

# Evaluation of Analgetic Use Rationality and Level of Patient Knowledge in Primary Healthcare Facility in Padang

Yoneta Srangenge<sup>1\*</sup>, Sri Oktavia<sup>2</sup>, Nur Hazizah<sup>2</sup>

<sup>1</sup>Faculty of Pharmacy, Andalas University

<sup>2</sup>College of Pharmacy (STIFARM) Padang

Corresponding author. Email: [yonetasrangenge@phar.unand.ac.id](mailto:yonetasrangenge@phar.unand.ac.id)

## ABSTRACT

Worldwide, oral analgesics are the most widely used drugs with prevalence ranging from 7% up to 35% in various countries. Naturally, this is accompanied by a high level of rationality of use as well. This study aims to evaluate the rationale of administering analgesic drugs and evaluate the level of patient knowledge of analgesic drugs at the Dadok Tunggul Hitam Public Health Center, Padang City. This type of research is non-experimental, with a descriptive design and prospective data collection, using the method *cross-sectional*, data obtained from medical records and questionnaires that were directly reviewed as data sources. The results showed that there were 95.6% patient accuracy, 100% dose accuracy, 15.9% drug selection accuracy, 100% indication accuracy, 100% route accuracy, 0% frequency accuracy and 18.6% potential drug interactions both physically and mentally. pharmacology and pharmacokinetics in the use of analgesic drugs. Meanwhile, the results of the assessment of the patient's knowledge level showed that 59.3% of patients had a good level of knowledge, it was also known that the level of education and age affected the patient's knowledge of analgesic drugs ( $P < 0.05$ ).

**Keywords:** Rationality, Analgesics, Osteoarthritis

## 1. INTRODUCTION

Rational use of drugs is the administration of drugs to patients according to clinical needs, appropriate doses and durations of treatment are sufficient and at a low cost [1]. The irrational use of drugs can affect the health of the world community and also cause a decrease in patient adherence to treatment [2]. Misuse of drugs can lead to unwanted drug reactions, for example, long-term use of paracetamol can lead to impaired liver function. The existence of limited knowledge by the public about drugs and their use can lead to sources of medication errors.

Analgesics are drugs used to relieve pain. Analgesics, both non-narcotic and narcotic, are prescribed to relieve pain, the choice of drug depends on the severity of the pain. Mild pain is often relieved by the use of non-narcotic analgesics. Moderate to severe pain in smooth muscles, organs and bones usually requires narcotic analgesics [3].

Pain is an unpleasant, subjective, sensory, emotional feeling associated with acute or potential tissue damage [4]. Pain is a major global health problem, with an estimated 1 in 5 adults suffering from pain and 1 in 10 adults being diagnosed with chronic pain each year. The four main causes of pain are cancer, osteoarthritis and rheumatoid arthritis, surgery and trauma, and spinal problems [5].

According to research that has been done by Afif, (2015) the accuracy of self-medication use of

analgesic drugs in the community of Demak district shows that it is rational as much as 46% and irrational as much as 54%. One of the studies that have been carried out to determine the relationship between the level of knowledge and the use of analgesic drugs, shows that there is an inaccuracy in the use of analgesic drugs because the respondents did not meet the appropriate aspect of the dose according to the standard [6].

## 2. METHOD

The study is non-experimental with a descriptive design using a cross-sectional method and prospective data collection. Data were obtained from outpatients' medical records and questionnaires.

### 2.1. Sample

#### 2.1.1. Rationality

Outpatients with a diagnosis of osteoarthritis, used analgesic during October to December 2019 and met the inclusion criteria.

#### 2.1.2. Level of knowledge

Outpatients who received analgesic drugs in October-December 2019 and met the inclusion criteria.

**2.2. Population**

Outpatients of Dadok Tunggul Hitam Primary Health Center (Puskesmas) in Padang City during October-December 2019.

**2.3. Inclusion Criteria**

**2.3.1. Rationality**

Patients with an age range of > 17 years.

**2.3.2. Level of Knowledge**

Patients who are prescribed analgesics.

