

# Perceptions and Beliefs Regarding NSAIDs in the Asia-Pacific Region

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**Background:** Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in the treatment of pain and inflammation. However, chronic NSAID use may result in gastrointestinal (GI), cardiovascular (CV), renal or other safety concerns, especially in high-risk populations. The aim of this review is to systematically identify relevant literature and to organize available evidence for perceptions or beliefs of physicians and patients about the safety and efficacy of NSAIDs.

**Methods:** A systematic literature search was conducted in MEDLINE<sup>®</sup> (through PubMed<sup>®</sup>), Embase<sup>®</sup> (through Ovid<sup>®</sup>), and the Cochrane Library. Additional unstructured searches were conducted using Google Scholar<sup>™</sup> and Google. The scope of this study did not include grey literature searches or handpicking of cross references. This systematic analysis was conducted with a special interest in studies conducted in the Asia-Pacific (APAC) region and information related to the COX-2 (cyclooxygenase-2) selective inhibitors.

**Results:** Out of a total of 2822 studies retrieved from different databases (PubMed<sup>®</sup>, Cochrane, Google Scholar<sup>™</sup> and Embase<sup>®</sup>), 99 (3.5%) met the inclusion criteria. Further, out of these 99 studies, 23 APAC region studies were analyzed. The common perceptions were related to GI, CV, renal and respiratory safety, efficacy and COX-2 inhibitors.

**Conclusion:** Overall, the level of awareness among patients regarding NSAIDs was observed to be considerably poor. Moreover, risk stratification by physicians must be practiced in order to decrease the incidence of adverse events.

**Keywords:** cardiovascular, COX-2 inhibitors, efficacy, gastrointestinal, renal, respiratory

## Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are extensively used in the management of symptomatic pain and inflammation in several acute and chronic conditions. NSAIDs can be purchased over-the-counter (OTC) in many countries, which in turn contributes to their increased use.<sup>1,2</sup>

Chronic use of NSAIDs is associated with gastrointestinal (GI), cardiovascular (CV), and renal toxicity.<sup>3</sup> Over the last few years, a large number of studies have been carried out to understand the toxic effects of NSAIDs and further evaluated the overall safety of non-selective and cyclooxygenase (COX)-2 selective inhibitors.<sup>3-6</sup> However, these updates may not have reached practicing physicians due to a lack of continuing education and appropriate scientific communication. In general, NSAID users were found to have poor knowledge of NSAID-associated risks.<sup>7</sup> As prescribers, physicians play an important role in conveying medication risk and safety information to the patients. Little is known about physicians' attitudes to NSAIDs or their perceptions of the risks associated

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with NSAID use.<sup>7</sup> The probability of under-prescription of NSAIDs due to bias among clinicians against the safety of NSAIDs cannot be eliminated, which may interfere with effective pain management strategies. The limited research in this area warrants the need to investigate the current perceptions or beliefs of physicians or patients with respect to the safety and efficacy of NSAIDs.

## Methods

### Definitions

#### Non-Steroidal Anti-Inflammatory Agents

As per Medical Subject Heading (MeSH<sup>®</sup>) dictionary of PubMed<sup>®</sup>, NSAIDs are

Anti-inflammatory agents that are non-steroidal in nature. In addition to anti-inflammatory actions, they have analgesic, antipyretic, and platelet-inhibitory actions. They act by blocking the synthesis of prostaglandins by inhibiting cyclooxygenase, which converts arachidonic acid to cyclic endoperoxides, precursors of prostaglandins. Inhibition of prostaglandin synthesis accounts for their analgesic, antipyretic, and platelet-inhibitory actions; other mechanisms may contribute to their anti-inflammatory effects.

