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CLINICAL FACTORS ASSOCIATED WITH PAIN INTENSITY AND ADJUVANT ANALGESIC USE IN OSTEOARTHRITIS PATIENTS

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ABSTRACT

Osteoarthritis (OA) is a degenerative joint disease that commonly causes chronic pain and functional limitations. In routine practice, adjuvant analgesics are frequently used as part of multimodal pain management; however, clinical factors associated with pain intensity and adjuvant analgesic use are not well characterized. This retrospective observational study aimed to identify clinical factors associated with final pain intensity and their relationship with adjuvant analgesic use in patients with OA. Medical records of OA patients treated at Sultan Agung Islamic Hospital, Indonesia, between 2020 and 2025 were reviewed. Data included patient characteristics, OA severity based on the Kellgren–Lawrence (KL) grading system, pain intensity assessed using the Visual Analog Scale (VAS), and types of adjuvant analgesics prescribed, Multivariate logistic regression analysis showed that severe OA (KL grade ≥3) was the strongest factor associated with higher final pain intensity (OR = 3.56; 95% CI: 2.9–4.3). Knee OA (OR = 1.70; 95% CI: 1.1–2.4) and hyperlipidemia (OR = 2.33; 95% CI: 1.3–4.1) were also independently associated with higher final pain intensity. The use of adjuvant analgesics, particularly joint supplements and neuropathic pain agents, was associated with higher final pain intensity, reflecting greater disease severity and clinical complexity rather than direct analgesic effectiveness. Muscle relaxants were not significantly associated with pain intensity. In conclusion, final pain intensity in OA is primarily associated with disease severity and clinical complexity, and causal relationships cannot be established due to the observational design.

Keywords: Adjuvant Analgesics, Kellgren–Lawrence, Osteoarthritis, Pain Intensity, Clinical Determinants

INTRODUCTION

Osteoarthritis (OA) is the most common musculoskeletal disorder worldwide and a leading cause of chronic pain and joint function limitations, particularly among older adults. In 2020, the global prevalence of OA was estimated at approximately 595 million individuals, contributing substantially to clinical burden and healthcare costs. The prevalence of OA is reported to be higher in women (7.9%) than in men (6.5%), influenced by

biological, metabolic, and behavioral factors that may affect disease progression (Collaborators, 2018; Steinmetz, 2023).

Clinically, structural changes in the joints include osteophyte formation, joint space narrowing, subchondral bone sclerosis, and joint deformities, which are associated with pain development and progressive functional decline. These conditions limit mobility and daily activities and are linked to reduced quality of life and increased healthcare utilization (He et al., 2020; Hunter & Bierma-Zeinstra, 2019). Given the complexity of these clinical manifestations, current OA management guidelines recommend a multimodal approach combining non-pharmacological and pharmacological interventions. In routine clinical practice, pharmacological therapy generally begins with paracetamol as first-line treatment, followed by non-steroidal anti-inflammatory drugs (NSAIDs) when pain is not adequately controlled; however, a substantial proportion of patients continue to experience persistent pain, leading to the frequent use of adjuvant therapies within a multimodal management strategy. Despite their widespread use, real-world evidence describing how sociodemographic and clinical characteristics relate to pain intensity and patterns of adjuvant therapy use remains limited (Bannuru et al., 2019; Bruyere et al., 2019).

The limitations of conventional analgesics have led to an increase in the use of adjuvant therapies, such as joint support supplements, agents that target neuropathic pain agents, and muscle relaxants as part of multimodal pain management. Several studies have demonstrated the benefits of adjuvant therapy in OA. Research in China has reported the effectiveness of oral hyaluronic acid in reducing pain and improving quality of life (Wang et al., 2021). Studies in Russia and Mexico have also reported that glucosamine, chondroitin, and vitamin B complex contribute to pain reduction and functional improvement (Delgado-García et al., 2024; Lila et al., 2023). Neuropathic pain agents such as mecobalamin, gabapentin, and pregabalin have also been reported to significantly reduce pain intensity (Han et al., 2018). However, most recommendations regarding the use of adjuvant therapy are still general and do not explicitly consider the specific clinical characteristics of patients.

