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Assessment of ADRS in Patients Undergoing NSAID Treatment in a Tertiary Care Centre

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Abstract
Non-steroidal anti-inflammatory drugs are extensively prescribed for pain and inflammation management in dental care. However, NSAIDs are associated with an important danger of adverse drug reactions, mainly affecting the gastrointestinal, renal, and cardiovascular systems. This study intended to assess the incidence, pattern, severity, and causality of ADRs related to NSAID use in patients attending a tertiary care dental hospital.A prospective observational study was conducted in the departments of orthodontics, prosthodontics, and oral surgery at a tertiary care teaching dental hospital in North India. Patients aged 18–70 years receiving NSAIDs for dental pain were enrolled after informed consent. Demographic data, NSAID prescription details, and medical history were recorded. ADRs were monitored during follow-up visits on Day 7 and Day 10. Pain intensity was assessed using the Visual Analogue Scale.
Among the study participants, 39 ADR cases (13%) were reported. Ketorolac was the most frequently implicated drug, responsible for 35 ADRs (11.67%), followed by Diclofenac with 4 ADRs (1.33%). Other NSAIDs like Ibuprofen, Indomethacin, Aceclofenac, and Acetaminophen showed no ADRs. The most common adverse events were gastrointestinal symptoms, including nausea (32 cases), heartburn (10 cases), abdominal pain (10 cases), and gastrointestinal bleeding (8 cases). The mean VAS score reduced from 5.53 ± 1.12 at baseline to 3.46 ± 1.4 at Day 10, representing significant pain relief. ADR severity analysis exposed that most reactions were moderate (mean Hartwig and Siegel score: 3.04 ± 0.94). A statistically significant association was observed between the type of NSAID and ADR occurrence ($\chi^2 = 180.931$; $P < 0.001$).This study shows that while NSAIDs are effective in managing dental pain, their use is associated with a substantial risk of gastrointestinal and systemic ADRs, particularly with Ketorolac.
Keywords: *NSAIDs, adverse drug reactions, gastrointestinal symptoms, pain management, tertiary care.*

INTRODUCTION

Non-steroidal anti-inflammatory drugs are one of the maximums extensively prescribed therapeutic classes. They help as first-line agents for relieving pain, reducing inflammation, and lowering fever by inhibiting cyclooxygenase enzymes, which suppress prostaglandin synthesis [1]. In spite of their proven efficacy, NSAIDs are associated with important adverse drug reactions, placing patients at danger of gastrointestinal, renal, cardiovascular, and hypersensitivity difficulties [2].

ADRs are defined by the World Health Organisation as "noxious, unintended responses to a drug at normal doses for prophylaxis, diagnosis, or therapy" [3]. As a leading cause of morbidity and mortality, ADRs contribute substantially to hospital admissions, length of stay, and healthcare costs globally [4]. In tertiary care situations, characterised by complex disease profiles and polypharmacy, the risk and impact of ADRs are exaggerated [3]. Moreover, NSAIDs frequently represent up to a third of ADRs reported in these environments.

Numerous observational studies from tertiary care hospitals across India have spoken to this problem. For example, a prospective study in Uttar Pradesh involving 600 orthopaedic outpatients found NSAIDs accounted for a 5.83% incidence of ADRs; gastritis via diclofenac being the most reported reaction [5].

Similarly, a descriptive analysis of 100 orthopaedic patients in a tertiary teaching hospital reported ADRs in 26%, where over 70% were linked to diclofenac. These results echo national trends: one multicentric tertiary care review found NSAIDs responsible for 32.4% of ADRs, second only to antimicrobials, with common reactions manifesting in skin and gastrointestinal systems [6].

Causality assessment, such as Naranjo's algorithm, WHO-UMC, and Hartwig-Siegel severity scale, are regularly used in pharmacovigilance to characterise and grade ADRs [7]. Thai and colleagues established that the majority of NSAID-related ADRs are mild to moderate in severity and largely classified as "probable" or "possible" via these tools [8]. However, serious ADRs, especially gastrointestinal bleeding and acute kidney injury, though less frequent, can result in hospitalisation or worse consequences if not anticipated and managed promptly.

