A Behavioural Study of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) in Relation to Risk Factors: Drug-Drug Interactions, Age, Elevated Serum Creatinine, and Pain Score Variations

Author- [1]Prapti Sonawane, [2]Gauri Thawali, [3]Dr.Vaishali Pardeshi, [4]Dr. Rahul Surve, [5]Dr.Trupti Tuse

[1]Student, [2]Student, [3]Assistant Professor, [4]Clinical Pharmacologist, [5]Principal

Department of Clinical Pharmacy, Abhinav Education Society's College of Pharmacy, Narhe, Pune 411041

Email- praptisonawane7932@gmail.com

ABSTRACT

Objective: This paper aims to examine the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on patients and promote the safe use of these medications. It includes a behavioural study of NSAIDs, focusing on outcomes such as changes in pain scores, drug-drug interactions, and variations in serum creatinine levels. Special attention is given to age-related differences in serum creatinine and the identification of high-risk groups that are more susceptible to elevated creatinine levels. These findings can contribute to better prevention of NSAID-induced nephrotoxicity.

Method: This is a prospective observational study conducted at a tertiary care hospital, with a total sample size of 223 participants.

Result: A total of 223 patients were included in the study. Of these, 133 (59.64%) were male and 90 (40.35%) were female. The commonly prescribed drugs in the study included diclofenac, aceclofenac, paracetamol, etoricoxib, aspirin, and naproxen.

A total of 24 drug interactions were identified, most of which were classified as minor drug-drug interactions. Pain scores were recorded using a numerical rating scale: 94 patients had a pain score of 0, 91 had a score of 1, 36 had a score of 2, and 2 patients had a score of 3.

Regarding renal function, 42 elderly patients (aged over 50 years) had serum creatinine levels greater than 1 mg/dL. In comparison, 15 patients aged between 15 and 50 years also had serum creatinine levels above 1 mg/dL.

Conclusion: The study aims to understand variations in drug effects based on different factors and conditions included in the analysis. These insights will assist healthcare providers in enhancing individual risk assessment and tailoring treatment plans accordingly.

Keywords: Safe use of NSAIDs, Risk factors, Drug interactions, Pain score observation, Polypharmacy, Serum Creatinine.

INTRODUCTION:

NSAIDs are commonly prescribed to manage conditions like rheumatoid arthritis, fever, pain and inflammation.[1]

Due to their wide range of therapeutic applications, NSAIDs are commonly used by patients. It is essential to educate individuals about the appropriate use of these medications. Healthcare professionals must ensure that each patient receives a dosage tailored to their specific condition and any coexisting medical issues a dose that is effective yet low enough to minimize adverse effects. One notable risk associated with NSAID toxicity is

nephrotoxicity. This occurs because NSAIDs reduce prostaglandin synthesis, which plays a crucial role in maintaining renal blood flow through vasodilation of renal arterioles.[2]

When multiple drugs are used simultaneously to treat one or more illnesses, drug-drug interactions may lead to unwanted effects, harmful side effects, or reduced clinical efficacy in certain patients.[3]One of the most frequent causes of adverse drug reactions is drug-drug interactions. Our findings indicate that older patients commonly experience these reactions due to polypharmacy.[4]

In practice, polypharmacy complicates medication management and increases the risk of clinically significant drug interactions, which may lead to adverse drug reactions and either diminish or enhance therapeutic outcomes. [5]When NSAIDs are taken alongside drugs administered more or less frequently, drug-drug interactions (DDIs) have been observed. These interactions can be categorized using several classification system

DDIs may result from pharmacokinetic mechanisms—such as changes in drug absorption, distribution, metabolism, or excretion—or from pharmacodynamic mechanisms, where enhanced, diminished, or antagonistic effects occur despite unchanged plasma drug levels. Additionally, some DDIs may arise from mechanisms that are not yet fully understood.[6]

Pain scales are tools that help patients communicate the intensity of their pain. These diagrams are also used by healthcare providers to assess and monitor a patient's condition. A pain scale typically presents a visual or numerical representation of pain levels, ranging from mild discomfort to extreme pain.[7]

