

## Correlation Between Analgesic Administration, Depression, and Knee Osteoarthritis Severity in Elderly

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### ABSTRACT

**Background:** Chronic diseases in the elderly, including osteoarthritis (OA), impact quality of life and can lead to depression. Pain caused by knee osteoarthritis may trigger stress and depression, while depression can worsen pain perception and disability. This study aimed to analyze the correlation between analgesic use, depression, and the severity of knee osteoarthritis in elderly patients.

**Subjects and Method:** A cross-sectional study was conducted at Dr. Moewardi Hospital, Surakarta, using medical records of 99 elderly patients diagnosed with primary knee osteoarthritis between January 2018 and January 2024. Analgesic administration data were obtained from prescription records. Depression levels were assessed using the Geriatric Depression Scale (GDS), while the severity of osteoarthritis was evaluated using the Kellgren and Lawrence radiological classification. Data were analyzed using the Spearman correlation test.

**Results:** Analgesic administration was negatively associated with depression (OR= 0.09; 95% CI= 0.03 to 0.32;  $p < 0.001$ ) and severity of knee OA (OR= 1.91; 95% CI= 0.60 to 6.08;  $p < 0.001$ ). Severity of knee OA was positively associated with depression (OR= 0.18; 95% CI= 0.05 to 0.62;  $p < 0.001$ ).

**Conclusion:** Analgesic administration is negatively associated with depression and severity of knee OA. Severity of knee OA is positively associated with depression.

**Keywords:** osteoarthritis, depression, elderly

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### BACKGROUND

Older age is defined as the final phase of an individual's life, beginning at the age of 55 years or older (Ahlawat et al., 2023). This stage is commonly accompanied by chronic diseases, which significantly contribute to morbidity and mortality among the elderly

population. Many of these chronic conditions are consequences of the natural aging process and can severely impact the quality of life of affected individuals, impose burdens on their families and caregivers, and strain healthcare systems (Anurogo, 2019). One of the most prevalent chronic

degenerative diseases in this population is osteoarthritis (OA), characterized by the formation of osteophytes, arthritis or synovitis, subchondral bone damage, and gradual cartilage degradation (Sen & Hurley, 2022).

Osteoarthritis is the leading cause of disability in older adults and is projected to become the sixth most common medical condition causing disability among the elderly worldwide (Arthritis Foundation, 2019). The incidence of OA has increased by 113.25% over the past three decades, with knee OA alone accounting for approximately 364 million cases globally (Long et al., 2022). This high prevalence is largely due to the knee joint bearing 40–70% of the total body weight. In Indonesia, the 2018 Basic Health Research (RISKESDAS) reported that 14.9% of elderly individuals over 65 years suffer from joint diseases, including OA, a figure significantly higher than that of younger populations. Local data from Surakarta also show an annual increase in joint disease prevalence, including OA (Surakarta Health Office, 2021). Among all joint locations, the tibiofemoral (knee) joint is most commonly affected.

Beyond physical symptoms, knee OA is strongly associated with psychological consequences, particularly depression. Parmelee et al. (2022) highlighted that chronic pain resulting from OA can trigger adverse psychological effects such as depression. The kindling hypothesis suggests that repeated depressive episodes lower the stress threshold, reducing individuals' ability to manage chronic stressors like persistent joint pain. Depression is reported to affect 8–16% of older adults in the community (Zheng et al., 2021). In patients with OA, depression can worsen pain perception, limit function, lower treatment response, reduce quality of life, and increase the risk of disability. This condition not only affects patients but also places a burden on their

families and society at large. Therefore, appropriate screening, assessment, and treatment for depression in elderly OA patients are essential.

Early diagnosis and accurate assessment of OA severity are crucial for optimal management. Conventional radiography remains the gold standard for OA diagnosis, particularly through the Kellgren & Lawrence classification system, which provides a widely accepted framework for grading radiographic OA severity (Kohn et al., 2016; Li & Argaez, 2020).

