

## Pattern of Use and Awareness of Side-Effects of Non-Steroidal Anti-Inflammatory Drugs in the General Population

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### ABSTRACT:

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly utilized to reduce pain, inflammation, and fever. This study aimed to assess patterns of use and awareness of NSAID-related side-effects in an adult Jordanian. And the associations with sociodemographic factors. This cross-sectional study among a representative sample of 604 adults >18 years. A validated, self-administered questionnaire was used to collect basic sociodemographic data from the participants, as well as information regarding NSAID use. Most respondents were NSAID users (65.7%), of which the majority were predominantly female (56.7%) and under 50 years of age (76.3%). Overall, 42.6% had been prescribed NSAIDs by a physician. Female respondents and those with government insurance more frequently utilizing NSAIDs ( $p = 0.029$  and  $0.032$ , respectively). In contrast, smokers and individuals with a history of diabetes mellitus or hypertension were less likely to use NSAIDs ( $p = 0.024$ ,  $0.026$ , and  $0.021$ , respectively). Overall, 65.1% were aware of kidney NSAID-related side-effects and 22.4% were aware of the increased risk of asthma and allergy. Despite the high frequency of NSAID use in the Jordanian general population, there is limited knowledge of their side-effects as well as drug interactions. This is cause for concern, particularly as many participants reported having been prescribed NSAIDs by physicians without adequate patient safety education.

**Key Words:** Anti-Inflammatory Agents, Non-Steroidal; Drug Utilization; Drug-Related Side-Effects and Adverse Reactions; Drug Interactions; Pharmacovigilance; Awareness; Jordan.

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## **INTRODUCTION;**

Non-steroidal anti-inflammatory drugs (NSAIDs) are a group of medications that act as painkillers and reduce fever and inflammation, but have concerning side-effects [1]. These medications are used to treat different conditions, including headache, fever, acute and chronic pain, biliary and ureteric colic, rheumatologic diseases, and dysmenorrhea. Such drugs are prescribed worldwide in clinics and hospitals and can also be purchased over the counter (i.e., without a prescription), as their use is believed to be safe even over long periods [2]. Moreover, purchasing an analgesic without a prescription is considered by many members of the public to be less time-consuming, less costly, and result in faster pain relief compared to visiting an emergency room or making an appointment to be examined by a general physician [3].

Nonetheless, it is vital that members of the public who use NSAIDs over a long period of time are aware of the maximum daily dose permissible and which side-effects can be harmful. Many adverse reactions can occur following NSAID use, including in the gastrointestinal (GI) tract, kidney, liver, skin, central nervous system, and blood [4]. According to a study conducted in an emergency department in California, most users (61%) are aware of the GI side-effects of NSAID use, while only a small proportion understand that utilization of these drugs can result in specific kidney problems and other adverse effects [5].

As such, the aim of this study was to assess the pattern of utilization of NSAIDs and level of awareness regarding NSAID-related side-effects among a representative sample of the Jordanian public. In addition, the study aimed to determine factors affecting NSAID use and awareness, such as sociodemographic factors, personal health, and family history of illness. It is important to assess the general public's knowledge of NSAIDs and their related side-effects, as their misuse may negatively impact health. A study conducted among medical students in India demonstrated that while most students were familiar with over-the-counter-medications, very few demonstrated

sufficient knowledge regarding the regulation and usage of self-medication [6].

## **METHODOLOGY;**

This cross-sectional study was conducted between June 2020 and September 2020. The target population included members of the general public in Jordan aged 18 years old and above, excluding healthcare providers. Written informed consent was obtained from all respondents prior to their participation in the study. A validated, self-administered questionnaire was used to collect basic sociodemographic data from the participants, as well as information regarding NSAID usage, patterns of use, and knowledge of their potential side-effects.

The self-administered questionnaire was divided into three sections. The first section assessed the participants' sociodemographic information, including their gender, age, marital status, level of education, type of work, insurance type, smoking status, and body mass index. The second part included relevant medical history, current medication use, and frequency of administration. The third and final part of the questionnaire sought details regarding the respondents' NSAID use, purpose of use, whether the medications had been purchased over-the-counter or prescribed by a physician or pharmacist, and the respondents' awareness of potential NSAID-related side-effects.

