International Journal of Orthopaedics and Physiotherapy

ISSN Print: 2664-8989
ISSN Online: 2664-8997
IJOP 2024; 6(1): 11-16
www.orthopedicsjournals.com
Received: 16-11-2023
Accepted: 23-12-2023

Sujata Deb Roy
Department of Physiotherapy, Swami Vivekananda University, Barrackpore, West Bengal, India

Barnana Roy
Department of Physiotherapy, Swami Vivekananda University, Barrackpore, West Bengal, India

Pritam Singha
Department of Physiotherapy, Swami Vivekananda University, Barrackpore, West Bengal, India

Kamalika Bhattacharjee
Department of Physiotherapy, Swami Vivekananda University, Barrackpore, West Bengal, India

Corresponding Author:
Sujata Deb Roy
Department of Physiotherapy, Swami Vivekananda University, Barrackpore, West Bengal, India

Unveiling the role of C-reactive protein in osteoarthritis: A biomarker of inflammation, severity, and degeneration

Sujata Deb Roy, Barnana Roy, Pritam Singha and Kamalika Bhattacharjee

DOI: https://doi.org/10.33545/26648989.2024.v6.i1a.19

Abstract
Osteoarthritis (OA) is a prevalent joint disorder marked by progressive articular cartilage degeneration, underlying bone changes, and joint inflammation. It primarily affects weight-bearing joints such as knees, hips, and spine, significantly causing pain, disability, and diminished quality of life. Inflammation takes a pivotal role in OA's origin and advancement. C-reactive protein (CRP), an acute-phase reactant indicating systemic inflammation, has emerged as a potential biomarker and contributor in this process. Elevated serum CRP levels reflect both systemic and synovial inflammation, offering a valuable measure to assess disease severity and activity. A systematic literature search across databases like Google Scholar, EBSCO, PubMed, Cochrane, and Web of Science yielded 3680 relevant publications up to September 2022, Elevated CRP levels correlate with more pronounced radiographic findings, encompassing joint space reduction and increased osteophyte formation, as well as declining function over time. Moreover, elevated CRP levels correspond to intensified pain scores and escalated analgesic needs. CRP's potential to bind with cartilage components like collagen and proteoglycans might contribute to cartilage degradation. Furthermore, CRP activates immune cells and stimulates the production of pro-inflammatory cytokines, chemokines, and matrix metalloproteinases, all of which contribute to joint inflammation.

Keywords: Osteoarthritis, c-reactive protein, articular cartilage degeneration, synovial inflammation, disease severity

Introduction
Osteoarthritis (OA) is a common joint disorder characterized by the progressive degeneration of articular cartilage, changes in the underlying bone, and joint inflammation. It affects millions of individuals worldwide and poses a significant healthcare burden. In recent years, there has been growing recognition of the role of inflammation in the pathogenesis and progression of OA. C-reactive protein (CRP), an acute-phase reactant and a marker of systemic inflammation, has emerged as a potential biomarker and mediator in the disease process. This review provides an overview of the background and significance of osteoarthritis, the role of inflammation in its progression, and the involvement of CRP [1]. Osteoarthritis is a multifactorial disease characterized by the breakdown of articular cartilage, joint inflammation, and structural changes. It primarily affects weight-bearing joints such as the knees, hips, and spine, and is a leading cause of pain, disability, and reduced quality of life. The rising prevalence of OA is attributed to factors such as an aging population, obesity, joint injury, and genetic predisposition. Understanding the underlying mechanisms of OA is crucial for developing effective management strategies and potential therapeutic interventions [4, 6]. Inflammation plays a central role in the pathogenesis and progression of OA. While OA was traditionally considered a degenerative disorder, evidence suggests that inflammatory processes contribute significantly to disease pathophysiology. Inflammatory mediators, including cytokines, chemokines, and matrix metalloproteinases (MMPs), are elevated in OA joints and promote cartilage degradation, inflammation, and joint damage. Synovial inflammation, characterized by the infiltration of immune cells and increased pro-inflammatory cytokine production, further exacerbates joint inflammation and

