ORIGINAL ARTICLE

Assessing Analgesic Use and Pain Perception among Orthopedic Patients With Chronic Non-cancer Pain

Hooi Li Chen¹, Retha Rajah², Shi Qi Lee¹, Sin Yu Tang¹, Stephanie Tang¹, Kuang Kian Khoo³, Phei Ching Lim⁴, *Chong Yew Lee⁴

¹ Department of Pharmacy, Hospital Pulau Pinang, Jalan Residensi, Georgetown, 10990 Penang, Malaysia.

² Department of Pharmacy, Hospital Seberang Jaya, Jalan Tun Hussein Onn, Seberang Jaya, 13700 Penang, Malaysia.

³ Department of Pharmacy, Hospital Balik Pulau, Jalan Balik Pulau, Balik Pulau, 11000 Penang, Malaysia.

⁴ School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, 11800 Penang, Malaysia.

ABSTRACT

Introduction: Chronic non-cancer pain (CNCP) negatively impacts patient quality of life. Analgesics remain the main treatment for CNCP. However, little is documented about analgesic use and the pain characteristics among orthopedic patients with CNCP. Objective: This study aimed to evaluate the analgesic use and pain characteristics among orthopedic patients with CNCP. We identified the reasons for analgesic underuse and examined the factors associated with analgesic underuse. Methods: A cross-sectional study was conducted involving orthopedic patients with CNCP from the Orthopedic Clinic between September and December 2021. Data was collected at initial clinic visit and at Week 4 via telephone follow-up. The Numerical Rating Scale was used to determine pain scores. Results: 156 patients (62.2% female, mean age 56.7 years) were recruited with most diagnosed with osteoarthritis (27.6%) and degenerative diseases (24.4%). More than one-third of the patients were on single oral analgesics and 7.1% were not on any oral analgesics. Paracetamol was the common choice of analgesic for both single or combination analgesics regimen. Most (47.2%) of the analgesics were prescribed as needed. The pain score reduced significantly with initial median pain score of 6 (IQR 4-7) to 5 (IQR 3-6) at Week 4, p<0.001. Almost three-quarter (67.4%) of the patients underused their analgesics with most citing the reason being that the pain was tolerable. Oral analgesic was found to be significantly associated with analgesic underuse (p=0.022). Conclusion: Analgesics were generally underused. Further exploration into patient perceptions, beliefs, and factors affecting the pain tolerance is warranted.

Keywords: Analgesic use; Chronic non-cancer pain; Orthopedic patients; Underuse

Corresponding Author:

Chong Yew Lee, PhD Email: chongyew@usm.my Tel: +604-6534086

INTRODUCTION

Chronic pain is defined as persistent or recurrent pain lasting longer than 3 months [1]. It is among the commonest chronic condition around the world [2,3]. Chronic pain arising from non-malignant sources is referred to as chronic non-cancer pain (CNCP). According to the World Health Organization (WHO), CNCP can be considered as a chronic condition, characterized by one or more of the following characteristics: it is permanent, leaves residual disability, is caused by non-reversible pathological alterations, requires special training of the patient for rehabilitation, or may be expected to require a long period of supervision, observation, or care [4]. A basic approach to pain management should include the ability to recognize pain, assess the type of pain and to provide appropriate treatment. Appropriate treatment may include a combination of interventional procedures, physical therapy and psychological measures. Medication however, remains the commonest treatment modality in pain management. The types of pain medications include non-opioid, opioid, and adjuvant analgesics.

CNCP negatively affects patient quality of life and poses a huge burden to resources-limited healthcare systems. Poorly managed chronic pain results in relapses and increasing patient dependence on the support system, the feeling of frustration, and continued consumption of healthcare resources. Patients with chronic pain were associated with more hospitalization and emergency care visits compared to patients without pain [5]. Although there has been a recent increase in awareness on the importance of pain management, inadequate pain control continues to be a significant problem among patients with CNCP. Moreover, there is paucity of research on CNCP in low to middle income countries, with most focusing on cancer pain and opioids in managing this type of pain [6].