Although adjuvant therapy is widely used in clinical practice, real-world evidence identifying clinical factors associated with pain intensity and guiding the rational use of adjuvant therapy remains

limited. Most existing evidence is derived from clinical trials or guideline-based recommendations, which may not fully reflect routine practice and patient heterogeneity. As a result, clinical decision-making is often based on empirical considerations rather than on data that account for individual sociodemographic and clinical characteristics. Therefore, this study aims to describe sociodemographic and clinical factors associated with pain intensity in patients with OA and to explore their relationship with the use of adjuvant therapy as part of a multimodal pain management approach in a real-world clinical setting.

METHODS

1. Study Design and Setting

This study was a retrospective observational study conducted at Sultan Agung Islamic Hospital, Semarang. Medical record data of patients diagnosed with OA between January 2020 and December 2025 were reviewed. Data collection was carried out from August to October 2025.

2. Study Population and Sample

The study population consisted of all patients diagnosed with OA recorded in the hospital medical records during the study period. A total sampling technique was applied. Inclusion criteria were patients aged ≥25 years who were diagnosed with OA based on the International Classification of Diseases, 10th Revision (ICD-10) codes M15–M19 and had complete medical records. Exclusion criteria included patients diagnosed with rheumatoid arthritis, osteoporosis, or those with a history of severe systemic diseases such as cancer, heart failure, or acute renal failure. A total of 1,124 patients met the inclusion and exclusion criteria and were included in the analysis.

3. Study Variables

The dependent variable in this study was pain intensity, measured using the VAS. Pain intensity was analyzed as two separate outcomes: initial pain intensity (initial VAS) and final pain intensity (final VAS).

The independent variables included age, sex, body mass index (BMI), education level, type of osteoarthritis (knee, hand, or hip), comorbidities, degree of disease severity based on KL grading system, and use of adjuvant therapy.

4. Definition and Timing of Pain Assessment

Initial VAS was defined as the pain intensity score recorded at the first clinical visit when osteoarthritis was diagnosed or when pharmacological treatment was

initiated. Final VAS was defined as the most recent pain intensity score documented during routine follow-up after pharmacological and/or adjuvant therapy. Due to the retrospective nature of the study, the time interval between initial and final VAS assessments varied among patients. Therefore, initial and final VAS were analyzed separately, and changes in pain intensity were interpreted as associations rather than treatment effects.

5. Definition of Adjuvant

Adjuvant therapy was defined as additional pharmacological agents prescribed alongside primary analgesics as part of a multimodal pain management approach. Adjuvant therapies included joint support supplements (glucosamine), neuropathic or nerve pain agents (mecobalamin, vitamin B1, vitamin B12, vitamin B complex, gabapentin, pregabalin, and amitriptyline), and muscle relaxants (eperisone). Information on dosage, duration of therapy, and specific combinations of adjuvant agents was not consistently available in the medical records and therefore was not included in the analysis.

6. Data Processing

All data were initially entered into Microsoft Excel for data management. The dataset was then imported into Google Colab and processed using the Python programming language. Data processing included checking data completeness and consistency, coding categorical variables into numerical form, and cleaning the dataset by removing duplicate entries, missing data, and implausible extreme values.

7. Data Analysis

Data analysis was conducted using univariate, bivariate, and multivariate approaches. Univariate analysis described patient characteristics, independent variables including the use of adjuvant therapy, as well as pain intensity categories (initial and final VAS) using frequencies and percentages.

Bivariate analysis assessed associations between independent variables (age, sex, BMI, education level, type of OA, comorbidities, KL grade, and use of adjuvant therapy) and both initial and final pain intensity categories using the Chi-square test. A p-value of <0.05 was considered statistically significant.

Multivariate logistic regression analysis was performed to identify factors independently associated with higher final pain intensity. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Given the retrospective observational design, all findings were

interpreted as non-causal associations. For multivariate logistic regression analysis, the dependent variable was higher final pain intensity, based on the final VAS assessment. Independent variables were categorized prior to analysis. Reference categories were defined as follows: age <60 years, female sex, non-obesity, hand or hip osteoarthritis, absence of comorbidities, non-severe OA (KL grade <3), and no use of adjuvant therapy. (Devi et al., 2024; Patil & Patil, 2024).

8. Ethical Aspects

This study has been approved by the Ethics Committee of Sultan Agung Islamic Hospital Semarang with Ethics Number 188/KEPK-RSISA/VIII/2025 and Research Permit Number 4098/B/RSI-SA/VIII/2025. The study uses anonymized secondary data, so there is no direct risk to the research subjects.