Pain is one of the most common symptoms encountered in clinical practice. Due to the high prevalence of polypharmacy among elderly patients, effective pain management can be particularly challenging. Drug interactions and adverse reactions must be carefully considered to minimize health risks in this population. This is especially important with the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which carry a significant risk of negative interactions and side effects.[8]

Age-related changes in serum creatinine levels should be carefully considered when evaluating renal function after clinical interventions.[9]

Serum creatinine levels are a key indicator of kidney function. Several factors, including age and gender, significantly influence the normal reference range. In general, men should have serum creatinine levels between 0.6 and 1.2 mg/dL, while women typically fall within the range of 0.5 to 1.1 mg/dL. As individuals age, serum creatinine levels may decrease due to a natural decline in muscle mass.[10]As a result, NSAIDs are associated with a range of adverse effects, which can vary in severity. In elderly patients, approximately 23.5% of hospitalizations are due to adverse drug reactions (ADRs).[11]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a class of medications that share a common mechanism of action despite differences in their pharmacological profiles and chemical structures. They reduce the synthesis of inflammatory mediators such as prostaglandins by inhibiting the enzymes cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). These enzymes also play key roles in maintaining physiological functions, including gastrointestinal, renal, and cardiovascular health. Due to the increased risk of serious side effects, particularly in older adults, NSAIDs should be used with caution in the elderly population.[12],[13

MATERIALS AND METHODS

This was a prospective observational study conducted over a period of six months at a tertiary care hospital. Clinical data were collected from patients treated with NSAIDs, and the associated risk factors were analyzed. The study focused on key criteria, including drug-drug interactions, pain scores, and age-related variations in serum creatinine levels. All observations were analyzed and presented in statistical form.

Study design and duration:

This was a prospective observational study conducted over a period of six months at a tertiary care hospital. A total of 223 patients were included in the study sample.

Study criteria

Inclusion criteria: Inpatient department and patients treated with NSAIDs.

Exclusion criteria: Outpatient department, pregnant women, breast feeding women.

RESULTS

A total of 223 patients were included in this observational study. Of these, 133 (59.64%) were male and 90 (40.35%) were female. The most commonly prescribed NSAIDs among the study participants were diclofenac, aceclofenac, paracetamol, etoricoxib, aspirin, and naproxen.

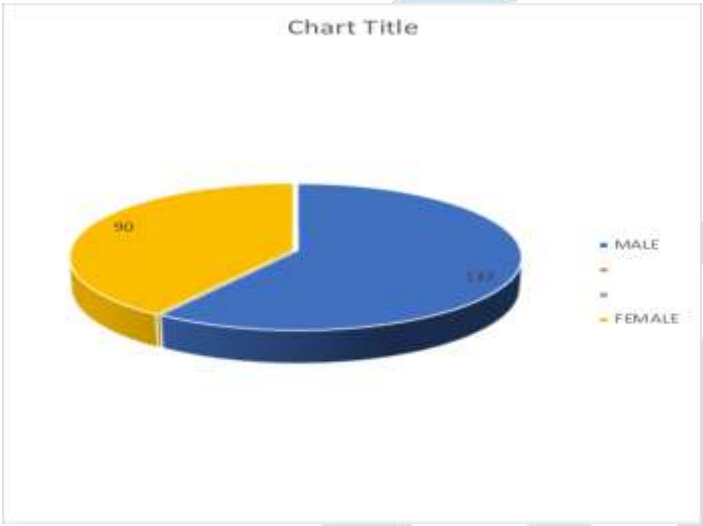

Figure1: Number of males and females prescribed with NSAIDs

Pain score observation

Pain scores were recorded for all 223 patients during treatment, following the administration of NSAIDs. Of these, 94 patients reported a pain score of 0, 91 reported a score of 1, 36 reported a score of 2, and 2 patients reported a score of 3.

