

# Characteristics of NSAIDs Prescription in Elderly Knee Osteoarthritis Patients

Janetta Wong<sup>1</sup>, Nicolaski Lumbuun<sup>1</sup>

*Faculty of Medicine Pelita Harapan University*

## Abstract

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**Correspondance:** Nicolaski Lumbuun. Faculty of Medicine Univ. Pelita Harapan

**E-mail:** [Nicolaski.lumbuun@uph.edu](mailto:Nicolaski.lumbuun@uph.edu)  
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**Introduction:** The prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) as pharmacological therapy for OA was found to be imprecise. In 2018, the rationality of NSAIDs prescribed at Wolter Monginsidi Hospital, Manado showed as much as 100% proper indication, 77% proper dose, and 89% proper medication. This shows that the rationality of NSAIDs prescription is still irrational. Irrational prescribing has the potential to result in side effects or the incidence of drug-related problems

**Aim:** To determine the characteristics and the rationality of NSAIDs prescriptions in elderly knee OA.

**Methods:** This is a descriptive study of 108 medical records for the period January 2020-April 2021 at BS Clinic, Semarang, using purposive sampling method.

**Result:** Results showed the characteristics of elderly knee OA patients at BS Clinic were 74.1% women, 47.2% belonging to obese group, and 41.7% experiencing severe pain. Patient's age had a median value of 66 years. In the number of comorbidity, the median value was 1. The rationality of NSAIDs prescription was 95.4% proper diagnosis, 100% proper drug, 97.2% proper dose, and 99.1% proper indication with the incidence of side effects of NSAIDs prescribing was 1.9%.

## Introduction

Elderly, in Law No. 13 of 1998, is defined as someone who has reached the age of 60 years and over. World Health Organization (WHO) defines elderly into the population group aged 60 years and over.<sup>1,2</sup> Statistics Indonesia shows that demographic data on the elderly in Indonesia in 2019 recorded 63.82% of 60-69 years, 27.68% aged 70-79 years, and 8.5% of elderly aged 80 years and above. The evidence of an increase in the elderly population every year has the various consequences on aspects of life, one of which is health.<sup>3</sup>

According to American College of Rheumatology (ACR), osteoarthritis (OA) is most common degenerative disease of joint cartilage. This disease affects knee, hip, and hand joints. Hence, OA becomes one of most common main causes of disability in elderly.<sup>4</sup> Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used pharmacological therapy in OA. NSAIDs are drugs that have analgesic, antipyretic, and anti-inflammatory properties by inhibiting the cyclooxygenase (COX) enzyme.<sup>5</sup> NSAIDs are commonly used in prescription so it is necessary to pay attention to the rationality of prescribing NSAIDs.

Drug rationality is defined by the compatibility of the diagnosis and drug administration with the reference used regarding diagnosis, dosage, and indications of usage.<sup>6</sup> Previous study in 2018 at Wolter Monginsidi Hospital, Manado, showed the rationality of NSAIDs prescription was found to be 100% proper indication, 77% proper dose, and 89% proper drug.<sup>7,8</sup> Another study in 2014 at the Subang District Hospital had the rationality of 100% proper diagnosis, 52% proper drug, 100% proper dose, 100% proper indication.<sup>8</sup> These studies show that administration of NSAIDs has not been fully rational. The rationality of NSAID prescribing needs to be a concern as the amount of elderly OA cases increase, which there is a danger of side effects if the prescribing pattern is inappropriate. Irrational prescribing of NSAIDs can lead to side effects such as gastrointestinal, cardiovascular, nephrotoxicity, cognitive deficits, and stroke.<sup>5,9,10</sup>

Although similar things have been studied, the rationality of NSAIDs prescription has not been completely perfect that can lead to the occurrence of side effects. In addition, the patient characteristics such as age, gender, presence of comorbid disease, body mass index (BMI), and degrees of pain play roles in NSAIDs prescription. Therefore, it is necessary to look further the characteristics of NSAIDs prescribed in elderly knee OA.