### Eligibility Criteria

Predefined unambiguous eligibility criteria have been established in order to carry out this systematic review. The types of studies, interventions and participants have been classified into the inclusion and exclusion criteria as mentioned below:

#### Inclusion Criteria

- Subjects of any age and sex
- Health-care professionals including specialist and general physicians or dentists, and allied health including pharmacists, nurses, physiotherapists, etc.
- Study conducted in any clinical setting or geographical area
- Any therapeutic area
- All NSAIDs
- Outcomes related to perception, knowledge, awareness, and prescribing pattern
- English language
- Human studies
- Original articles
- Opinion-based articles
- Publication between 2008 and 2018

#### Exclusion Criteria

- Preclinical studies
- Meta-analysis/systematic review
- Narrative reviews summarizing previously published data only
- Case reports
- Case series
- Conference abstracts
- Clinical practice guidelines
- Non-NSAIDs with anti-inflammatory activity (such as plant oils of omega-3-fatty acids)
- Outcomes related to pain perception (effect of a drug on pain intensity/pain score/patient's perception of pain, ie, clinical efficacy endpoints of NSAIDs)

### Search Strategy

A literature search through electronic platforms was conducted to identify relevant peer-reviewed, bibliographic publications. The scope of search included freely accessible data sources, except Embase<sup>®</sup>.

#### PubMed<sup>®</sup> Search Strategy

A MEDLINE<sup>®</sup> search through PubMed<sup>®</sup> was conducted on 30 July 2018 using the search strategy summarized in Table 1.

#### Embase<sup>®</sup> Search Strategy

An Embase<sup>®</sup> search through Ovid<sup>®</sup> was conducted using same entry terms that were used for PubMed<sup>®</sup> search on 12 September 2018 (Table 2).

### Data Collection and Analysis

#### Data Management and Storage

References retrieved from electronic databases were imported using the reference manager, EndNote<sup>™</sup> X8 and de-duplicated using the inbuilt de-duplication functionality of EndNote. De-duplicated references were exported to Microsoft Excel from EndNote and further screened manually to validate accuracy.

#### Screening and Study Selection

The study selection process took place in two steps. In the first step, two reviewers independently reviewed the title and abstract of each study obtained from the electronic searches and made a decision about selection using pre-defined inclusion/exclusion criteria. Discrepancies were discussed, and if unresolved, a third reviewer took the final decision. The second step was based on the full-text review of the articles included in the first step by a single reviewer.

**Table 1** MEDLINE® Search Strategy Through PubMed®

#	Queries	Hits
1	"cyclooxygenase inhibitors"[MeSH®] OR "anti-inflammatory agents, non-steroidal"[MeSH®] OR "non-steroidal anti-inflammatory"[tiab] OR "nonsteroidal anti-inflammatory"[tiab] OR "non-steroidal antiinflammatory"[tiab] OR "nonsteroidal antiinflammatory"[tiab] OR "non-steroid anti-inflammatory"[tiab] OR "non-steroid antiinflammatory"[tiab] OR "nonsteroid antiinflammatory"[tiab] OR "NSAIDs"[tiab] OR "NSAID"[tiab] OR "Non-steroid anti-inflammatory drugs"[tiab]	97,389
2	"Perception"[tiab] OR "Perceptions"[tiab] OR "preference"[tiab] OR "preferences"[tiab] OR "perspective"[tiab] OR "opinion"[tiab] OR "opinions"[tiab] OR "Prescribing Pattern"[tiab] OR "Practice Patterns"[tiab] OR "awareness"[tiab] OR "Belief"[tiab] OR "Believe"[tiab] OR "Prescription pattern"[tiab]	803,722
3	"Biological Therapy"[MeSH®] OR "Plant Oils"[MeSH®] OR "Spectrum Analysis" [MeSH®] OR "Molecular Dynamics Simulation"[MeSH®] OR "Protein Aggregates"[MeSH®] OR "Amyloid beta-Peptides"[MeSH®] OR drug evaluation studies, preclinical[MeSH® Terms] OR medicinal plants testing, preclinical[MeSH®] OR "systematic review"[tiab] OR "Case reports"[ptyp] OR "Case report"[tiab] OR "case series"[tiab] OR "case study"[tiab] OR "meta-analysis"[Publication Type] OR "meta-analysis"[tiab] OR "Cost-effectiveness" [tiab] OR "rat" OR "rats" OR "mouse" OR "mice" OR "pig" OR "pigs" OR "horse" OR "equine" OR "veterinary" OR "Animal" OR "Animals" OR "Birds" OR "bird" OR "virus" OR "brolga" OR "Avian"	10,160,450
5	(((((#1 AND #2) NOT #3) Publication date: 2008–2018) Human) English)	601