RESULTS AND DISCUSSION

Table 1. Baseline clinical characteristics of osteoarthritis patients (n = 1,124)

Characteristics		n (%)
Age (years)	25-44	87 (7.7)
	45-59	366 (32.6)
	≥ 60	671 (59.7)
Sex	Female	667 (59.3)
	Male	457 (40.7)
BMI	Underweight	7 (0.6)
	Normal	871 (77.5)
	Overweight	144 (12.8)
	Obesity	102 (9.1)
Education Level	Junior High School	165 (14.7)
	Senior High School	615 (54.7)
	Diploma	186 (16.5)
	Bachelor	158 (14.1)
Type of OA	Knee	1,011 (89.9)
	Hand	81 (7.2)
	Hip	32 (2.8)
Comorbidities	Hypertension	584 (52.0)
	Diabetes Mellitus	242 (22.5)
	Hyperlipidemia	81 (7.2)

Characteristics		n (%)
OA Severity	Normal	6 (0.5)
	Doubtful	254 (22.6)
	Mild	462 (41.1)
	Moderate	280 (25.0)
	Severe	122 (10.8)

Notes:
BMI = Body Mass Index, OA = Osteoarthritis.
Bivariate analysis demonstrated that BMI and OA severity grade were significantly

A total of 1,124 patients with OA were included in this study. Pain intensity was assessed using the Visual Analog Scale (VAS) and analyzed separately as initial and final pain intensity. Most patients were aged ≥60 years (59.7%) and female (59.3%). The majority had a normal body mass index (77.5%), and the most common education level was senior high school (54.7%). Knee OA was the predominant type (89.9%). Hypertension was the most frequent comorbidity (52.0%), followed by diabetes mellitus (22.5%) and hyperlipidemia (7.2%). Based on radiographic severity using the KL grading system, most patients had mild (41.1%) or moderate OA (25.0%) (Table 1).

Associated with both initial and final pain intensity ($p < 0.05$), while hyperlipidemia was significantly associated only with final pain intensity. In contrast, age group, sex, education level, type of OA, hypertension, and diabetes mellitus were not significantly associated with pain intensity at either assessment (Table 2). These findings suggest that pain intensity in OA is more strongly influenced by disease-related and metabolic factors than by sociodemographic characteristics, consistent with previous studies reporting inconsistent associations between age, sex, and pain severity across different populations (Saraf et al., 2023;He et al., 2024; Hu et al., 2025;Sananta et al., 2022).

Multivariate logistic regression analysis further identified independent factors associated with final pain intensity (Table 3). OA severity was the strongest determinant of pain intensity, with higher KL grades associated with more than threefold increased odds of greater pain intensity (OR 3.56; 95% CI 2.94–4.33). This finding reflects the progressive structural joint damage in advanced OA, including cartilage loss, osteophyte formation, and subchondral bone changes, which increase nociceptive stimulation and may involve inflammatory and neuropathic pain mechanisms (Sananta et al., 2022; Radhakrishnan et al., 2024; Song et al., 2025).

Table 2. Bivariate association between clinical factors and pain intensity

Variable	Initial VAS (p-value)	Final VAS (p-value)
Age	0.848	0.530
Sex	0.005*	0.223
BMI	< 0.001*	0.006*
Education Level	0.943	0.107
Type of OA	0.233	0.087
Hypertension	0.698	0.079
Diabetes Mellitus	0.291	0.222
Hyperlipidemia	0.086	0.006*
OA severity	< 0.001*	< 0.001*

Notes:
*Significant at $p < 0.05$
VAS = Visual Analog Scale, BMI = Body Mass Index ,OA = Osteoarthritis.

Table 3. Multivariate logistic regression of factors associated with higher final pain intensity

Variable	Adjusted OR (95% CI)	p-value
Older age	0.80 (0.6-1.0)	0.061
Male sex	0.81 (0.5-1.1)	0.188
Obesity	0.67 (0.5-0.8)	0.005*
Lower Education level	0.98 (0.8-1.1)	0.825
Knee OA	1.70 (1.1-2.4)	0.003*
Hypertension	1.58 (0.8-2.9)	0.144
Diabetes Mellitus	0.64 (0.4-1.0)	0.067
Hyperlipidemia	2.33 (1.3-4.1)	0.004*
More Severe OA	3.56 (2.9-4.3)	< 0.001*
Joint supplements	1.91 (1.2-2.9)	0.002*
Neuropathic pain agents	1.73 (1.2-2.4)	0.001*
Muscle relaxants	1.04 (0.6-1.5)	0.833

Notes:
The dependent variable was higher final pain intensity based on the final VAS assessment. Odds ratios (ORs) >1 indicate higher odds of experiencing higher pain intensity, while ORs <1 indicate lower odds.
*Statistically significant at $p < 0.05$.
BMI = Body Mass Index, OA = Osteoarthritis, KL = Kellgren–Lawrence.

