

## Enhancing Awareness of Diclofenac as an Over-the-Counter Analgesic in the Northern Border Region of Saudi Arabia

### ABSTRACT

**Introduction:** Diclofenac was identified by the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency as a high-risk NSAID in terms of its effects on the heart and circulation when administered systemically, i.e. capsules, tablets or injections.

**Objective:** To evaluate the knowledge and awareness about over the counter analgesic medication (Diclofenac) among people living in northern border region – Saudi Arabia.

**Methodology:** Self-administered cross-sectional study conducted during a period of two months (October and November 2023) on random sample of 430 Saudi people living in the Northern Border Region. The data was analyzed by Microsoft excel program by means of Descriptive statistics.

**Results:** Toothache and headache were the most worried pain among participants (32%) and (31%) respectively, majority (72%) of participants buy OTC medication for pain from community pharmacy on the advice of pharmacist. Small percentage (20%) thought that medications containing diclofenac have very few side effects, 76% didn't know any side effect of diclofenac, 47% didn't know that diclofenac in high dose has adverse effects on kidney, 71% didn't know that diclofenac cause gastrointestinal adverse effects. About one fifth of participants (21%) didn't know the maximum dose of diclofenac when they use it, tablet is the preferred dosage form of diclofenac (27%) followed by granules (16%), dosage of 100 mg is the most frequently used (36%) followed by 50 mg (16%).

**Conclusion:** Saudi people's knowledge about diclofenac as one member of non-steroidal anti-inflammatory drugs was insufficient. Knowledge about related adverse effects of diclofenac was lacked which exposes to misuse that may carry accidents and severe side effects especially among high-risk population.

## INTRODUCTION

“Pain is a common condition and has a significant influence on the quality of life”<sup>1,2,3</sup>. It was defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”<sup>4</sup>.

“Analgesics, commonly known as painkillers, are substances which work in various ways to relieve different types of pain experienced in the body”<sup>5</sup>. “Non-prescription over-the-counter (OTC) analgesics are widely used by patients to control aches, pain, and fever”<sup>6,7</sup>. Over-the-counter (OTC) (non-prescribed) analgesics that are generally used by the public are paracetamol, weak opioids such as codeine, and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, diclofenac and aspirin.

“NSAIDs produce analgesic effects, reduce inflammation and are anti-pyrexial”<sup>8</sup>. “NSAIDs inhibit COX. There are two main isoforms of COX, COX-1 (expressed in most tissue and blood platelets and with a homeostatic role) and COX-2 (induced in inflammatory cells by cytokines)”<sup>9</sup>. “The inhibition of COX-1 and COX-2 by NSAIDs causes inhibition of the biosynthesis of prostaglandins. This produces the anti-inflammatory effect of NSAIDs with a decrease in vasodilatory prostaglandins. Prostaglandins are responsible for increasing the body’s core temperature set point during fever. NSAIDs reverse this effect by causing inhibition of prostaglandin production”<sup>10</sup>. “By contrast with the above beneficial effects, NSAIDs increase the risk of gastrointestinal mucosal damage by reducing COX-1-derived prostaglandin production. The amount of damage to the upper gastrointestinal depends on many factors, such as prior history of peptic ulcer and age”<sup>11</sup>. Hargreave et al. demonstrated that “age is closely associated with continuous analgesic use, which may explain why age can also have an effect on the prevalence of gastrointestinal damage due to analgesics”<sup>12</sup>.

“Successful pharmacotherapy is largely dependent on patient adherence and a rational choice of drug. Information regarding the pharmacological properties of the drugs including instructions for use and warnings, as well as the indication and justification should be delivered to the patients effortlessly via education”<sup>13,14</sup>.

“A readable and correct prescription does not guarantee appropriate use by the patient”.<sup>13,14</sup> Failure to provide such information may lead to poor compliance,<sup>15,16</sup> where physician as well as the pharmacist can play an important role in delivering the information in order to improve patient compliance.

## **RATIONALE OF THE STUDY**

“The reason of high usage of analgesics was explained by an American study which revealed that public perceive analgesics as safe, effective and with fewer side effects”.<sup>17</sup>

“Previous studies have indicated that self-medication should be done under special caution. Even for OTC medications like diclofenac, most people are not familiar with the possible risks and should be advised by health professionals before side effects occur”.<sup>18</sup> “However, little is known about what people believe about mild analgesics, especially diclofenac, and whether these beliefs are associated with the way they use them” .[18] To our knowledge there are little studies evaluate knowledge about analgesic and their side effects in Saudi Arabia.