**2.4. Exclusion Criteria**

**2.4.1. Rationality**

Patients who are referred to the Hospital, Patients who seek treatment at the KIA poly (Maternal and Child Consultation) and dental poly.

**2.4.2. level of Knowledge**

Patients who are not willing to be included in the study, patients who seek treatment and do not take drugs at the pharmacy.

**2.5. Data analysis**

Data are presented in the form of tables and graphs.

**3. RESULTS AND DISCUSSION**

This study was conducted at the Dadok Tunggul Hitam Health Center Padang City from October until December 2019. The number of patients obtained was 113 patients who met the inclusion and exclusion criteria. The next step is to collect data starting from patient demographic data, the demographics of osteoarthritis patients include gender, namely 23 male patients (20.4%) and 90 female patients (79.6%). The number of female respondents aged 36-45 years was 2 patients (1.8%), 46-55 years 23 patients (20.3%), 56-65 years 22 patients (19.5%) and aged >65 years totaled 66 patients (58.4%). There are no male respondents aged 36-45, age 46-55 years are 4 patients (3.5 %), age 56-65 years are 2 patients (1.8%) and age 65 years and over are 17 patients (15 %).

**Table 1.** Basic data of osteoarthritis patient by gender, age, history of OA, first time OA prescription

No	Variable	Category	Frequency	Percent %
1	Gender	Male	23	20.4
		Female	90	79.6
2	Age	36-45	2	1.8
		46-55	23	20.3
		56-65	22	19.5
		>65	66	58.4
3	History of OA Yes	Yes	29	25.7
		None	84	74.3
4	First time prescription OA	Diclofenac sodium	67	59.3
		Paracetamol	18	15.9
		Ibuprofen	27	23.9
		mefenamic acid	1	0.9

These results are in accordance with research conducted by Nur where the prevalence of osteoarthritis in female respondents was 46 respondents (40.7%), and male respondents were 14 respondents (23.3%). Another study conducted at the Arifin Achmad Hospital in Riau gave the results of 126 female respondents (63.6%) and 72 male respondents (36.4%) [7]. And another study conducted at the TNI AD Robert Wolter Mongosidi Hospital Manado gave the results of 27 female respondents (77%) and 8 patients (23%) male respondents [8]. This is because one of the risk factors for osteoarthritis is women who experience menopause. Women experience menopause occurs at the age of 45-55 years. When women experience menopause, there is a hormone whose production decreases, namely the hormone estrogen. The decrease in the female hormone estrogen causes women to be more at risk of developing OA than men [9]. The decrease in this hormone causes the cartilage to become rougher and thinner. This hormone has the function of reducing the rate of decline in bone mass [10].

Based on the patient's age, there were 2 patients with osteoarthritis (36-45 years old) (1.8%), early elderly (46-55 years old) 23 patients (20.4%), late elderly (56-65 years old) years as many as 22 patients (19.4%) and seniors (> 65 years) as many as 66 patients (58.4%) based on the data obtained found the same results as the study conducted by Siti (2018) where the most patients experienced osteoarthritis are patients aged 65 years and over, patients aged 65 years and over are susceptible to osteoarthritis because at this age the patient's physical body begins to decline. At this age, there is an increase in weakness around the joints, a decrease in joint flexibility, cartilage classification and a decrease in chondrocyte function so that it supports the occurrence of osteoarthritis [11].

Based on the history of osteoarthritis, the distribution of patients with osteoarthritis who had been diagnosed with osteoarthritis was 25.7% with a total of 29 patients and in patients who did not have a history of osteoarthritis, the percentage was 74.3% with a total of 84 patients from 113 osteoarthritis patients.

Analysis based on patients prescribed medication with a diagnosis of osteoarthritis for the first time. It was found that 59.3% of 67 prescriptions were given to the drug diclofenac sodium when the patient was first diagnosed with osteoarthritis (OA). For paracetamol drugs obtained 15.9% with a total of 18 prescriptions, for prescription ibuprofen obtained 23.9% with a total of 27 prescriptions and for prescribing mefenamic acid drugs obtained 0.9% with a total of 1 prescription from a total of 113 patients who were prescribed analgesic drugs for patients diagnosed with osteoarthritis for the first time.