## Data Extraction

Data from the full-text selected papers were extracted using a pre-approved data extraction form (DMF) and stored in MS Excel. Data extraction was carried out by a single reviewer. Since most of the data obtained were textual, large fragments of text were extracted in DMF from source articles and summarized as text documents.

## Results

### Overview of Search results

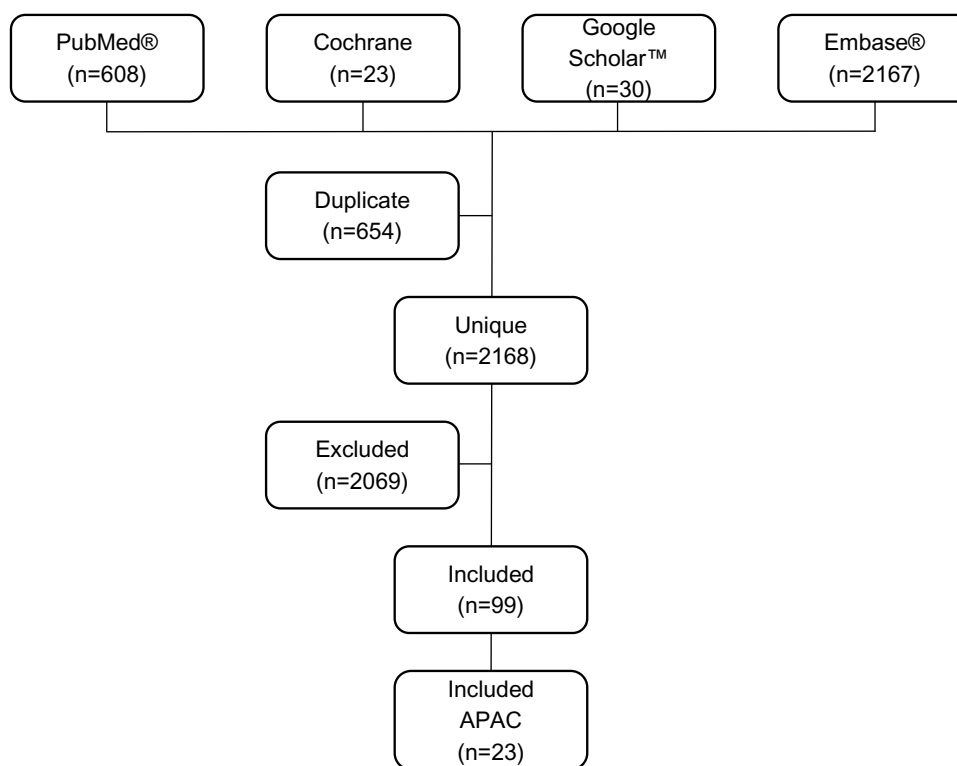
Of 2,822 studies retrieved from different databases, 99 (3.5%) were included in the analysis (Figure 1). Out of