## **OBJECTIVE OF THE STUDY**

### **Primary objective:**

To evaluate the knowledge and awareness about over the counter analgesic medication (Diclofenac) among people living in northern border region – Saudi Arabia

### **Secondary objective:**

To evaluate Saudi people’s awareness about the diclofenac side effects

To determine the most commonly used **drug** form and dose of diclofenac

## **LITERATURE REVIEW**

“Non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, naproxen and ibuprofen, have analgesic/ antipyretic and anti-inflammatory properties across a wide range of dosing regimens. Various prescription-strength NSAIDs are effective for relief

of chronic musculoskeletal pain and inflammation in conditions such as rheumatoid arthritis (RA) or osteoarthritis (OA). Lower, Over-The-Counter (OTC) doses of NSAIDs are effective for short-term (e.g.,  $\leq 10$  days) relief of minor aches and pains due to headache, toothache, backache, menstrual cramps, common cold, muscular aches, and arthritis. NSAIDs taken at OTC doses can also be effective at relieving painful episodes in patients with chronic diseases such as OA".<sup>19</sup>

"NSAIDs are the most commonly used drugs in the United States (U.S.), with approximately 90 million prescriptions being filled yearly, which account for about 5% of all prescriptions".<sup>20</sup>"It is estimated that over-the-counter (OTC) NSAIDs are used 6 to 8 times more often than prescription NSAIDs".<sup>21,22</sup> Most oral NSAIDs are now available as generics and are generally considered to be safe and effective.

"Both oral and topical NSAIDs inhibit the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzymes that catalyze the synthesis of prostaglandins from arachidonic acid. These prostaglandins are partially responsible for the development of pain and inflammation associated with various medical conditions. COX-1 has a major role in maintaining normal gastric mucosa and influences kidney function. COX-2 activity is rapidly upregulated during inflammatory pain conditions and may be involved in the pathogenesis of some malignancies".<sup>23-26</sup>

"First pass metabolism may impact oral administration and has the potential for systemic adverse effects".<sup>27</sup> "A route of administration that bypasses the systemic exposure would provide an alternative that consequently minimize adverse effects, allow for a fewer administration, improve patient adherence, and serve as a substitute to conventional therapy. NSAIDs reduce swelling and ease inflammation that can cause pain".<sup>[27]</sup>

"NSAIDs are used for pain from different etiologies and commonly used to treat osteoarthritis. Oral and topical NSAIDs are among pharmacologic therapies recommended for osteoarthritis of the hand, knee, and hip by the 2012 American College of Rheumatology (ACR)".<sup>28</sup>"The 2013 treatment guidelines from the American Association of Orthopedic Surgeons for the treatment of osteoarthritis of the knee do not specify a specific NSAID or route of administration for osteoarthritis symptoms".<sup>29</sup>"If the risk of GI adverse events is increased, the topical route is preferred among other

treatment strategies. Similarly, the American Academy of Orthopedic Surgeons clinical practice guidelines (2017) on the management of osteoarthritis of the hip note strong evidence to support NSAIDs to improve short-term pain, function, or both in patients with symptomatic osteoarthritis of the hip however, does not specify a specific NSAID”.<sup>30</sup>“The American College of Physicians (ACP) in an update to their former 2007 guidelines, recommends nonpharmacological therapy (e.g., heat, massage, acupuncture, spinal manipulation) as first-line for acute/subacute low back pain lasting 12 weeks or more”.<sup>31</sup> For acute or subacute pain, NSAIDs or skeletal muscle relaxants may be used. For chronic pain (> 12 weeks), the first-line recommendation is non-drug therapy (e.g., exercise, multi-approach rehab, acupuncture, stress reduction); however, NSAIDs may be added if needed, followed by tramadol or duloxetine. If prior therapy fails and the potential benefits outweigh risks, opioids for chronic pain can be considered.

“In addition, American College of Physicians published new guidelines forgout in 2016 recommending corticosteroids, NSAIDs, and colchicine to treat patients with gout flare”.<sup>32</sup> Use of NSAIDs is based on high-quality evidence demonstrating their ability to reduce pain in this patient population. NSAIDs (including selective agents) have similar efficacy and have similar efficacy to corticosteroids. In addition, NSAIDs for prophylactic therapy can also reduce the risk for gout flare in patients starting urate-lowering therapy.

“NSAIDs are associated with adverse effects including peptic ulcer disease, gastrointestinal (GI) bleeding, renal disease hypertension and edema. In addition, NSAIDs have been linked with an increased risk of myocardial infarction (MI) which is reflected in the boxed warning for all NSAIDs. In July 2015, the Food and Drug Administration (FDA) issued a Safety Alert strengthening the existing warning on the increased risk of heart attack and stroke risk associated with NSAIDs”.<sup>33</sup>“GI adverse effects induced by NSAIDs lead to significant morbidity and mortality. Ulcers are found by endoscopy in 15% to 30% of patients who are using NSAIDs regularly, and the incidence of upper GI clinical events due to NSAIDs is 2.5% to 4.5%. In the U.S., GI side effects due to NSAIDs in patients with arthritis account for approximately 107,000 hospitalizations and result in 16,500 deaths each year”.<sup>34</sup>

“Diclofenac was identified by the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency as a high-risk NSAID in terms of its effects on the heart and circulation when administered systemically, i.e. capsules, tablets or injections”.<sup>35</sup>“Individual drugs carry differing degrees of risk within the larger group of NSAIDs. Naproxen and low-dose ibuprofen carry the lowest cardiovascular risk, while diclofenac, at available OTC doses, carries a higher risk”.<sup>36</sup>

## **MATERIALS AND METHODS**

### **3.1. Study Design and area**

This is a Cross-sectional study in Northern Border Region-Saudi-Arabia

### **3.2. Sampling and sample size**

Random sample of 430 Saudi people

All data were processed and analyzed using Microsoft excel Statistical program by means of Descriptive statistics with representation by bar graph.