Number of patients	Pain score
94	0
91	1
36	2
2	3

Table 1: Pain score report

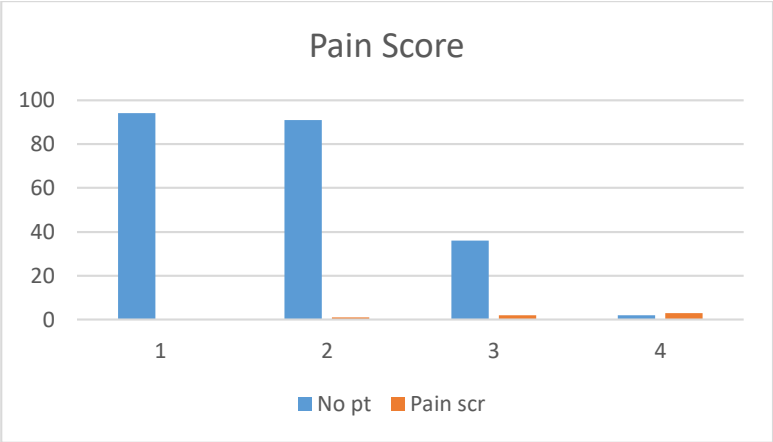

Figure 2: Pain score graph

Nonsteroidal Anti-inflammatory Drug Interaction with other drugs.

According to the study, nonsteroidal anti-inflammatory drugs (NSAIDs) were prescribed alongside other medications, resulting in minor drug-drug interactions in some cases. A total of 223 patients were included in the drug interaction analysis. Of these, 24 patients were prescribed drug combinations that showed minor interactions, while no interactions were observed in the remaining 199 patient.

DRUGS	NO. OF INTERACTION
Paracetamol - Ondansetron	18
Aceclofenac - Enoxaparin	1
Aceclofenac - Tramadol	2
Diclofenac - Dexamethasone	1
Naproxen - Aspirin	1
Naproxen - Metformin	1
None	199

Table 2: Number of drug interactions

Variations in serum creatinine according to age

Variations in serum creatinine levels were analyzed based on patient age. A total of 223 patients were included in the study. Of these, 112 patients were in the age group of 15 to 50 years, while111 patients were aged over 50 years.

Age group (15 to 50)

According to the study findings, serum creatinine levels varied with age, indicating age-related differences in renal function among the participants.

In this study, serum creatinine levels were observed in patients aged 15 to 50 years. A total of 112 patients were included in this age group. Among them, 15 patients had serum creatinine levels greater than 1 mg/dL, while 97 patients had levels between 0.6 and 1 mg/dL. These findings indicate that a smaller proportion of patients in

this age group showed a slight increase in serum creatinine, while the majority were within the normal or low-risk range.

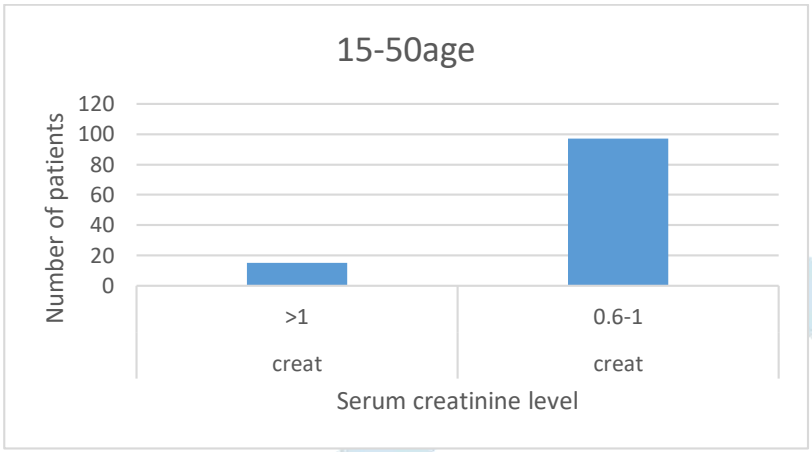

Figure 3: Representation of Variations in serum creatinine

Age group (> 50)

In this study, serum creatinine levels were also observed in patients aged over 50 years. A total of 111 patients were included in this age group. Among them, 66 patients had serum creatinine levels in the range of 0.6 to 1 mg/dL, while 42 patients had levels greater than 1 mg/dL, indicating a higher risk of elevated serum creatinine. These results suggest that elderly patients are at increased risk of impaired renal function.

