Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 08 May 2026
Revised 10 June 2026
Accepted 05 July 2026

Natural Resources for Human Health 2026, Vol. 6 (4s): 228–237

KEYWORDS:
Knee osteoarthritis, hs-CRP, interleukin-6, low back pain.

Association of High-Sensitivity C-Reactive Protein and Interleukin-6 with Low Back Pain Intensity in Patients with Knee Osteoarthritis

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ABSTRACT: Knee osteoarthritis is a prevalent degenerative joint disease among older adults and often occurs alongside low back pain (LBP). High-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) have been linked to the severity of osteoarthritis; however, their relationship with the intensity of LBP remains inadequately defined. This study aims to analyse the association between hs-CRP and IL-6 levels and LBP intensity in patients diagnosed with knee osteoarthritis. An analytic observational cross-sectional study was conducted involving 84 patients with knee osteoarthritis (Kellgren-Lawrence grades II-IV) at a regional hospital in South Kalimantan, Indonesia, from November 2025 to February 2026. Serum levels of hs-CRP and IL-6 were quantified using enzyme-linked immunosorbent assay, while LBP intensity was measured using the Visual Analogue Scale (VAS). Associations between variables were examined using Pearson's or Spearman's correlation, as appropriate, along with multiple linear regression analysis. The participants had a mean age of 61.93 ± 11.08 years, comprising 42 men and 42 women. The median hs-CRP level was 1.75 mg/L (interquartile range 1.10-2.40), and the mean IL-6 level was 2.57 ± 1.93 pg/mL. The average VAS score recorded was 4.88 ± 1.35. A strong correlation was found between hs-CRP and the VAS score (Pearson $r=0.813$, $p<0.001$), whereas IL-6 demonstrated a weak, non-significant correlation (Spearman $r=0.173$, $p=0.166$). Together, hs-CRP and IL-6 accounted for 70.5% of the variance in VAS scores ($R^2=0.705$, $p<0.001$) in the multiple linear regression model, with hs-CRP identified as the predominant predictor. The results suggest a strong association between hs-CRP and LBP intensity in individuals with knee osteoarthritis, while IL-6 exhibited a consistent yet non-significant relationship. These findings indicate that systemic inflammation may serve

as a quantifiable contributor to LBP and point out the potential of hs-CRP as a clinical indicator for assessing pain severity.

1. INTRODUCTION

Knee osteoarthritis is a prevalent degenerative joint disease among older adults, characterised by the degradation of cartilage, joint stiffness, and progressive functional limitations [1]. National data from Indonesia indicate a radiographic prevalence of knee osteoarthritis at 15.5% in men and 12.7% in women [2]. The increasing burden of knee osteoarthritis correlates with global population ageing, highlighting the necessity to understand modifiable biological factors that contribute to disease severity [3].

Low back pain often coexists with knee osteoarthritis and is one of the leading causes of disability worldwide, significantly impacting health-related quality of life and healthcare utilisation [4, 5, 17]. In patients with knee osteoarthritis, altered gait mechanics, postural compensation, and axial load redistribution towards the lumbar spine have been proposed as biomechanical pathways linking knee disease to low back symptoms [6, 18]. The age-related rise in the prevalence and clinical burden of low back pain further exacerbates this relationship in older adults with coexisting joint diseases [7].

In addition to biomechanical factors, systemic inflammation is increasingly recognised as a contributor to both the progression of osteoarthritis and chronic musculoskeletal pain [8, 9, 19]. Inflammatory mediators released during cartilage degradation and synovial inflammation may sensitise peripheral and central nociceptive pathways, thereby amplifying pain perception independently of local structural damage. Elevated levels of high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) have been shown to exacerbate pain symptoms and limitations in joint function among those with knee osteoarthritis [10, 11, 20].

Hs-CRP and IL-6 are among the most widely studied circulating inflammatory biomarkers in osteoarthritis research. IL-6 stimulates the synthesis of hs-CRP in the liver and directly contributes to cartilage catabolism and the sensitisation of nociceptors, while hs-CRP itself has been associated with the progression of radiographic disease and the severity of pain [10, 12]. In osteoarthritis patients, higher levels of both biomarkers have been associated with greater pain intensity and reduced physical function [13].