**Table 2** Embase® Search Strategy Through Ovid®

#	Queries	Hits
1	cyclooxygenase inhibitors.mp. or prostaglandin synthase inhibitor/	10,018
2	(cox adj inhibitor\$1).ti,ab.	2898
3	Non-steroidal anti-inflammatory drugs.mp. or Non-steroidal anti-inflammatory drugs/	14,587
4	non?steroid\$ anti?inflammatory.ti,ab.	5774
5	nsaid\$1.ti,ab.	38,506
6	perception\$1.ti,ab.	257,798
7	*prescription/or *prescription drug misuse/	34,212
8	(prescribing adj pattern\$1).ti,ab.	4358
9	(prescription adj pattern\$1).ti,ab.	2154
10	(practice adj pattern\$1).ti,ab.	10,692
11	exp Biological Therapy/	1,443,475
12	exp preclinical study/	15,294
13	exp Plant Oils/	74,624
14	exp Spectrum Analysis/	348,769
15	exp Molecular Dynamics Simulation/	114,549
16	exp Protein Aggregates/	2135
17	exp Amyloid beta-Peptides/	35,915
18	systematic review\$1.ti,ab.	153,199
19	case report/	2,266,125
20	case series.mp. or case study/	108,437
21	meta analysis/	147,444
22	(Cost adj effectiveness).ti,ab.	72,337
23	exp rats/	1,629,941
24	exp mouse/	1,620,316
25	exp pig/	42,843
26	exp horse/	59,383
27	veterinary.mp. or veterinary.ti,ab.	100,448
28	exp Birds/	203,853
29	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	7,679,003
30	preference\$1.ti,ab.	157,129
31	believe.ti,ab.	108,989
32	belief.ti,ab.	35,558
33	awareness.ti,ab.	172,345
34	1 or 2 or 3 or 4 or 5	58,942
35	nsaid/	113,774
36	34 or 35	139,170
37	6 or 7 or 8 or 9 or 10 or 30 or 31 or 32 or 33	740,140
38	36 and 37	4674
39	38 not 29	3810
40	limit 39 to (english language and yr="2008–2018")	2167

these 99 studies, 23 were related to the APAC (Asia-Pacific) region only, as described in Table 3.<sup>7–29</sup>

Studies that had findings related to prescription patterns only and did not report perceptions/beliefs/practices leading to those patterns were excluded from the final analysis. A wide variety of population samples were studied, which were classified as general physicians, specialists (eg,



**Figure 1** PRISMA flow diagram, study selection flow.

**Abbreviation:** APAC, Asia-Pacific.

anesthesiologists, rheumatologists), paramedics, medical students, general population, subpopulation of patients, or prescriptions. The population samples were classified into four categories: physicians, patients, students, and prescriptions. Among the 23 APAC studies that were included in this review, patients comprised the highest population sample (30%) (Figure 2). Different outcomes included perceptions related to NSAIDs' safety, efficacy, and usage; level of awareness, extent of self-medication, polypharmacy, and inappropriate usage.

## Physicians' Perceptions on NSAID Risks

A retrospective study from the APAC region (Hong et al, Korea) compared the prescription patterns of internists and physicians.<sup>9</sup> Internists were unaware of the hepatic effects of acetaminophen and prescribed it to patients with liver cirrhosis, while physicians were cautious and preferred prescribing NSAIDs over acetaminophen in the same group of patients. In the study by Choudhary et al, among health-care professionals, physicians (66.7%), nurses (60.9%), and pharmacists (47.8%) displayed a moderate level of awareness regarding the major AEs (adverse events) associated with NSAID use.<sup>22</sup> On the

contrary, Phueanpinit et al, found that majority of orthopedic physicians took patients' history (GI, CV, renal, allergy to NSAIDs, patient's age) into consideration before prescribing non-selective NSAIDs.<sup>7</sup>

## Perceptions Related to Gastrointestinal Safety

In Thailand, 95.5% (n=63) orthopedic physicians were aware that a history of GI ulcers or bleeding must be considered before prescribing NSAIDs.<sup>7</sup> The risk of GI ulceration or bleeding was the second most common concern after a patient's medical history of renal impairment.<sup>7</sup> Around 63.1% of physicians had a moderate attitude towards providing information on AE management and monitoring to patients.<sup>7</sup>

Although prescription of gastro-protective agents, such as histamine type-2 (H2) blockers and proton pump inhibitors (PPIs) is common practice in the rest of the world, only a few professionals in a few APAC regions, namely, Malaysia and Pakistan preferred prescribing PPIs and H2 receptor blockers for gastroprotection.<sup>20,26</sup> Prescribers in the APAC region preferred COX-2 inhibitors to avoid GI AEs, especially in high-risk populations.<sup>20</sup>