#### **3.2.1. Inclusion criteria:**

- Age is  $\geq$  18 years
- Saudi in nationality
- Currently or previously used analgesic
- Willing to respond to the study questionnaire

#### **3.2.2. Exclusion criteria:**

- Incompletely answered questionnaires
- Age is  $<$ 18 years
- Healthcare practitioners

### **3.3. Data Collection Process and duration**

The data was collected for two months (October and November 2023)using questionnaire.

### **3.4. Data collection tool**

The data was collected by using closed ended self-administered questionnaire in Arabic language, the questionnaire designed through searching in related scientific references (e.g. pharmacology and pharmaceutic text books).

The questionnaire included 5 parts

- Demographic characteristics of Participants
- Participantsexperiences about pain sensation
- Attitude of participants toward OTC analgesics
- Knowledge of participants about diclofenac
- Practices of participants toward diclofenac use

The questionnaire was tested for its readability and understanding to the public before distribution. All participants were asked to answer all questions. All incomplete questionnaires were omitted from the study.

## **RESULTS**

### **4.1. Demographic characteristics of respondents**

Demographic characteristics of respondents represented in (Fig.1.)Regarding the gender, 91% of participants were females. More than two thirds of participants (61%) had university education. Furthermore, majority of participants (72%) of were in the age group (18-25) years.

### **4.2. Participants answer about pain sensation**

More than one third of participants (32%) reported frequency of pain as once monthly, 13% reported once weekly. Teeth pain and head pain were the most worried pain among participants (32%) and (31%) respectively. 31% of participants usually buy themselves OTC drugs without prescription when treating pain. (Fig. 2)

### **4.3. Attitude of participants toward OTC analgesics**

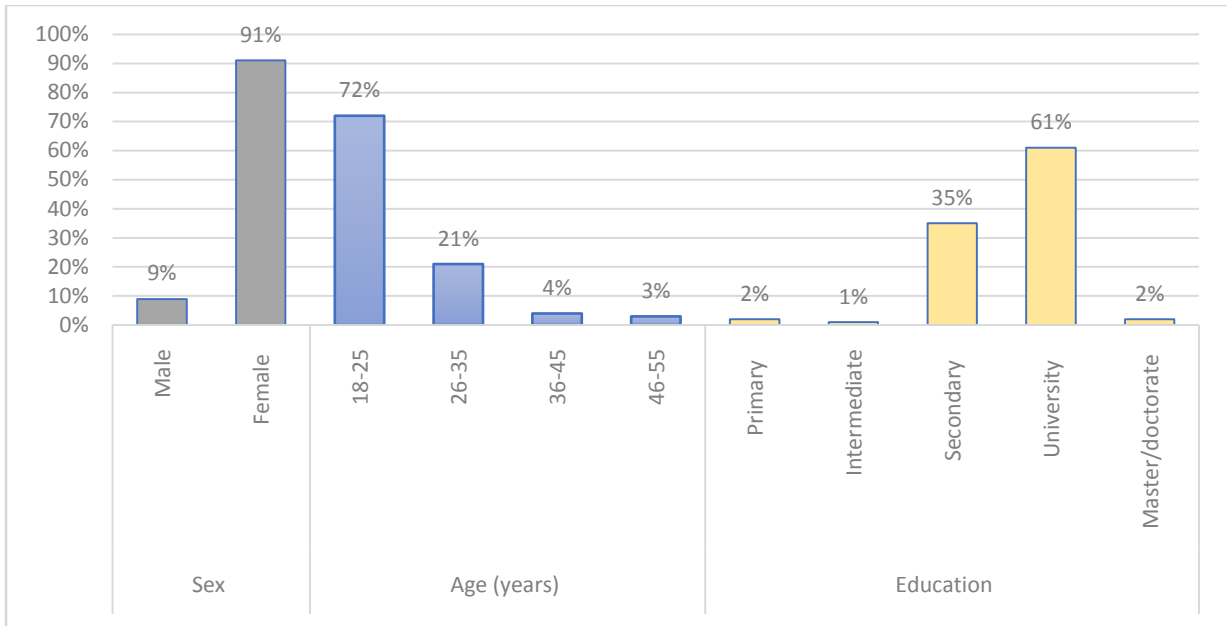
Majority (72%) of participants believe that OTC medication for pain can be bought from a pharmacy/medical store on the advice of pharmacist, (74%) keep analgesic medicine in their homeand (10%)only buy it when necessary.(Fig 3)