The questionnaire was validated using a pilot study of 20 participants and reviewed by two academically oriented physicians. This provided feedback regarding the cohesion and coherence of the instrument, as well as its clarity and ease of use. During the main study, investigators assisted respondents in answering the questionnaire to minimize the possibility of respondents not understanding specific questions.

### ***Statistical analysis***

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 25 (IBM Corp., Armonk, New York, USA). Results were summarized using descriptive statistics, including frequencies (n) and

percentages (%). A Chi-squared test ( $\chi^2$ ) was used to determine whether associations existed between variables, with a  $p$  value of  $<0.05$  considered to indicate statistically significant differences. During analysis, when assessing the relationship between NSAID use and awareness of its side-effects, respondents were divided into four categories: (1) individuals who were aware of side-effects and who continued to use these medications; (2) those who did not use these medications and knew of their side-effects; (3) those who neither used such medications nor knew of their side-effects; and (4) those who used these medications, but did not know of their side-effects.

**RESULTS;**

A total of 604 members of the Jordanian general public were surveyed, of which 65.7% were NSAID users. The majority of NSAID users were female (56.7%) and less than 50 years old (76.3%). In addition, 49.4% of NSAID users were non-smokers. Most users had been prescribed NSAIDs by a physician (42.6%) or pharmacist (17%), while 28.6% were taking these medications on an over-the-counter basis. Only 29.6% of NSAID users were warned about the potential side-effects of these medications. The majority of the population without health insurance were NSAID users (73%). Overall, headache (30%) was the most common indication for NSAID utilization, followed by toothache (21%), while the least common indication was abdominal pain (6%) (Fig. 1).

Most respondents (81%) utilized NSAIDs once per month or less, with 10.5% using them once

per week, 4.6% two to three times per week, and 3.7% on a daily basis. Factors associated with NSAID use included gender ( $p = 0.029$ ) and type of health insurance ( $p = 0.032$ ), with female respondents and those with government insurance more frequently utilizing NSAIDs compared to their respective counterparts. In turn, those who smoked or had a history of diabetes mellitus or hypertension were significantly less likely to use NSAIDs, with  $p$  values of 0.024, 0.026, and 0.021, respectively (Table 1).

With regards to awareness of NSAID-related side-effects, respondents were initially asked if they knew that NSAIDs could interact with each other or different medications, of which 37.9% affirmed that they could. As for organ- or system-specific side-effects, 65.1% and 52.6% of respondents were aware of possible kidney and GI problems, respectively, but only 22.4% were aware of the increased risk of asthma and allergy (Fig. 2). Overall, only 29.6% of NSAID users reported having received patient education regarding the potential side-effects of these medications.

