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RESEARCH ARTICLE

Proton Pump Inhibitor-Induced Nephrotoxicity: A Study on the Prevalence of Acute Interstitial Nephritis

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Abstract: ***Background***: Proton pump inhibitors (PPIs) are widely prescribed for acid-related gastrointestinal disorders, with prolonged use becoming increasingly common. Recent evidence has raised concerns about potential renal complications, particularly acute interstitial nephritis (AIN), a reversible cause of acute kidney injury. This study evaluated the association between long-term PPI use and AIN and determined its prevalence among chronic users. ***Methods***: A retrospective observational study was conducted at Sree Balaji Medical College and Hospital, Chennai, using 10,000 archived medical records (2020–2025). From these, 638 patients with documented long-term PPI exposure were identified, and 120 met inclusion criteria (age ≥18 years, PPI use ≥2 weeks to 6 months, no pre-existing chronic kidney disease). Patients on nephrotoxic drugs or with autoimmune disorders were excluded. Clinical, biochemical, urinary, inflammatory, and imaging data were analyzed. Associations were assessed using chi-square tests and logistic regression. ***Results***: Of the 120 patients, 29 (24.2%) developed AIN. A significant association was found between PPI use exceeding six months and AIN occurrence ($p = 0.013$). Affected patients frequently presented with hematuria (45%), proteinuria (23.3%), and eosinophiluria ($p < 0.001$). Imaging revealed cortical scarring or renal enlargement in 71.7% of AIN cases, while inflammatory markers were significantly elevated. Omeprazole (29.2%) and lansoprazole (28.3%) were the most commonly implicated agents, although nephrotoxicity risk did not differ significantly between PPI types ($p = 0.31$). Withdrawal of PPIs with supportive therapy, including corticosteroids, resulted in full recovery in 82.75%, while 17.24% progressed to chronic kidney disease. ***Conclusion***: Long-term PPI use is significantly associated with AIN, particularly with therapy beyond six months. Early recognition, routine renal monitoring in chronic users, and prompt drug withdrawal are essential to prevent progression to chronic kidney disease. These findings underscore the importance of cautious prescribing, physician awareness, and stronger pharmacovigilance regarding PPI safety.

Keywords: Proton pump inhibitors, acute interstitial nephritis.

INTRODUCTION

Acute interstitial nephritis (AIN) is an immune-mediated form of acute kidney injury (AKI), defined histologically by interstitial inflammation and tubular epithelial cell injury. The majority of cases are drug-induced, accounting for 70–90%, with antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and, more recently, proton pump inhibitors (PPIs) being the principal culprits. Other causes include infections such as Streptococcus, Leptospira, and cytomegalovirus, as well as systemic autoimmune diseases including sarcoidosis, Sjögren's syndrome, and systemic lupus erythematosus. The underlying pathophysiology is most often a delayed-type (type IV) hypersensitivity reaction, characterized by infiltration of lymphocytes, eosinophils, plasma cells, and occasionally granulomas within the renal interstitium. Clinical recognition remains challenging, as AIN frequently presents with nonspecific features. The classical triad of fever, rash, and eosinophilia occurs in fewer than 15% of patients. More commonly, findings include hematuria, sterile pyuria, and rising serum creatinine. Although renal biopsy remains the diagnostic gold standard, the subtle and variable presentation often leads to underdiagnosis. Timely withdrawal of the offending drug usually results in recovery, while delayed recognition may lead to chronic interstitial nephritis and irreversible renal impairment.

Since their introduction in the late 1980s, PPIs have become integral to the management of acid-related gastrointestinal disorders such as gastroesophageal reflux disease, peptic ulcer disease, Zollinger–Ellison syndrome, and NSAID-induced gastropathy. Their efficacy, tolerability, and availability—often over the counter—have contributed to their widespread and frequently prolonged use. Although historically regarded as safe, accumulating evidence indicates a possible link between long-term PPI therapy and renal complications, particularly AIN.

Several retrospective cohort and registry-based studies have shown a consistent association between prolonged PPI exposure and biopsy-proven AIN, with some reporting a 1.5- to 2-fold increased risk compared to non-users. These risks are particularly pronounced in elderly individuals and those on multiple medications. While such studies cannot establish definitive causation, they provide strong evidence of a temporal and clinical relationship between chronic PPI therapy and AIN.

In India, the extensive and often empirical use of PPIs—fueled by over-the-counter availability—raises concern for under-recognized renal adverse effects. Despite this, local data on the prevalence of AIN in chronic PPI users remain scarce.