In 2008, pain has been recognized as the 5th vital sign in the management of patients in Malaysian public healthcare facilities, and later in 2011, the Pain Free Hospital initiative was launched to implement effective pain management involving multidisciplinary healthcare providers using a multimodality approach. Besides, all pain free health care facilities were required to have mandatory criteria, including a written policy on pain free program, implement pain as the 5th vital sign, practice standardized treatment protocols, conduct training for all health care staff on knowledge and skills in pain assessment and management, educate patients and get them involved in their own pain management and carry out regular audit [7]. The impact of the Pain Free Hospital initiative was apparent from the more timely and effective pain management by hospital staff, better knowledge and attitude of staff towards patients with pain and better patient satisfaction with their pain management [8]. Pain is highly prevalent among orthopedic patients; however available evidence mostly documents the general patient population [9-11] or patients under specialized services such as the pain clinic [12]. Thus, little is known on CNCP among orthopedic patients in Malaysia. This study aimed to evaluate the analgesic use and pain characteristics among orthopedic patients with CNCP particularly the type of analgesic medications used to manage their pain, the pain perception and scores and to identify underuse of the medications among these population. The reasons for the underuse and the factors associated with the underuse were also evaluated.

MATERIALS AND METHODS

Study Design

This was a cross-sectional study registered with the National Medical Research Registry (NMRR-20-2114-55753) and obtained approval from the Medical Research and Ethics Committee Ministry of Health, Malaysia.

Study sample and setting

This study was conducted at the Orthopedic Clinic, Hospital Pulau Pinang, Malaysia from September 2021 to December 2021. Patients aged 18 years and above with CNCP on at least one oral or topical analgesics, able to speak and write in either the English or Malay language, able to self-report their pain scores and could be reached by telephone were recruited using convenient sampling method. Patients were excluded if the diagnosis was malignant related pain, acute pain, or when the patient refused to participate. CNCP patients were patients who suffered from chronic pain continuously or intermittently for 3 months or more.

The sample size was determined with finite population formula. The total population of outpatient orthopedic

patients prescribed with analgesic was accessed through a computerized system namely the Pharmacy Hospital Inventory System (Phis). Sample size was calculated using the Raosoft® software. The number of participants required was 156 with an estimation of the orthopedic population with at least one prescribed analgesic was 260 with an alpha of 5%, confidence level of 95% and 50% response rate.

Study procedure and data collection

The eligible patients were briefed on the study objectives and procedure and written informed consents were obtained. The data were collected by two pharmacists (KKK, ST) using a structured data collection form. The pharmacists were trained on the data collection method and the telephone followup at Week 4. Data of demographic, pain-related characteristics such as diagnosis, location of pain and the pain score using the Numerical Rating Scale (NRS), prescribed analgesic for the pain, contact details, suitable date and time for telephone follow-up at Week 4 were collected and documented in the data collection form. At Week 4, the patients were contacted via telephone to assess the pain score based on the NRS, their balance of medication at home and reasons for not taking the analgesic if there was balance. The telephone follow-up length was about 15 minutes for most conversations. For patients who missed the call, three attempts were made on the same day and one attempt the following two days. If there was no response for the telephone follow-up could be obtained, the patients were deemed lost on follow-up.

Data analysis

Data was analyzed using the IBM SPSS Statistics version 25.0. A descriptive analysis was performed on the overall characteristics of the study population. Additionally, the analgesic type, dosing and the analgesic underuse were reported as frequencies and percentages. The pain scores at baseline and during the telephone follow-up were tested for normality, and noted to be not normally distributed. Median and interquartile range (IQR) were therefore calculated as a measure of central tendency. Only respondents who could be contacted for follow-up were included in the comparative analyses for pain severity scores at baseline and at Week 4 using the Wilcoxon Signed-rank test. The factors associated with analgesic underuse were analyzed using the Chi-square test. Underuse was defined as occurrence of balance of analgesic disclosed during the telephone follow-up. The pain was categorized a mild (1 - 4), moderate (5 - 6) and severe (7 - 10) based on the Chronic Pain Classification for International Classification of Disease 11th edition (ICD-11). Data was statistically significant when p value was <0.05.

RESULTS

A total of 156 orthopedic patients with CNCP were recruited. The majority of patients were female (62.2%), and of Chinese ethnicity (44.9%). The mean age was 56.69 ± 13.90 years with a large proportion of patients were in the age group of 40-79 years. More than three-quarter of the patients (77.6%) obtain a minimum level of secondary education. Table I detailed the demographic data.

 Table I : Demographic characteristics of orthopedic patients with CNCP.