## Objectives

This study aimed to determine the characteristics of NSAIDs prescribed in elderly knee OA in *Fasilitas Kesehatan Tingkat Pertama/FKTP* (general clinic) since the previous study focused on hospital prescriptions mostly given by specialists.

## Material And Methods

### Study Design

This research was a retrospective descriptive cross-sectional study design.

### Sample

108 medical records of period January 2020 to April 2021 were obtained from BS Clinic, Semarang. Sampling was carried out from December 2020 to April 2021.

### Data Collection Method

Data were collected using purposive sampling method (total sampling) in the number of samples. 108 samples were taken and met the inclusion criteria consisting of (1) medical records of male and female OA outpatients aged 60 years; (2) medical records of patients who made the next visit at least a month after receiving NSAIDs. Meanwhile, OA patients who came but were referred to a higher-level health facility without receiving any treatment at the clinic were excluded from the research data. Data such as name, gender, age, BMI, number of comorbidity, degree of pain, diagnostic statement, NSAIDs use (type, dosage, and prescription duration), and any side effect of prescription were obtained from medical records. Several data on the patient's pain degree in January-November 2020 period were completed through primary data collection of online interviews with the patients. All the collected data were recorded in Case Report Form (CRF).

### Data Analysis

Data were analysed using Statistic Package for the Social Sciences 26<sup>th</sup> version. Univariate analyses were

performed to assess the characteristics and the rationality of NSAIDs prescription compared to literatures.

## Results

### Patient Characteristics

A total sample of 108 medical records was obtained from the data collection. Research obtained that 74.1% of OA patients were women. In the context of BMI, the largest amount of data was 51 people (47.2%) in the obese group. The median age was 66 years with the youngest of 60 years and the oldest of 92 years. Patients aged 60 years had the most frequent visit to the clinic. In the number of comorbidity, the median value was 1 with the smallest number of 0 means patients didn't have any comorbidity and the most being 3 diseases. Numeric Rating Scale (NRS) was used to assess pain degree felt by the OA patients. The majority of the samples experienced severe pain with the prevalence of 41.7%.

**Table 1.** Patient Characteristics

Characteristics	n	%
<b>Gender</b>		
Male	28	25.9
Female	80	74.1
<b>BMI</b>		
Underweight	7	6.5
Normal	28	25.9
Overweight	22	20.4
Obese	51	47.2
<b>Pain degree</b>		
Mild	20	18.5
Moderate	43	39.8
Severe	45	41.7
	<b>Age</b>	<b>Number of Comorbid</b>
Median	66	1
Mode	60	0
IQR	7	1
Min-Max	60-92	0-3

### Prescription Characteristics

Based on 2016 ACR Revised Criteria for Early Diagnosis of Knee Osteoarthritis, the research found that NSAIDs prescriptions in BS Clinic had the level of proper diagnosis of 95.4%. 100% of proper drug obtained in this study referred to Rekomendasi IRA 2014. Based on British National Formulary (BNF) 80, research got 97.2% of proper dose and 99.1% of proper indication on NSAIDs prescription.

**Table 2.** Characteristics of Prescription

Characteristics	%
Proper Diagnosis	95.4
Proper Drug	100
Proper Dose	97.2
Proper Indication	99.1

**Table 3.** Types of NSAID prescribed

NSAIDs	Degree of Pain		
	Mild	Moderate	Severe
<b>Celecoxib</b>	1	4	1
<b>Meloxicam</b>	4	10	12
<b>Ibuprofen</b>	6	11	3
<b>Diclofenac</b>	9	18	29
<b>Total</b>	<b>20</b>	<b>43</b>	<b>45</b>

In the context of prescription duration, result showed the median value was 3 days with the shortest being 3 days and the longest was 7 days

**Table 4.** Duration of NSAIDs Prescription

Duration of NSAIDs Prescription			
Median	Mode	IQR	Min-Max
3	3	0	3-7

## Side Effects

Two (1.9%) out of 108 samples experienced the side effect of NSAIDs prescription manifested as dyspepsia. Table 5 showed the division of patient groups based on the administration of gastroprotective agent, given as proton pump inhibitor (PPI). About 84 samples did not get PPI, including those 2 samples with dyspepsia. As for 24 samples got PPI and didn't experience any side effect caused by NSAIDs prescription.