This study was designed to evaluate whether a significant association exists between long-term PPI use and the development of AIN and to estimate the prevalence of AIN among chronic PPI users in an Indian tertiary-care setting.

METHODOLOGY

Study Design and Ethical Approval

This retrospective cross-sectional observational study evaluated the relationship between long-term proton pump inhibitor (PPI) use and acute interstitial nephritis (AIN). The protocol was reviewed and approved by the Institutional Human Ethics Committee of Sree Balaji Medical College and Hospital, Chennai. All data were derived from archived medical records in accordance with ethical standards, with confidentiality maintained throughout.

Study Setting and Duration

The research was conducted at Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai, a tertiary referral center with multidisciplinary services. Medical records from January 2020 to January 2025 were screened, covering admissions across General Medicine, Nephrology, Medical Gastroenterology, Intensive Care, and the Medical Records Department (MRD).

Study Population and Sampling

Patients aged ≥18 years with documented continuous PPI use for at least two weeks were eligible. A purposive sampling technique was adopted, given the retrospective design. Out of 10,000 archived records reviewed, 638 patients had a history of prolonged PPI use. After applying inclusion and exclusion criteria, 120 patients were included in the final analysis.

Sample Size Determination

The sample size was calculated using OpenEpi software (CDC) based on the following statistical parameters:

- Z = 1.96 (95% Confidence Interval)
- p = 16% (expected proportion of PPI-associated AIN)
- q = 84% (100 − p)
- d = 7% (absolute precision)

Applying the formula:

$$n = \frac{Z^2 \cdot p \cdot q}{d^2} = \frac{(1.96)^2 \cdot 16 \cdot 84}{49} \approx 106$$

adjusting for a 10% potential non-response or exclusion rate, the final sample size was set at **120 participants**.

The reference for estimated prevalence was based on data from Sierra et al. (2007), who reported a 16% incidence of PPI-associated AIN in their systematic review.

Inclusion Criteria

- Age ≥18 years
- Minimum two weeks of continuous PPI therapy (omeprazole, pantoprazole, lansoprazole, esomeprazole, rabeprazole)
- Adequate clinical and laboratory documentation

Exclusion Criteria

- Known chronic kidney disease (CKD)
- Concurrent nephrotoxic medications (e.g., aminoglycosides, cisplatin)
- Other intrinsic renal pathologies (e.g., renal tubular acidosis)
- Autoimmune diseases, systemic infections, or vasculitis linked to interstitial nephritis
- Pregnant women, individuals <18 years, incomplete or illegible records

Data Collection

From the 10,000 screened records, eligible cases were identified using a structured proforma. Data extracted included:

- Demographics: age, sex, comorbidities
- Clinical presentation: admission details, presenting complaints
- Drug history: PPI molecule, dose, frequency, duration
- Laboratory investigations: serum creatinine, blood urea nitrogen, eGFR, electrolytes, complete hemogram, ESR, CRP, urine microscopy (proteinuria, hematuria, eosinophiluria)
- Radiological findings: ultrasonography for echotexture and corticomedullary differentiation
- Confounders: history of nephrotoxic drug exposure, infections, or autoimmune conditions

Operational Definitions

- **Acute Interstitial Nephritis (AIN)**: A clinical condition characterized by acute deterioration in renal function associated with inflammatory infiltrates and edema in the renal interstitium and tubules (1). Although histopathological confirmation with biopsy remains the gold standard investigation for the diagnosis of acute interstitial nephritis, a modified consensus including biochemical and radiological findings have been used to diagnose AIN, as Renal biopsy is an invasive test and may not indicated in some patients (e.g geriatric age group). (1)

- **Proton Pump Inhibitors (PPIs)**: A class of drugs that reduce gastric acid secretion by irreversibly inhibiting the hydrogenpotassium ATPase enzyme system in gastric parietal cells. Commonly prescribed for gastroesophageal reflux disease, peptic ulcer disease, and dyspepsia. (2)
- **Long-Term PPI Use**: Continuous administration of any PPI agent for more than two weeks, with or without dosage modification, and irrespective of indication. This operational definition is consistent with prior literature that identifies durations beyond two weeks as a potential threshold for renal adverse effects. (3,4)

Statistical Analysis

Data were compiled in Microsoft Excel and analyzed using IBM SPSS Statistics (Version 24.0). Categorical variables were expressed as frequencies and percentages, while continuous data were presented as mean ± standard deviation. Associations between categorical variables were assessed using chi-square or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee prior to data collection. Due to the retrospective nature of the study, informed consent for review of medical records was waived. However, in cases requiring clarification or missing information, verbal or written consent was obtained from patients or their representatives. All procedures adhered to the principles outlined in the Declaration of Helsinki.

