



Research Article

Section: Pathology & Orthopaedics

Comparison of Erythrocyte Sedimentation Rate and C-Reactive Protein with Clinical and Radiographic Severity in Patients with Osteoarthritis

Dr. Deepti Gangwar^{*1}, Dr. Amitosh Mishra² & Dr. Siddharth Gangwar³

¹Associate Professor, Department of Pathology, Hind Institute of Medical Science, Mau, Ataria

²Associate Professor, Department of Orthopaedics, Integral Institute of Medical Sciences and Research, Lucknow

³Assistant Professor, Department of Pathology, Hind Institute of Medical Sciences, Safedabad, Barabanki

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*Corresponding author:

Dr. Deepti Gangwar

Associate Professor, Department of
Pathology, Hind Institute of Medical
Science, Mau, Ataria.

ABSTRACT

Introduction: This research examines the possible connection between C-reactive protein and erythrocyte sedimentation rate levels, their relationship to clinical observations and radiographic severity. The study utilizes the Kellgren Lawrence grading system and physical examination methods to assess the potential correlation among these factors. The aim of the study is to assess the association between C-reactive proteins and erythrocyte sedimentation rate with the clinical and radiographic severity/progression in patients with osteoarthritis. **Material & Methods:** The research was carried out in a tertiary care facility's Pathology and Orthopedics departments. A total of 300 patients with clinically diagnosed osteoarthritis were examined. The clinical evaluation took place in the outpatient department, considering the patient's history and physical examination, which included assessment of swelling, pain/tenderness using a visual analogue scale and range of motion. The patient's height, weight, and body mass index were documented. The radiographic examination involved anteroposterior standing and lateral views, categorized according to the Kellgren Lawrence classification. The Westergren method was employed to measure erythrocyte sedimentation rate, while C-reactive protein was evaluated using latex immunoassay. The study compared inflammatory markers with clinical and radiological grades. **Results :** The study population's age spanned from 40 to 80 years, with a mean of 50. Among the 300 participants, 142 (47.3%) were men and 158 (52.6%) were women. Approximately 75% of subjects reported pain levels between 3 and 6 on the visual analogue scale. The severity of symptoms correlated with increased swelling and reduced mobility. Patients with radiological grades III and IV exhibited a notable elevation in inflammatory markers. **Conclusion:** Patients clinically diagnosed with osteoarthritis exhibited elevated levels of erythrocyte sedimentation rate and C-reactive protein concentration. The increased presence of these inflammatory markers in such patients indicates that osteoarthritis progression and its severity correlate with a rise in inflammatory indicators.

INTRODUCTION

Radiographic examinations are typically employed to evaluate the advancement and intensity of osteoarthritis (OA). Nevertheless, these imaging techniques may prove inadequate for identifying OA in its nascent stages. Consequently, there exists a demand for alternative methods to assess arthritis during its initial phases and track the efficacy of treatments. Biochemical indicators detected in blood serum and/or urine samples could potentially fulfill this role. Furthermore, existing research indicates that localized inflammatory processes might contribute to the onset and

progression of OA. ESR and CRP are the two primary laboratory indicators used to assess systemic inflammatory diseases. RA, a severe inflammatory condition, typically presents with elevated ESR and CRP levels in affected patients [1]. Historically, OA, a common joint disorder, was not considered an inflammatory disease, and it was believed that inflammatory markers in the blood remained normal in OA patients. Nevertheless, recent research has suggested that individuals with OA may exhibit slight increases in both ESR and CRP values [2].

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are two prominent biosensors used to evaluate systemic inflammation. Elevated levels of these indicators often correspond to increased disease activity and unfavorable clinical outcomes in osteoarthritis [3]. Women are more commonly affected by OA due to a decrease in estrogen levels in the blood, leading to reduced bone density with advancing age. In premenopausal women, a significant correlation exists between osteoarthritis (OA) and both body mass index (BMI) and C-reactive protein (CRP) levels. Management may require focusing on weight control and regular CRP monitoring as part of standard medical practice [4]. Osteoarthritis is marked by symptoms including discomfort, short-lived stiffness in the morning, and challenges in carrying out everyday tasks, which adversely affect an individual's well-being. Following an osteoarthritis diagnosis, engaging in basic exercises that do not involve bearing weight could lead to enhanced patient care and an improved quality of life [5].