Effective pharmacovigilance programs in tertiary hospitals are serious to mitigate NSAID-related risks. Structured ADR reporting, regular training of healthcare professionals, and integration of monitoring protocols have been shown to enhance ADR detection and preventability [1]. However, under-reporting remains an important task, compounded by variable consciousness among clinicians and the absence of systematic surveillance systems [2].
Evaluating ADRs due to NSAIDs in tertiary care situations is vital to improve therapeutic safety, guide prescribing practices, and inform institutional policies. The present study purposes to assess the frequency, pattern, severity, causality, and preventability of NSAID-induced ADRs in patients at a tertiary care centre, thereby contributing indication to reinforce pharmacovigilance and patient safety initiatives.

METHODS

Research Design

A prospective observational study was conducted in the departments of orthodontics, prosthodontics, and oral surgery at a tertiary care teaching dental hospital in North India. The primary objective of the study was to assess the incidence, pattern, and severity of adverse drug reactions associated with the use of nonsteroidal anti-inflammatory drugs in dental patients. The study population included patients visiting the outpatient departments of these specialities who were prescribed NSAIDs for the management of pain related to dental procedures or conditions. For each enrolled patient, detailed demographic information, medical history, and NSAID prescription details, including the specific drug name, dosage, frequency, and route of administration, were systematically recorded. ADR monitoring was carried out during follow-up visits on Day 7 and Day 10 to identify and document any side effects or complications arising from NSAID therapy. In addition, pain levels were assessed using the Visual Analogue Scale at baseline and during the follow-up visits to assess the effectiveness of pain management. In cases where suspected ADRs were identified, a thorough evaluation was performed using established criteria. The World Health Organisation definition of ADRs was applied for identification, while the Naranjo Probability Scale was used to determine the causality assessment, categorising reactions as definite, probable, or possible. The Hartwig and Siegel Scale was employed to assess the severity of ADRs, classifying them into mild, moderate, or severe categories. This structured method ensured accurate monitoring of both the therapeutic consequences and the safety profile of NSAID usage in dental practice.

Inclusion Criteria:

- Patients prescribed NSAIDs for pain or inflammation.
- Male and female patients aged 18 to 70 years.
- Patients willing to participate and who provided written informed consent.

Exclusion Criteria:

- Patients with known liver or kidney disease.
- Patients with a history of cardiovascular disorders.
- Patients with a history of peptic ulcer disease.
- Patients receiving chronic glucocorticoid therapy or anticoagulant therapy.
- Pregnant or lactating women.
- Unconscious or critically ill patients.

Statistical analysis

Statistical analysis was performed using SPSS version 26 to assess the study data. For categorical variables, such as the gender distribution of adverse drug reactions, the Chi-square test was primarily used. In cases where the expected cell frequencies were low, Fisher's exact test was applied to ensure accurate statistical interpretation. To compare pain scores before and after NSAID administration, the Wilcoxon signed-rank test was utilised, as this non-parametric test is appropriate for analysing paired data when the normality assumption is not met. Through the analysis, a P-value of less than 0.05 was considered statistically significant, indicating the threshold for rejecting the null hypothesis and confirming the presence of meaningful associations or differences in the data.

RESULTS

In the 20–29 years age group, there were 22 female patients (61.1%) and 14 male patients (38.9%), totalling 36 patients. For the 30–39 years group, 51 females (70.8%) and 21 males (29.2%) were recorded, summing to 72 patients. In the 40–49 years category, the trend was similar, with 44 females (66.7%) and 22 males (33.3%), totalling 66 patients. The 50–59 years group comprised 52 females (67.5%) and 25 males (32.5%), accounting for 77 patients. Lastly, in the 60–69 years group, there were 34 female patients (69.4%) and 15 male patients (30.6%), making up 49 patients. Across all age groups, female patients consistently outnumbered male patients, representing a higher rate of dental care utilisation among women. This may reflect greater health-seeking behaviour and awareness of dental health among females compared to males, which is a trend often observed in healthcare utilisation studies. The Chi-square test value (χ^2 = 1.134) with a P-value of 0.889 indicates that there is no statistically significant association between age group and gender distribution. This suggests that while there is a numerical predominance of female patients in each group, the variation in male and female proportions across age categories is not statistically significant. The relatively uniform pattern across all age groups implies that gender preference for dental care does not significantly change with age (Table 1).