**Table 3** Characteristics of Asia-Pacific (APAC) Studies

No.	Author (Year)	Country (Region)	Population Studied	Study Design	Sample Size	Outcomes Studied
1	Gupta (2014) <sup>8</sup>	India (APAC)	Students	Cross-sectional study	591	Patient awareness/perception
2	Hong (2016) <sup>9</sup>	Korea (APAC)	Patients with cirrhosis	Retrospective review	125,505	Prescription pattern
3	Imtiaz (2013) <sup>10</sup>	Pakistan (APAC)	Students	Descriptive cross-sectional study	320	Patient awareness/perception
4	Jagdish (2018) <sup>11</sup>	India (APAC)	Patients with rheumatological diagnosis	Prospective study	500	Patient awareness/perception
5	Tanwar (2015) <sup>12</sup>	India (APAC)	Undergraduate medical students	Cross-sectional questionnaire-based Study	130	Awareness/Perception
6	Mudhaliar (2016) <sup>13</sup>	India (APAC)	Patients at orthopedic outpatient	Retrospective Study	150	Prescription pattern
7	Phueanpinit (2017) <sup>7</sup>	Thailand (APAC)	Orthopedic physicians	Cross-sectional study	66	Prescription pattern/physician perception
8	Saurabh (2010) <sup>14</sup>	India (APAC)	Physicians	Survey	NA	Prescription pattern
9	Purkayastha (2016) <sup>15</sup>	India (APAC)	Prescriptions	Prospective, observational, non-interventional study	300	Prescription pattern
10	Khan (2016) <sup>16</sup>	Pakistan (APAC)	Physicians	Non-interventional, cross sectional study	45 inpatient prescriptions	Prescription pattern
11	Saurabh (2011) <sup>17</sup>	India (APAC)	Prescriptions	Cross-sectional descriptive study	600	Prescription pattern
12	Sonal Sekhar (2011) <sup>18</sup>	India (APAC)	Patients	Hospital based retrospective study	575	Prescription pattern
13	Ahmad (2015) <sup>19</sup>	India (APAC)	Patients	Cross-sectional study	380	Patient perception
14	Chan (2014) <sup>20</sup>	Malaysia (APAC)	Medical records	Cross-sectional study	365	Physician perception/awareness
15	Chen (2014) <sup>21</sup>	Pakistan (APAC)	Medical/Non-medical Teachers	Cross-sectional study	250	Patient awareness/perception
16	Choudhary (2013) <sup>22</sup>	India (APAC)	Doctors, nurses and pharmacists	Questionnaire Survey	72 doctors, 46 pharmacists, 23 nurses	Physician awareness
17	De leon (2008) <sup>23</sup>	Philippines (APAC)	General surgeons	Survey	167	Physician perception/preference

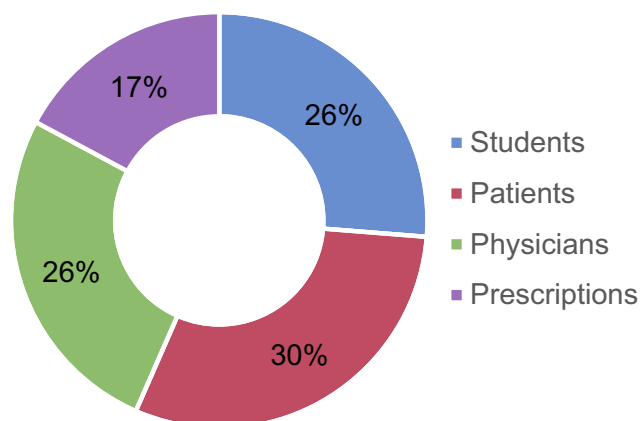
(Continued)