The ESR test is a basic, nonspecific measure of inflammation that assesses the rate at which red blood cells settle at the bottom of a test tube. Conversely, CRP is a more sensitive indicator for detecting low levels of systemic inflammation and is frequently used in chronic inflammatory disorders. These biomarkers may correlate with clinical manifestations and radiographic findings in osteoarthritis, facilitating the evaluation of early detection of disease. Compared to the erythrocyte sedimentation rate, C-reactive protein serves as a superior marker for inflammation. It exhibits greater sensitivity and demonstrates a quicker response to shifts in clinical conditions. Factors such as kidney disorders, being female, and advanced age tend to elevate the erythrocyte sedimentation rate. Despite this, the erythrocyte sedimentation rate remains useful for identifying mild bone infections and monitoring individuals with autoimmune disorders [6].

This investigation compared ESR and CRP with clinical symptoms and radiographic severity in patients with osteoarthritis to explore whether these markers can function as reliable indicators for assessing disease severity. Understanding these correlations may contribute to more targeted therapeutic approaches and enhance disease management in individuals with osteoarthritis.

MATERIAL AND METHODS

A cross-sectional investigation was carried out at a tertiary level medical facility, from October 2022 to March 2023 involving both the Orthopedics and Pathology departments. This hospital-based study in corporate 300 [7] patients with clinically diagnosed osteoarthritis from the Orthopaedics department. Approval for this study was granted by the Institutional Ethics Committee (IEC/IIM S&R/2022/09). The medical assessment encompassed an analysis of the patient's medical history and a physical examination, which evaluated pain, swelling using a visual

analogue scale, and mobility range. The patient's height, weight, and BMI were recorded. The radiographic evaluation consisted of standing anteroposterior and lateral views, classified according to the Kellgren-Lawrence system. For each participant, blood samples were collected to measure the erythrocyte sedimentation rate in an ESR tube and C-reactive protein in a plain vial.

In conventional blood analysis protocols, specialized tubes were utilized for ESR measurements, with the Westergren technique serving as the primary assessment method. ESR values surpassing 20 mm/h were categorized as elevated. For CRP evaluation, blood samples were obtained in plain vials and analyzed using immunoturbidimetric methods. CRP levels exceeding 5 mg/L were considered high. All blood specimens underwent examination within a two-hour time frame following collection. Regular analyzer calibrations and daily inspections were implemented as part of quality assurance protocols. In the outpatient clinic, patient evaluations encompassed a thorough review of medical histories, comprehensive physical examinations, and the collection of anthropometric data, including weight, height, and body mass index for each individual. Radiological assessments, consisting of standing anteroposterior and lateral views, were conducted and subsequently categorized using the Kellgren Lawrence classification system. Participants with a history of rheumatoid arthritis (RA) or other forms of inflammatory arthritis/autoimmune disorders (immunosuppressant drugs), acute or chronic infectious diseases, heart disease, chronic obstructive pulmonary disease, injury within the past two months, musculoskeletal surgery, hormone replacement therapy, oral hypoglycemic agents, oral insulin pregnancy, hormone replacement therapy, thrombosis, malignancy, and chronic renal insufficiency were excluded from the study

SPSS (version 16.0; SPSS Inc., Chicago, IL, USA) was used to conduct statistical analyses. The Shapiro-Wilk test was used to assess variable distributions. Results are expressed as mean \pm standard deviation. To compare continuous variables, the researchers planned to use the Student's t-test and Mann-Whitney's U test. Spearman's correlation test was applied to examine relationships between pairs of variables. Statistical significance was set at a p-value of <0.05 .

RESULTS

The age of the patient ranged from 40 to 80 years, with an average age of 50 years. Males were 142 and females were 158. Neuropathic pain and severity were assessed on the visual analogue scale from 01 to 10. Patients had pain from 03 to 06 grade, mild swelling was present in 225 patients, moderate in 50 patients, and others did not have any swelling. Three-fourths of the patients had difficulty in flexion and there was limitation in daily activity. Body mass index varied from 25 to 32 with an average of 29. According to Kellgren Lawrence, grade I had 110 patients, grade II had 99 patients,

grade III had 60 patients, and grade IV had 31 patients. CRP radiological severity of knee joint osteoarthritis, with and ESR levels consistently increased with clinical and increasing severity in clinical and radiological findings.

Table1: Distribution of patients according to demographic profile.