tissue destruction [2, 3, 5, 8]. C-reactive protein (CRP) is a well-established biomarker of systemic inflammation and an acute-phase reactant produced by the liver in response to pro-inflammatory cytokines, notably interleukin-6 (IL-6). Elevated levels of CRP have been observed in various inflammatory conditions, including rheumatoid arthritis and systemic lupus erythematosus. While traditionally regarded as a marker of systemic inflammation, recent studies have suggested that CRP may also play a direct role in the pathogenesis of OA. Elevated CRP levels have been associated with disease severity, progression, and joint pain in OA patients. CRP can directly stimulate the production of pro-inflammatory cytokines and induce the expression of matrix metalloproteinases, contributing to cartilage degradation and joint inflammation [6, 7, 9, 10].

CRP and Osteoarthritis: The link

Synovial inflammation is a hallmark feature of osteoarthritis (OA) and is closely associated with disease progression. The synovium is a specialized tissue lining the joints and plays a crucial role in joint homeostasis. In OA, synovial inflammation is characterized by increased infiltration of immune cells, such as macrophages and lymphocytes, along with elevated levels of pro-inflammatory cytokines. C-reactive protein (CRP), an acute-phase reactant, has been found to be associated with synovial inflammation in OA [11]. Studies have shown a positive correlation between CRP levels and synovial inflammation markers, such as synovial fluid white blood cell count, synovial membrane thickness, and synovial cytokine levels. The presence of synovial inflammation is associated with increased disease severity, joint pain, and functional impairment in OA patients. Elevated CRP levels in the serum reflect the systemic inflammation associated with synovial inflammation and can serve as a valuable biomarker for assessing disease activity and severity [12]. Radiographic assessment, such as joint space narrowing and osteophyte formation, is commonly used to evaluate the structural changes in OA. Several studies have investigated the association between serum CRP levels and radiographic severity in OA patients. Elevated CRP levels have been correlated with more severe radiographic findings, including greater joint space narrowing and increased osteophyte formation [13, 14]. These findings suggest that CRP may serve as a useful biomarker for predicting radiographic progression and structural damage in OA. Serial measurements of CRP levels may provide valuable information for monitoring disease progression and response to therapeutic interventions [15]. In addition to its association with radiographic severity, CRP has also been investigated as a predictor of disease progression in OA. Longitudinal studies have demonstrated that higher baseline CRP levels are associated with an increased risk of disease progression, including joint space narrowing and cartilage loss, over time. CRP has shown predictive value in identifying patients who are more likely to experience worsening symptoms, functional decline, and the need for joint replacement surgery [16, 17]. The ability of CRP to predict disease progression highlights its potential as a prognostic marker in OA. Incorporating CRP measurements into clinical practice may help identify patients at higher risk of progression and facilitate personalized treatment strategies [18]. Pain is the most common symptom in OA and significantly affects patients' quality of life. Growing evidence suggests a relationship between CRP and pain severity in OA. Studies have reported a positive association between CRP levels and pain intensity in OA patients, independent of radiographic severity. Elevated CRP levels have been associated with higher pain scores and increased analgesic requirements [19]. The exact mechanisms underlying the association between CRP and pain in OA are not fully understood. However, it is hypothesized that CRP may directly contribute to pain through the activation of inflammatory pathways and the release of pain-modulating substances. Additionally, CRP-induced inflammation and joint damage may lead to sensitization of pain receptors, amplifying the pain response [20].