Analgesic medications are a cornerstone of OA management, primarily used to reduce pain and improve function. Interestingly, some studies have also revealed a relationship between analgesic use and psychological symptoms such as depression. For example, certain NSAIDs like celecoxib have demonstrated antidepressant properties, suggesting a potential dual benefit in managing both pain and mood disorders in OA patients (Wang et al., 2022).

While several studies have explored the relationship between pairs of variables, such as analgesic use and depression, analgesic use and OA severity, or depression and OA, few have simultaneously examined all three. Moreover, most previous research was conducted outside of Surakarta, and regional differences may influence the prevalence and clinical presentation of these conditions.

Given this gap, the current study seeks to investigate the relationship between analgesic administration and depression, the association between analgesic use and radiological severity of knee OA, and the link between OA severity and depression in elderly patients with knee osteoarthritis in Surakarta. The findings of this study are expected to provide new insights that can

enhance clinical management strategies for this population.

## SUBJECTS METHOD

### 1. Study Design

This was a cross-sectional study. The study was conducted at the Geriatrics and Internal Medicine clinic, medical records installation, PACS Room, and Radiology Department at Dr. Moewardi Regional General Hospital, in Surakarta, Central Java, Indonesia. Data were collected from patients' medical records and X-ray results from January 2018 to February 2024.

### 2. Population and Sample

The study subject was elderly aged  $\geq 60$  years old. Data were collected purposively.

#### a. Inclusion Criteria

- 1) Patients aged 60 years or older.
- 2) Patients with a history of primary knee osteoarthritis diagnosis based on clinical and radiological criteria according to ICD-10 code M17.
- 3) Patients who have undergone knee X-rays.
- 4) Patients who have been assessed for depression using the Geriatric Depression Scale (GDS).

#### b. Exclusion Criteria

- 1) Patients with a history of taking medications that could alleviate depression other than analgesics, such as Fluoxetine or Levodopa.
- 2) Patients with a history of severe kidney disorders or peptic ulcer.
- 3) Patients with incomplete medical records.

### 3. Study Variables

The independent variable was administration of analgesic medication. The dependent variables were severity of knee OA and depression.

### 4. Operational Definition of Variables

**Depression** is the severity of psychological disorders in the form of depression

experienced by elderly patients with a diagnosis of knee OA.

**Osteoarthritis severity** is the severity of osteoarthritis that is radiologically assessed using the Kellgren & Lawrence classification. Osteoarthritis is a disease characterized by joint incompetence or pathological changes in joint structures.

**Analgesic administration** is the patient's history of analgesic drug consumption since the diagnosis of osteoarthritis seen from the history of analgesic drug prescriptions given to patients. Analgesics can include non-opioid analgesic drugs, combined opioid and non-opioid analgesics, and opioid/ narcotic analgesics.

### 5. Study Instruments

All of the data on the patients' analgesic administration, knee OA and depression severity were obtained from medical record.

### 6. Data analysis

Sample characteristics was described in count and percent. Pearson correlation test was used to determine the relationship between analgesic administration, OA severity, and depression.

### 7. Research Ethics

Research ethical issues including informed consent, anonymity, and confidentiality, were addressed carefully during the study process. The research ethical clearance approval letter was obtained from the Research Ethics Committee at Dr. Moewardi Hospital, Surakarta, Indonesia, No. /119/HREC/2017, on January 16<sup>th</sup>, 2024.

## RESULTS

### 1. Sample Characteristics

Table 1 presents the demographic and clinical characteristics of the study participants. The majority of the 99 samples were female, comprising 75 individuals (75.75%). The most common age group was 70–79 years, with 66 participants (66.66%),

falling within the middle elderly age range. Bilateral knee osteoarthritis was the most frequently observed condition, affecting 86 participants (86.86%). In terms of pharmacological management, paracetamol was the most commonly used analgesic, administered to 43 participants (53.75%). Additionally, most patients (59 individuals or 59.59%) received only one type of analgesic medication.