Characteristics	Number (%)	
Gender		
Male	59 (37.8)	
Female	97 (62.2)	
Age, years, mean ±SD	56.69 ±13.90	
Age group, years		
20-39	21 (13.5)	
40-59	62 (39.7)	
60-79	68 (43.6)	
>80	5 (3.2)	
Ethnicity		
Malay	50 (32.1)	
Chinese	70 (44.9)	
Indian	28 (17.9)	
Others	8 (5.1)	
Highest Education Level		
No formal education/Primary Education	35(22.4)	
Secondary Education	83 (53.2)	
Tertiary Education	38 (24.4)	

The most common diagnosis for prescribing analgesic medications among outpatient orthopedic patients were osteoarthritis (27.6%) and degenerative diseases including spondylosis (24.4%), followed by trauma (21.8%) caused by injury, fall, accident or tear (Table II). More than half (51.9%) of the patients were on combination oral analgesics regimen and 7.1% were not on any oral analgesics. Paracetamol was a common choice of analgesic for both as single or combination analgesics to treat CNCP among orthopedic patients. Most (47.2%) of the analgesics were prescribed on a need basis. Methyl salicylate cream (26.3%) was the most prescribed topical analgesic followed by ketoprofen patch (14.1%). Similarly, these two topical preparations were preferred as combination for CNCP.

During the follow-up, 144 (92.3%) patients were able to be contacted and completed the study. The

Table II : Pain and analgesic related data for orthopedic patients with CNCP.

Characteristics	Number (%)
Duration of pain	
3- 6 months	78 (50.0)
7-12 months	37 (23.7)
> 12 months	41 (26.3)
Diagnosis for analgesic prescribing	
Osteoarthritis (OA)	43 (27.6)
Degenerative Diseases/Spondylosis	38 (24.4)
Trauma (Injury/Fall/Accident/Tear)	34 (21.8)
Slipped Disc	8 (5.1)
Shoulder Pain	7 (4.5)
Hand Pain	6 (3.8)
Arthritis	5 (3.2)
Spondylolisthesis	3 (1.9)
Others	12 (7.7)
Oral analgesics prescribed for CNCP	
Not on oral analgesic	11 (7.1)
Single oral analgesic	64 (41.0)
Paracetamol	19 (12.2)
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	
Celecoxib	26 (16.7)
Etoricoxib	3 (1.9)
Diclofenac	2 (1.3)
Opioids	
Tramadol	14 (8.9)
Combination of oral analgesics	81 (51.9)
Paracetamol + Celecoxib	15 (9.6)
Paracetamol + Diclofenac	3 (1.9)
Paracetamol +Tramadol	55 (35.3)
Tramadol + Celecoxib	2 (1.3)
Paracetamol + Tramadol+ Celecoxib	6 (3.8)
Topical analgesics	
Not on topical analgesics	36 (23.1)
Single topical analgesic	
Methyl Salicylate Cream	41 (26.3)
Diclofenac Gel	10 (6.4)
Ketoprofen Patch	22 (14.1)
Combination of topical analgesics	
Methyl Salicylate Cream + Ketoprofen Patch	34 (21.8)
Methyl Salicylate Cream + Diclofenac Gel	3 (1.9)
Diclofenac Gel + Ketoprofen Patch	9 (5.8)
Methyl Salicylate Cream + Diclofenac Gel + Ketoprofen Patch	1 (0.6)
Oral analgesic dosing (n=144)	
Regular dosing	35 (24.3)
As Needed	68 (47.2)
Regular and As Needed	41 (28.5)

	Number of patients with CNCP N (%)		Changes (%)
Pain severity category	Baseline	Follow-up	
Mild pain (1-4)	38 (26.4)	61 (42.4)	Increased 16.0 %
Moderate pain (5-6)	52 (36.1)	49 (34.1)	Reduced 2.1%
Severe pain (7-10)	54 (37.5)	34 (23.6)	Reduced 13.9 %

Table III : Self-reported pain scores at baseline and at follow-up (n = 144 patients)

Table IV : Factors associated with the prescribed analgesic underuse among orthopedic patients with CNCP (n = 132 patients)