#### **4.4. Knowledge of participants about diclofenac**

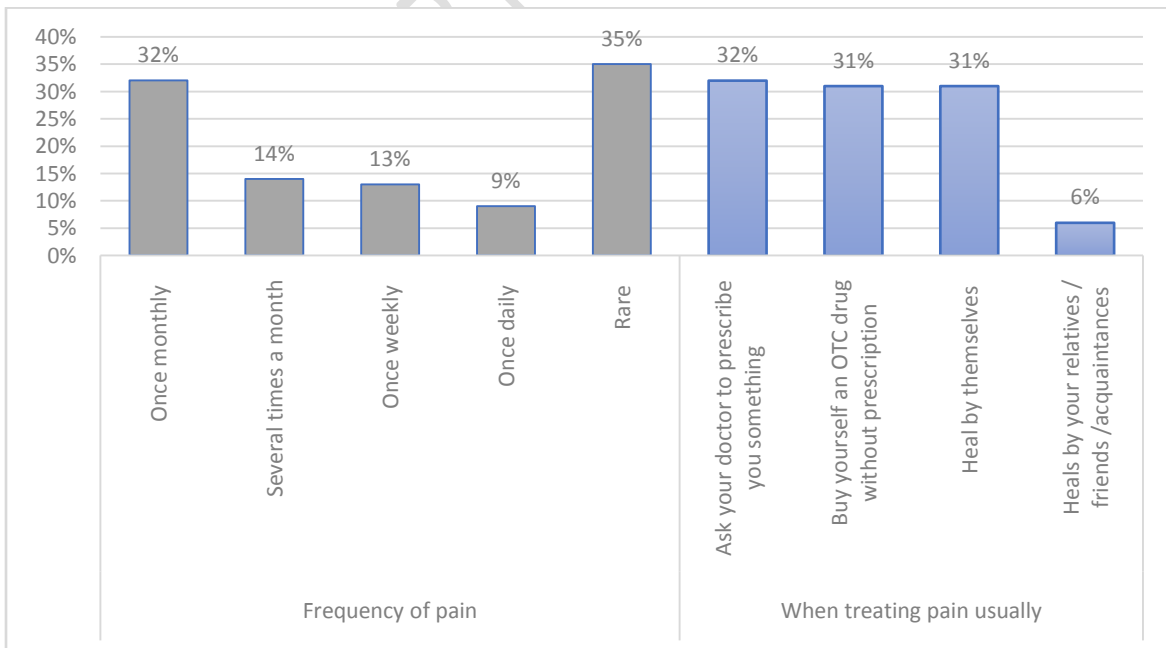
Less than half (46%) of participants were aware that diclofenac is a major component of dosage regimen for pain, 20% thought that medications containing diclofenac have very few side effects, 76% didn't know any side effect of diclofenac, 60% didn't know that diclofenac in high dose has adverse effects on heart, 47% didn't know that diclofenac in high dose has adverse effects on kidney, 70% didn't know that diclofenac is not recommended for elderly, 71% didn't know that diclofenac is not recommended for hypertensive patients, 72% didn't know that diclofenac is not recommended for asthma patients, 71% didn't know that diclofenac causes gastrointestinal adverse effects and 71% didn't know about drug interactions of diclofenac. (Fig 4)

#### **4.5. Practices of participants toward diclofenac use**

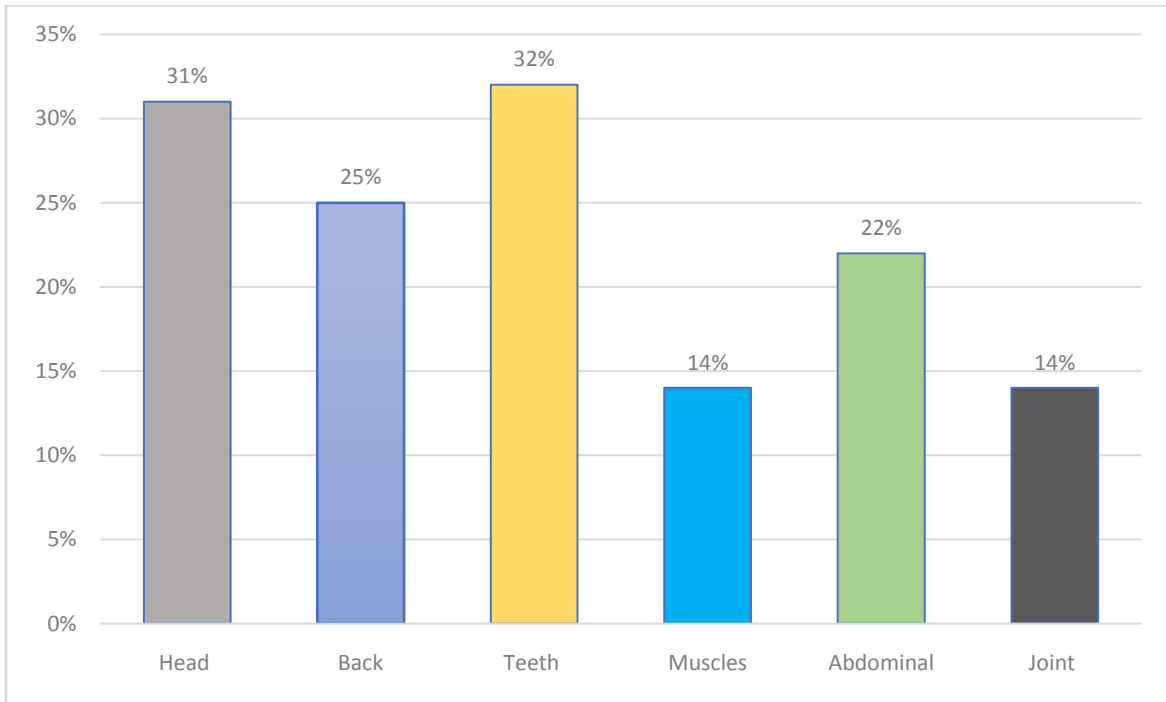
More than half of participants (57%) will stop the drug and try another analgesic if they didn't feel better after taking analgesic drug while 20% will increase dose. About one fifth of participants (21%) didn't know the maximum dose of diclofenac when they use it. 24% of participants use analgesic without prescription while 37% sometimes use it with prescription and sometimes without. Tablet is the preferred dosage form of diclofenac (27%) followed by granules (16%). Dosage of 100 mg is the most frequently used (36%) followed by 50 mg (16%). More than one half (26%) reported that pharmacist never asks them about other medications they are taking when they purchase diclofenac however, 31% of the participants had been informed by the pharmacists about maximum daily dose and 24% informed about the proper use of NSAIDs. (Table 1)