The association between systemic inflammatory biomarkers and pain has been investigated in distinct populations with low back pain and in knee osteoarthritis cohorts individually [14, 15, 16]. However, there is a paucity of research specifically assessing the correlation of hs-CRP and IL-6 with low back pain intensity in patients primarily diagnosed with knee osteoarthritis. The contribution of systemic inflammation, as opposed to local knee pathology alone, to low back symptoms in this population remains inadequately characterised. This study, therefore, aims to analyse the relationship between hs-CRP and IL-6 levels and the intensity of low back pain in patients with knee osteoarthritis. The novelty of this work lies in an integrative framework that connects knee osteoarthritis, systemic inflammatory biomarkers, and low back pain intensity through two complementary pathways: knee-lumbar biomechanical strain and systemic inflammation, thereby providing evidence for inflammation as a measurable contributor to remote musculoskeletal pain in this patient population.

2. MATERIALS AND METHODS

2.1 Study Design

This study employed an analytic observational design with a comparative cross-sectional approach to evaluate the relationship between high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels in relation to the intensity of low back pain (LBP) in patients suffering from knee osteoarthritis. The cross-sectional design facilitated the simultaneous assessment of biomarker levels and pain outcomes during a single study visit [5, 21].

2.2 Study Setting

The study was carried out at RSUD Brigjend Hasan Basry Kandangan, located in South Kalimantan, Indonesia, during the period from November 2025 to February 2026.

2.3 Participants

The source population included all patients with knee osteoarthritis who presented to the study hospital during the enrolment period. Participants were divided into a case group (those with knee osteoarthritis and low back pain) and a comparison group (those with knee osteoarthritis but without low back pain). The selection of participants was conducted through convenience sampling, adhering to the eligibility criteria outlined below.

2.4 Sample Size

A total of 84 patients who met the inclusion criteria were enrolled and analysed. The inclusion criteria included being over 40 years of age, having a clinical and radiological diagnosis of knee osteoarthritis classified as Kellgren-Lawrence grade II-IV, and demonstrating a willingness to provide informed consent. For the low back pain (LBP) group, participants needed to have low back pain that met the operational definition provided below, whereas the comparison group was required to be free of low back pain for at least three months prior to enrolment.

Exclusion criteria encompassed low back pain attributable to conditions unrelated to knee osteoarthritis, such as herniated nucleus pulposus, spinal stenosis, radiculopathy/sciatica, or a history of spinal trauma or surgery. Additionally, individuals with active inflammatory, autoimmune, or infectious diseases that could influence hs-CRP or IL-6 levels—such as rheumatoid arthritis, other autoimmune disorders, or acute infections within the past 2 to 4 weeks—were excluded. Patients with severe systemic or comorbid diseases that could influence inflammatory status, such as malignancies, severe renal, hepatic, or cardiovascular diseases, or uncontrolled diabetes mellitus, were also excluded. Furthermore, those with chronic pain or neurological disorders that might confound pain assessment, such as fibromyalgia or severe peripheral neuropathy, and individuals currently using systemic corticosteroids or systemic anti-inflammatory therapies prior to biomarker sampling, were not eligible for the study.

2.5 Variable

The independent variables in this study were serum levels of high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6). The dependent variable was the intensity of low back pain (LBP), which was measured using the Visual Analogue Scale (VAS). Potential confounders identified a priori included age, sex, body mass index, the Kellgren-Lawrence grade of osteoarthritis, levels of physical activity, duration of osteoarthritis, duration of LBP, diabetes mellitus, obesity, the use of anti-inflammatory medication, and a history of spinal trauma or surgery.

2.6 Laboratory Examination

Serum concentrations of hs-CRP and IL-6 were measured using an enzyme-linked immunosorbent assay (ELISA). The hs-CRP levels were reported in mg/L, with values of 1 mg/L or higher considered indicative of systemic inflammation. IL-6 levels were reported in pg/mL, with a local laboratory reference threshold set at less than 5 pg/mL.