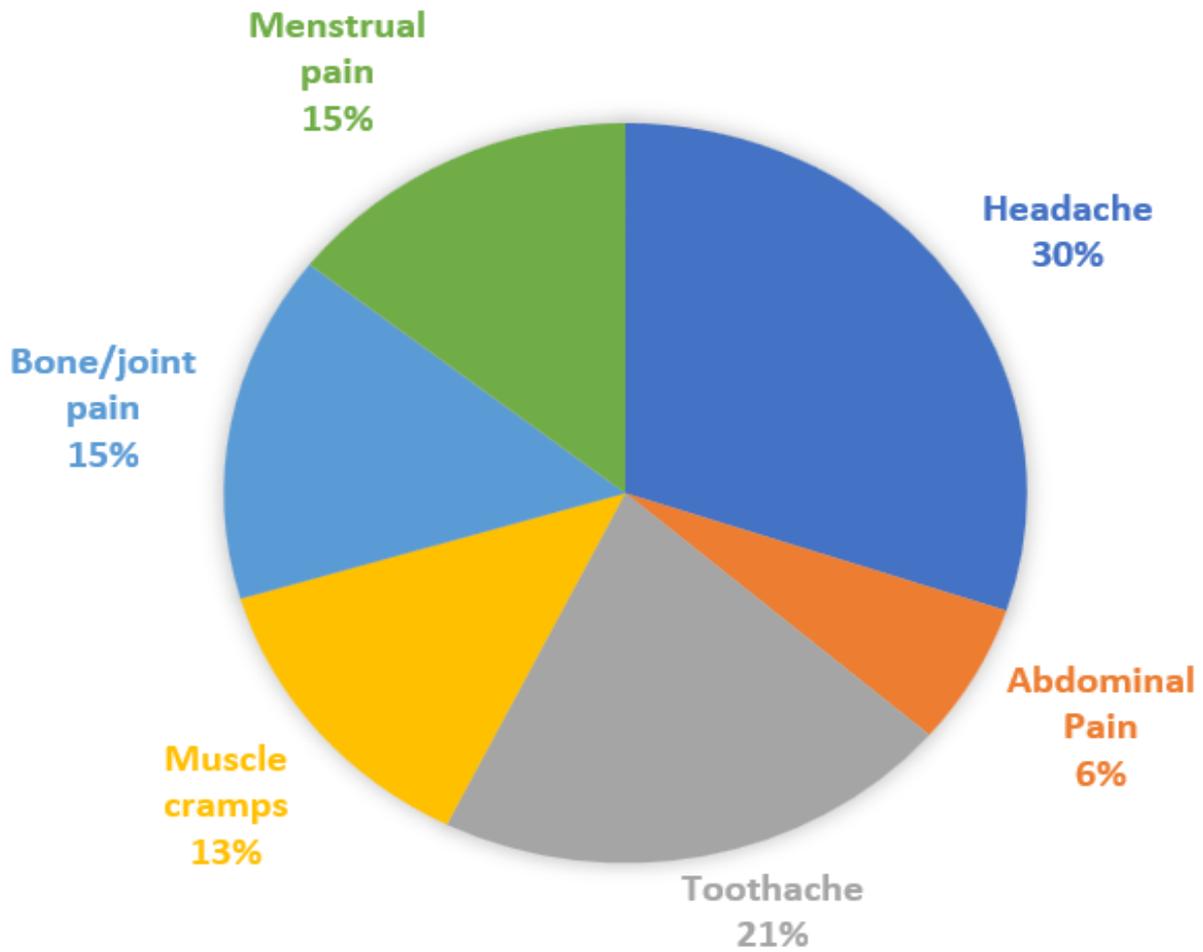
With regards to specific adverse effects, 51.2% of respondents used NSAIDs but did not know of their effects on asthma and allergies, whereas 14.5% continued to use such medications despite this knowledge. As for GI side-effects, 37.4% used NSAIDs yet were aware of these particular side-effects, while 28.3% used such medications while remaining unaware of these effects. Finally, 45.7% of the respondents used NSAIDs despite understanding the risk of potential kidney disease, while 20% used them without being aware of this potential side-effect (Fig. 3).