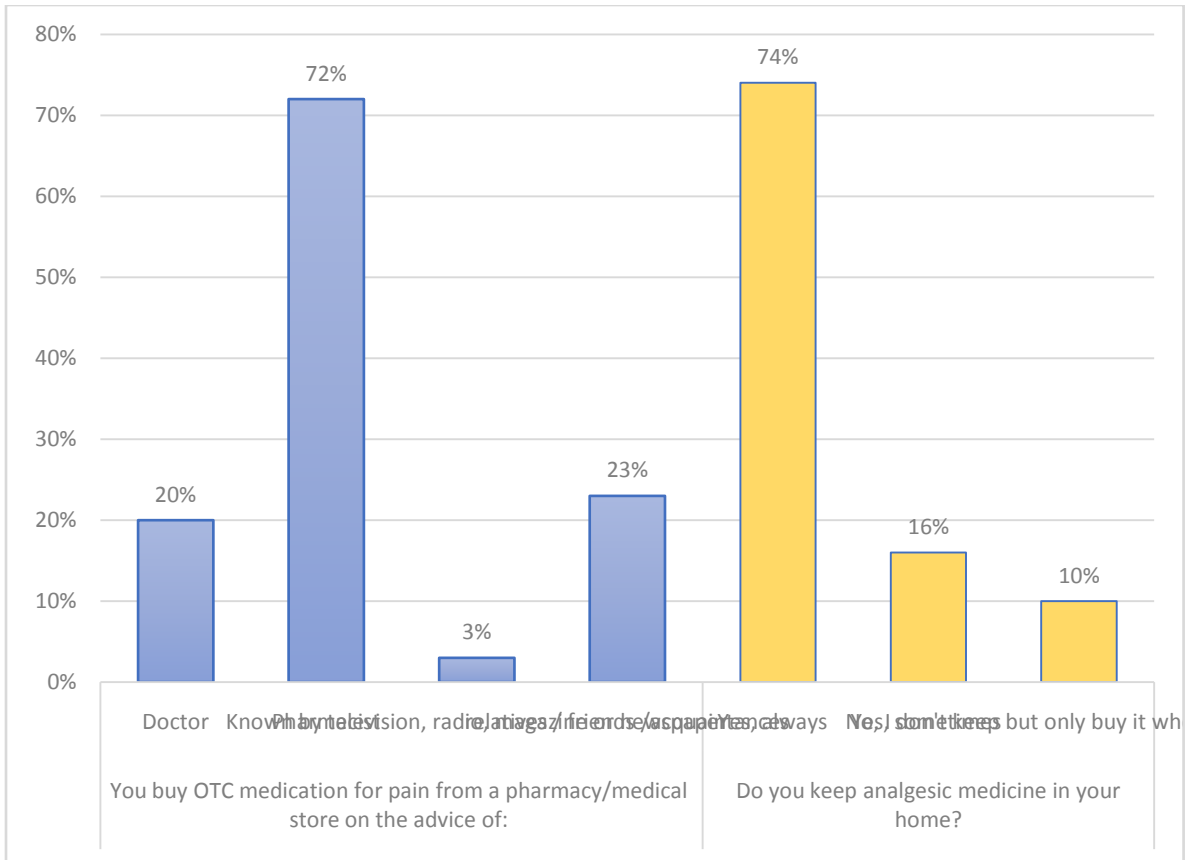
**Figure 1. Demographic characteristics of respondents**