Analysis based on the frequency of polypharmacy for osteoarthritis patients. The percentage of 0.9% of drugs whose use is combined with 1 prescription (0.9%). Drugs whose use is said to be a combination are the use of drugs simultaneously with the aim of overcoming disease problems other than osteoarthritis. The combination of drugs in question is between the drug diclofenac sodium with paracetamol where diclofenac sodium is used for osteoarthritis and paracetamol for fever. In the percentage of duplication, it was found that 1.8% of drugs whose use was duplicated with a total of 2 prescriptions. Drugs whose use is said to be duplication are the use of drugs simultaneously with the aim of increasing the effect of the drug itself. The duplication of the drug itself includes the use of the drug diclofenac sodium with paracetamol where in this case the patient does not experience fever or other diseases according to the use of the drug itself.

**Table 2.** Analgesics prescribing frequency in osteoarthritis patients

		<b>Frequency</b>	<b>Percent</b>
Valid	Diclofenac sodium	81	69.8
	Paracetamol	17	14.6
	Ibuprofen	17	14.6
	Mefenamic acid	1	0.9
	<b>Total</b>	<b>116</b>	<b>100.0</b>

**Table 3.** Polypharmacy frequency (Duplication and Combination)

		<b>Frequency</b>	<b>Percentage</b>
Frequency of prescriptions	Duplicate	2	1.8
	Combinations	1	0.9
	No	110	97.3
	<b>Total</b>	<b>113</b>	<b>100.0</b>

**Table 4.** Data on the rationality of analgesic drug use in patients with OA

The rationality of drug use		Frequency	Percentage	Valid Percent	Cumulative Percent
Patient	Rational	108	95.6	95.6	95.6
	Irrational	5	4.4	4.4	100.0
Dose	Rational	113	100.0	100.0	100.0
Indication	Rational	113	100.0	100.0	100.0
Route	Rational	113	100.0	100.0	100.0
Frequency	Irrational	113	100.0	100.0	100.0
Drugs	Rational	18	15.9	15.9	15.9
	Irrational	95	84.1	84.1	100.0
Drug interaction	Not potential	92	81.4	81.4	81.4
	Potential	21	18.6	18.6	100.0

In this study evaluate the rationality of analgesic use in patients with a diagnosis of osteoarthritis in the form of the right patient, the right dose, the right indication, the right route, the right frequency, the right drug and drug interactions. The use of drugs is said to be appropriate when prescribing drugs is based on medical indications or diagnoses found in the patient. In this study, 113 patients (100%) had the right indication, this was because the patient was diagnosed with osteoarthritis.

The right drug is a drug that is given according to the *drug of choice*, which is safe to use for osteoarthritis patients according to what has been previously determined [12, 13, 14]. Based on the treatment of osteoarthritis in osteoarthritis patients, 18 patients received the right medication (15.9%) the result was said to be correct because it was in accordance with the literature used, namely the Ministry of Health of the Republic of Indonesia and Dipro edition 8 for patients with osteoarthritis. The use of osteoarthritis drugs in OA patients at the Dadok Tunggal Hitam Health Center in Padang City in 2019 was diclofenac sodium, ibuprofen, paracetamol and mefenamic acid. Paracetamol is the first line in the management of mild to moderate pain because it is relatively safe to use, the price is cheaper than NSAIDs, does not irritate the stomach so it is safe for elderly patients and patients with a history of peptic ulcers and paracetamol is the *drug of choice* for patients who have kidney problems. Paracetamol should be considered in patients with liver disease and alcoholics. The mechanism of action of paracetamol is by inhibiting the synthesis of prostaglandins (increasing the sensation of pain) by blocking the work of central cyclooxygenase [15]