**Table 1:** Factors associated with NSAIDs use (univariate associations)

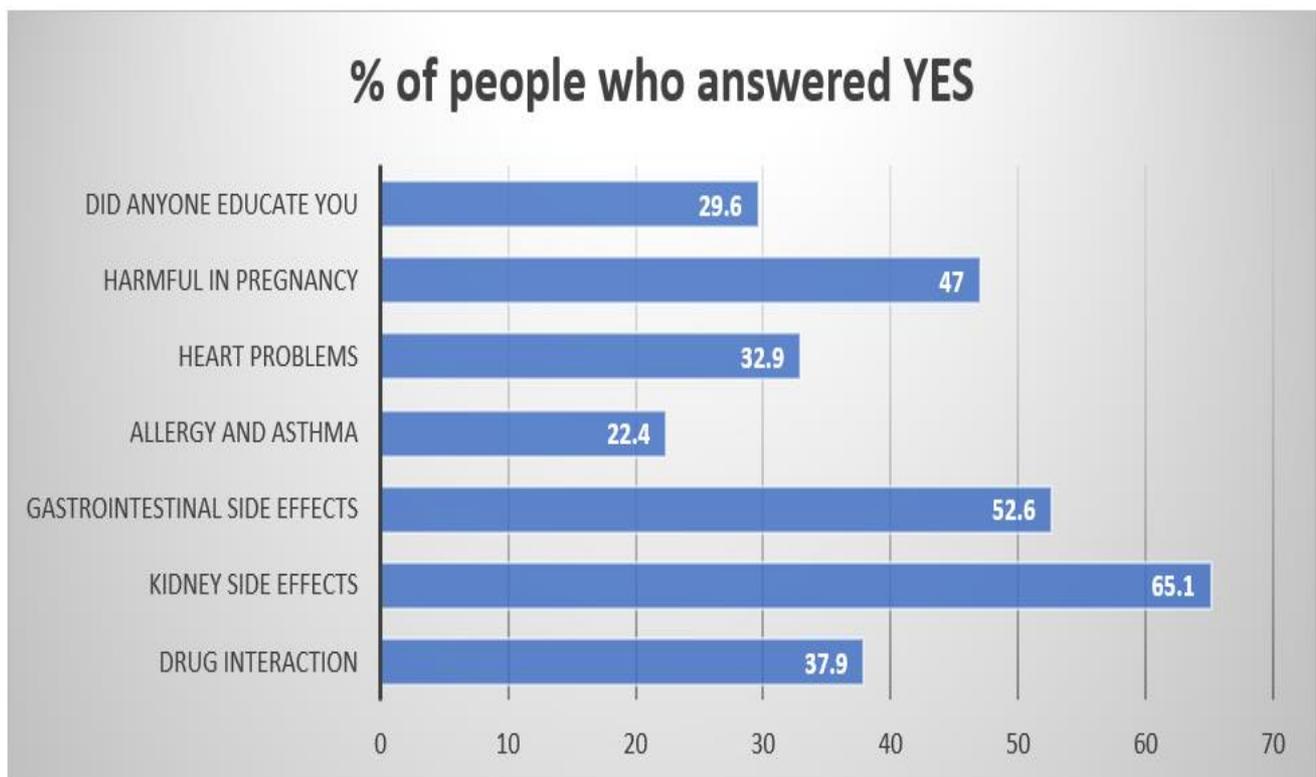
		NSAIDs Users count (%)	Non-NSAIDs User count (%)	Total numbers 604 (%)	P value
<b>Gender</b>	Male	172 (43.3)	109 (52.7)	281 (46.5)	0.029*
	Female	225 (56.7)	98 (47.3)	323 (53.4)	

<b>Age</b>	< 50	303 (76.3)	147 (71.0)	450 (74.5)	0.155
	>=50	94 (23.7)	60 (29.0)	154 (25.5)	
<b>Social Status</b>	Married	223 (56.2)	120 (57.9)	343 (56.8)	0.914
	Single	164 (41.3)	82 (39.6)	246 (40.7)	
	Other	10 (2.5)	5 (2.4)	15 (2.5)	
<b>Education Level</b>	Middle school	26 (6.5)	21 (10.1)	47 (7.8)	0.100
	High school	98 (24.7)	64 (30.9)	162 (26.8)	
	Bachelor's degree	245 (61.7)	109 (52.6)	354 (58.6)	
	Masters/PhD	28 (7.1)	13 (6.2)	41 (6.8)	
<b>Working Status</b>	Student	81 (20.4)	50 (24.1)	131 (21.7)	0.066
	Working	204 (51.4)	88 (42.5)	292 (48.3)	
	Housewife	77 (19.4)	39 (18.8)	116 (19.2)	
	Retired	35 (8.8)	30 (14.4)	65 (10.7)	
<b>Smoking Status</b>	Smoker	186 (46.9)	74 (35.7)	260 (43)	0.029*
	Non-smoker	192 (49.4)	123 (59.4)	315 (52.1)	
	Ex-smoker	19 (4.8)	10 (4.8)	29 (4.8)	
<b>Insurance</b>	Private	112 (28.2)	48 (23.2)	160 (26.5)	0.032*
	Ministry of Health	125 (31.5)	88 (52.5)	213 (35.3)	
	University	60 (15.1)	33 (15.9)	93 (15.4)	
	None	100 (25.2)	38 (18.3)	138 (22.8)	
<b>Body-Mass-Index</b>	Normal				0.809
	Underweight	142 (35.8)	66 (31.9)	208 (34.4)	
	Overweight	33 (8.3)	19 (9.1)	52 (8.6)	
	Obese	136 (34.3)	76 (36.7)	212 (35.0)	
		86 (21.7)	46 (22.2)	132 (21.8)	
<b>Comorbidities</b>	Hypertension	53 (13.4)	42 (20.3)	95 (15.7)	0.026*
	Diabetes Mellitus	35 (8.8)	31 (14.9)	66 (10.9)	0.021*
	Gastrointestinal disease	23 (5.8)	8 (3.8)	31 (5.1)	0.308
	Heart Disease	10 (2.5)	7 (3.3)	17 (2.8)	0.543
	Asthma	8 (2.0)	2 (1)	10 (1.7)	0.338
	Musculoskeletal disease	23 (5.8)	8 (3.8)	31 (5.1)	0.308
	Thyroid disease	16 (4.0)	12 (5.8)	28 (4.6)	0.327

