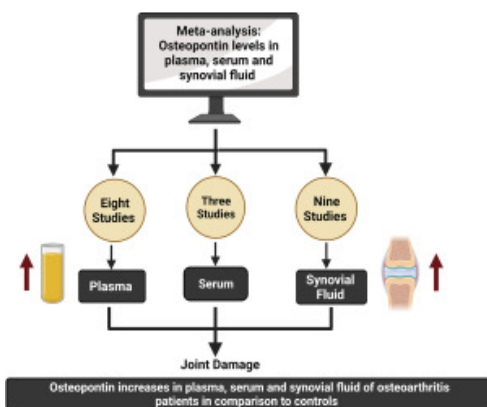


Figure 1:

takes only a few months to observe changes and joint damage through while observing the effectiveness of treatment through traditional radiographs (anteroposterior) based on the modified Sharp/Van der Heijde scoring method, may take 1 year or more.[4]another study was performed in American college of rheumatology on 21 patients that concluded plasma OPN levels are increased in idiopathic hip OA and are directly related with severity. Thus giving an assumption that measurements of plasma OPN levels could be used as a biochemical marker for diagnosis and the determining of severity in hip osteoarthritis.^[4]

Biochemical markers including OPN may offer a great opportunity, not only to help evaluate the severity and progression of arthritis, but also to diagnose the disease in its early stages and to monitor responsiveness to treatment. The need to detect plasma OPN in hip OA and its correlation to the disease is very desirable. And hence modification of the initiation and regulation of the immune pathogenesis pathways has a possible role in revealing new targets for future therapeutic modalities in OA. ^[4]

The request for non-invasive and elaborative biochemical markers (biomarkers) is increasing for better and earlier diagnosis and prognosis of osteoarthritis; furthermore it can allow for early drug development (including translational research),. The Purpose of this review is to comment on current availability of such biomarkers. we can identify new markers that can distinguish different subtypes, this can greatly facilitate drug development from early discovery to late clinical development.^[5]

In one study sample of cartilage was taken from patients with osteoarthritis, and osteopontin detected by immunohistochemistry, Western blot analysis, in situ hybridization, and Northern blot analysis. And the qualitative analysis indicated that the deposition of osteopontin protein and its mRNA expression rise with the severity of the osteoarthritic lesions and with the destruction of the cartilaginous matrix.^[6]

Biochemical markers including OPN enable clinicians, not only to assess the severity and progression of arthritis, but also helps, to diagnose

the disease in its early stages ,earlier intervention and to monitoring response to treatment. The necessity to detect plasma OPN in OA and its correlation to the disease is very preferable. And hence moderation of the commencement and regulation of the immune-pathogenesis pathways has a possible role in disclosing new targets for future therapeutic modalities in OA.^[4]

OPN in synovial fluid and articular cartilage is associated with progressive joint damage and is likely to be a useful biomarker for determining disease severity and progression in knee OA. The patients with OA had higher levels of synovial fluid OPN compared with healthy controls. OPN concentrations in plasma ,serum and synovial fluid and articular cartilage greatly related with the severity of disease. Further studies are in progress to elaborate and clarify the part of OPN to the pathogenesis of the degenerative process of OA.^[1]

Recommendations

Here are few points to consider regarding the potential use of OPN as a diagnostic marker for osteoarthritis:

- **Conduct further research:** Continue conducting in-depth studies to establish a strong association between OPN levels and osteoarthritis.
- **Validate findings:** Validate the findings from different research studies to ensure the accuracy and reliability of OPN as a diagnostic marker.
- **Standardize testing methods:** Develop standardized testing methods to measure OPN levels consistently across different healthcare settings.
- **Establish reference ranges:** Establish reference ranges for OPN levels in individuals with and without osteoarthritis to aid in diagnosis.
- **Explore different sample types:** Investigate the feasibility of using various sample types (e.g., blood, synovial fluid) to measure OPN levels accurately.
- **Consider different stages of osteoarthritis:** Determine whether OPN levels vary at different stages of osteoarthritis, allowing for early detection and intervention.

- **Assess specificity and sensitivity:** Evaluate the specificity and sensitivity of OPN as a diagnostic marker compared to existing diagnostic methods.
- **Incorporate OPN into clinical guidelines:** Consider including OPN as part of clinical guidelines for osteoarthritis diagnosis and monitoring.
- **Collaborate with healthcare professionals:** Foster collaboration between researchers and healthcare professionals to ensure the practicality and applicability of OPN as a diagnostic marker.
- **Monitor long-term outcomes:** Track the long-term outcomes of using OPN as a diagnostic marker to assess its effectiveness in improving patient outcomes and guiding treatment decisions.

These recommendations aim to highlight the importance of further research, standardization, and collaboration to fully explore the potential of OPN as a diagnostic marker for osteoarthritis.

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