Table 1: Gender Distribution Across Age Groups in Dental Patients

Age Group		Female	Male	Total	χ 2	P-value
20-29 years	Number of patients	22	14	36	1.134	0.889
	% within Age Group	61.1%	38.9%	100.0%		
30-39 years	Number of patients	51	21	72		
	% within Age Group	70.8%	29.2%	100.0%		
40-49 years	Number of patients	44	22	66		
	% within Age Group	66.7%	33.3%	100.0%		
50-59 years	Number of patients	52	25	77		
	% within Age Group	67.5%	32.5%	100.0%		
60-69 years	Number of patients	34	15	49		
	% within Age Group	69.4%	30.6%	100.0%		

The majority of alcohol users belonged to the 60–69 years (72 patients) and 40–49 years (75 patients) categories, indicating a significant prevalence of alcohol use in middle-aged and elderly populations. Non-alcoholic individuals were still most represented in these age groups, but in comparatively lower numbers, suggesting lifestyle-related risk behaviours are prominent in older adults. The tendency was similar for smoking, where a higher prevalence was noted in the 60–69 years and 40–49 years cohorts. Non-smokers were relatively evenly distributed across age groups but comprised fewer individuals in the older population compared to smokers (Fig.1).

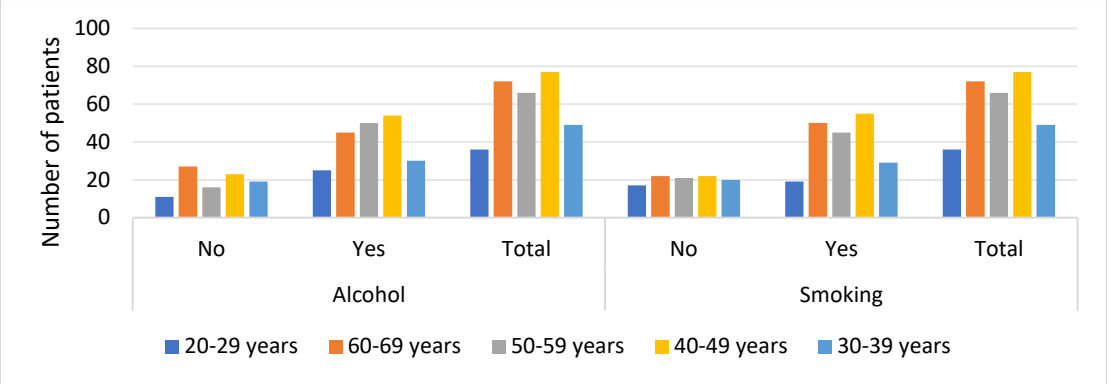

Fig. 1 Relationship Between Alcohol/Smoking Habits and Age

The Visual Analogue Scale was used to quantify pain intensity on Day 0 (baseline) and Day 10. On Day 0, the mean VAS score was 5.53 ± 1.12, indicating that most patients initially experienced moderate to severe pain at the time of presentation. This level of pain is typical in conditions such as dental abscesses, post-extraction inflammation, or temporomandibular joint disorders. By Day 10, the mean VAS score decreased to 3.46 ± 1.4, reflecting a significant reduction in pain intensity following dental interventions and pharmacological management. Even though some discomfort persisted, the decline in VAS scores demonstrates effective pain control and healing progression over the treatment period. The Hartwig and Siegel Severity Scale was used to assess the severity of ADRs related to prescribed medications. The mean severity score was 3.04 ± 0.94, suggesting that most adverse reactions were moderate in nature. A score around 3 typically corresponds to ADRs that required medical management but did not result in permanent harm or life-threatening events. Common reactions likely included gastrointestinal symptoms such as nausea, heartburn, or mild gastrointestinal bleeding, which were managed symptomatically without hospitalisation (Table 2).