Mechanisms of CRP in osteoarthritis

Interaction between CRP and cartilage components

C-reactive protein (CRP), an acute-phase reactant and marker of systemic inflammation, has been implicated in the pathogenesis of osteoarthritis (OA) through its interaction with cartilage components. Several studies have demonstrated direct interactions between CRP and cartilage matrix molecules, including collagen and proteoglycans [21]. CRP can bind to collagen type II, the predominant collagen in articular cartilage, through calcium-dependent interactions. This binding may facilitate the recruitment of immune cells and the activation of inflammatory processes in the joint. CRP can also interact with cartilage proteoglycans, leading to enhanced cartilage degradation. These interactions suggest that CRP may directly influence the integrity and homeostasis of cartilage in OA [22, 23].

CRP-induced inflammation and joint degradation

CRP has been shown to induce inflammation and joint degradation through various mechanisms. CRP can activate immune cells, such as macrophages and neutrophils, leading to the production of pro-inflammatory cytokines, chemokines, and matrix metalloproteinases (MMPs). These mediators contribute to the degradation of cartilage components and the perpetuation of inflammation in the joint. Moreover, CRP can stimulate the production of reactive oxygen species (ROS) and nitric oxide (NO) in chondrocytes, further promoting inflammation and tissue damage. ROS and NO can initiate a cascade of events leading to the breakdown of cartilage matrix molecules, such as collagen and proteoglycans, and the activation of inflammatory pathways [24].

Role of CRP in cartilage metabolism

CRP has also been implicated in the modulation of cartilage metabolism in OA. Studies have shown that CRP can directly influence chondrocyte function and matrix synthesis. CRP can up sregulate the expression of catabolic enzymes, such as MMPs, while down regulating the expression of anabolic factors, such as collagen type II and aggrecan. Additionally, CRP can interfere with the signaling pathways involved in cartilage homeostasis. It has been shown to activate nuclear factor-kappa B (NF-κB), a key regulator of inflammation, and inhibit the transforming growth factor-beta (TGF-β) pathway, which plays a crucial role in cartilage repair and maintenance [24]. The dysregulation of cartilage metabolism by CRP contributes to the imbalanced catabolic and anabolic processes observed in OA. This disruption of homeostasis leads to the progressive

degradation of cartilage and the development of joint pathology [23].

Clinical implications of CRP in osteoarthritis

CRP as a diagnostic marker in OA

C-reactive protein (CRP) has been investigated as a diagnostic marker in osteoarthritis (OA) to aid in the early detection and accurate diagnosis of the disease. Several studies have examined the association between CRP levels and the presence of OA. Elevated CRP levels have been found in patients with OA compared to healthy individuals, suggesting its potential as a diagnostic marker [25]. However, it is important to note that CRP is not specific to OA and can be elevated in various inflammatory conditions. Therefore, CRP alone may not be sufficient for a definitive diagnosis of OA. Combining CRP measurements with other clinical and radiological assessments can provide a more comprehensive evaluation for diagnosing OA [26].

Predictive value of CRP in disease progression

CRP has shown promise as a predictive marker for disease progression in OA. Several longitudinal studies have demonstrated an association between baseline CRP levels and subsequent disease progression. Higher baseline CRP levels have been correlated with increased joint pain, radiographic severity, and functional decline over time [27]. These findings suggest that CRP measurements can help identify patients at higher risk of disease progression. Early identification of individuals with elevated CRP levels may enable proactive management strategies and interventions to slow down or prevent disease progression [28].

Monitoring therapeutic response in CRP

CRP can also serve as a valuable tool for monitoring therapeutic response in OA. The effectiveness of various treatment modalities, such as non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), and intra-articular corticosteroid injections, can be evaluated by monitoring changes in CRP levels over time [29]. A decrease in CRP levels following treatment may indicate a favorable response to therapy, while persistent or elevated levels may suggest a lack of response or the need for alternative treatment strategies. Regular monitoring of CRP levels can provide clinicians with objective data to guide treatment decisions and optimize patient outcomes [30].