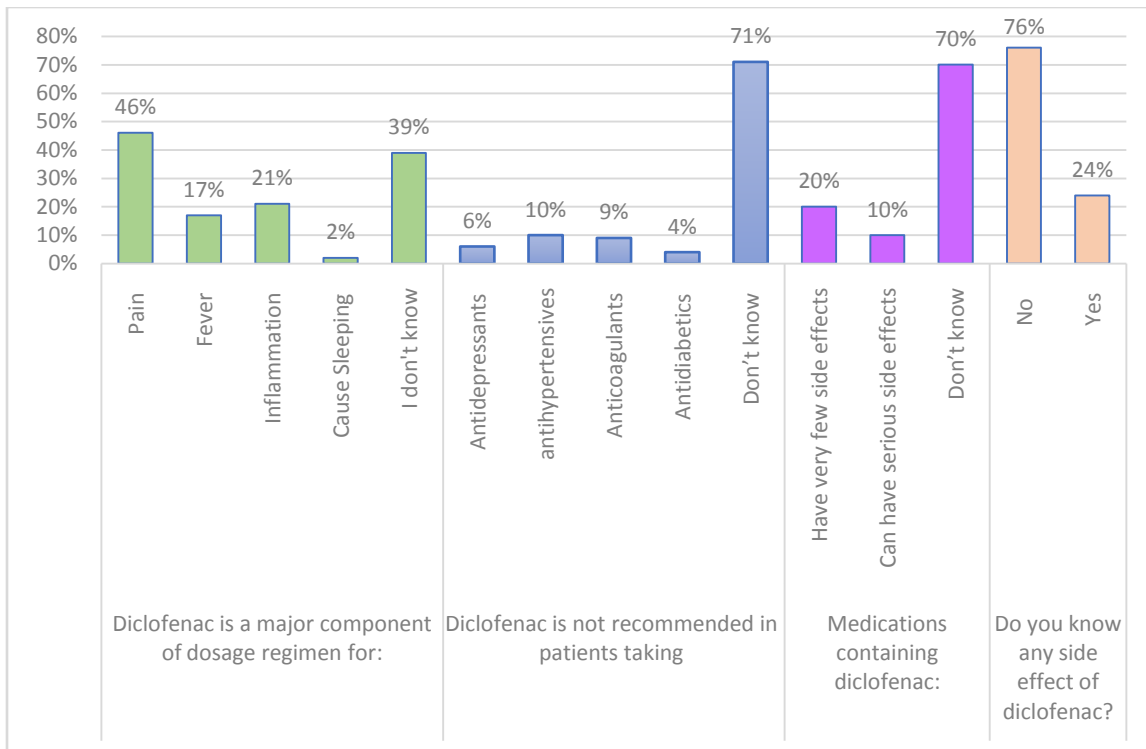
**Figure 2 (a). Participants answer about pain sensation**