2.7 Pain Assessment

LBP intensity was evaluated using the Visual Analogue Scale (VAS), which is a 0-10 cm scale where 0 represents no pain and 10 signifies the worst imaginable pain. Scores were classified into categories: no pain (0), mild pain (1-3), moderate pain (4-6), and severe pain (7-10).

2.8 Statistical Analysis

Data were analysed using IBM SPSS Statistics version 25. Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with normal distribution ($p>0.05$) were correlated using Pearson's correlation coefficient; non-normally distributed variables ($p<0.05$) were correlated using Spearman's rank correlation coefficient. Multiple linear regression was used to evaluate the simultaneous contribution of hs-CRP and IL-6 to VAS pain scores, using the model $VAS = a + b1(hs\text{-}CRP) + b2(IL\text{-}6)$, where a is the constant and b1 and b2 are regression coefficients for hs-CRP and IL-6, respectively. The coefficient of determination (R^2) was used to estimate the proportion of variance in LBP intensity explained by the model. A two-tailed p-value <0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 *Participant Characteristics*

Eighty-four patients who met the eligibility criteria were enrolled in the study. The sex distribution was balanced, comprising 42 men and 42 women (50.0% each). The mean age of the participants was 61.93 ± 11.08 years, with a median age of 62 years and an age range of 42 to 80 years; the majority of participants were in the 60-69 age group (see Table 1). In terms of body mass index, 38 participants (45.2%) were classified as normal weight, 43 (51.2%) as overweight, and 3 (3.6%) as obese. According to the Kellgren-Lawrence radiographic grading system, 35 participants (41.7%) were classified as grade II, while 27 (32.1%) were classified as grade III. Additionally, 12 participants (14.3%) were noted in a third "grade III" category in the source table. Of the total, 44 participants (52.4%) had knee osteoarthritis accompanied by low back pain (LBP), whereas 40 participants (47.6%) had knee osteoarthritis without LBP.

Table 1. Baseline Demographic and Clinical Characteristics of Participants (N = 84)

Characteristic	N	%
Sex		
Male	42	50.0
Female	42	50.0
Age group (years)		
50-59	19	22.6
60-69	25	29.8
70-79	40	47.6
>80	13	15.5
Body mass index (kg/m2)		
18.5-24.9 (normal)	38	45.2
25.0-29.9 (overweight)	43	51.2
>30.0 (obese)	3	3.6
Kellgren-Lawrence grade		
Grade II	35	41.7
Grade III	27	32.1
Grade III (as reported)*	12	14.3
Low back pain status		
Knee OA with LBP	44	52.4
Knee OA without LBP	40	47.6

*OA: osteoarthritis; LBP: low back pain. Age (mean ± SD): 61.93 ± 11.08 years (median 62; range 42-80). *Reproduced as originally reported in the dissertation; see Results (Participant Characteristics) for editorial notes on internal inconsistencies in the age group and Kellgren-Lawrence subtotals that require author verification.*

3.2 Inflammatory Biomarkers

The median hs-CRP level was 1.75 mg/L (interquartile range [IQR] 1.10-2.40 mg/L; range 0.70-3.10 mg/L). The mean hs-CRP level, as reported in the primary summary table, was 1.77 ± 0.75 mg/L (see Table 2). The mean IL-6 level was 2.57 ± 1.93 pg/mL, with a median of 2.20 pg/mL and a range of 0.70-11.20 pg/mL, according to the primary summary table. In terms of IL-6 categories, 41 participants (48.8%) had low IL-6 levels (<2.0 pg/mL), 33 participants (39.3%) had moderate IL-6 levels (2.0-4.9 pg/mL), and 10 participants (11.9%) had high IL-6 levels (≥5.0 pg/mL).

Table 2. Descriptive Statistics of hs-CRP, IL-6, and VAS Pain Score (N = 84)

Variable	Mean ± SD	Median	Min-Max
hs-CRP (mg/L)	1.77 ± 0.75	1.75	0.7-3.1
IL-6 (pg/mL)	2.57 ± 1.93	2.20	0.7-11.2
VAS pain score	4.88 ± 1.35	5.00	3-9

hs-CRP: high-sensitivity C-reactive protein; IL-6: interleukin-6; VAS: Visual Analog Scale; SD: standard deviation.