Non-steroidal anti-inflammatory drugs; NSAIDs, \*Significant value.

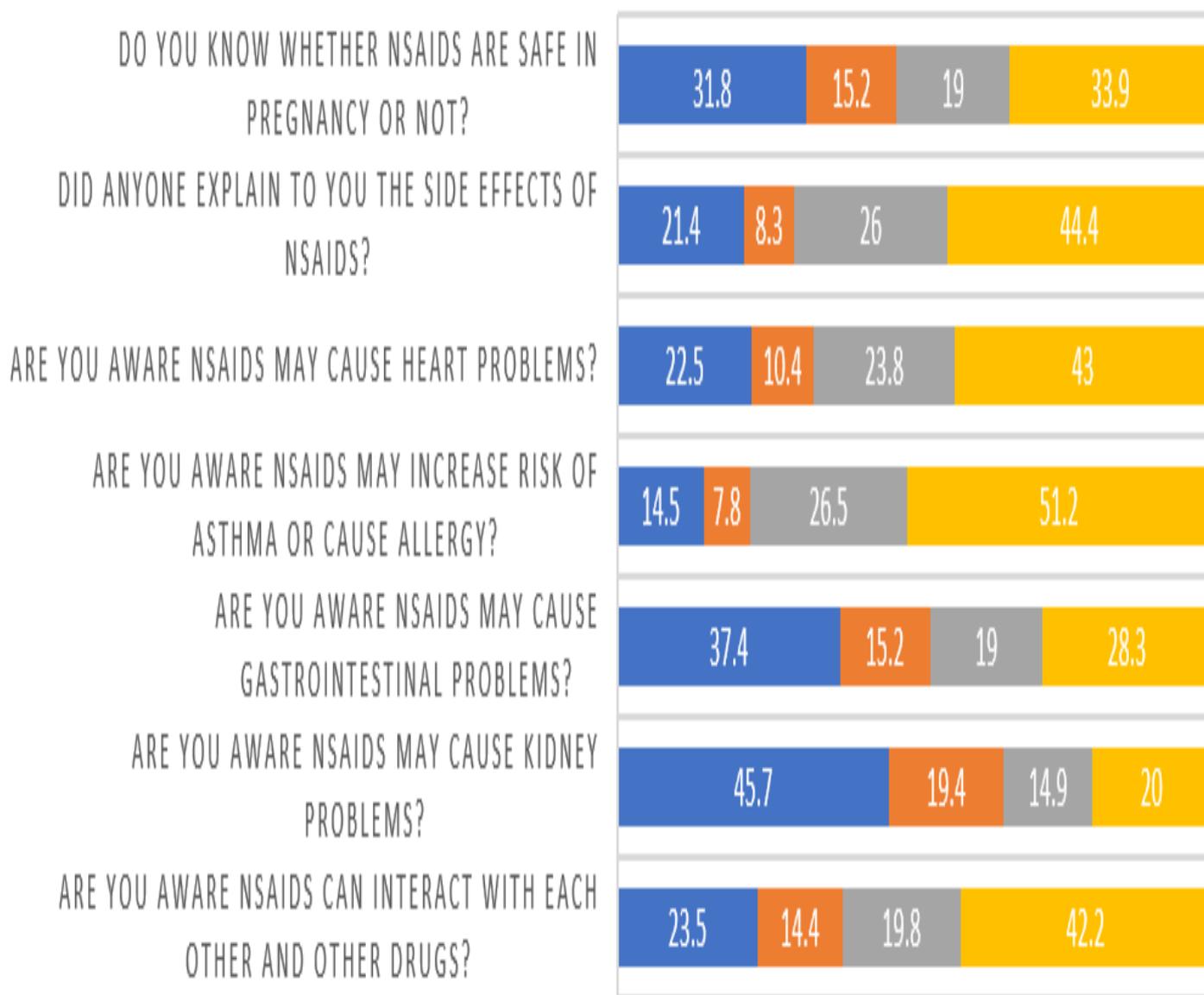


**Figure 1:** Indications for NSAID use among members of the Jordanian public.  
 NSAID = non-steroidal anti-inflammatory drug.



**Figure 2:** Awareness of NSAID-related side-effects among members of the Jordanian public.  
 NSAID = non-steroidal anti-inflammatory drug.

- percentage of people who use NSAIDS AND answered and are aware of side-effects
- percentnage of people who do not use NSAIDs and ARE aware of side-effects
- percentage of people who are do NOT use NSAIDs and answered are NOT aware of side-effects
- percentage of people who answered use NSAIDS and are NOT aware of side-effects



**Figure 3:** Awareness of NSAID-related side-effects among members of the Jordanian public according to patterns of utilization.

*NSAID = non-steroidal anti-inflammatory drug.*

**DISCUSSION;**

According to global estimates, NSAIDs comprise some of the most frequently utilized medications worldwide and taken by approximately 30 million people per day.[7] However, despite their frequency of use, NSAIDs also have the potential to cause considerable harm due to the risk of avoidable adverse drug reactions, including myocardial infarction, stroke, bleeding, and kidney damage.[8,9] NSAIDs are responsible for just under one-third of hospital admissions due to adverse drug reactions, predominantly affecting vulnerable patient populations such as the elderly, individuals taking multiple medications, and those with comorbid conditions such as cardiovascular disease, diabetes, hypertension, and pre-existing renal or liver impairment.[8]