**Figure 2 (b). Types of pain require using analgesic among study participants**

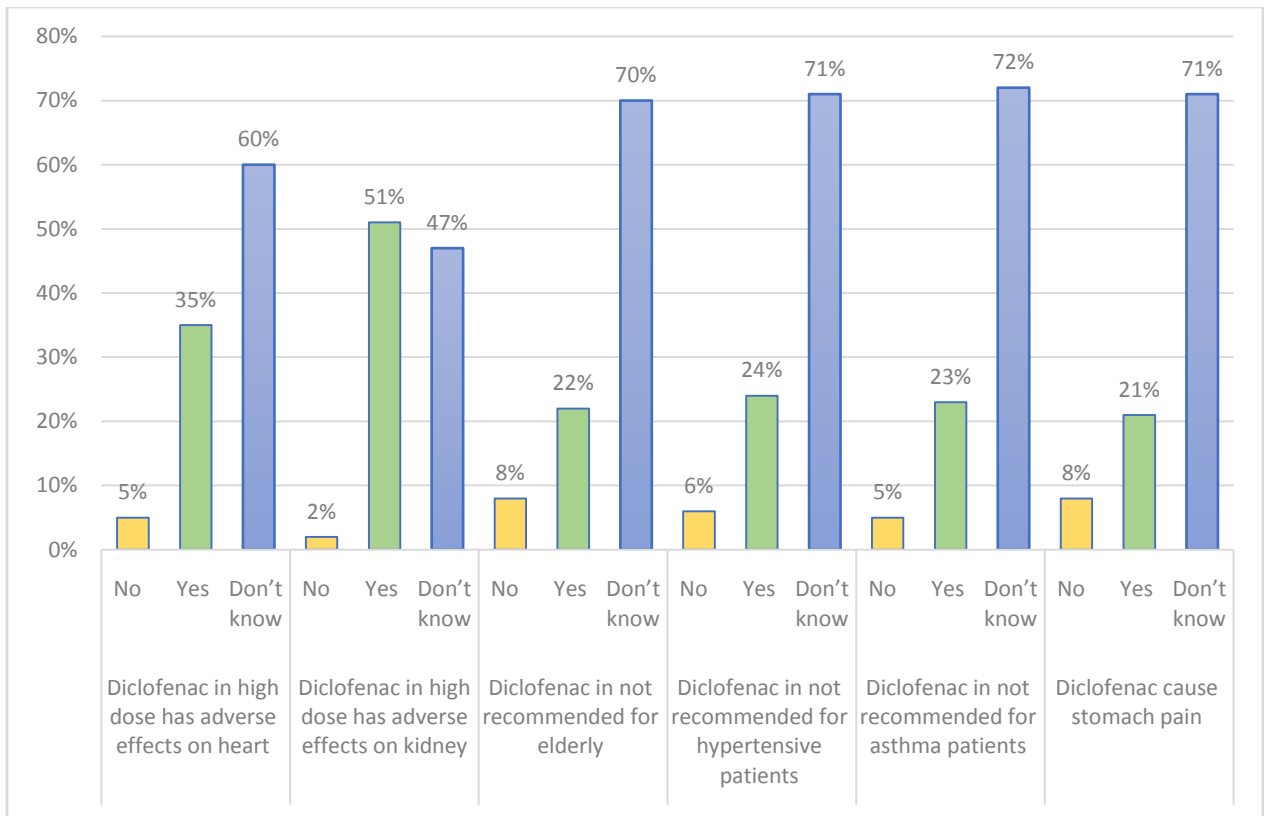


**Figure 3. Attitude of participants toward OTC analgesics**



**Figure 4 (a). Knowledge of participants about diclofenac**

UNDER PEER REVIEW



**Figure 4 (b). Knowledge of participants about diclofenac**

**Table 1. Practices of participants toward diclofenac use (n=430)**

Variable	Categories	Frequency	Percentage (%)
If you didn't feel better after taking analgesic drug	Increase the dose	85	20%
	Continue with the same dose	98	23%
	Stop the drug and try another analgesic	247	57%
When you take analgesic e.g., diclofenac, you know the maximum daily dose?	Yes	167	39%
	No	89	21%
	I don't take diclofenac as analgesic	174	40%
You use analgesic	With prescription	165	38%
	Without prescription	105	24%

likediclofenac	With and without prescription	160	37%
Preferred dosage form of diclofenac	Tablet	115	27%
	Injection	19	4%
	Patch	15	3%
	Suppository	7	2%
	Cream	33	8%
	Granules	71	16%
Amount of diclofenac frequently used	12.5 mg	12	3%
	25 mg	42	10%
	50 mg	67	16%
	75 mg	32	7%
	100 mg	114	26%
If you purchase Diclofenac, your pharmacist asks you what other medications you are taking:	Always	45	10%
	Sometimes	137	32%
	Never	113	26%
	I don't buy medication containing Diclofenac	135	32%
If you purchase Diclofenac, the pharmacist tells you	Maximum daily dose	134	31%
	For use with / after meals	99	23%
	To drinking sufficient amount of water	3	1%
	About drugs which should not be combined with diclofenac	40	9%
	About the cost of medication	46	11%
	Nothing	107	25%

## DISCUSSION

“The frequent and often everyday use of OTC medication for various indications has been common practice amongst adults. Almost half (42%) of adults in the United States take at least one form of OTC medication regularly”.<sup>37</sup>“The ease, at which these medications are accessed, as well as the potential lack of any guidance from health professionals regarding the correct dosage and precautions, results in the public having to rely on their own level of health literacy to access the information provided with the medication. A previous study in substance abuse treatment centers found that the second most frequently reported medicines which are abused or overused are OTC analgesics. OTC medicines as a primary and secondary substance of abuse accounted for 2.6% and 5.2% of all patients admitted, respectively”.<sup>38</sup> As this study was completed in substance abuse centers, the authors of the study suggest that the prevalence of OTC misuse in the general population is predicted to be more extensive than the misuse reported in the study.

“The present study conducted with the aim to evaluate the awareness about over the counter analgesic medication (Diclofenac) among people living in northern border region – Saudi Arabia. It was found that females received OTC analgesics more than males and the highest proportion (93%) of the participants were under 35 years old”. [39, 40] The higher use of OTC analgesics in female and younger ages has been reported in previous studies by Duong et al. and Sarganas et al.<sup>39,40</sup>“In the present study, the education level of most of OTC analgesic users (63%) were university and master/doctorate. Consistently, it was previously shown that the higher the educational and socioeconomical level, more the consumption of OTC NSAIDs”.<sup>41,42</sup>

In the present study, the most common reason for OTC use of analgesics was teeth pain (32%) and head pain (31%) followed by back pain (25%) and 20% of the respondents indicated that they increase dose if they didn't feel better. Our results is different from another study, conducted by Wilcox et al in the United States, where musculoskeletal pain was the most common reason for OTC use of NSAIDs. <sup>41</sup>“In another study undertaken in Scotland, Porteous et al found that the most common reason for using nonprescription analgesics was headache (59%)”. <sup>43</sup>