Second-line treatment in osteoarthritis patients with NSAIDs is diclofenac sodium, ibuprofen. NSAIDs are drugs that can suppress inflammation through cyclooxygenase (COX) enzyme inhibitors, the effectiveness of NSAIDs is to relieve pain in low doses and eliminate inflammation in high doses so as to provide comfort in patients with chronic joint problems. serious, heart failure, asthma. If the use of NSAIDs is not effective, combination therapy can be used or

corticosteroid drugs such as methylprednisolone, glucosamine sulfate, and tramadol can be used which are weak opioids used to treat moderate to severe pain [15]. There were 95 patients (84.1%) who did not take the right medication, because they received diclofenac sodium or ibuprofen therapy directly without a history of previous use of acetaminophen in a history of osteoarthritis, even though the first line of treatment for osteoarthritis is acetaminophen based on the literature of the Ministry of Health of the Republic of Indonesia and Dipro edition 8 and also when the patient is receiving diclofenac sodium therapy should be accompanied by a gastric protective drug in the form of (lansoprazole, omeprazole or ranitidine). Diclofenac sodium has side effects on the gastrointestinal tract, gastrointestinal bleeding and the formation of ulcers or perforation of the wall [16]. Because most people with osteoarthritis are aged 60 years and over, it is necessary to consider the selection of diclofenac sodium in therapy [16]. And also, if the patient receives mefenamic acid therapy, it means it is not appropriate because this drug has a side effect of diarrhoea to bloody diarrhoea [17]. This is dangerous because most osteoarthritis patients are elderly patients.

The right patient is the drug that is given does not have contraindications to the patient's condition that can worsen the patient's condition. Based on the evaluation results, there were 108 patients who were right patients (95.6%) and 5 patients who were not patients (4.4%). Comorbidities or a history of dyspepsia should not be given with NSAIDs because the mechanism of NSAIDs inhibits COX 1 and COX 2, COX1 functions as gastric protection so that when COX 1 is inhibited, it can worsen gastric conditions. Inappropriate treatment of osteoarthritis of the patient needs to be replaced according to drugs that are not contraindicated in the patient so as not to aggravate the patient's condition [18].

Drug dose is the amount of drug used by a patient to obtain the expected therapeutic effect. Dosage is one of the most important aspects in determining drug efficacy, if the dose given is too low or below the therapeutic range then the expected

therapeutic effect will not be achieved, and vice versa if the dose given is too high, especially if the drug has a narrow therapeutic-range it will very risky to cause overdose [14]. There were 113 patients (100%) who had the right dose. The accuracy in dosing was adjusted based on the literature Drug Information Handbook (DIH), British National Formulary (BNF), AHFS Drug Information Essential.

Route accuracy analysis was 100%. The exact route in question is seen from the right way of using the drug so that it can provide the right therapeutic effect. In this study, all patients received the oral route of administration.

The right frequency is said to be the right frequency if the drug is given continuously

according to a predetermined distance or time interval, there are 113 patients who do not have the right frequency (100%). In this study, the inaccuracy occurs because the prescription given is incomplete where the use of analgesic drugs must be clearly stated because in the use of analgesics the drug is used only when necessary or in pain and the accuracy of the frequency cannot be analyzed accurately because pain parameters cannot be measured with so that in outpatients it cannot be monitored how many times the frequency of drug use is per day.

**Table 5.** Socio-demographic data of respondents by chi-square

variable	Range	Total	Min-Max	Mean	Median	Standard Deviation	category	P <0.05
Age	late adolescents (17-25 years)	15	8-19	13.53	13	± 2.800	good	0.008
	Early Adults (26-35 years old)	17	10-18	15.18	16	± 2.215	better	
	Late Adults (36-45 years old)	17	9-18	14.18	14	± 3.321	good	
	Early Elderly (46-55 years)	25	7-17	12.40	12	± 2.500	good	
	Elderly (56-65 years)	22	6-18	12.14	12	± 2.336	both	
	Geriatry (> 65 years)	17	7-17	11.53	12	± 2.961	both	
Gender	Women	78	6-19	13.12	13	±2.998	good	0.557
	male	35	7-18	12.91	13	± 2.694	good	
Education	Elementary	19	6-15	10.74	10	±2,705	low	0.000
	Junior High School	22	7-18	11.45	11	2.304 ±	good	
	Senior High School	51	8-18	13 ,08	13	± 2,106	good	
	Higher Education	21	15-19	16,76	17	± 1,179	Very good	