Table 2: Assessment of Pain Reduction and Adverse Drug Reaction Severity in Dental Patients: A Prospective Analysis

Scoring	Mean Score
VAS at Day 0	5.53±1.12
VAS at Day 10	3.46±1.4
Hartwig and Siegel Severity Scale	3.04±0.94

Nausea emerged as the most common ADR, affecting 32 patients, making it the leading side effect, probably due to the gastrointestinal sensitivity induced by medications such as NSAIDs or opioids commonly prescribed for dental pain. Heartburn and abdominal pain were the next prevalent complaints, each reported by 10 patients, indicating the gastrointestinal side effects of analgesic therapy. Diarrhoea was reported in a small subset of patients, possibly linked to antibiotic-associated gastrointestinal upset. Less frequently reported reactions included gastric irritation (4 patients), constipation, flatulence, and peptic ulcers, each occurring in very few cases. Particularly, gastrointestinal bleeding was reported by 8 patients, a significant finding that underscores the need for cautious prescribing, especially in patients with pre-existing GI risk factors or those on long-term NSAIDs (Fig. 2).

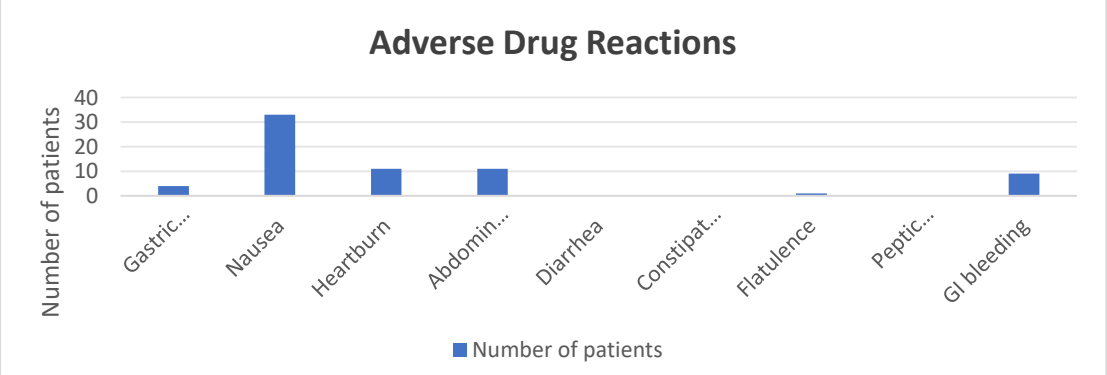

Fig. 2 Associated Adverse Drug Reactions in Dental Patients: An Observational Analysis

The presented data evaluate the occurrence of adverse drug reactions linked to the use of commonly prescribed analgesics in dental practice. Among the six drugs assessed, Ketorolac was found to be associated with the highest number of ADR cases, with 35 reported events, accounting for 11.67% of total drug exposures. Diclofenac was responsible for 4 ADR cases, representing 1.33% of the total. Particularly, Ibuprofen, Indomethacin, Aceclofenac, and Acetaminophen (Paracetamol) did not report any ADR cases in this dataset. The overall incidence of ADRs across all analgesics was 39 cases, corresponding to a 13% ADR rate in the study population. The high number of reactions associated with Ketorolac suggests a significant potential for gastrointestinal and systemic side effects with its use, consistent with its known pharmacological profile, which includes risks of gastrointestinal irritation, bleeding, and renal complications, especially in prolonged or high-dose therapy. The statistical analysis using the Chi-square test yielded a χ^2 value of 180.931 with a P-value < 0.001, indicating a highly significant association between the type of drug used and the incidence of ADRs. This strongly suggests that not all analgesics carry the same risk profile for adverse events in dental patients. The data imply that Ketorolac carries a substantially higher risk of ADRs compared to other analgesics in the study (Table 3).

Table 3: Incidence of Adverse Drug Reactions Associated with Analgesic Use in Dental Patients: A Statistical Analysis

Drugs	Number of ADR cases	%	χ 2	P-Value
Ibuprofen	0	0		
Ketorolac	35	11.67		
Indomethacin	0	0		
Diclofenac	4	1.33	180.931	<0.001
Aceclofenac	0	0		
Acetaminophen	0	0		
Total	39	13		

DISCUSSION

Non-steroidal anti-inflammatory drugs remain an essential component of clinical therapeutics for pain and inflammation management, particularly in orthopaedic, rheumatologic, and general medicine situations. In spite of their efficacy, the present study reinforces the substantial burden of adverse drug reactions associated with NSAID use in a tertiary care hospital environment. The observed ADR frequency in this study is parallel with previous literature, signifying that NSAIDs rank among the top contributors to drug-induced adverse events altogether [9].