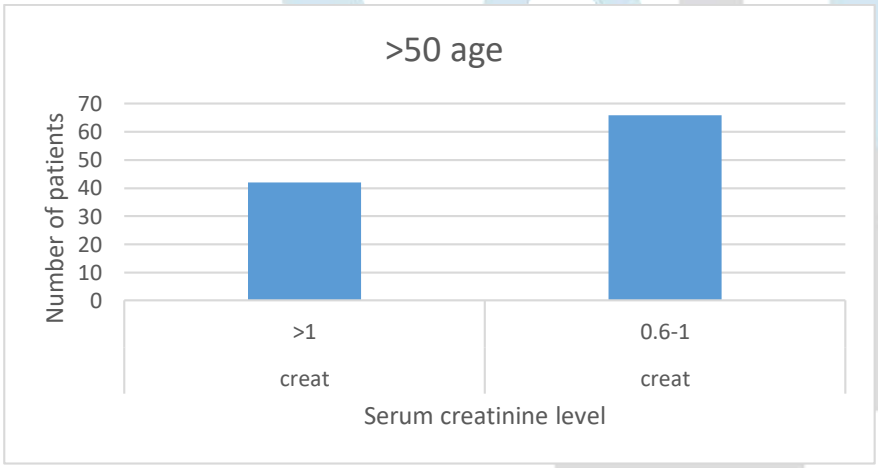

Figure 4: Representation of variations in serum creatinine

Discussion

Drug interactions can result in either diminished therapeutic effects or unintended adverse outcomes. As the number of prescribed medications increases, so does the risk of these interactions. This risk is particularly elevated in older adults due to the high prevalence of polypharmacy in this population. According to a meta-analysis, up to 7% of hospitalizations are related to adverse drug events.[14]

The aim of this paper is to enhance healthcare practitioners' awareness of potential drug interactions involving nonsteroidal anti-inflammatory drugs (NSAIDs). It seeks to provide healthcare providers with comprehensive and up-to-date information on NSAID-related interactions to support effective treatment of various conditions while minimizing patient risk.[15] The American Geriatrics Society advises against the concurrent use of

ibuprofen and aspirin, referencing a 2006 warning from the U.S. Food and Drug Administration (FDA). Evidence also suggests that this caution may extend to naproxen, but not to celecoxib.[16],[17]

Age is a known risk factor for NSAID-related kidney complications. As the prevalence of self-reported chronic pain increases with age, older adults are more frequently prescribed pain medications.[18]

Among individuals over the age of 65, up to 90% of all prescriptions include NSAIDs. This review highlights both the widespread use of NSAIDs in older adults and the associated risks.[19]

Most studies have found that the use of cyclooxygenase-2 (COX-2) selective NSAIDs significantly reduces the incidence of gastrointestinal, cardiovascular, and renal adverse drug reactions compared to non-selective NSAIDs.[20]

Older age and pre-existing renal disease are significant risk factors. Ibuprofen may slightly increase the risk of acute renal failure in individuals who are already experiencing renal stress due to factors such as physical activity in hot environments and dehydration.[21]

As people age, the incidence of comorbidities and polypharmacy increases, along with the prevalence of chronic musculoskeletal conditions such as osteoarthritis, which are commonly treated with NSAIDs.[22]

Older adults often have one or more chronic conditions that require analgesic treatment and are more susceptible to gastrointestinal complications. Therefore, it is essential to closely monitor their use of over-the-counter (OTC) NSAIDs.[23]

Acetaminophen, aspirin, ibuprofen, and naproxen are the four over-the-counter oral analgesics currently available in the United States.[24]

When used as directed, these over-the-counter analgesics provide a relatively safe, effective, and cost-efficient treatment option for mild to moderate pain, fever, and inflammation.[25]

Limitation

While this study provides valuable insights, it has certain limitations. The analysis primarily identified minor drug interactions, with no major drug interactions reported, which may limit the generalizability of the findings. Additionally, the sample size varied across different risk factor analyses, potentially affecting the consistency of subgroup comparisons. The study was limited to raising awareness of risk factors during treatment but did not evaluate whether these findings led to changes in prescribed drugs or dosages.