RESULTS

TABLE-1: DISTRIBUTION OF AIN IN LONG TERM PPI USERS

Acute Interstitial nephritis	No. of Patients	Percentage
Present	29	24.2
Absent	91	75.8
Total	120	100.0

Acute Interstitial nephritis Among Study Participants

Among the 120 patients analyzed, acute interstitial nephritis (AIN) was identified in 24.2% (n = 29), while the remaining 75.8% (n = 91) showed no evidence of the condition. Thus, AIN was observed in less than one-quarter of the study population, suggesting it remains relatively uncommon in this cohort. The clustering of AIN in a subset of patients may indicate the influence of specific risk factors—such as prolonged proton pump inhibitor (PPI) therapy—which is a well-recognized cause of drug-induced interstitial nephritis. The disparity between affected and unaffected groups emphasizes the need to delineate clinical and demographic variables, including age, treatment duration, and urinary findings, that could predispose individuals to AIN. This distribution further underscores the importance of detailed evaluation into its pathogenesis, diagnostic markers, and optimal management approaches to enable early recognition and timely intervention in at-risk patients.

Graph-1: Distribution of Acute interstitial nephritis in long term PPI users

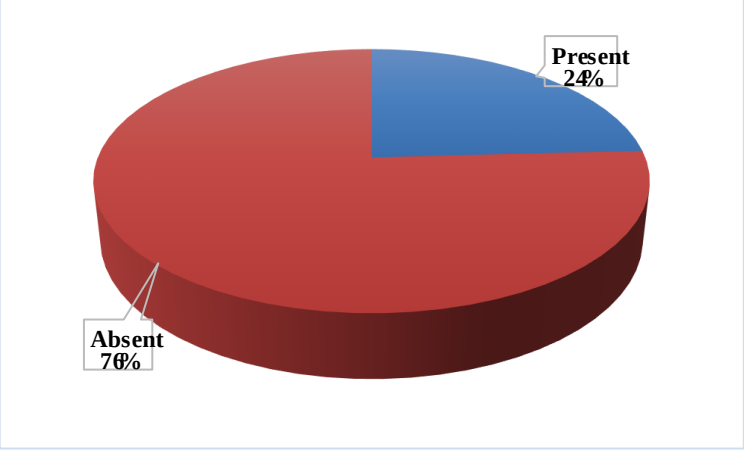


TABLE-2: AGE DISTRIBUTION OF STUDY POPULATION

Age	Frequency	Percent
18-30	10	8.3

31-40	25	20.8
41-50	22	18.3
>50	63	52.5
Total	120	100%

Age-Wise Distribution of Study Population

Analysis of the age distribution showed that more than half of the study population (52.5%, n = 63) were above 50 years, representing the largest subgroup within the cohort (N = 120). This predominance of older adults may reflect their increased susceptibility to chronic gastrointestinal disorders and the consequent long-term use of proton pump inhibitors (PPIs). The next most represented groups were patients aged 31–40 years (20.8%, n = 25) and 41–50 years (18.3%, n = 22). By contrast, the youngest category, 18–30 years, accounted for only 8.3% (n = 10), indicating limited representation of younger individuals.