Table 2 shows the distribution of OA severity, analgesic administration, and depression status. The majority of patients were classified as having grade 2 knee osteoarthritis according to the Kellgren & Lawrence criteria, with 43 participants (43.43%). Analgesic medications were prescribed to 69 participants (69.69%). Notably, most participants—83 individuals (83.83%)—did not exhibit symptoms of depression.

**Table 1. Distribution Data of Research Data Characteristics**

Characteristics	Frequency	Percentage (%)
<b>Gender</b>		
Male	24	24.24%
Female	75	75.75%
<b>Age</b>		
60-69 years old	12	12.12%
70-79 years old	66	66.66%
≥ 80 years old	21	21.21%
<b>Location of OA</b>		
Dextra	6	6.06%
Sinistra	7	7.07%
Bilateral	86	86.86%
<b>Type of Analgesic</b>		
Paracetamol	43	53.75%
Natrium Diclofenac	14	17.5%
Celecoxib	9	11.25%
Analsik	6	7.5%
Mefenamic acid	2	2.5%
Meloxicam	3	3.75%
Celebrex	1	1.25%
Kalium Diclofenac	2	2.5%
<b>Analgesic Dose</b>		
Without analgesic	30	30.30%
Single dose	59	59.59%
≥2 doses	10	10.10%

**Table 2. Distribution Data of Research Variables**

Variable	Frequency	Percentage (%)
<b>Analgesic Administration</b>		
Yes	69	69.69%
No	30	30.30%
<b>Depression Level</b>		
Normal	83	83.83%
Mild depression	16	16.16%
<b>OA Severity</b>		
Grade 1	9	9.09%
Grade 2	43	43.43%

Variable	Frequency	Percentage (%)
Grade 3	37	37.37%
Grade 4	10	10.10%

## 2. Bivariate Analysis

Table 3 showed that there was a negative relationship between analgesic administra-

tion and depression ( $r = -0.35$ ;  $p < 0.001$ ) and severity of knee OA ( $r = -0.43$ ;  $p < 0.001$ ) in elderly patients with knee OA.

**Table 3. The results of Spearman correlation analysis between analgesic administration, depression, and severity of knee OA**

Independent variables	Depression		Severity of knee OA	
	r	p	r	p
Analgesic Administration	-0.35	<0.001	-0.43	<0.001

## DISCUSSION

### 1. Sample Characteristics Study Subjects

The results of this study indicate that knee osteoarthritis (OA) is more prevalent in elderly women than in elderly men. This finding aligns with the study by Hoxha et al. (2015), which reported that females are at a higher risk of developing OA compared to males. Several factors may contribute to this increased risk in women, including hormonal influences, particularly related to estrogen, as well as genetic predisposition, anatomical differences, and a higher incidence of joint injuries or trauma. At the molecular level, women exhibit elevated levels of macrophage stimulators and pro-inflammatory mediators, such as inflammatory interleukins, along with greater expression of estrogen receptors. In contrast, men tend to have higher levels of catabolic enzymes responsible for extracellular matrix degradation, but they also benefit from more robust anabolic compensatory mechanisms, including increased levels of growth factors and testosterone (Franconi, 2021).

In this study, patients with grade 4 osteoarthritis (OA), as classified by the Kellgren & Lawrence criteria, were rarely found. This may be because individuals

with advanced OA are more likely to undergo total knee arthroplasty (TKA). In fact, OA grade 4 is widely recognized as a major risk factor for TKA (Goh et al., 2023).

Additionally, the majority of elderly patients in this study were found to have bilateral knee OA. This finding is consistent with research by Anggraini and Sjarqiah (2021), which reported that a significant proportion of elderly individuals with knee OA experienced osteoarthritis in both knee joints.

This study also observed that many elderly patients received treatment involving analgesic medications. This aligns with findings from Bichsel et al. (2021), who noted that pharmacological interventions, including the use of analgesics, are commonly administered to manage symptoms in patients with knee OA.