	Is there still balance of oral analgesic available at home?		p-value
_	Yes (n= 89)	No (n=43)	_
Socioeconomic variables			
Gender			p=0.904
Male	32	15	
Female	57	28	
Age			p=0.649
20-39	13	5	
40-59	36	15	
≥60	40	23	
Ethnicity			p=0.216
Malay	33	11	
Chinese	35	20	
Indian	14	11	
Others	7	1	
Highest education level			p=0.943
No formal education/Primary Education	21	9	
Secondary Education	46	23	
Tertiary Education	22	11	
Pain related characteristics			
Duration of pain			p=0.334
3- 6 months	43	23	
7-12 months	19	12	
> 12 months	27	8	
Oral analgesic use			р=0.022
Single	33	25	
Combination	56	18	
Pain severity			p 0 524
Mild (1-4)	37	19	p=0.524
Moderate (5-6)	33	12	
Severe (7-10)	19	12	
Oral analgesic dosing			p=0.738
Regular dosing	23	12	
	46	15	
Regular and As Needed	19	17	

 $^{\rm b}$ p ≤0.05 using the χ2 test.

median reported pain score of the study population at baseline was 6 (IQR 4-7), and at Week 4 was 5 (IQR 3- 6) indicating a significant reduction in the pain score (p<0.001). Number of patients with severe pain (pain score range from 7 to 10) had reduced from 54 patients to 34 patients at the fourth week. Table III shows self-reported pain severity at baseline and follow-up.

Out of 132 patients on oral analgesics, almost threequarter (67.4%) of the patients claimed that they still had balance of the medication dispensed to them at Week 4. When asked the reason for having balance of the medication, most of the patients claimed that their pain was tolerable (67.0%), followed by the reason that they were seeking for alternative approach for their pain (9.1%) (Fig. 1). Only oral analgesic use as single or in combination was associated with the underuse of prescribed analgesics among the patients with CNCP (Table IV).

DISCUSSION



Fig. 1 : Factors contributing for balance of oral analgesic.

To our best of knowledge, this was the first study to provide valuable findings on pain characteristics and analgesic medication use, the underuse of prescribed pain medication and potential reason for the underuse among orthopedic patients with CNCP in Malaysia.

In this study, analgesics were most commonly prescribed for CNCP due to osteoarthritis and degenerative disease. A prior study conducted among general patients attending outpatient clinics in Malaysia reported a similar trend [9]. However, several other studies revealed fracture as the main indication for analgesic prescribing in orthopedic patients [13, 14]. Notably, these studies were conducted outside Malaysia and in inpatient settings. As the population age in Malaysia, musculoskeletal disorders with pain have become an important disease burden and the commonest reason for patients to seek medical attention [10]. Physiological processes such as structural changes and reduced body functions in the elderly increase the prevalence of CNCP among the elderly.

Our findings indicated that knee osteoarthritis (OA) was the most common diagnosis that cause CNCP among the elderly patients. The modifiable risk factors of developing knee OA include body mass index (BMI) and history of knee injury [15]. Identifying the modifiable risk factors above can help in prevention of OA and its progression. Lifestyle interventions, including weight reduction and physical activity or exercise are effective in pain reduction and prevention of disease progress [16]. Therefore, these interventions should be emphasised as the preventive measures in the pain management and should be started as soon as possible to improve pain. Furthermore, patient education is an important approach in the disease management. Patient education should include nature of the disease, therapeutic options and the importance of patient participation in the disease management. Patients who have better understanding of their disease tend to cope better and report less pain. The growing burden borne by these diseases especially in the elderly, creates a need for a more careful approach in their pain management as this population is vulnerable with altered organ functions that may affect the pharmacokinetics and pharmacodynamics of the prescribed analgesics. Pharmacists as the accessible medication expert have important roles to assess the history of patients' prescribed analgesics to minimize risk of adverse effect, in addition to providing effective advice on analgesics use. However, a study showed both physicians and pharmacists lacked in the aspects of CNCP management for elderly population. A continuing education program to improve knowledge and competency in managing CNCP is relevant and perceived as necessary by clinicians. Continuing education program was found to improve the longitudinal pain management in this population [17].