Graph-2: Age Distribution of study population

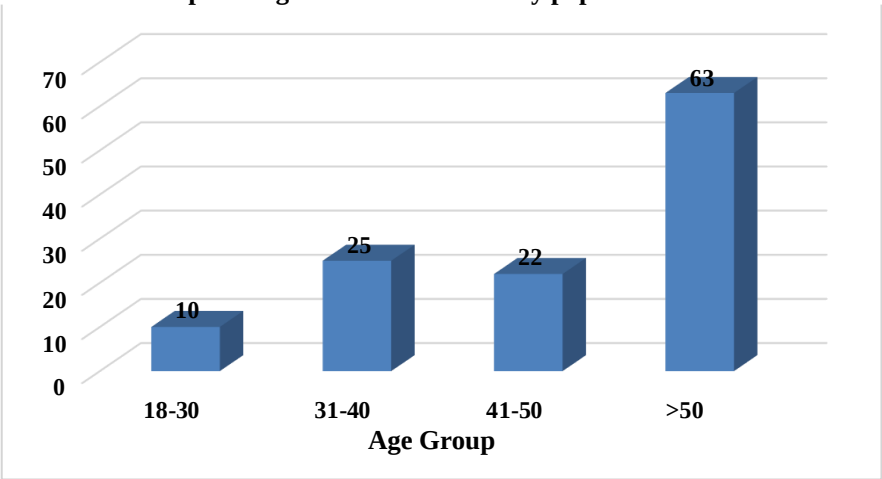


TABLE-3: GENDER DISTRIBUTION OF STUDY POPULATION

Gender	Frequency	Percent
Female	63	52.5%
Male	57	47.5%
Total	120	100%

Gender Distribution of the Study population

The study population exhibited a nearly equal gender distribution, with females representing 52.5% (n=63) and males comprising 47.5% (n=57) of the total sample (N=120). This balanced representation allows for a comprehensive and unbiased analysis of sex-based differences, if any, in the development of AIN associated with long-term proton pump inhibitor (PPI) use.

Graph-3: Gender Distribution of study population

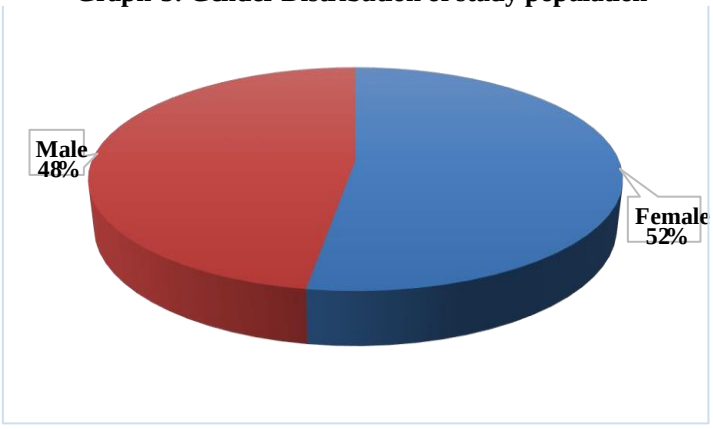


TABLE-4: DISTRIBUTION OF VARIOUS PPI TYPES USED BY STUDY POPULATION

PPI Type	Frequency	Percent
Esomeprazole	24	20%
Lansoprazole	34	28.3%
Omeprazole	35	29.2%
Pantoprazole	27	22.5%
Total	120	100%

Distribution of types of Proton Pump Inhibitor Agents

Within the study cohort, omeprazole (29.2%, n = 35) and lansoprazole (28.3%, n = 34) emerged as the most frequently prescribed proton pump inhibitors. The near-equal distribution of PPI use indicates no strong preference for a single agent, reflecting a relatively balanced prescribing pattern. Such variability in drug selection offers an opportunity for subgroup analyses to determine whether particular PPI formulations are associated with differing risks of renal injury. Establishing molecule-specific nephrotoxic profiles would aid in optimizing prescription practices and strengthening pharmacovigilance, especially for patients requiring prolonged acid suppression.

Graph-4: Duration of PPI Use Distribution

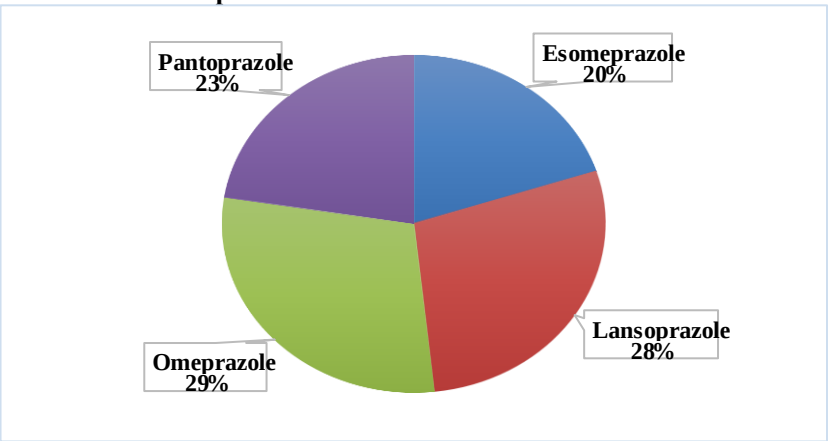


TABLE-5: DURATION OF PPI USE DISTRIBUTION

Duration of PPI Use	Frequency	Percent
2 weeks - 1 month	25	20.8%
1 month – 3 months	28	23.3%
3 months – 6 months	28	23.3%
>6 months	39	32.5%
Total	120	100%

Duration of Proton Pump Inhibitor Usage

A substantial proportion of participants had a history of extended proton pump inhibitor (PPI) use, with 32.5% (n = 39) receiving therapy for more than six months and 23.3% (n = 28) for three to six months. In total, 75.8% of the cohort had been on PPI treatment for longer than one month. This pattern highlights the widespread practice of prolonged PPI administration and underscores the relevance of assessing its renal implications. Duration of exposure emerges as a critical determinant in evaluating potential nephrotoxicity, particularly the risk of acute interstitial nephritis (AIN), among chronic PPI users.