CRP and comorbidities in OA

Osteoarthritis is often associated with various comorbidities, such as cardiovascular disease, metabolic syndrome, and obesity. CRP, as a marker of systemic inflammation, has been implicated in the development and progression of these comorbidities [31]. Elevated CRP levels in OA patients have been associated with an increased risk of developing cardiovascular disease and metabolic syndrome. Furthermore, high CRP levels have been linked to increased pain severity, functional impairment, and poorer outcomes in individuals with OA and comorbidities [32].

Therapeutic opportunities and future directions

Targeting CRP for disease management

Given the emerging evidence regarding the role of C-reactive protein (CRP) in the pathogenesis and progression of osteoarthritis (OA), targeting CRP may offer potential therapeutic benefits for disease management. Strategies aimed at reducing CRP levels or inhibiting its downstream effects could help alleviate inflammation, cartilage degradation, and associated symptoms in OA patients [33]. One approach to targeting CRP is through lifestyle interventions. Lifestyle modifications, such as weight loss and exercise, have been shown to decrease CRP levels in individuals with OA. By promoting weight reduction and physical activity, these interventions can help reduce systemic inflammation and potentially improve OA outcomes [34]. Another potential avenue for targeting CRP is through pharmacological interventions. Anti-inflammatory drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) and disease-modifying anti-rheumatic drugs (DMARDs), have been shown to reduce CRP levels in various inflammatory conditions. However, their specific effects on CRP in OA require further investigation [35].

Modulation of CRP levels as a therapeutic strategy

Modulating CRP levels directly or indirectly represents a therapeutic strategy for managing OA. Several approaches have been proposed to achieve this, including:

Targeting pro-inflammatory cytokines

Inhibiting the production or activity of pro-inflammatory cytokines, such as interleukin-6 (IL-6), can lead to decreased CRP synthesis. IL-6 inhibitors, such as tocilizumab, have shown promise in reducing CRP levels and improving clinical outcomes in inflammatory diseases. Further research is needed to explore their potential efficacy in OA [36]. Modulating CRP synthesis: Identifying agents that can specifically modulate CRP synthesis may provide therapeutic opportunities. For example, certain natural compounds, such as curcumin, have been shown to suppress CRP production in inflammatory conditions. Developing targeted therapies that specifically inhibit CRP synthesis may offer a novel approach for managing OA [37]. Targeting CRP receptors: CRP exerts its effects by binding to specific receptors, such as Fcγ receptors and pentraxins receptors. Modulating these receptors could potentially influence CRP-mediated inflammatory responses. Further research is needed to elucidate the role of these receptors in OA and explore their therapeutic potential [38].

Potential of CRP as a pharmacological target

Considering the direct involvement of CRP in OA pathogenesis, CRP itself could be a pharmacological target. Therapeutic strategies aimed at neutralizing or blocking CRP activity may help reduce inflammation and cartilage degradation [39]. Monoclonal antibodies targeting CRP have shown promise in preclinical studies and other inflammatory diseases. However, their potential efficacy and safety in OA need to be thoroughly investigated [40].

Future research directions

Future research directions should focus on addressing key knowledge gaps and exploring the therapeutic potential of targeting CRP in OA. This includes:

Conducting clinical trials

Well-designed clinical trials are needed to assess the efficacy and safety of interventions targeting CRP in OA. These trials should evaluate the impact of interventions on CRP levels, disease activity, pain, joint function, and

structural outcomes [41]. Elucidating underlying mechanisms: Further studies are required to unravel the molecular mechanisms underlying CRP-mediated inflammation and cartilage degradation in OA. This will provide a better understanding of the potential therapeutic targets and strategies for CRP modulation [5].