**Table 6.** Questionnaire respondent data based on the knowledge level

Variable		Frequency	Percent	Valid Percent
Level of knowledge	Poor	22	19.5	19.5
	Good	67	59.3	59.3
	Very good	24	21.2	21.2
	Total	113	100.0	100.0

In the elderly, the majority experience a decrease in body function or changes in the structure of the entire organ so that they can experience conditions with two or more diseases. The existence of complications of this disease makes medical personnel give several kinds of drugs to elderly patients which can later cause drug side effects and drug interactions. Of the 113 osteoarthritis patients who used analgesic drugs, 18.6% (21 patients) had the potential for interactions, in this case, the drug interactions that occurred were pharmacological and pharmacokinetic. The drugs that interact pharmacologically are diclofenac sodium and corticosteroid class drugs (dexamethasone) which increase the effect of diclofenac sodium, then diclofenac sodium and ARB drugs (candesartan) whose effects are decreased by diclofenac sodium and diclofenac sodium with an antacid class that can slow down the absorption of diclofenac sodium. For pharmacokinetic interactions, namely ibuprofen, ibuprofen with diuretics (hydrochlorothiazide) can reduce the natriuretic effect. This is in accordance with the British national formulary (BNF), drug information handbook (DIH) and (AHFS) literature.

Respondent analysis based on gender male 31% (35 respondents) female 69% (78 respondents). Analysis based on age, namely late adolescents 17-25 years (13.3%), early adults 26-35 years (15%), late adults 36-45 years (15%), early elderly 46-55 years (22.1%), the elderly aged 56-65 years (19.5%) and Geriatriy >65 years (15%) [14]. Analysis based on the latest education, namely elementary school as much as 16.8% (19 respondents), junior high school as much as 19.5% (22 respondents), Senior high school as many as 45.1 % (51 respondents), and Higher education as many as 18.6% (21 respondents).

Analysis of the patient's level of knowledge, in this case using a questionnaire. The questionnaire used in this study has been tested for validity and reliability with a random distribution of 30 respondents from the test results, the questionnaire is feasible and can be used. A questionnaire is said to be valid if the r count is greater than 0.362 and a questionnaire is said to be reliable. If the value of > 0.70 then all questions are reliable, meaning that the instrument is feasible and can be used for validity and reliability test results.

Analysis of the sociodemographic relationship obtained a value for the relationship between age

and knowledge level of (0.008). Based on the results of research that has been done, it can be explained that age is a factor that affects a person's level of knowledge. This is in accordance with the research conducted by Yeni (2015) where the p-value of  $0.007 < 0.05$  can be said to be rejected, which means that there is a relationship between age and knowledge. There are several factors that can affect a person's knowledge about something, one of which is the age factor [19], which states that age can affect a person's perception and mindset. Analysis of the sexual relationship with the level of knowledge obtained a value of (0.557). Based on the research that has been done, it can be explained that gender has no relationship with a person's level of knowledge. This is in accordance with the research conducted by Forid *et al* (2015) that gender does not have a significant relationship or does not affect a person's level of knowledge. Analysis of the relationship between the level of education and the level of knowledge obtained a value of (0.000). Based on the results of the research that has been done, it can be explained that the level of education has a significant relationship with the level of knowledge. This is in accordance with the research conducted by Yeni (2015) which results in 0.046, which means that there is a relationship between the level of education and knowledge [19]. In Istianah's (2013) research, the result is also 0.000, which means that there is a relationship between the level of education and the level of knowledge [20].