**Table 5.** Side Effects of NSAIDs Prescription

PPI	Side Effects	
	Dyspepsia	Nothing
Given	-	24
Not	2	82
<b>Total</b>	<b>2</b>	<b>106</b>

## Discussion

### Patient Characteristics

The gender distribution of knee OA patients at BS Clinic shows the largest number of data in the female group, which is 80 people (74.1%). This research resembles a study in 2020 at *RSUD dr. Mohamad Soewandhie* with a prevalence of OA in women by 77.9% and a research in 2015 at Subang District Hospital with a prevalence of OA in women of 63%.<sup>8,11</sup> Hence, it can be concluded that the gender characteristics of knee OA patients in *FKTP* correspond with those who come to the hospital in terms of more women than men.<sup>12-15</sup>

Fifty one (47,2%) out of 108 samples were categorized as obese group that resembles a study in 2014 at *Posyandu Lansia Surakarta* which showed the prevalence of knee OA in obese patients

was 48.1%.<sup>16</sup> According to the findings, it can be concluded that knee OA patients who came to *FKTP* had the same BMI characteristics in the terms of being obese. The prevalence of this study increased in the obese group because the knee is a weight-bearing joint. Several studies have stated that obesity is one of the risk factors for knee OA due to increasing load in joint.<sup>13</sup> A study in 2016 proved that there was a significant relationship between BMI and the degree of joint damage in OA patients.<sup>17</sup>

This study has an age profile with a median value of 66 years, which is similar to a study in 2014 by Hasiibi at *Puskesmas Susut, Bali* with the median age of 66.5 years. So that, OA patients who come to *FKTP* have the characteristics of same population average age.<sup>18</sup> Increasing age as the aging process contributes to the development of OA. Chondrocyte cells undergo aging through the degradation of cartilage and tissue by increasing the production of pro-inflammatory mediators in arthritis-affected joints.<sup>19,20</sup>

This study obtained data on the number of comorbidity with a median value of 1. This is in accordance with the CDC statement that most of joint disease patient suffers from one other chronic disease.<sup>21</sup> Hypertension was the most comorbidity as in 20 samples (15.3%). NSAIDs use has the side effect of increasing blood pressure. So that, prescribing in the patients with a history of hypertension needs to be considered. Research has also shown that aging factors contribute to an increase in systolic pressure and heart rate due to increased stiffness of the arteries thereby reducing the reservoir function of the heart arteries.<sup>22</sup> NSAIDs work by inhibiting the COX enzyme that will decrease the rate of prostacyclin (PGI<sub>2</sub>) synthesis as a vasodilator and platelet inhibitor that are

produced in inflammatory conditions. Reduced amount of PGI<sub>2</sub> will trigger an increase in blood pressure, leading to hypertension and thrombosis.<sup>23</sup>

In the assessment of pain degree, NRS was used in accordance with the study population that is elderly group. NRS has the advantage of being practically since any equipment isn't needed, is easy to understand, and isn't influenced by feelings of being disturbed due to the pain felt.<sup>24,25</sup> A study by Gallasch, et al. showed that NRS has a high level of reliability in the elderly population and is appropriate for all levels of education.<sup>26</sup> Measurement with Visual Analog Scale (VAS) is hampered by the need for equipment, the patient's level of education to understand measurement instructions, and the patient's medical history related to the visual acuity and cognitive function. Thereof, VAS is more difficult to be applied in the elderly population.<sup>24,25</sup> Verbal Rating Scale (VRS) has been shown to be influenced by conditions that affect patient's quality of life, such as the emotional feeling due to the pain felt or as the result of limitations in daily activities.<sup>25</sup>