This study showed that 65.7% of respondents were using NSAIDs, of which the majority were female and less than 50 years old. Several previous studies have also reported a greater frequency of NSAID use among women [10,11], possibly because female patients are more likely to develop migraines and suffer from menstrual pain. In turn, previous studies have shown that younger patients are more frequent users of NSAID medications [12-14]; this may be attributed to the fact that older people are more likely to suffer from comorbidities [15] and may therefore be wary of taking NSAIDs because of the increased opportunities for patient education of NSAID-related side-effects during doctor appointments. As for tobacco use, 49.4% of NSAID users in the current study were non-smokers. It is believed that smoking might increase pain threshold and tolerance levels [16,17], thereby lowering usage of analgesics.

We also noted that 73% of our population without health insurance were NSAID users. Lack of health insurance may result in affected individuals being unable to visit physicians or having access to follow-up care, thereby leading to increased self-medication practices [18]. Moreover, respondents with comorbidities reported decreased NSAID consumption compared to those without comorbidities. This was surprising as the

opposite trend was elicited in a study from Egypt, which reported that 63.5% of hypertensive patients used NSAIDs [19]. Our varying results may be explained by the fact that patients with comorbidities tend to visit physicians more often and may therefore be more educated about how such medications can worsen chronic health conditions like hypertension or diabetes [20-22].