The gastrointestinal system was the most frequently involved organ system in NSAID-induced ADRs in this cohort. This result is consistent with multiple studies reporting NSAID-induced gastritis, dyspepsia, and peptic ulcers as predominant problems [10]. NSAIDs inhibit prostaglandin synthesis via COX-1 inhibition, leading to compromised gastric mucosal protection and subsequent ulcer formation [11]. A study by Lanas et al. reported that long-term NSAID therapy increases the risk of upper gastrointestinal bleeding by up to fourfold, even with intermittent use [12]. In our population, gastritis and epigastric pain were the most frequently reported symptoms, and the need for routine gastroprotective measures, such as proton pump inhibitors, when prescribing NSAIDs, especially in high-risk patients [13].

Renal ADRs, though less common than GI difficulties, were also reported. NSAID-induced nephrotoxicity is primarily due to altered renal perfusion and acute interstitial nephritis [14]. Elderly patients and those with pre-existing renal impairment are predominantly vulnerable [15]. A study by Whelton emphasises that even short-term NSAID use can lead to important renal events, which may be preventable with early recognition and avoidance in threatened populations [16].

Hypersensitivity reactions, including urticaria and skin rashes, were less predominant but still clinically important. NSAID-induced hypersensitivity is typically non-immunologic and related to COX-1 inhibition-mediated shifts in arachidonic acid metabolism, resulting in leukotriene overproduction [17]. Some patients may require drug desensitisation or alternative analgesic regimens, such as selective COX-2 inhibitors, which have a lower frequency of hypersensitivity reactions but are not devoid of risks [18].

Causality assessments in this study, based on the WHO-UMC scale and Naranjo's algorithm, classified most ADRs as "probable," reflecting the temporal relationship with NSAID administration and positive rechallenge results. These results corroborate earlier research by Ramesh et al., who observed similar patterns in NSAID-related ADR causality assessments [19]. Severity assessments using the Hartwig and Siegel scale indicated that the majority of ADRs were mild to moderate, but about 10–15% required hospitalisation or involvement, echoing data from previous pharmacovigilance reports [20].

Under-reporting of ADRs remains an important task in tertiary care hospitals due to a lack of awareness, time constraints, and fear of medico-legal consequences [21]. Establishment of hospital-based pharmacovigilance systems, including regular training of healthcare professionals and simplifying ADR reporting processes, is essential to improve patient safety [22]. Moreover, patient education about early recognition of ADR symptoms can reduce delays in search of medical attention, potentially preventing complications [23].

In this study, the need for vigilant NSAID prescribing practices, regular monitoring for ADRs, and robust pharmacovigilance methods in tertiary care situations. Implementing preventive measures such as risk stratification, co-prescription of protective agents, and timely recognition of ADRs can mitigate the illness associated with NSAID use.

CONCLUSION

The results of this study emphasise the important problem of adverse drug reactions associated with NSAID use in dental practice, especially in a tertiary care setting. Ketorolac was identified as the major contributor to ADRs, predominantly gastrointestinal side effects such as nausea, heartburn, and gastrointestinal bleeding. Diclofenac was associated with fewer ADRs, and no adverse events were reported with Ibuprofen, Aceclofenac, Indomethacin, or Acetaminophen in this study. In spite of the effective reduction in pain scores over the treatment period, the occurrence of moderate severity ADRs emphasises the need for cautious prescribing practices, especially in patients with gastrointestinal risk factors. The study promotes the implementation of robust pharmacovigilance protocols, routine ADR monitoring, and preventive methods such as co-prescription of gastroprotective agents. In addition, patient education regarding early recognition of ADRs and timely medical consultation can play an essential role in mitigating severe consequences. Complete, this study contributes to the growing indication that NSAID safety monitoring is essential in dental care and the need for individualised therapeutic methods to balance efficacy with safety.

List of abbreviations

ADR – Adverse Drug Reaction
NSAID – Non-Steroidal Anti-Inflammatory Drug
VAS – Visual Analogue Scale
WHO-UMC – World Health Organization – Uppsala Monitoring Centre
COX – Cyclooxygenase (enzyme)
GI – Gastrointestinal
SPSS – Statistical Package for the Social Sciences

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