In CNCP, medication continues to be the main component of treatment modality. In line with the World Health Organization (WHO) analgesic ladder, paracetamol was the most common analgesic prescribed for both single or combination analgesics to treat CNCP in this study population followed by celecoxib, a nonsteroidal anti-inflammatory drug (NSAID). A six years data on the trend and pattern of analgesic prescribing in two tertiary Malaysian public hospitals showed that NSAIDs were most commonly prescribed in orthopedic patients [11]. Paracetamol is recommended as a first line treatment for musculoskeletal pain due to its efficacy and good safety profile. However, there are contraindications to paracetamol. These include active hepatic disease and severe hepatic impairment. Malnutrition, chronic alcohol misuse and concomitant use of drugs that induce cytochrome P450 enzymes may increase the risk of hepatotoxicity induced by paracetamol. Therefore, it is important to educate patients not to exceed the recommended maximum daily dose of 4 grams [18]. It was suggested that paracetamol doses

should be titrated to its lowest for optimum analgesic effect, which are different for every elderly individual to prevent liver complications [19]. Furthermore, tramadol was another common analgesic found to be highly prescribed as combination with either paracetamol or NSAIDs in the present study. The local guide on the management of OA recommended the use of tramadol as combination if the first line fails to relieve the pain [20]. Tramadol, a remarkable opioid analgesic often provides modest improvement in pain with substantial safety profile in terms of gastrointestinal and cardiovascular side effects compared to NSAIDs. However, it may cause confusion in older people. The use in older people have been associated with increased risk of falls and fractures [21]. The potential adverse effects include nausea, vomiting, drowsiness, dizziness and sweating. Tramadol should also be used with caution in patients taking other serotonergic drugs. Therefore, this opioid drug should only be prescribed in exceptional circumstances when other treatments have failed, and when there is evidence of use, efficacy, side effects and potential interaction with their prescription medication.

Effective pain management is achieved when there is reduction in pain intensity. In this study, despite significant improvement reported in the pain scores at the follow-up, a substantial percentage of patients still experienced severe pain (pain scores of 7 to 10). Inadequate pain control has negative implication to the patient's quality of life. In a study among 61.5% employed patients with CNCP, more than half reported their pain affected work performance and some raised concern on losing their job [22]. Similarly, in a survey conducted in ten Asian countries involving 1,305 patients experiencing CNCP showed 62.6 % of them stated work performance was disrupted by their chronic pain. Additionally, disruption of sleep patterns and focus were reported in 80% and 79.4% of the patients respectively [23].

Most of our study orthopedic patients claimed there was balance of pain medication at home during the follow-up indicating underuse of the pain medication dispensed to them. Underuse of analgesic among patients with CNCP was a common issue reported widely in studies investigating pain medication adherence [24, 25]. Underuse of analgesic was reported more frequently than overuse which could lead to inadequate pain control among CNCP patients [24]. Several factors cited in the literature for the underuse of pain medication were lower pain intensity, non-pharmacological coping strategies and higher number of prescribed analgesics [24]. Consistently, that the pain was tolerable and has resolved were the same reasons offered for underuse of the analgesic in the present study. The high percentage of analgesic underuse due to tolerable pain warrants further exploration into factors affecting the patients' pain

tolerance. Besides, the oral analgesic use as single or combination was significantly associated with underuse of analgesic of our study population. Furthermore, approximately 3.4% of the orthopedic patients claimed their medication was ineffective. A prior study reported one-quarter of the patients with pain described their opioid analgesic was ineffective.[26] Interestingly, some of the patients claimed they intentionally underuse the pain medication out of fear that the medication would finish. Besides, 5.7% of the patients concern about side effects. These findings highlighted the need for an immediate action to strengthen healthcare providerpatient communication. Communication is the key in chronic conditions such as CNCP; communication with patient-centered approach that focuses on patients' experiences and views, being non-judgmental and open about their concerns, tailoring the regime and fostering shared decision-making are crucial [27]. Communication should also address personal barriers and beliefs on pain medication. Given the significant underuse of analgesics reported, future studies could delve into understanding patient perceptions, beliefs, and barriers related to analgesic use. Besides, these findings also highlighted that patient education is needed to ensure appropriate use of pain medication and increase patients' understanding on their medication. A study showed that knowledge of the prescription significantly contributes to the prediction of adherence to pain medication [28]. Furthermore, involvement of the family members and caregivers are important in the management of CNCP as they contribute to the treatment plan including reporting the pain, filling of prescription, and administration of the medication and emotional support especially in elderly patients [29].

Pharmacists play a vital role in the care of CNCP patients. The study findings addressed that pharmacists need to do more in educating patients about the safe use of their pain medication, in addition to reviewing patients' past and current medication to minimise risk of adverse effect. Pharmacists should actively collaborate with other healthcare providers to optimise the pain management [30]. Pain medication therapy management clinic (Pain MTM Clinic) is conducted by pharmacists in collaboration with other healthcare providers to provide pain pharmacotherapy service. This service was limited to pain clinic in Hospital Pulau Pinang. The finding of this study suggested the need to expand the service to orthopedic clinic.