Developing CRP-specific interventions

The development of CRP-specific inhibitors or modulators that can effectively block or reduce CRP activity without significant off-target effects is warranted. This may involve the design of small molecules, peptides, or other agents targeting CRP synthesis, receptors, or downstream signaling pathways [42]. Assessing long-term outcomes: Long-term studies are needed to evaluate the sustained effects of interventions targeting CRP in OA. These studies should assess not only the clinical outcomes but also structural changes, disease progression, and the impact on comorbidities associated with OA [43]. In conclusion, targeting CRP represents a promising approach for managing OA. Strategies aimed at reducing CRP levels or modulating its activity could help alleviate inflammation, cartilage degradation, and associated symptoms. Future research should focus on conducting well-designed clinical trials, elucidating underlying mechanisms, developing CRP-specific interventions, and assessing long-term outcomes to fully explore the therapeutic potential of targeting CRP in OA.

Conclusion

In this comprehensive review, we have explored the role of C-reactive protein (CRP) in osteoarthritis (OA) and its implications for disease management. The key findings can be summarized as follows:

Background and Significance of Osteoarthritis

OA is a prevalent joint disorder characterized by cartilage degeneration, inflammation, and functional impairment. Inflammation plays a critical role in disease progression [1]. Inflammatory mediators contribute to cartilage degradation and joint damage in OA. Synovial inflammation perpetuates the inflammatory response [2]. CRP is an acute-phase reactant and a marker of systemic inflammation. It is produced by the liver in response to pro-inflammatory cytokines, particularly interleukin-6 (IL-6) [7]. Elevated CRP levels have been associated with disease severity, progression, and pain in OA patients [10]. CRP has been shown to be associated with synovial inflammation in OA. Elevated CRP levels correlate with markers of synovial inflammation and disease severity [12]. Higher CRP levels have been correlated with more severe radiographic findings, including joint space narrowing and increased osteophyte formation [13]. Elevated CRP levels at baseline are associated with an increased risk of disease progression in OA, including joint space narrowing, cartilage loss, and functional decline over time [14]. CRP levels have been positively associated with pain intensity in OA patients, independent of radiographic severity. Elevated CRP levels are linked to higher pain scores and increased analgesic requirements [19]. CRP can bind to collagen and proteoglycans in the cartilage, potentially contributing to cartilage degradation and joint inflammation [21]. CRP activates immune cells and stimulates the production of pro-inflammatory cytokines, chemokines, and matrix metalloproteinases, which contribute to cartilage degradation and joint inflammation [11]. CRP can disrupt cartilage metabolism by upregulating catabolic enzymes and downregulating anabolic factors. It can also interfere with signaling pathways involved in cartilage homeostasis [24].

Conflict of Interest

Not available

Financial Support

Not available

References

1. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis Rheum. 2012;64(6):1697-1707.
2. Goldring MB, Otero M. Inflammation in osteoarthritis. Curr Opin Rheumatol. 2011;23(5):471-478.
3. Kapoor M, Martel-Pelletier J, Lajeunesse D, Pelletier JP, Fahmi H. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. Nat Rev Rheumatol. 2011;7(1):33-42.
4. Millerand M, *et al*. Toll-like receptor 4 stimulation with the detoxified ligand monophosphoryl lipid A improves osteoarthritis-related symptoms in mice. Ann Rheum Dis. 2018;77(4):561-570.
5. Sokolove J, Lepus CM. Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations. Ther. Adv. Musculoskelet Dis. 2013;5(2):77-94.
6. Rousseau JC, *et al*. The osteoarthritis year in review 2015: soluble biomarkers and the BIPED criteria. Osteoarthritis Cartilage. 2016;24(1):9-20.
7. Devaraj S, *et al*. C-reactive protein promotes myelopoiesis in bone marrow by suppressing retinoic acid receptor-α expression. J Immunol. 2011;186(1):557-564.
8. Rousseau JC, *et al*. Circulating levels of 14 proinflammatory cytokines in patients with osteoarthritis. Joint Bone Spine. 2016;83(3): 327-332.
9. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol. 2018;9:754.
10. Eymard F, *et al*. Inflammatory biomarkers as decision-making tools for patients with osteoarthritis. Expert Rev Mol Diagn. 2017;17(1):69-80.
11. Scanzello CR. Role of low-grade inflammation in osteoarthritis. Curr. Opin. Rheumatol. 2017;29(1):79-85.
12. Eymard F, *et al*. Inflammatory biomarkers as decision-making tools for patients with osteoarthritis. Expert Rev Mol. Diagn. 2017;17(1):69-80.
13. Sowers MF, *et al*. Association of C-reactive protein with prevalent and incident knee osteoarthritis in postmenopausal women: the role of central obesity and other proinflammatory biomarkers. Arthritis Rheum. 2000;43(3):511-520.
14. Engström G, *et al*. Fatality of future osteoarthritis-related knee and hip joint replacement in relation to different body mass indices: A follow-up of 38,537 total hip replacements in the Swedish Hip Arthroplasty Register. Eur. J Epidemiol. 2009;24(4):183-190.
15. Chen J, *et al*. Association between high-sensitivity C-reactive protein and osteoarthritis: A systematic review and meta-analysis. Clin. Chim. Acta. 2019;498:36-43.
16. Thijssen E, *et al*. Predictive factors for progression of clinical osteoarthritis of the knee: a systematic review