### Prescription Characteristics

The compatibility of the OA diagnosis in this study was 95.4%. This was based on the 2016 ACR criteria which states that patients are diagnosed with knee OA if they have symptoms of knee joint pain plus at least 3 out of 6 other symptoms, consist (1) patients aged >50 years; (2) morning joint stiffness <30 minutes; (3) crepitus; (4) bone tenderness; (5) joint enlargement; and/or (6) warmth isn't palpable on the joint surface.<sup>27</sup>

Several factors may influence the discrepancy in the diagnostic accuracy of this study. The diagnostic decision was made based on clinical complaints and physical examination which was not supported by a comprehensive supporting examination. Furthermore, the research population, which was the elderly could be a factor because doctors and patients themselves tend to perceive complaints as a natural process of aging. This is in line with the results of a 2014 study by Paskins, et al.<sup>28</sup> In addition, some patients may have undergone therapy or taken medication previously that it could affect the diagnosis due to differences in symptoms felt before and after the therapy. Besides, patients' own opinions and ideas based on disease information from the internet and the financial limitations in the cost of necessary health care could also hinder the diagnostic accuracy.

This is also supported by research in 2018 by Egerton, et al., published the factors that hindered the accuracy of diagnosis in GPs' practice were as follows<sup>29</sup>

- 1) Doctors tend to underestimate the patient's complaints.<sup>28,29</sup>
- 2) Gaps in the knowledge and abilities of doctors.<sup>29,30</sup>
- 3) Lack of access and awareness to update references or guidelines related to diagnosis.
- 4) Time-limited consultation.<sup>30,31</sup>

The results showed that the accuracy of the NSAIDs types of knee OA patients at the BS Clinic was 100% that resembles the research at *RSUP dr. Soeradji Tirtonegoro, Klaten* in 2018 with 100% drug type accuracy.<sup>32</sup> As seen that NSAIDs prescribing in *FKTP* corresponds hospital prescriptions in terms of the accuracy of NSAIDs type. The selection of

NSAIDs in this study was based on COX-2 selective, in the form of celecoxib and meloxicam that were administered to patients with a history of GI and cardiovascular and in patients without contraindications. While the non-selective prescribed as ibuprofen and diclofenac sodium were administered to patients with a history of cardiovascular given with gastroprotective agent (PPI) and in patients without contraindications.

The dosing accuracy profile in this study was 97.2% in 105 of 108 prescriptions, which is comparable to a study in 2014 at *Apotek X Kuningan* with an exact dose of 94.45%. The discrepancy occurred in 3 prescriptions with meloxicam given as 3 x 7.5 mg/day while the recommended dose in the literature is 7.5-15 mg/day.

The accuracy of indications in this study was 99.1%, which resembles a similar study at the Subang District Hospital with 100% proper indication.<sup>8</sup> A prescription of diclofenac sodium was given inappropriate. It was prescribed to a patient with a stroke that is classified as cerebrovascular disease which is included in the contraindication of diclofenac sodium. Diclofenac has the highest COX-2 selectivity compared to other types in non-selective group. In turn, increases the inhibition rate of prostacyclin production and causes vasoconstriction. In addition, renal action-induced hypertension may occur due to volume expansion. NSAIDs

also induce thrombosis due to platelet aggregation due to inhibition of prostaglandin production.<sup>23,33</sup>

Research obtained the median value of prescription duration in this study was 3 days as well as being the shortest duration and the longest was 7 days. NSAID is a dose-response agent where the amount of dose affects the side effects of the prescription. Research in 2017 by Al Khaja, et al. showed that NSAID prescriptions are recommended with the shortest duration to minimize side effects that may arise with long-term use.<sup>34</sup>

In the study, it was found that two (1.9%) patients experienced side effect in the form of dyspepsia and were not given PPI as gastroprotective agent. This study is comparable to a study in 2020 which stated that the most common side effects of NSAIDs is in the GI system.<sup>35,36</sup> Gastroprotective agents should be given to patients on NSAID treatment, especially those with GI history. The selection of PPI is based on its mechanism of action that reduce gastric acid production for 36 hours and is recommended to be given in the smallest dose NSAID prescriptions.<sup>35,37,38</sup>

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