Analysis of high and low levels of patient knowledge of the use of analgesic drugs. The distribution was carried out to 113 respondents at random with the record that the respondents (patients) received a prescription for analgesic drugs. In this study, the patient's level of knowledge was divided into four, namely very poor, poor, good and very good. From the results of the analysis, the highest percentage was at the level of good knowledge of 59.3% (76 respondents) and the lowest was at the level of poor knowledge of 19.5% (22 respondents). A respondent (patient) is said to have a very poor level of knowledge getting a score of 5 which is answered correctly from the 20 questions given. For the level of knowledge that is said to be poor, it gets a score of 10 which is answered correctly from the 20 questions given. For the level of knowledge that is said to be good, it gets a score of 15 which is answered correctly from the 20 questions given. For the level of knowledge that is said to be very good, it gets a score of > 15 which

is answered correctly from the 20 questions given. Meanwhile, the level of very good knowledge was 21.2% (24 respondents), and there were no respondents with a very poor level of knowledge. In the research conducted by Meilina (2017), the score for respondents who have good knowledge is 11-20, while for respondents who have poor knowledge the score is 0-10. For respondents with high knowledge, the result is 98.3% (115 respondents) while respondents with low knowledge are 1.7% (2 respondents) [21].

Analysis based on each question found that the questions that most respondents could not answer correctly were in questions 8, 11, 12, 13 and 18. In question 8 regarding what types of drugs were consumed when they had a toothache, many respondents answered using antibiotics, compared to analgesic drugs to relieve toothache. Of the 113 respondents who answered correctly as many as 50 respondents with a percentage of 44.2% and the rest answered incorrectly. In question 11 regarding the dose of analgesic drug used for children over 12 years old, is it the same as the dose of analgesic drug used for children under 12 years old, the average answer from the respondents is yes. Of the 113 respondents who answered correctly as many as 48 respondents with a percentage of 42.5% and the rest answered incorrectly. In question 12 regarding the impact experienced when using analgesic drugs more than specified, the average answer from the respondents answered that the body was weak, where the answer should be kidney damage. Of the 113 respondents who answered correctly, 41 respondents with a percentage of 36.3% answered incorrectly. In question 13 regarding whether analgesic drugs can be taken continuously even though the pain has disappeared, the average answer is yes where the answer should be no. If the patient takes analgesic drugs continuously, side effects may occur, analgesic drugs themselves have side effects such as liver damage, stomach pain, dyspepsia, ulcers, gastrointestinal disturbances, flatulence, therefore long-term use of analgesic drugs is not recommended. Of the 113 respondents who answered correctly as many as 34 respondents with a percentage of 30.1% and the rest answered incorrectly. In question 18 regarding whether patients with blood clotting disorders (haemophilia, thrombocytopenia, uremia and cirrhosis) can take NSAIDs to relieve pain, the average answer from respondents answered yes, where the answer should be no. This is because patients who use NSAIDs in these conditions will worsen the patient's condition because NSAIDs are blood thinners. Of the 113 respondents who answered correctly as many as 51 respondents with a percentage of 45.1% and the rest answered incorrectly.

#### 4. CONCLUSION

1. The results of the evaluation of the rationality of therapy in osteoarthritis patients at the Dadok Tunggul Hitam Public Health Center, Padang City is there were 108 patients (95.6 %) included which having accuracy of dose in 113 patients (100 %), accuracy of drug selection in 18 patients (15.9 %), accuracy of indications in 113 patients (100 %), route accuracy in 113 patients (100 %), frequency accuracy (0 %), and 21 patients (18.6%) with potential drug interactions.
2. The results of the assessment of the patient's level of knowledge is poor (19.5%), good (59.3%) and very good (21.2%). Based on the results of the study, the patient's level of knowledge on the use of analgesic drugs, education level and age factors affect the respondent's level of knowledge in the use of analgesic drugs.

#### 5. SUGGESTIONS

1. There is a need for further research regarding the evaluation of the use of analgesic drugs in osteoarthritis patients and the level of patient knowledge of the analgesic class
2. The need for education about self-medication knowledge regarding the use of analgesic drugs to minimize errors in drug use.