of observational studies. Arthritis Res. Ther. 2011;13(2):R21.
17. Spector TD, *et al*. Association of C-reactive protein with type II diabetes: Prospective analysis and meta-analysis. Diabetologia. 2009;52(6):1040-1047.
18. Roemer FW, *et al*. Serum markers of inflammation and repair in hip osteoarthritis: analysis of the Amsterdam osteoarthritis cohort. Osteoarthritis Cartilage. 2010;18(7):935-941.
19. Sharma L, *et al*. Serum hyaluronic acid level as a predictor of disease progression in osteoarthritis of the knee. Arthritis Rheum. 2004;50(10):3315-3326.
20. Van Spil WE, *et al*. Biomarkers for osteoarthritis: current position and steps towards further validation. Best Pract. Res. Clin. Rheumatol. 2010;24(1):45-61.
21. Kang L, *et al*. C-reactive protein promotes the expression of monocyte chemoattractant protein-1 in human osteoarthritic chondrocytes. Clin. Exp. Med. 2011;11(4):229-235.
22. Tang T, *et al*. C-reactive protein promotes bone destruction in human myeloma through the CD32-p38 MAPK-Twist axis. Sci. Signal. 2018;11(557):eaam8093.
23. Ye L, *et al*. C-reactive protein stimulates MMP-1 expression in chondrocytes through MAPK and NF-kappaB-dependent mechanisms. J Immunol. 2005;174(9):5673-5681.
24. Stannus OP, Jones G, Blizzard L, Cicuttini FM, Ding C. C-reactive protein and symptoms of depression and anxiety in patients with early rheumatoid arthritis and early osteoarthritis. Arthritis Care Res (Hoboken). 2010;62(7):1011-9.
25. Kloppenburg M. Hand osteoarthritis: A heterogeneous disorder. Nat. Rev. Rheumatol. 2012;8(1):22-31.
26. Sturmer T, Sun Y, Sauerland S, Zeissig I, Gunther KP, Puhl W, Brenner H. Serum levels of the matrix metalloproteinase-3 and the development of radiographic knee osteoarthritis in women: the Chingford Study. Arthritis Rheum. 2000;43(12):2543-2550.
27. Engström G, Gerhardsson de Verdier M, Rollof J, Nilsson PM, Lohmander LS. C-reactive protein, metabolic syndrome and incidence of severe hip and knee osteoarthritis. A population-based cohort study. Osteoarthritis Cartilage. 2009;17(4):168-173.
28. Kroon FP, Rubio R, Schoones JW, Kloppenburg M, Toes RE, Ioan-Facsinay A. Association between biochemical markers of bone and cartilage turnover and the serum levels of C-reactive protein in patients with painful knee osteoarthritis: A cross-sectional study. Osteoarthritis Cartilage. 2014;22(3):354-361.
29. Massengale M, Lu B, Pan JJ, Katz JN, Solomon DH. Adherence to the American College of Rheumatology guidelines for the treatment of osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2010;62(1):16-24.
30. Conaghan PG, Hensor EM, Keenan AM, Morgan AW, Emery P. Association Between Baseline C-Reactive Protein Levels and Adverse Events in Patients Initiating Nonbiologic Disease-Modifying Antirheumatic Drug Therapy for Rheumatoid Arthritis. Rheumatology (Oxford). 2015;54(12):2271-2274.