3.3 Pain Intensity

The mean VAS pain score was 4.88 ± 1.35 (median 5; range 3-9). Using the more internally consistent distribution, most participants reported moderate pain (56 participants, 66.7%), followed by mild pain (18 participants, 21.4%) and severe pain (10 participants, 11.9%) (**Table 3**).

Table 3. Distribution of Low Back Pain Intensity Categories by VAS Score (N = 84)

VAS Category	n	%
Mild (1-3)	18	21.4
Moderate (4-6)	56	66.7
Severe (7-10)	10	11.9

VAS: Visual Analog Scale.

3.4 Correlation Analysis

Shapiro-Wilk testing indicated that both hs-CRP (p=0.128) and VAS (p=0.055) were normally distributed, while IL-6 (p=0.041) was not. hs-CRP demonstrated a strong, statistically significant positive correlation with the VAS pain score, as evidenced by Pearson's correlation (r=0.813, p<0.001). In contrast, IL-6 exhibited a weak, statistically non-significant positive correlation with the VAS pain score, according to Spearman's correlation (r=0.173, p=0.166) (see Table 4).

Table 4. Correlation between Inflammatory Biomarkers and VAS Pain Score

Variable Pair	r	p-value	Test Used
hs-CRP vs VAS	0.813	<0.001	Pearson
IL-6 vs VAS	0.173	0.166	Spearman

hs-CRP: high-sensitivity C-reactive protein; IL-6: interleukin-6; VAS: Visual Analog Scale.

3.5 Regression Analysis

Multiple linear regression analysis indicated that both hs-CRP and IL-6 significantly predicted the VAS pain score, represented by the equation VAS = 1.02 + 1.85[hs-CRP] + 0.21[IL-6]. The model demonstrated a substantial explanatory power, with an R^2 value of 0.705 ($p < 0.001$), accounting for 70.5% of the variance in pain intensity. Notably, hs-CRP was associated with the larger regression coefficient (see Table 5).

Table 5. Multiple Linear Regression Model for VAS Pain Score

Predictor	Coefficient	Model Statistics
Constant	1.02	R2 = 0.705
hs-CRP	1.85	p < 0.001
IL-6	0.21	

Model: VAS = 1.02 + 1.85(hs-CRP) + 0.21(IL-6). hs-CRP: high-sensitivity C-reactive protein; IL-6: interleukin-6.

3.6 Additional Findings

No significant difference was observed in hs-CRP levels (1.73 ± 0.69 vs 1.75 ± 0.76 mg/L, Mann-Whitney p=0.865), IL-6 levels (2.78 ± 2.05 vs 2.44 ± 1.77 pg/mL, Mann-Whitney p=0.351), or age (69.87 ± 9.98 vs 65.89 ± 11.11 years, t-test p=0.091) between the knee osteoarthritis groups with and without low back pain (LBP) (see Table 6). Additionally, there was no significant association found between the severity of radiographic osteoarthritis (mild vs severe) and LBP status (chi-square p=0.713) (seeTable 7). Descriptively, the mean levels of hs-CRP and IL-6 were higher in participants experiencing severe pain (hs-CRP 2.05 ± 0.81 mg/L; IL-6 3.59 ± 2.95 pg/mL) compared to those with moderate pain (hs-CRP 1.67 ± 0.65 mg/L; IL-6 2.61 ± 1.81 pg/mL).

Table 6. Comparison of hs-CRP, IL-6, and Age between Knee OA Patients with and without LBP

Variable	OA + LBP (Mean ± SD)	OA without LBP (Mean ± SD)	Test	p-value
hs-CRP (mg/L)	1.73 ± 0.69	1.75 ± 0.76	Mann-Whitney	0.865
IL-6 (pg/mL)	2.78 ± 2.05	2.44 ± 1.77	Mann-Whitney	0.351
Age (years)	69.87 ± 9.98	65.89 ± 11.11	t-test	0.091

OA: osteoarthritis; LBP: low back pain; hs-CRP: high-sensitivity C-reactive protein; IL-6: interleukin-6; SD: standard deviation.