Demographic Profile of Patients			
Sex	Osteoarthritis patients (n)	Test Statistic (Chi-Square)	Pvalue
Male	142 (47.3%)	0.852	0.356
Female	158 (52.6%)		
Age(Years)			
50-59	41	39.26	<0.001
60-69	60		
70-79	113		
>80	86		
Kellegren-Lawrencegrade (Clinicalcharacteristics)			
1	110	34.56	<0.001
2(Mild)	99		
3(Moderate)	60		
4(Severe)	31		

Out of 300 patients, males were 142(47.3%), and 158 common grade in KELLGREN LAWRENCEGRADE was (52.6%) were females. The most commonly affected age gradeIwhichwas110(p=<0.001). group was between70-79 (p=<0.001) years. The most

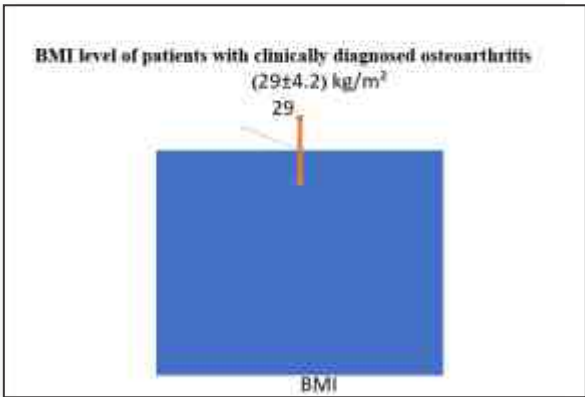


Figure 1: Body mass index (BMI) of the patients with osteoarthritis varied between 25 to 31with an average of (29±4.2) the range suggests that patients fall predominantly in the overweight category.

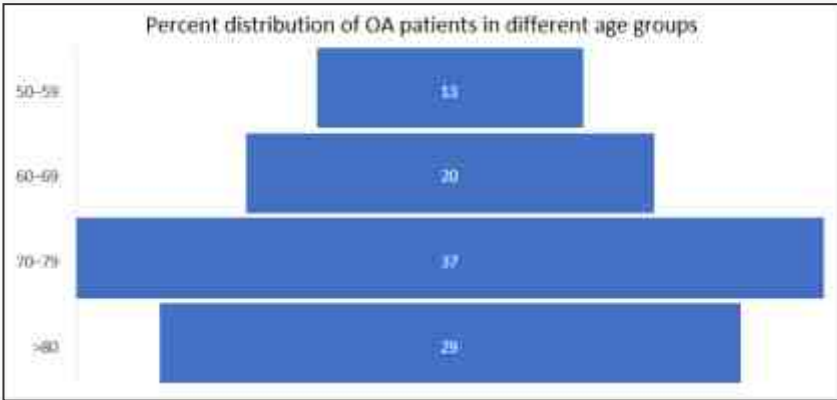


Figure 2: Percent distribution of patients reveals maximum number of patients were seen in the age group of 70-79 years (37%).

Table 2: Kellgren Lawrence Grades with ESR and CRP Levels in Patients with OA.

Radiological Grades	No. of Patients	Normal ESR (mm/h)	Median (interquartile range)	Normal CRP (mm/Dl)	CRP Median (interquartile range)
Grade-I	110	20 mm/h	20.02mm/h	<5mg/L	3.3
Grade-II	99	20 mm/h	21.12mm/h	<5mg/L	4.8
Grade-III	60	20 mm/h	21.82mm/h	<5mg/L	5.1
Grade-IV	31	20 mm/h	22.06mm/h	<5mg/L	5.3

The comparison of ESR and CRP concentrations at each Kellgren-Lawrence grade demonstrates that ESR levels were elevated in grade III and grade IV osteoarthritis, but only marginally increased in grade I. The CRP concentration in Grade I was slightly lower than in Grades II, III and IV as shown in table 2. Kellgren-Lawrence (KL) grading system assesses osteoarthritis severity: Grade 0 indicates no OA radiological features; Grade 1 shows possible osteophytic lipping and uncertain joint space narrowing; Grade 2 exhibits clear osteophytes and potential joint space narrowing; Grade 3 demonstrates multiple moderate osteophytes, definite joint .

space narrowing, some sclerosis, and possible bone end deformity; Grade 4 presents large osteophytes, significant joint space narrowing, severe sclerosis, and definite bone end deformity

The erythrocyte sedimentation rate (ESR) was significantly elevated in patients exhibiting tenderness and patellar ballottment. Analysis of the relationship between C-reactive protein (CRP) levels and clinical manifestations of pain and patellar ballottment revealed significant elevation of values. Correlation was observed between inflammatory markers and disease severity as shown in table 3.