**Table 3** (Continued).

No.	Author (Year)	Country (Region)	Population Studied	Study Design	Sample Size	Outcomes Studied
18	Nguyen (2014) <sup>24</sup>	India (APAC)	Medical students/ residents, and GI fellows	Survey	543	Perception/ preference
19	Fatima (2017) <sup>25</sup>	India (APAC)	Medical and paramedical students	Cross-sectional study	250	Awareness/ perception
20	Gul (2014) <sup>26</sup>	Pakistan (APAC)	Prescriptions	Retrospective study	200	Prescription pattern
21	Phueanpinit (2016) <sup>27</sup>	Thailand (APAC)	Orthopedic patients	Cross-sectional study	474	Patient awareness/ perception
22	Ravinthar (2017) <sup>28</sup>	India (APAC)	Post graduates and dental practitioners	Survey	100	Physician perception/ awareness
23	Antappan (2017) <sup>29</sup>	India (APAC)	Orthopedic patients	Prospective observational study	105	Prescription pattern

## Perceptions Related to Cardiovascular Safety

Amongst untoward CV effects, risk of hypertension in susceptible populations was the only identified concern.<sup>7</sup> In an interview of 100 dentists in Chennai, India (Ravinthar et al, India), 6% of the participants identified hypertension as a contraindication of NSAIDs, indicating a low level of awareness among prescribers.<sup>28</sup> In another study from the APAC region (Chen et al, Pakistan), it was clearly stated that physicians prescribing NSAIDs or pharmacists who dispense NSAIDs do not query patients regarding comorbidities and concomitant medications, which may further increase the incidence of CV-related AEs among patients.<sup>21</sup>

**Figure 2** Distribution of included studies (Asia-Pacific) by population studied.

In a Thai study conducted among 206 orthopedic physicians, 72.1% of participants reported to have observed hypertension in patients taking NSAIDs.<sup>7</sup> A very small proportion of physicians (15.6%) informed patients regarding the CV effects of NSAIDs.

## Perceptions Related to Renal Safety

In north-eastern Thailand, most physicians (98.5%) were aware that NSAIDs might be associated with renal impairment and considered this factor before prescribing NSAIDs to patients who were already at a higher risk of developing renal complications.<sup>7</sup> Renal function was deemed the risk factor of greatest concern for prescribing any NSAID. Three out of four orthopedic physicians claimed that they provided adverse drug reaction (ADR) information related to prescription NSAIDs, but ADR monitoring and management (29.7%, and 37.5%, respectively) information was provided less frequently to patients.<sup>7</sup>

## Perceptions Related to Respiratory Safety

In a study involving dentists (Ravinthar et al, India), 25% of participants reported that bronchial asthma was the second most common contraindication to the use of NSAIDs.<sup>28</sup>

## Patients' Perceptions on NSAID Risks

The awareness of NSAID risks varied among patients. One Indian study (Jagdish et al) reported low NSAID awareness among patients (21.3%) while another study



(Ahmad et al, India) found that a considerable proportion (75%) of patients were aware that chronic use of NSAIDs may be associated with the occurrence of AEs.<sup>11,19</sup>

## Perceptions Related to Gastrointestinal and Renal Safety

Lack of awareness among patients regarding safe usage of NSAIDs was a common finding in APAC as well as the rest of the world, especially among patients practicing self-medication. One study (Phueanpinit et al, Thailand) showed that 80% of the patients (n=140) were aware that long-term therapy, high dose, and the presence of underlying GI or renal disease could increase the risk of AEs.<sup>27</sup> In this questionnaire-based study, approximately half of NSAID users had received information about potential side effects, whether from physicians or pharmacists,<sup>27</sup> which corroborates with the lack of sufficient knowledge transfer reported.<sup>7</sup> They believed that physicians may be more likely to inform patients about GI risks than other risks.<sup>27</sup>