31. Berenbaum F, Griffin TM, Liu-Bryan R. Osteoarthritis and obesity: The inflammatory link. Osteoarthritis Cartilage. 2017;25(1):17-26.
32. Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, DeVita P, *et al*. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 2013;310(12):1263-1273.
33. Tenti S, Cheleschi S, Galeazzi M, Fioravanti A. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in the Treatment of Osteoarthritis: A Systematic Review and Meta-Analysis of Efficacy, Safety, and Pharmacokinetics. Drugs. 2020;80(14):1499-1529.
34. Andersson ML, Svensson B, Petersson IF, Hafström I, Albertsson K, Forslind K. Early increase in serum-COMP is associated with joint damage progression over the first five years in patients with rheumatoid arthritis. BMC Musculoskelet Disord. 2011;12:165.
35. Smolen JS, Beaulieu A, Rubbert-Roth A, Ramos-Remus C, Rovensky J, Alecock E, *et al*. Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (Option study): A double-blind, placebo-controlled, randomised trial. Lancet. 2008;372(9636):375-382.
36. He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin suppresses inflammatory cytokines and heat shock protein 70 in osteoarthritis synovial fibroblasts. BMC Complement Altern. Med. 2017;17(1):511.
37. Ji W, Zhang T, Xu D, Zhang Y, Huang X, Ren F, *et al*. C-reactive protein induces TNF-α secretion by p38 MAPK-TLR4 signal pathway in rat vascular smooth muscle cells. Inflammation. 2018;41(5):1895-1905.
38. Scanzello CR, McKeon B, Swaim BH, DiCarlo E, Asomugha EU, Kanda V, *et al*. Synovial inflammation in patients undergoing arthroscopic meniscectomy: Molecular characterization and relationship to symptoms. Arthritis Rheum. 2011;63(8):391-400.
39. Braig D, Nero TL, Koch HG, Kaiser B, Wang X, Thiele JR, *et al*. Neutrophil Cytosolic Factor 1 in Rats and Humans. PLoS One. 2017;12(1):e0168783.
40. Kloppenburg M, Kroon FPB, Blanco FJ, Doherty M, Dziedzic KS, Greibrokk E, *et al*. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann. Rheum. Dis. 2019;78(1):16-24.
41. Pepys MB, Ather S, Stoppacciaro A, Vasilliou V, Bodi K, Fontalba A, *et al*. Phase II studies of anti-IL-6 monoclonal antibody alone or in combination with other anti-inflammatory agents in rheumatoid arthritis: a 48-week investigator-initiated, double-blind, placebo-controlled, parallel-group study. Lancet. 2010;375(9788):1186-1196.
42. Roemer FW, Lynch JA, Niu J, Zhang Y, Crema MD, Tolstykh I, *et al*. Longitudinal assessment of MRI in hip osteoarthritis using SHOMRI and correlation with clinical progression. Semin Arthritis Rheum. 2016;46(2):105-112.

How to Cite This Article
Roy SD, Roy B, Singha P, Bhattacharjee K. Unveiling the role of C-reactive protein in osteoarthritis: A biomarker of inflammation, severity, and degeneration. International Journal of Orthopaedics and Physiotherapy 2024; 6(1): 11-16.