### 2. Relationship Between Depression and Severity of Knee Osteoarthritis

There is a positive and significant correlation between osteoarthritis (OA) severity and depression. A study by Zheng et al. (2021) demonstrated that symptoms of knee OA, such as pain, are commonly associated with depression and may even play a role in its pathogenesis. As the severity of knee OA increases, symptoms such as joint pain, stiffness, and limited

function become more pronounced, often leading to decreased quality of life and disability. These limitations can contribute to multidimensional burdens, including financial stress. Furthermore, OA is frequently associated with comorbid conditions such as cardiovascular disease, diabetes, hypertension, falls, fractures, and depression. Approximately 19.9% of individuals with OA experience depressive symptoms, with a relative risk of 1.17 compared to those without OA.

The co-occurrence of depression in OA patients may be mediated by both biological and behavioral mechanisms. For instance, a neurobiological link may exist between chronic pain and depression. Additionally, the physical limitations imposed by OA can result in reduced participation in meaningful and social activities, potentially exacerbating depressive symptoms. Understanding the mechanisms behind depression in OA patients is essential for identifying modifiable risk factors and developing effective interventions. Joint pain, impaired physical performance, and an elevated risk of chronic comorbidities are key features of OA that may contribute to the development of depression (Zheng et al., 2021).

### **3. Relationship Between Analgesic Administration and Severity of Knee Osteoarthritis**

There is a significant relationship between analgesic administration and the severity of knee osteoarthritis. As the most common joint disease in the elderly, osteoarthritis is a progressive condition marked by cartilage degeneration, tendon and ligament damage, and synovial inflammation, all of which contribute to chronic pain and functional impairment. Since there is no definitive cure for OA, management strategies focus on pain control and improving physical function. According to a study by

Li and Argaez (2020), the analgesic drug codeine provides moderate benefits in alleviating pain in OA patients.

### **4. Relationship Between Analgesic Administration and Depression**

There was a negative association between analgesic administration and depression, suggesting that the use of analgesics may help reduce the risk of depression in elderly patients with knee osteoarthritis, regardless of disease severity. This finding is supported by a systematic review and meta-analysis conducted by Wang et al. (2022), which demonstrated that the analgesic celecoxib has antidepressant effects. The study explained that depression often co-occurs with inflammatory conditions, and celecoxib showed efficacy in reducing depressive symptoms in both acute (less than four weeks) and chronic (more than four weeks) cases.

In addition to celecoxib, other NSAIDs were also found to be beneficial in lowering depression levels. Wang et al. (2022) noted that depression is often characterized by a pro-inflammatory state and is causally linked to neurotransmitter dysregulation. Inflammation, typically a result of infection, physical trauma, or immune responses, can also be triggered by psychological stress. This connection highlights the interplay between physical and mental health.

The inflammatory response is often mediated by microglia in the hippocampus and other brain regions involved in mood regulation. These areas are particularly vulnerable to the effects of chronic stress, which can initiate or exacerbate depression. Stress-induced immune activation disrupts neurotransmitter systems, leading to imbalances such as serotonin deficiency, an important mechanism in the development of depression. Thus, inflammation plays a

central role in the pathogenesis of depression for some individuals.

Further, a study by Michaelides and Zis (2019) described the bidirectional relationship between pain and depression. They reported that depression is associated with increased perception of pain severity, while prolonged pain can impair mood regulation and lead to depressive symptoms. Each condition may act as both a cause and consequence of the other, reinforcing their interdependent nature.

### Research Limitations

This study has several limitations. First, it did not assess patients' adherence to taking the prescribed analgesic medications, which may influence the relationship between analgesic use and depression or osteoarthritis severity. Second, the use of a cross-sectional study design limits the ability to determine causal relationships between the variables studied, as data were collected at a single point in time.

### AUTHOR CONTRIBUTIONS

All authors have read and agreed to the published version of the manuscript.

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### CONFLICT OF INTEREST

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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