## Physicians' Perceptions Related to COX-2 Inhibitors

An observational study evaluated the use of celecoxib in hospitals across Malaysia (Chan et al, Malaysia) and assessed the perceptions of physicians regarding the use of celecoxib and non-selective NSAIDs.<sup>20</sup> The study demonstrated that physicians considered GI safety profile (65.9%), efficacy (23.7%), and CV safety profile (3.8%) when choosing between COX-2 selective inhibitors and non-selective NSAIDs. Most physicians (51.8%) believed that celecoxib was more effective as an anti-inflammatory and analgesic agent.<sup>20</sup> Most physicians (90%) perceived that celecoxib had a better GI safety profile than a non-selective NSAID and preferred COX-2 selective inhibitors over a combination of non-selective NSAIDs and PPIs in patients with GI risk.<sup>20</sup> The reasons cited were similar efficacy between celecoxib and non-selective NSAIDs as well as affordability.<sup>20</sup>

A study among Filipino surgeons (de Leon et al, Philippines) observed that COX-2 selective inhibitors were preferred as the first-line treatment for pain management followed by weak opioid + COX-2 selective NSAID, weak opioid alone, and non-selective NSAID + weak opioid.<sup>23</sup> Preference for COX-2 selective inhibitors for pain management was because of the greater efficacy and better safety profile of this class of drug.<sup>23</sup> Also, COX-2

selective inhibitors were being marketed widely and were popular among the Filipino surgeons.<sup>23</sup>

## Patients' Perceptions Related to COX-2 Inhibitors

In an observational study (Antappan et al, India) conducted in an orthopedic department, patients were asked about risk factors including concomitant use of anticoagulants or selective serotonin reuptake inhibitors, comorbidities (CV, renal, hepatic diseases, diabetes), old age (>65 years), poor health status, history of GI symptoms, heavy smoking and drinking.<sup>29</sup> COX-2 selective inhibitors were prescribed to patients with these risk factors in order to prevent GI-related AEs. However, the frequency of COX-2 selective inhibitors usage was lower, ranging from 1% to 11.4% of patients with these risk factors.<sup>29</sup>

## Polypharmacy and Self-Medication Risks

Polypharmacy was found to be a widespread practice in the APAC region. Two Indian studies (Mudhaliar et al; Purkayastha et al) reported prevalent use of NSAID fixed dose combinations (FDCs).<sup>13,15</sup> The authors concluded that the indiscriminate use of FDCs may increase the incidence of AEs while, combining opioid analgesics may be a better option to achieve the desired analgesic efficacy.<sup>13,15</sup> Another study (Saurabh et al, India) found that NSAIDs or their combinations were unnecessarily used in as many as 50% of all prescriptions.<sup>14</sup> Similarly, in a study from Pakistan (Khan et al), polypharmacy of NSAIDs was found to be prevalent.<sup>16</sup> More than half of the study population (55.6%) had two analgesics in their prescription while 24.4% of the patients had three to four.<sup>16</sup> Another study (Gul et al, Pakistan) showed that majority of the prescriptions (69%) included more than one NSAID. The study reported that the use of two NSAIDs was often observed in patients with arthritis or those who experienced intense unbearable pain.<sup>26</sup>

In an Indian study, Tanwar et al reported that undergraduate medical students were widely practicing self-medication, which may increase the risk of health hazards.<sup>12</sup> The common reasons for self-medication included: unwillingness to visit a doctor; considering pain as a mild illness; and busy schedules. It was observed that a patient receiving treatment for bronchial asthma took a combination of ibuprofen and paracetamol. The authors considered this as a significant finding because NSAIDs are known to precipitate asthma attack.<sup>12</sup>

Self-medication was reported to be common among 67% of the patients in one study (Imtiaz et al, Pakistan).<sup>10</sup> In another study (Fatima et al, India), female medical students were commonly found practicing self-medication whereas, the female paramedical students usually preferred medical consultation or use of home remedies.<sup>25</sup> In an Indian study, Tanwar et al reported that undergraduate medical students were widely practicing self-medication, which may increase the risk of health hazards.<sup>12</sup> It was observed that a patient receiving treatment for bronchial asthma took a combination of ibuprofen and paracetamol. The authors considered this as a significant finding because NSAIDs are known to precipitate asthma attack.<sup>12</sup>