Regarding patterns of NSAID usage, our findings showed that the most frequent indication for NSAIDs was headache (30%), similar to results reported from a study conducted in Scotland [23]. The most common frequency of usage was once per month or less often. Infrequent analgesic users should therefore be targeted for additional awareness initiatives, as well as close monitoring for possible side-effects. Our data indicated that 42.6% and 17% of users had NSAID prescriptions from a physician or pharmacist, respectively. However, 28.6% of respondents had self-prescribed themselves NSAIDs, indicating overuse of these medications in the public health system [24]. Moreover, only 29.6% of NSAID consumers in the current study were warned about the potential side-effects of such medications. A study from Switzerland found that physicians and pharmacists informed 47.3% and 25.6% of their patients, respectively, about potential side-effects [25]. Thus, healthcare professionals have an important role to play in adequately informing patients of the possible interactions and complications which may arise from NSAID utilization.

Most respondents were aware of NSAID-related kidney (65.1%) and GI (52.6%) side-effects, but few were aware of other possible side-effects such as asthma and allergies (22.4%). Similar findings have been reported among elderly citizens living in the Midwestern USA, in which 65.3% were aware of kidney problems, while only 25.0% knew of the increased risk of asthma and allergies [26]. These results indicate that awareness of NSAID-related side-effects is still inadequate in Jordan, suggesting that healthcare providers who prescribe or sell these drugs do not provide sufficient information. This could have serious

implications with regards to potential side-effects, toxicity, and illness resulting in utilization of these drugs, as illustrated by a prior study showing a possible relationship between lack of awareness of proper medication use and frequency of side-effects in the Jordanian population [27]. Moreover, this is supported by a study conducted in New Zealand in which lack of knowledge about adverse effects, along with taking the maximum dosage, placed consumers at risk of NSAID-related complications [28].

According to a review of the clinical and economic burden of adverse events resulting from NSAID utilization, it is estimated that more than 100,000 patients in the USA are hospitalized every year for GI complications alone, resulting in approximately 16,500 deaths [29]. While no similar data yet exist to illustrate the burden of NSAID-related hospitalizations in the developing world, it is highly probable that complications arising from the usage of such medications cause significant morbidity and mortality. Further studies would be useful in quantifying the burden that NSAID-related complications place on the healthcare systems of developing countries.

## **CONCLUSION;**

More than two-thirds of the study participants utilized NSAIDs. Given that most users were under 50 years of age, did not suffer from comorbidities, and were unaware of NSAID-related side-effects other than GI and renal problems, it can be concluded that there is a need to educate NSAID users outside of clinic and hospital settings. Additionally, healthcare workers must make additional efforts to educate their patients with regards to both acute problems related to NSAID utilization, such as an allergic reaction which may progress to life-threatening anaphylaxis, as well as long-term complications like kidney failure and peptic ulcer disease. The findings of this study may help define priorities in the Jordanian healthcare system, establish health policies on the national level, and aid in the counseling of patients regarding the appropriate use and possible adverse effects of NSAIDs.

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## **DECLARATIONS**

## **ETHICAL CONSIDERATIONS**

This a cross-sectional study was approved by our Institutional Review Board and all procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the World Medical Association Declaration of Helsinki. Written informed consent was obtained from all participants.

## **CONSENT FOR PUBLICATION**

Not applicable.

## **DATA AVAILABILITY**

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## **COMPETING INTERESTS**

The authors declare that they have no conflicts of interest.

## **FUNDING**

The authors received no specific funding for this work.

## **AUTHOR CONTRIBUTIONS**

Randa I. Farah contributed to the conception and design of the work. Aseil E. Khatib, Hiba J. Abu Ziyad, Dareen K. Jiad, and Lara R. Al Qusous contributed to the acquisition of data. Randa I. Farah and Aseil E. Khatib, Hazem Jaber contributed to the interpretation of data. Randa I. Farah and Aseil E. Khatib contributed to the analysis of data. Randa I. Farah, Aseil E. Khatib, Hiba J. Abu Ziyad, Dareen K. Jiad, and Lara R. Al Qusous contributed to drafting of the manuscript. Randa I. Farah and Aseil E. Khatib, Salma Alajarmeh critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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