This study has few limitations. The patients included was from only one tertiary public hospital, hence the findings might not be generalizable. However, the setting was one of the few tertiary public facilities that offer orthopedic specialty in Penang state of Malaysia. Besides, 7.7 % of the patients were unable to be contacted during the follow-up that might affect the findings, however this loss to follow-up was relatively small. Furthermore, the recruitment of the patients with CNCP involved convenience sampling that could overestimate or underestimate the findings. The follow-up data was solely based on self-reporting, which could be influenced by recall bias or social desirability. Yet, this method has been demonstrated to be a reliable and non-judgmental way of getting pain related information from patients. The factors affecting the pain tolerance were not studied. Hence, future research includes factors related to pain tolerance needs to be conducted.

CONCLUSION

Based on this study conducted among orthopedic patients with CNCP, the findings showed the majority were prescribed with at least one analgesic and paracetamol was the most frequently prescribed oral analgesic as single or in combination with other analgesic. The pain score reduced significantly although some patients were still experiencing severe pain during the follow-up after 4 weeks. A large percentage of analgesic underuse was mainly due to the tolerable pain. Only oral analgesic use as single or combination was significantly associated with their analgesic underuse. These study findings suggested the need for training and communication skills to healthcare providers to optimize the management of CNCP among orthopedic patients.

ACKNOWLEDGEMENT

The authors thank the Director General of Health Malaysia for the permission to publish this paper.

REFERENCES

- 1. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. A classification of chronic pain for ICD-11. Pain. 2015;156(6):1003-7. doi: 10.1097/j. pain.00000000000160.
- 2. Mohamed Zaki LR, Hairi NN. A Systematic Review of the Prevalence and Measurement of Chronic Pain in Asian Adults. Pain Manag Nurs. 2015;16(3):440-52. doi: 10.1016/j.pmn.2014.08.012.
- 3. Ospina M, Harstall C. Prevalence of chronic pain: an overview. Vol. 28. Alberta: Alberta Heritage Foundation for Medical Research Edmonton; 2002.
- 4. Sabaté E. Adherence to long-term therapies: evidence for action. World Health Organization; 2003.
- 5. Blyth FM, March LM, Brnabic AJ, Cousins MJ. Chronic pain and frequent use of health care. Pain. 2004;111(1-2):51-8. doi: 10.1016/j. pain.2004.05.020.
- 6. Morriss WW, Roques CJ. Pain management in low- and middle-income countries. BJA Educ. 2018;18(9):265-270. doi: 10.1016/j.

bjae.2018.05.006.

- 7. Pain Free Program: Pain Free Manual 3rd Edition. Ministry of Health Malaysia; 2023.
- 8. Mary Suma Cardosa. Pain Free Hospital and its implementation. Malaysian Orthopedic Journal. Current Issue MOA Scientific Meeting Abstract Supplement; 2017 Vol. 11.
- 9. Cheah HM, Harun MA, Ahmad NFAnalgesic Dosing Behaviours in Patients with Chronic, Non- Cancer Pain: Does it Affect the Pain Control. Malaysian Journal of Pharmacy. 2021; 28-33. doi: 10.52494/AVKA5257.
- 10. Zailinawati AH, Teng CL, Kamil MA, Achike FI, Koh CN. Pain morbidity in primary care preliminary observations from two different primary care settings. Med J Malaysia. 2006;61(2):162-7.
- 11. Zin CS, Nazar NI, Rahman NS, Alias NE, Ahmad WR, Rani NS, et al. Trends and patterns of analgesic prescribing in Malaysian public hospitals from 2010 to 2016: tramadol predominately used. J Pain Res. 2018; 11:1959-1966. doi: 10.2147/JPR. S164774.
- 12. Ang JY, Leong EL, Chan HK, Shafie AA, Lee SQ, Mutiah P, et al. Health-related quality of life of Malaysian patients with chronic non-malignant pain and its associated factors: a cross-sectional study. BMC Musculoskelet Disord. 2022;23(1):400. doi: 10.1186/s12891-022-05354-1.
- 13. Choudhury DK, Bezbaruah BK. Prescribing pattern of analgesics in orthopedic in-patient department at tertiary care hospital in Guwahati, Assam, Northeast India. Indian J Pharmacol. 2016;48(4):377-381. doi: 10.4103/0253-7613.186207.
- 14. Abhilash S, Rao RR. Assessment of prescribing pattern among orthopedic in-patients using WHO prescribing indicators. Asian journal of pharmaceutical and clinical research. 2018;11(12):505-509.
- 15. Blagojevic M, Jink, C, Jeffery A, et al. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2010 Jan;18(1):24-33
- 16. Pendleton A, Arden N, Dougados M, et al. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis. 2000 Dec;59(12):936-44.
- 17. Lalonde L, Leroux-Lapointe V, Choinière M, Martin E, Lussier D, Berbiche D, et al. Knowledge, attitudes and beliefs about chronic noncancer pain in primary care: a Canadian survey of physicians and pharmacists. Pain Res Manag. 2014;19(5):241-50. doi: 10.1155/2014/760145.
- 18. Claridge LC, Eksteen B, Smith A, Shah T, Holt AP. Acute liver failure after administration of paracetamol at the maximum recommended daily dose in adults. Br Med J 2010; 341: c6764.
- 19. Ministry of Health Malaysia. Guidelines for pain