#### REFERENCES

- [1] World Health Organization. *The Rational Use of Drugs*. Geneva: World Health Organization Geneva, 1985.
- [2] Ministry of Health. *Rational Drug Use National Action Plan*. Ankara Turkiye: Ministry of Health, 2017.
- [3] Kee, J. L. & Hayes, E. R. *Farmakologi pendekatan proses keperawatan*. Jakarta: Penerbit Buku Kedokteran EGC, 1996.
- [4] Dipiro, J.T., Wells, B.G., Schwinghammer, T.L., Dipiro, C.V. *Pharmacotherapy Handbook* (8<sup>rd</sup> ed). New York: The McGraw-Hill Companies, 2011.
- [5] Goldberg, D. S. & McGee, S. J. *Pain as a Global Public Health Priority*. Greenville: BMC Public Health, 2011.
- [6] Damayanti, D. *Hubungan Tingkat Pengetahuan dengan Penggunaan Obat Analgetik Pada Swamedikasi Nyeri Gigi di Masyarakat Kabupaten Sukohardjo*. (Skripsi). Surakarta: Fakultas Farmasi Universitas Muhammadiyah Surakarta, 2017.
- [7] Suari. *Gambaran Penderita Osteoarthritis di Bagian Bedah RSUD Arifin Achmad Periode*

Januari 2011-Desember 2013. JOM FK, 2015, 2 (2). 1-10.

[8] Isngadi, S. *Evaluasi Penggunaan Obat NSAID (Non-Steroid Anti Inflammatory Drug) Pada Pasien Osteoarthritis Rawat Jalan di RS TNI AD Robert Wolter Mongisidi Manado*. 2018, Malang: Universitas Islam Negri Malang.

[9] Felson, D. T. & Yuqing, Z. An Update on the Epidemiology of Knee and Hip Osteoarthritis with a View to Prevention. *Journal of America Collage of Rheumatology*, 1998, 41 (8). 1343-1355

[10] Guyton, A. C. & Hall, J. E. (1997). *Buku ajar fisiologi kedokteran* (9<sup>th</sup> ed). Jakarta: Penerbit Buku Kedokteran EGC.

[11] Maharani, E. *Faktor-Faktor Resiko Osteoarthritis Lutut (Studi Kasus di Rumah Sakit Dokter Karadi Semarang)*. 2007, Universitas Diponegoro.

[12] Departemen Kesehatan Republik Indonesia. *Klasifikasi Umur Menurut Kategori*. Jakarta: Direktorat Jenderal Pelayanan Kesehatan, 2009.

[13] Dipiro, J.T., Wells, B.G., Schwinghammer, T.L., Dipiro, C.V. *Pharmacotherapy Handbook* (8<sup>rd</sup> ed). New York, 2011, The McGraw-Hill Companies.

[14] Ikatan Rheumatoid Indonesia. *Diagnosis dan Penatalaksanaan Osteoarthritis*. Jakarta, 2014, PAPDI.

[15] Departemen Kesehatan Republik Indonesia. *Pharmaceutical Care Untuk Pasien Penyakit Arthritis Rematik*. 2006, Departemen Kesehatan Republik Indonesia. Jakarta

[16] Gilman, A. G. *Goodman & Gilman Dasar Farmakologi Terapi*. Diterjemahkan Oleh Tim Alih Bahasa Sekolah Farmasi ITB. Edisi 10, 2007. Jakarta: Penerbit Buku Kedokteran EGC.

[17] Ganiswarna, G. S. *Farmakologi dan terapi* (5<sup>rd</sup> ed). Jakarta, 2007, Fakultas Kedokteran Universitas Indonesia.

[18] Dipiro, J.T., Wells, B.G., Schwinghammer, T.L., Dipiro, C.V. *Pharmacotherapy Handbook*, 2009, (7<sup>rd</sup> ed). New York: The McGraw-Hill Companies.

[19] Yeni, P. S. I. *Faktor-faktor yang berhubungan di wilayah kerja puskesmas padang payang*

*kabupaten nagan raya tahun 2015*. Aceh, 2015. Fakultas Kesehatan Universitas Tengku Umar.

[20] Istianah. *Hubungan karakteristik masyarakat dengan pengetahuan tentang obat generik dipuskesmas wonoaya*, 2013. Access on 20 Februari 2020 at [http:// academica. Edu. Id](http://academica.Edu.Id)

[21] Meilina, A. A. *Pengaruh Edukasi Terhadap Tingkat Pengetahuan Swamedikasi Analgetik di Kecamatan Parang Kabupaten Jember*, 2017, Fakultas Farmasi Universitas Jember.