Conclusion

This study highlights the importance of understanding risk factors associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs) during treatment. It emphasizes the need for increased awareness of potential drug interactions, particularly in patients with comorbidities, where careful drug monitoring is essential. In elderly patients, the study identifies an increased likelihood of elevated serum creatinine levels, underlining the need for caution when prescribing NSAIDs. By analyzing variations in drug effects under different risk conditions, the study provides valuable insights to support individualized risk assessment and more informed treatment decision by healthcare providers.

Acknowledgement:

The successful completion of this study would not have been possible without the support, guidance, and efforts of many individuals.

We are sincerely grateful to Dr. Trupti Tuse, Principal of our institute, for her leadership and encouragement throughout this journey. Our deepest appreciation goes to our mentor, Dr. Vaishali Pardeshi, from the Department of Clinical Pharmacy. Dr. Rahul Surve Clinical Pharmacologist.Their expert advice, ongoing motivation, and insightful feedback played a crucial role in shaping our thesis.We also want to express our heartfelt gratitude to our families and friends, whose continuous support, patience, and belief in us gave us the strength to carry on.

Finally, we thank everyone who contributed to this project, whether directly or indirectly. Your support has truly meant a lot to us.

With sincere thanks,

Prapti Sonawane, Gauri Thawali

References

1) Farah RI, Albashaireh LE, AbuTaha A, Aldahlan WS, et al. Pattern of use and awareness of side-effects of non-steroidal anti-inflammatory drugs in the Jordanian population. **Ann Med.** 2023;55(2):2242248. doi:10.1080/07853890.2023.22422
2) Ghlichloo I, Gerriets V. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) [Internet]. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated 2023 May 1 [cited 2025 Jun 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547742/
3) Pichini S, Di Trana A, García-Algar O, Busardò FP. Drug-drug interactions in pharmacology.**Front Pharmacol.** 2023;14:1155738. doi:10.3389/fphar.2023.1155738.
4) allelli L, Colosimo M, Pirritano D, Ferraro M, De Fazio S, Marigliano NM, et al. Retrospective evaluation of adverse drug reactions induced by nonsteroidal anti-inflammatory drugs. **Clin Drug Investig.** 2007;27(2):115-22. doi:10.2165/00044011-200727020-00004.
5) Franceschi A, Tuccori M, Bocci G, Vannozzi F, Di Paolo A, Barbara C, et al. Drug therapeutic failures in emergency department patients: a university hospital experience. **Pharmacol Res.** 2004;49(1):85-91. doi:10.1016/j.phrs.2003.08.001.
6) Freedman MD. Drug interactions: classification and systematic approach. **Am J Ther.** 1995;2(6):433-43.
7) Zambon V. Pain scale types: benefits and limitations [Internet]. *Medical News Today*. 2020 Oct 22 [cited 2025 Jun 17]. Available from: https://www.medicalnewstoday.com/articles/pain-scale medicalnewstoday.com
8) Gosch M, Schramm W, Füllerer F, et al. Polypharmazie und Schmerztherapie. **Wien Med Wochenschr.** 2010;160(11-12):286-92. doi:10.1007/s10354-010-0788-z.
9) Tiao JY-H, Sykes KSL, Thompson MM, Nasim A, London NJ, Boyle JR, et al. Effect of age on serum creatinine levels in an aging population: relevance to vascular surgery. **Cardiovasc Surg.** 2002;10(5):445-51. doi:10.1016/S0967-2109(02)00056-X.
10) Garg P, Rohra D. Serum creatinine test normal range by age: complete values [Internet]. *MyHealth (Redcliffe Labs)*. 2022 Feb 24; updated 2025 Jan 9 [cited 2025 Jun 17]. Available from: https://redcliffelabs.com/myhealth/lab-test/serum-creatinine-normal-range-by-age-can-creatinine-levels-change-quickly/ scribd.com

11) American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. **J Am Geriatr Soc.** 2009;57:1331-46. doi:10.1111/j.1532-5415.2009.02376.x.