BMI was independently associated with pain intensity, indicating a metabolic contribution to pain perception (OR 0.67; 95% CI 0.52–0.89). Although most patients had normal BMI, this finding indicates that metabolic and inflammatory pathways related to adipose tissue may influence pain perception beyond mechanical joint loading alone, as reported in previous studies from Korea and India (Chang et al., 2021;Hasan et al., 2024;Raud et al., 2020)

Joint location was also an important factor, with knee OA associated with higher pain intensity compared to non-knee OA (OR 1.70; 95% CI 1.19–2.44). As a primary weight-bearing joint, the knee is exposed to repetitive mechanical stress during daily activities, which may accelerate cartilage

degeneration and contribute to increased pain levels (Innmann et al., 2023; Steenkamp et al., 2022; Khella et al., 2021)

Among comorbidities, hyperlipidemia was significantly associated with higher pain intensity (OR 2.33; 95% CI 1.31–4.15). This association supports evidence linking metabolic dysfunction and chronic low-grade inflammation with OA progression and pain sensitization (Nukala et al., 2021; Xiong et al., 2020;Zhang et al., 2023). In contrast, hypertension and diabetes mellitus were not independently associated with pain intensity after adjustment, suggesting a lesser contribution to pain outcomes in this cohort.

The use of adjuvant therapy was significantly associated with pain intensity. Patients receiving joint supplements (OR 1.91; 95% CI 1.25–2.91) and neuropathic pain agents (OR 1.73; 95% CI 1.23–2.45) had higher odds of greater pain intensity, whereas muscle relaxants were not significantly associated. These findings likely reflect real-world prescribing patterns, in which patients with higher pain intensity and more complex pain mechanisms are more likely to receive adjuvant therapy. Therefore, the observed odds ratios should not be interpreted as evidence of therapeutic effectiveness but rather as indicators of clinical decision-making within a multimodal OA management strategy (Purwata et al., 2021;Salman et al., 2022; Kaur et al., 2021;Taguchi et al., 2021;Ruan & Li, 2025). Conversely, age, sex, and education level were not independently associated with pain intensity in the multivariate model. Although education level has been linked to occupational exposure, physical activity, and health literacy in previous studies its influence on pain intensity appears to be outweighed by disease severity and clinical factors in routine OA management

Overall, these findings indicate that pain intensity in OA is primarily driven by disease severity, joint involvement, and metabolic factors, while the use of adjuvant therapy reflects the complexity of pain mechanisms encountered in clinical practice rather than direct treatment effects. Given the retrospective design and the lack of detailed data on dosage, duration, and combinations of adjuvant therapy, causal interpretation is limited. Prospective studies incorporating standardized functional outcomes and stratification by disease severity are needed to better define the clinical role of adjuvant therapy in multimodal OA pain management.

CONCLUSIONS

This study demonstrates that pain intensity in osteoarthritis (OA) is primarily determined by disease severity and clinical complexity. The Kellgren–Lawrence (KL) grade showed the strongest association with pain intensity, indicating that progressive structural joint damage is accompanied by more complex pain mechanisms. Body mass index, joint location, and metabolic comorbidities such as hyperlipidemia also contributed to higher pain intensity, highlighting the role of both mechanical and metabolic factors in OA pain.

Importantly, these clinical factors have direct implications for the use of adjuvant therapy in routine practice. Patients with more severe OA and higher pain intensity were more likely to receive joint support supplements and neuropathic pain agents, reflecting clinicians' tendency to escalate treatment in response to complex and refractory pain rather than evidence of therapeutic effectiveness. Thus, adjuvant therapy use appears to be driven by disease severity and pain characteristics rather than by sociodemographic factors.

These findings support a selective and clinically guided use of adjuvant analgesics based on individual patient profiles, particularly radiographic severity, joint involvement, and metabolic comorbidities, as part of a multimodal OA management strategy. However, due to the observational nature of this study and the lack of detailed information on dosage and duration of adjuvant therapy, causal relationships cannot be established. Prospective studies are needed to clarify whether specific adjuvant therapies provide additional clinical benefit beyond reflecting prescribing patterns in patients with more complex pain presentations.

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