Majority of respondents were not aware about the side effects of diclofenac; 60% of respondents don't know that diclofenac in high dose has cardiovascular adverse effects, 47% don't know that diclofenac in high dose has adverse effects on kidney, 72% don't know that diclofenac is not recommended for asthma patients and 71% don't know that diclofenac cause gastrointestinal side effects. This result is consistent with the study of Wilcox et al.<sup>41</sup>, who revealed that 60% of OTC users were not aware of NSAIDs side effects and also the researchers in the study of Porteous et al., warned about inappropriate use of nonprescription analgesics.<sup>43</sup>“Additionally, while it is recommended to avoid NSAIDs use in patients with chronic kidney disease, OTC use of NSAIDs has been reported by nearly 7.5% of population with mild to severe CKD in the United States. However, awareness of this comorbidity did not reduce the use of NSAIDs in the mentioned population”.<sup>44</sup>

“Moreover, it was found 71% of OTC consumers of NSAIDs were not aware about drug interactions of NSAIDs. Indermitte et al investigated the awareness of patients concerning potential drug interactions between OTC medications and their prescribed medications in Switzerland. It was found that less than half (47%) of their participants were aware of these potential drug interactions. The prescribing physicians had informed only 47% and the community pharmacists had informed only 26% of the participants, respectively”.<sup>45</sup> This study highlighted the essential roles of physicians and pharmacists to increase patients' awareness of potential drug interactions.

“In the present study, large proportion of respondents(72%) use OTC NSAIDs upon recommendation from pharmacists. However, 31% of the them had been informed by the pharmacists about maximum daily dose, 9% informed about the drug interactions, 24% informed about the proper use of NSAIDs. So, the majority of the respondents of the present study take NSAIDs without professional guidance. This finding could be explained by the following firstly, during rush-hours, pharmacists are too busy to evaluate patients' conditions and to provide them with necessary information about proper medication use”.<sup>46</sup> Second, the false assumption by patients that OTC medications are harmless and can be self-consumed might lead to unsupervised usage of NSAIDs<sup>41</sup> and might cause patients to take OTC medications without getting advice.

This current study findings indicate that some respondents (24%) take diclofenac without medical prescription. This result is lower when compared with previous study findings in Saudi Arabia by Bawazir<sup>47</sup> who found that 51% of participants buy the medications without prescription.

“Due to overdosing and dependence on OTC medication becoming a common phenomenon, certain countries such as the United Kingdom and the United States have attempted to control the consumption of OTC medications by implementing limits on the daily consumption of certain products”.<sup>48</sup>“Similar guidelines are followed in the USA and Canada. However, studies have found it difficult to determine whether this limitation has had any significant effect on the overuse of paracetamol amongst the population”.<sup>48</sup>

“It is generally found that information provided with medication usually includes information at a higher level than the reading ability of the patient”.<sup>49</sup>“It is important to acknowledge that individuals who have access to medication don’t necessarily understand it. Therefore, it needs to be highlighted that providing access to information is not sufficient for informing the population about safe medication use, the information needs to be conveyed in a way that is effective and appropriate for the context”.<sup>49</sup>

“When patients have an understanding of the benefits and potential risks of their medication, as well as an understanding of how to administer the medication, they are empowered to make appropriate decisions about using the medication safely”.<sup>50</sup>“Patients should receive counseling and education in how to administer the medication, as well as the risks and benefits of the medication from their doctor and/ or pharmacists”.<sup>50</sup>

## **STUDY LIMITATIONS**

The small number of participants is limitation of the study.

## **CONCLUSION AND RECOMMENDATIONS**

In conclusion, Saudi people’s knowledge about diclofenac as one member of non-steroidal anti-inflammatory drugs was insufficient. Knowledge about related adverse effects of diclofenac was lacked which exposes to misuse that may carry

accidents and severe side effects especially among high-risk population. The lack of knowledge about diclofenac highlights the need for targeted information. The pivotal role of pharmacists in educating patients should not be ignored.

Tablets are the most commonly used dosage form and dose of 100 mg is the most frequently used dose of diclofenac.

Programs to increase patient knowledge and adherence to medication therapy will affect positively on their use for analgesic medication. Factors such as knowledge, attitudes and motivation are particularly important in terms of patient compliance and the effectiveness of therapy.

Further larger scale studies to evaluate awareness of patients about adverse effects of analgesic medications should be undertaken in the near future.

### **Conflicts of interest**

The authors declare that there are no conflicts of interest.

### **Declaration of competing interest**

The authors declare that there are no competing interest.

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## **LIST OF ABBREVIATIONS**

NSAIDs: Non-steroidal anti-inflammatory drugs

ACP: American College of Physicians

ACR: American College of Rheumatology

COX: Cyclooxygenase

FDA: Food and drug administration

GI: Gastrointestinal

IASP: International Association for the Study of Pain

OA: Osteoarthritis

OTC: Over-the-counter

RA: Rheumatoid arthritis

U.S.: United States

UNDER PEER REVIEW