management in the elderly. 1st ed. Ministry of Health Malaysias; 2018.

- 20. Academy of Medicine Malaysia. Clinical Practice Guidelines. Management of Osteoarthritis. 2nd ed. [Internet] [Cited on 2023, January 15] Available from: http:// www.acadmed.org.my/index. cfm?&menuid=67.
- 21. Yoshikawa A, Ramirez G, Smith ML, Foster M, Nabil AK, Jani SN, et al. Opioid Use and the Risk of Falls, Fall Injuries and Fractures among Older Adults: A Systematic Review and Meta-Analysis. J Gerontol A Biol Sci Med Sci. 2020;75(10):1989-1995.doi: 10.1093/gerona/glaa038.
- 22. Ho KY, Ahn JS, Calimag MM, Chao TC, Kim YC, Moon H, et al. Inadequate treatment practices for pain relief and adverse event management in cancer patients across 10 countries/regions in Asia: a call for greater efforts to improve standards for patient care. Asia Pac J Clin Oncol. 2018;14(3):159-166. doi: 10.1111/ajco.12696.
- 23. Cheung CW, Choo CY, Kim YC, Lin FS, Moon SH, Osio-Salido E, et al. (2016) Collaborative Efforts May Improve Chronic Non-Cancer Pain Management in Asia: Findings from a Ten-Country Regional Survey. J Pain Relief 5:225.doi:10.4172/2187-0846.1000225
- 24. Broekmans S, Dobbels F, Milisen K, Morlion B, Vanderschueren S. Determinants of medication underuse and medication overuse in patients

with chronic non-malignant pain: a multicenter study. Int J Nurs Stud. 2010;47(11):1408-17. doi: 10.1016/j.ijnurstu.2010.03.014.

- 25. McCracken LM, Hoskins J, Eccleston C. Concerns about medication and medication use in chronic pain. J Pain. 2006;7(10):726-34. doi: 10.1016/j. jpain.2006.02.014.
- 26. Lewis ET, Combs A, Trafton JA. Reasons for underuse of prescribed opioid medications by patients in pain. Pain Med. 2010 Jun;11(6):861-71. doi: 10.1111/j.1526-4637.2010.00868.x.
- 27. Butow P, Sharpe L. The impact of communication on adherence in pain management. Pain. 2013;154 Suppl 1:S101-S107. doi: 10.1016/j. pain.2013.07.048.
- 28. Timmerman L, Stellema R, Stronks DL, Groeneweg JG, Huygen FJ. Adherence to pharmacological pain therapy: the role of patients' knowledge of pain medication. Pain Pract 2013 Nov 13;. doi:10.1111/ papr.12139.
- 29. Glajchen M. Chronic pain: treatment barriers and strategies for clinical practice. J Am Board Fam Pract. 2001;14(3):211-8
- 30. Murphy L, Ng K, Isaac P, Swidrovich J, Zhang M, Sproule BA. The Role of the Pharmacist in the Care of Patients with Chronic Pain. Integr Pharm Res Pract. 2021 Apr 30; 10:33-41. doi: 10.2147/IPRP. S248699