Table 3: The Relationship of ESR and CRP with clinical features

Clinical Findings	Number Of Patients	Normal ESR (Mm/H)	Esr Median (Interquartile Range)	Normal Crp (Mm/Dl)	Crpmedian (Interquartile Range)
Tenderness	280	20mm/H	22.7mm/H	<5mg/L	5.8
Patellar Ballottment	160	20mm/H	23.0mm/H	<5mg/L	5.6
Swelling	275	20mm/H	21.9mm/H	<5mg/L	5.01
Flexioncontracture	107	20mm/H	20.8mm/H	<5mg/L	5.2
Decreased Flexion	216	20mm/H	20.6mm/H	<5mg/L	5.3

The study found a significant correlation between erythrocyte sedimentation rate (ESR) levels and C-reactive protein (CRP) with osteoarthritis's clinical and radiographic severity. It was observed that ESR and CRP concentrations were high in patients with clinically diagnosed osteoarthritis. The study suggests that the progression of osteoarthritis and its severity were synchronous with an increase in inflammatory markers. The CRP and ESR concentration in patients with swelling, tenderness and patellar ballottment was significantly high. The study found that average CRP levels increased homogeneously with increasing radiological grades according to the Kellgren Lawrence classification. The study found that osteoarthritis was more common in females, with 158 (56%) of the 300 patients being female. Pain was assessed using the visual analog scale (VAS), with patients reporting pain levels between 3 to 6.

These findings support the study's aim of determining the correlation between C-reactive proteins and erythrocyte sedimentation with clinical and radiographic severity/progression of osteoarthritis. They also high light the role of inflammation in osteoarthritis progression and suggest that CRP may be a more sensitive marker compared to ESR in the early stages of the disease.



Figure 3: Patient with clinically diagnosed osteoarthritis & varus deformity of bilateral knee and X-rays of bilateral knees anterior-posterior (standing) and lateral views showing moderate multiple osteophytes, definite narrowing of joint space, small pseudo cystic areas with sclerosis and possible deformity of bone contour (Kellgren -Lawrence grade 3)

DISCUSSION

The research results indicate that osteoarthritis is closely related to aging. Recent studies reveal elucidated inflammation and aging with OA. Age-related OA shows changes in tissues and articular cartilage. Multiple factors, such as low reactivity to growth factors, oxidative stress, mitochondrial dysfunction, and abnormal accumulation of advanced glycation end products, all play important roles in the etiopathogenesis of OA. Swadi et al [4] showed that obesity is a robust indicator of osteoarthritis, and BMI was found to increase in postmenopausal women older than 40 years. There was a change in the female hormone estrogen, which decreased with age. In our study also we saw that osteoarthritis was common in females, 158 (52.6%) average age of patients was 50 years. Research by Deepti et al [5] indicated that osteoarthritis manifestations, such as pain, short-lived morning stiffness, and compromised physical capabilities (fig.3) in routine activities, can exert broad influences on health, eventually affecting an individual's life quality. In their study revealed that Sananta P et al [8], Suyasa, I.K. et al [9] in a study revealed that the severity of osteoarthritis increased with advancing age. In the present study also OA was also common in the age group of 70-79 years, that is 37%. Women were more affected.

Jadhao AR [10] et al in their study showed a higher prevalence of OA in individuals above the age of 60 years. In the present study also elderly individuals were more commonly affected. Most patients were between the ages of 70-79 years.

Kherani et al [11] in their study on knee joint OA found a significant difference in CRP or ESR levels when classified according to KL grades, despite these markers being associated with pain and movements. Observations in their

study suggest that inflammatory markers like ESR and CRP play a role in the progression and severity of osteoarthritis. These findings highlight the potential significance of inflammatory markers like ESR and CRP in assessing and monitoring the progression of osteoarthritis. Understanding the relationship between these markers and disease severity could improve OA patient's diagnostic and treatment strategies, potentially enhancing clinical outcomes and quality of life. The relationship between these markers and radiographic findings, as measured by the Kellgren Lawrence (KL) grading system, appears to be complex and may vary across different patient populations. Further research is needed to elucidate the precise mechanisms linking inflammatory markers to OA severity and to determine their potential utility as diagnostic or prognostic tools in clinical practice.