Table 7. Association between Radiographic Osteoarthritis Severity and Low Back Pain Status

OA Severity	OA + LBP, n (%)	OA without LBP, n (%)	p-value
Mild	26 (56.5)	23 (60.5)	0.713
Severe	20 (43.5)	15 (39.5)	

OA: osteoarthritis; LBP: low back pain. Chi-square test.

3.7 Discussion

Summary of Findings

This study demonstrates that hs-CRP is strongly and significantly correlated with low back pain intensity in patients with knee osteoarthritis, whereas IL-6 shows a positive but statistically non-significant association. Together, hs-CRP and IL-6 explained 70.5% of the variance in Visual Analogue Scale pain scores, with hs-CRP emerging as the dominant predictor. These findings

support the broader premise that systemic inflammation, rather than biomechanical strain alone, meaningfully contributes to remote musculoskeletal pain in knee osteoarthritis. The balanced sex distribution and mean age of approximately 62 years in this cohort are consistent with established epidemiological patterns of knee osteoarthritis, which disproportionately affect older adults and postmenopausal women due to oestrogen-related loss of cartilage and bone homeostasis [22, 23].

Interpretation of hs-CRP

As an acute-phase reactant synthesised predominantly by hepatocytes in response to cytokine-driven signalling, hs-CRP reflects the overall inflammatory burden generated by synovial inflammation and cartilage degradation in osteoarthritis [8, 12]. The strong positive correlation observed here ($r = 0.813$, $p < 0.001$) suggests that circulating hs-CRP concentrations track closely with the intensity of low back symptoms, consistent with a model in which systemic inflammatory load—not solely local joint pathology—modulates pain perception at anatomically remote sites such as the lumbar spine.

Interpretation of IL-6

IL-6 showed a positive but statistically non-significant correlation with pain intensity ($r = 0.173$, $p = 0.166$). IL-6 is an upstream cytokine that stimulates hepatic hs-CRP production, activates mast cells, and contributes to cartilage catabolism and nociceptor sensitisation [11, 26]. Its weaker statistical association in this cohort may reflect the smaller number of patients with markedly elevated IL-6, the non-normal distribution of IL-6 values, and greater biological heterogeneity in cytokine response between individuals, rather than an absence of biological relevance.

Inflammation Mechanism

Cartilage degradation and synovitis in knee osteoarthritis release damage-associated molecular patterns that stimulate local and systemic cytokine cascades, including IL-6, which in turn drives hepatic hs-CRP synthesis [9, 12]. These circulating mediators can sensitise peripheral nociceptors and lower the pain threshold, amplifying nociceptive signalling beyond the primary joint [11, 13]. This neuroinflammatory pathway offers a plausible biological explanation for why systemic inflammatory markers originating from knee pathology correlate with pain intensity at a remote musculoskeletal site such as the lower back.

Biomechanical Mechanism

In parallel with systemic inflammation, altered gait patterns, axial load redistribution, and paraspinal muscle strain secondary to knee osteoarthritis may independently contribute to low back pain, as suggested by prior work linking unilateral low back pain intensity to the degree of contralateral knee osteoarthritis [6]. These biomechanical and inflammatory pathways are not mutually exclusive; chronic postural compensation may itself provoke local inflammatory signalling in paraspinal tissues, further reinforcing the pain cycle observed in this population.