## Discussion

This study observed that physicians in the APAC region generally have lower awareness of the potentially harmful side effects of NSAIDs. Among AEs associated with NSAIDs, GI-related AEs were most commonly reported. However, physicians seldom take an adequate history to assess a patient's risks before prescribing NSAIDs.<sup>7</sup> There were also differences in NSAID prescription patterns when compared by physician practice type.<sup>9</sup> In a study of Thai orthopedic surgeons, majority of surgeons reported providing patients with side effects information related to prescription NSAID.<sup>7</sup> In the same study, surgeons who did not provide patients with the side effects information perceived that sharing AE information with patients would likely increase their anxiety and encourage non-adherence. However, there is no evidence of association between patients receiving AE information and NSAID treatment discontinuation.<sup>7</sup>

Physicians were perceived by patients as the most reliable source of information on knowledge of NSAID side effects and contraindications followed by media and relatives/friends, according to a study conducted in a Pakistan university.<sup>21</sup> Pharmacists were perceived as a source of NSAID information by only a quarter of the participants.<sup>21</sup> Awareness of non-prescription drugs, mostly NSAIDs, was higher among urban population compared with rural population, however the use of NSAIDs was higher among rural population, according to an Indian study.<sup>19</sup> Age was also inversely associated with awareness of NSAID use.<sup>19</sup> A study in Thai population observed that the perception of risks and knowledge of risk factors for NSAID use was generally low but was higher among those who were provided with NSAID side effects information. This lack of awareness may lead to inappropriate use of NSAIDs. Thus,

there is a need for educational programs to bridge the knowledge gap in patients, particularly in rural populations, older patients and those with low educational levels.<sup>27</sup>

Widespread use of NSAID FDCs has been reported in several APAC studies.<sup>13–16,26</sup> Combining two NSAIDs is not likely to improve efficacy as NSAIDs act on the same pathway, however the FDCs may increase the chances of AEs and drug interaction compared with both drugs administered individually.<sup>13</sup> Use of multiple concomitant NSAIDs was attributed to irrational prescription by physicians, lack of awareness among patients and inadequate pain relief with one NSAID.<sup>26</sup> Self-medication of NSAIDs is also prevalent in the region with high consultation costs, shortage of time, easy accessibility to drugs and lack of awareness about complications of NSAIDs contributing to the practice.<sup>10,25</sup> The common reasons for self-medication among students included unwillingness to visit a doctor, considering pain as a mild illness and busy schedules.<sup>12</sup>

## Limitations

There are some limitations to the studies sampled in this review. Several studies have limitations due to their small sample size (Table 3). The generalizability of the results of few studies were also limited as they used convenience sampling or were single-center experience.<sup>10,11</sup> Studies that employed survey-based methodology had varied response rates and may invariably have recall bias.<sup>7,20</sup> Use of health insurance databases, prescription databases or patient medical records in some studies may not provide accurate diagnosis information for patients which may lead to over or underestimation of the study population. Finally, most studies did not include information on the mode of NSAID administration.

## Conclusion

The prescription pattern of NSAIDs was influenced by the perceptions related to the safety of NSAIDs. Physicians are also generally unaware of contraindications to NSAID use. Risk stratification and individualization of prescription were not evident. Lack of communication regarding NSAID-associated risks and AEs between patients and prescribers may also expose patients to a higher risk for AEs associated with NSAIDs. Lack of awareness among patients, tendency to self-medicate, polypharmacy of NSAIDs further escalate these risks.

Based on the findings of this review, the following recommendations are proposed:



1. Greater educational efforts to teach physicians on the risks of NSAIDs, contraindications to NSAID use, risk stratification of patients and appropriate use of NSAIDs
2. A treatment algorithm to assist physicians in making a choice to use COX-2 selective NSAIDs over non-selective NSAIDs in high-risk patients
3. Raise public awareness of risks and AEs of NSAIDs, risks of self-medication and avoidance of NSAID polypharmacy

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## Disclosure

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