12) Wongrakpanich S, Wongrakpanich A, Melhado K, Rangaswami J. Comprehensive review of non-steroidal anti-inflammatory drug use in the elderly. **Aging Dis.** 2018;9:143-50. doi:10.14336/AD.2017.0306.

13) McDonald DD. Predictors of gastrointestinal bleeding in older persons taking nonsteroidal anti-inflammatory drugs: results from the FDA adverse events reporting system. **J Am Assoc Nurse Pract.** 2019;31:206-13. doi:10.1097/JXX.0000000000000130.

14) Cascorbi I. Drug interactions—principles, examples and clinical consequences. **Dtsch Arztebl Int.** 2012;109(33-34):546-55; quiz 556. doi:10.3238/arztebl.2012.0546.

15) Vostinaru O. Adverse effects and drug interactions of the non-steroidal anti-inflammatory drugs [Internet]. In: *Nonsteroidal Anti-Inflammatory Drugs*. London: InTech; 2017 [cited 2025 Jun 17]. Available from: http://dx.doi.org/10.5772/intechopen.68198.

16) Capone ML, Sciulli MG, Tacconelli S, Tontini C, Patrignani P, et al. Pharmacodynamic interaction of naproxen with low-dose aspirin in healthy subjects. **J Am Coll Cardiol.** 2005;45(8):1295-301. doi:10.1016/j.jacc.2005.01.045.

17) Renda G, Tacconelli S, Capone ML, Di Francesco L, Patrignani P, et al. Celecoxib, ibuprofen, and the antiplatelet effect of aspirin in patients with osteoarthritis and ischemic heart disease. **Clin Pharmacol Ther.** 2006;80(3):264-74. doi:10.1016/j.clpt.2006.05.004.

18) Nathan K. 3 absolute dangers of NSAIDs in elderly! Clinician's thoughts [Internet]. *Geriatric Academy*. 2023 Dec 10 [cited 2025 Jun 17]. Available from: https://geriatricacademy.com/nsaids-in-elderly/ geriatricacademy.com

19) Togo K, Ebata N, Yonemoto N, Abraham L. Safety risk associated with use of nonsteroidal anti-inflammatory drugs in Japanese elderly compared with younger patients with osteoarthritis and/or chronic low back pain: a retrospective database study. **Pain Pract.** 2021;22(2):200-9. doi:10.1111/papr.13079.

20) Monteiro C, Pereira P, Soares M, et al. Safety of non-steroidal anti-inflammatory drugs in the elderly: an analysis of published literature and reports sent to the Portuguese Pharmacovigilance System. **Int J Environ Res Public Health.** 2022;19(6):3541. doi:10.3390/ijerph19063541.

21) Weir MR. Renal effects of nonselective NSAIDs and coxibs. **Cleve Clin J Med.** 2002;69(Suppl 1):SI53-8. doi:10.3949/ccjm.69.suppl_1.si53.

22) Masclee GM, Valkhoff VE, Coloma PM, et al. Risk of upper gastrointestinal bleeding from different drug combinations. **Gastroenterology.** 2014;147(4):784-92.e9. doi:10.1053/j.gastro.2014.06.007.

23) 23) Silverstein FE, Graham DY, Senior JR, Davies HW, Struthers BJ, Bittman RM, Geis GS. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis

receiving nonsteroidal anti-inflammatory drugs: a randomized, double-blind, placebo-controlled trial. **Ann Intern Med.** 1995;123:241-9. doi:10.7326/0003-4819-123-4-199508150-00001.

24) *Physicians' Desk Reference for Nonprescription Drugs, Dietary Supplements, and Herbs.* 27th ed. Montvale (NJ): Thomson PDR; 2006. p. 194-216.

25) Wazaify M, Kennedy S, Hughes CM, McElnay JC. Prevalence of over-the-counter drug-related overdoses at Accident and Emergency departments in Northern Ireland: a retrospective evaluation. **J Clin Pharm Ther.** 2005;30:39-44. doi:10.1111/j.1365-2710.2004.00607.x.