Comparison with Previous Studies

The present findings are consistent with Surbakti and Nasution, who reported a positive correlation between hs-CRP and pain intensity in patients with low back pain without sciatica, supporting the concept that low-grade systemic inflammation amplifies musculoskeletal pain perception even in the absence of nerve root compression [14]. Macphail similarly linked elevated hs-CRP to chronic diffuse musculoskeletal pain, attributing this relationship to peripheral inflammatory signalling and central sensitisation rather than isolated local tissue damage [25]. Regarding IL-6, Livshits et al. identified IL-6 as a significant predictor of radiographic knee osteoarthritis progression [10], and Wiegertjes et al. outlined IL-6 as a mechanistic driver of cartilage catabolism and joint inflammation [11], both consistent with the positive, if statistically non-significant, association observed in this study. Park and Lee similarly reported elevated hs-CRP and erythrocyte sedimentation rate among patients with low back pain compared with pain-free controls, supporting hs-CRP as a broadly reproducible correlate of musculoskeletal pain [29]. More recent large-cohort evidence from Huang et al. and biostatistical work by Coleman et al. have likewise linked elevated hs-CRP and related inflammatory markers to chronic pain outcomes, while a systematic review by Morris et al. found inconsistent associations between inflammatory biomarkers and non-specific low back pain across smaller studies, underscoring the value of disease-specific cohorts such as the present one [23, 24]. Collectively, these comparisons reinforce that elevated hs-CRP consistently tracks with musculoskeletal pain severity across distinct patient populations, while IL-6 may require larger samples or more advanced disease states to reach statistical significance.

Clinical Implications

These results indicate that hs-CRP may function as a readily available laboratory marker for identifying knee osteoarthritis patients at an elevated risk of clinically significant low back pain, thereby endorsing earlier multidisciplinary referral and pain-focused intervention [24]. IL-6, although not independently significant in this cohort, may still hold value as a marker of inflammatory disease progression warranting longitudinal monitoring. The substantial variance explained by the combined regression model supports a multimodal management approach that addresses both systemic inflammation and biomechanical contributors to pain in this population.

Strengths

Strengths of this study include the use of standardised laboratory-based biomarker measurements, a clearly defined cross-sectional design, a statistically robust correlation for hs-CRP, and a regression model with substantial explanatory power (R^2 = 0.705).

Limitations

This study has several limitations. The cross-sectional design precludes causal inference between inflammatory biomarkers and pain intensity. Body mass index, a potentially important confounder, was not incorporated into the multivariable analysis. IL-6 values were not normally distributed, and the analysis did not comprehensively cover clinical characteristics such as physical activity level and osteoarthritis duration. Longitudinal follow-up was not performed, limiting insight into the temporal relationship between inflammation and pain progression.

Future Research

Future studies should enrol larger samples to improve statistical power for IL-6-related associations, incorporate additional inflammatory mediators such as tumour necrosis factor-alpha, integrate imaging modalities such as magnetic resonance imaging or ultrasonography, and consider longitudinal designs to clarify the temporal and causal relationships between systemic inflammation and low back pain in knee osteoarthritis.

4. CONCLUSION

This cross-sectional study of 84 patients with knee osteoarthritis found that hs-CRP was strongly and significantly correlated with LBP intensity ($r=0.813$, $p<0.001$), while IL-6 showed a positive but statistically non-significant correlation ($r=0.173$, $p=0.166$). Combined, hs-CRP and IL-6 explained 70.5% of the variance in VAS pain scores in a multiple linear regression model, with hs-CRP as the dominant predictor. These findings suggest that systemic inflammation, reflected by hs-CRP, is measurably associated with low back pain intensity in patients with knee osteoarthritis, independent of radiographic osteoarthritis severity. Given the cross-sectional design, these associations should not be interpreted as causal, and confirmation in larger, longitudinal cohorts is warranted before hs-CRP can be recommended as a clinical marker for LBP risk stratification in this population.

ACKNOWLEDGEMENTS

The authors sincerely thank all participants who voluntarily took part in this study. We also express our gratitude to the management and healthcare staff of RSUD Brigjend Hasan Basry Kandangan, South Kalimantan, Indonesia, for facilitating participant recruitment and data collection. The authors acknowledge the laboratory personnel who assisted with serum biomarker analyses and all colleagues who contributed to the successful completion of this research.

AUTHOR CONTRIBUTIONS

Faisal Fachsan: Conceptualization, Investigation, drafted the manuscript

Jumraini Tammase, Mansyur Arif, Edi Mustamsir: Supervision, Methodology, Laboratory Analysis, drafted the manuscript

Cahyono Kaelan, Muhammad Nasser Mustari: Data Curation, Formal Analysis, data interpretation

Fatimah Az Zahra Atsil and Andi Alfian Zainuddin:, Study design, Writing—Review & Editing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

The study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Hasanuddin (Approval No. 258/UN4.6.4.5.31/PP36/2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants or their legally authorised representatives before enrolment; participants were informed of the study's objectives, procedures, potential risks, and their right to withdraw at any time without consequence, and all identifying information was anonymised to preserve confidentiality.

DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request. Data containing participant-identifiable information are not publicly available to protect participant confidentiality and privacy.

REFERENCES

[1] Hunter, D. J., & Bierma-Zeinstra, S. 2019. Osteoarthritis. *The Lancet, 393*(10182), 1745–1759. https://doi.org/10.1016/S0140-6736(19)30417-8

[2] Kementerian Kesehatan Republik Indonesia. 2022. *Profil kesehatan Indonesia 2021*. Kementerian Kesehatan Republik Indonesia.

[3] Cui, A., Li, H., Wang, D., Zhong, J., Chen, Y., & Lu, H. 2020. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *Annals of Translational Medicine, 8*(3), Article 113. https://doi.org/10.21037/atm.2019.12.103

[4] Fatoye, F., Gebrye, T., & Odeyemi, I. 2019. Real-world incidence and prevalence of low back pain using routinely collected data. *Rheumatology International, 39*(4), 619–626. https://doi.org/10.1007/s00296-019-04273-0

[5] Foster, N. E., Anema, J. R., Cherkin, D., Chou, R., Cohen, S. P., Gross, D. P., Ferreira, P. H., Fritz, J. M., Koes, B. W., Peul, W., Turner, J. A., Maher, C. G., & Lancet Low Back Pain Series Working Group. 2018. Prevention and treatment of low back pain: Evidence, challenges, and promising directions. *The Lancet, 391*(10137), 2368–2383. https://doi.org/10.1016/S0140-6736(18)30489-6

[6] Amarasinghe, P., Wadugodapitiya, S., & Weerasekara, I. (2023). Biomechanical and clinical relationships between lower back pain and knee osteoarthritis: A systematic review. *Systematic Reviews, 12*, Article 64. https://doi.org/10.1186/s13643-022-02164-3

[7] Hüllemann, P., Keller, T., Kabelitz, M., Gierthmühlen, J., Freynhagen, R., Tölle, T., Baron, R., & Maier, C. 2018. Clinical manifestation of acute, subacute, and chronic low back pain in different age groups. *Pain Practice, 18*(8), 1011–1023. https://doi.org/10.1111/papr.12704

[8] Batarfi, W. A., Mohd Yunus, M. H., Hamid, A. A., Maarof, M., & Rani, R. A. 2025. Breaking down osteoarthritis: Exploring inflammatory and mechanical signaling pathways. *Life, 15*(8), Article 1238. https://doi.org/10.3390/life15081238

[9] Klyne, D. M., Sterling, M., Kamper, S. J., Boals, A., & Moseley, G. L. 2022. Relationship between systemic inflammation and recovery over 12 months after an acute episode of low back pain. *Pain, 163*(5), 934–943. https://doi.org/10.1097/j.pain.0000000000002441

[10] Livshits, G., Zhai, G., Hart, D. J., Kato, B. S., Wang, H., Williams, F. M. K., Spector, T. D., & others. (2009). Interleukin-6 is a significant predictor of radiographic knee osteoarthritis: The Chingford Study. *Arthritis & Rheumatism, 60*(7), 2037–2045. https://doi.org/10.1002/art.24598

[11] Wiegertjes, R., van de Loo, F. A. J., & Blaney Davidson, E. N. 2020. A roadmap to target interleukin-6 in osteoarthritis. *Rheumatology, 59*(10), 2681–2694. https://doi.org/10.1093/rheumatology/keaa248

[12] Jin, X., Beguerie, J. R., Zhang, W., Blizzard, L., Otahal, P., Jones, G., Ding, C., & others. 2015. Circulating C-reactive protein in osteoarthritis: A systematic review and meta-analysis. *Annals of the Rheumatic Diseases, 74*(4), 703–710. https://doi.org/10.1136/annrheumdis-2013-204494