Mckenzie et al [12] in their study revealed that clinical indicators strongly suggest an inflammatory process; CRP testing should be considered a primary diagnostic tool, as it effectively identifies most inflammatory conditions. Mckenzie et al in their study revealed that CRP testing should be considered a primary diagnostic tool, as it effectively identifies most inflammatory conditions. Lapić et al [13] and Pearle et al [14] in their study observed that C- reactive-protein (CRP) is associated with disease progression in patients with osteoarthritis(OA). They hypothesized that higher CRP levels would be related to local inflammatory findings in the joints of patients with OA. These findings suggest that systemic CRP levels reflect synovial inflammation in patients with OA by means of synovial IL-6 production. Future studies are needed to clarify how IL-6 infiltrates and its products contribute to disease pathogenesis. In the present study also CRP levels were also high in patients

with clinical features of pain/tenderness and patellar ballotment and KL grades III and IV.

Rafnsson et al [15] conducted a study in Göteborg, Sweden, focusing on women between 44 and 66 years old. The study revealed that women exhibiting signs of joint disease had higher average erythrocyte sedimentation rates (ESR) and a greater frequency of elevated ESR values (defined as ≥ 30 mm) than those without such conditions. These differences were statistically significant in women presenting with swollen or deformed finger joints and wrist symptoms. Women showing active joint disease symptoms during the examination displayed even higher ESR values, with statistically significant differences observed in those experiencing finger joint symptoms. Elevated ESR values were more prevalent among women who tested positive for rheumatoid factor and exhibited joint manifestations that were indicative of arthritis and osteoarthritis. The study concluded that while ESR values are moderately increased in individuals with various joint disease manifestations, the vast majority of these subjects still maintain ESR values below 30mm. In the present study, we also observed that ESR was raised in patients with osteoarthritis.

Sanchez-Ramirez et al [16] examined the elevation of CRP and ESR with reduced muscle strength and restricted joint movements in patients with OA and the link inflammatory markers (CRP and ESR) with muscle strength. In the present study, elevation of the inflammatory markers CRP and ESR was seen with tenderness and restricted movements, further supporting the connection of biomarkers ESR and CRP with clinical findings.

Sharif M et al [17] investigated the relationship between serum CRP levels and osteoarthritis. These researchers found that patients with OA exhibited elevated CRP levels suggesting inflammation in OA, which was traditionally considered a non-inflammatory disease. This finding indicates that CRP could serve as a biomarker for inflammation in OA patients.

Takashaki M et al [18] observed that patients with generalized osteoarthritis, identified through radiographs, exhibited significantly elevated levels of CRP. Zhenghai et al [19] in a study found a correlation between higher grades of OA and elevated inflammatory markers. In OA patients, serum levels of ESR and CRP were positively correlated. Taşoğlu et al [20] in their research found mean ESR was significantly higher in the severe OA group (KL grade 3- 4) compared to mild-moderate. In the present study also CRP and ESR biomarkers were markedly higher in KL grades III & IV, which was in line with previous studies.

CONCLUSION

Patients clinically diagnosed with osteoarthritis exhibited an elevated erythrocyte sedimentation rate and C-reactive protein concentration. An increased presence of these inflammatory markers in such patients indicates that osteoarthritis progression and its intensity correlate with an

increase in inflammatory indicators. This may lead to the development of new biomarkers for early detection and monitoring of osteoarthritis progression, potentially enabling more targeted and personalized treatment approaches. Furthermore, this shift in understanding could inspire innovative research into anti-inflammatory interventions specifically tailored for osteoarthritis management, opening up new avenues for drug development and therapeutic strategies.

LIMITATIONS

This study had several limitations that warrant consideration. The restricted scope of this research, involving a small participant pool and a single institution, may hinder the widespread application of our observations. To establish the validity of these findings and investigate the potential utility of CRP and ESR levels across diverse patient groups and medical conditions, it is crucial to conduct additional research encompassing larger cohorts and multiple research centers.

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Conflict of interest-

The authors declare that they have no conflict of interest regarding the publication of this article.

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