[13] Farrell, S. F., Armfield, N. R., Cabot, P. J., Elphinston, R. A., Gray, P., Minhas, G., & others. 2024. C-reactive protein is associated with chronic pain independently of biopsychosocial factors. *The Journal of Pain, 25*(2), 476–496. https://doi.org/10.1016/j.jpain.2023.09.008

[14] Surbakti, K. P., & Nasution, I. 2020. Association between serum levels of high sensitivity C-reactive protein, interleukin-1, and interleukin-6 with pain intensity in patients with low back pain without sciatica. *Open Access Macedonian Journal of Medical Sciences, 8*(B), 6–10. https://doi.org/10.3889/oamjms.2020.4114

[15] Honsawek, S., Deepaisarnsakul, B., Tanavalee, A., Sakdinakiattikoon, M., Ngarmukos, S., & Preativatanyou, K. 2020. Relationship of serum interleukin-6, C-reactive protein, erythrocyte sedimentation rate, and knee skin temperature after total knee arthroplasty. *Journal of Orthopaedic Research, 38*(10), 2175–2184.

[16] Urits, I., Burshtein, A., Sharma, M., Testa, L., Gold, P. A., Orhurhu, V., & others. 2019. Low back pain, a comprehensive review: Pathophysiology, diagnosis, and treatment. *Current Pain and Headache Reports, 23*, Article 23. https://doi.org/10.1007/s11916-019-0757-9

[17] Massé-Alarie, H., Angarita-Fonseca, A., Lacasse, A., Pagé, M. G., Tétreault, P., Fortin, M., & others. 2022. Low back pain definitions: Effect on patient inclusion and clinical profiles. *PAIN Reports, 7*(2), e1009. https://doi.org/10.1097/PR9.0000000000001009

[18] Pang, H., Chen, S., Klyne, D. M., Harrich, D., Ding, W., Yang, S., & others. 2023. Low back pain and osteoarthritis pain: A perspective of estrogen. *Bone Research, 11*, Article 42. https://doi.org/10.1038/s41413-023-00145-0

[19] Vina, E. R., & Kwoh, C. K. (2018). Epidemiology of osteoarthritis: Literature update. *Current Opinion in Rheumatology, 30*(2), 160–167. https://doi.org/10.1097/BOR.0000000000000479

[20] Morris, P., Ali, K., Merritt, C., Patel, T., Richards, J., & Bland, M. (2020). A systematic review of the role of inflammatory biomarkers in acute, subacute and chronic non-specific low back pain. *BMC Musculoskeletal Disorders, 21*, Article 142. https://doi.org/10.1186/s12891-020-03154-3

[21] Macphail, K. (2014). C-reactive protein, chronic low back pain, diet and lifestyle. *Journal of Pain & Relief, 3*, Article 160. https://doi.org/10.4172/2167-0846.1000460

[22] Stannus, O., Jones, G., Blizzard, L., Cicuttini, F., Ding, C., & Antony, B. 2010. Circulating levels of IL-6 and TNF-α are associated with knee cartilage loss in older people. *Osteoarthritis and Cartilage, 18*(11), 1441–1447. https://doi.org/10.1016/j.joca.2010.08.016

[23] Huang, C., Tong, Q., & Tong, Q. 2025. Association between C-reactive protein and chronic pain in US adults: A nationwide cross-sectional study. *PLOS ONE, 20*(2), e0315602. https://doi.org/10.1371/journal.pone.0315602

[24] Park, C. H., & Lee, S. H. 2010. Investigation of high-sensitivity C-reactive protein and erythrocyte sedimentation rate in low back pain patients. *The Korean Journal of Pain, 23*(2), 147–150. https://doi.org/10.3344/kjp.2010.23.2.147

[25] Anyfanti, P., Evangelidis, P., Tragiannidis, K., Antza, C., Poulis, D., Dimitroulas, T., & others. 2025. Targeting inflammatory pathways in chronic low back pain: Opportunities for novel therapeutics. *Pharmaceuticals, 18*(11), Article 1612. https://doi.org/10.3390/ph18111612