Graph-5: Duration of PPI Use Distribution

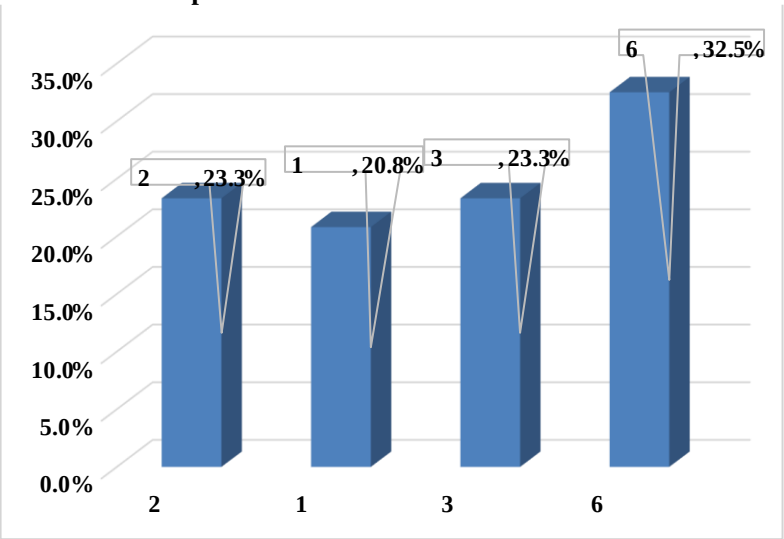


TABLE-6: COMPARISON OF AGE IN AIN

	Acute interstitial nephritis				
	No		Yes		
Age	**Count**	**% without AIN**	**Count**	**% with AIN**	**P value**
18-30	8	8.79	2	6.9	0.034
31-40	15	16.48	10	34.48	
41-50	14	15.38	8	27.59	
>50	54	59.34	9	31.03	
Total	91	100.0%	29	100.0%	

Age-Specific Susceptibility to Acute Interstitial Nephritis

Comparative analysis of age distribution and acute interstitial nephritis (AIN) demonstrated a statistically significant association (p = 0.034). Among participants without AIN (n = 91), the majority were over 50 years (59.3%, n = 54), with smaller proportions in the 31–40 (16.5%, n = 15), 41–50 (15.4%, n = 14), and 18–30 (8.8%, n = 8) groups. In contrast, of the 29 patients with AIN, the largest subgroup was aged 31–40 years (34.5%, n = 10), followed by those over 50 years (31.0%, n = 9), 41–50 years (27.6%, n = 8), and 18–30 years (6.9%, n = 2). These findings indicate that middle-aged adults (31–50 years) appear more susceptible to AIN compared to older adults, in whom chronic PPI exposure did not correspond to as high an incidence. This age-related variation suggests a possible differential risk profile for PPI-associated nephrotoxicity, emphasizing the need for targeted, age-specific monitoring strategies in clinical practice.

Graph-6: Comparison of Age in AIN

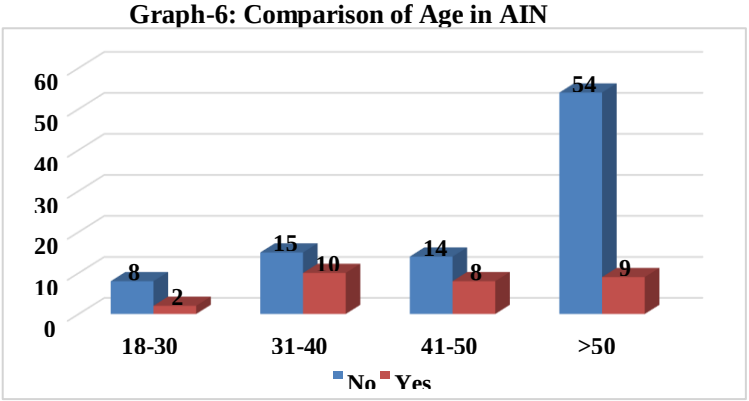


TABLE-7: GENDER-BASED COMPARISON AND RISK OF ACUTE INTERSTITIAL NEPHRITIS

	A		N		
	N	o	Yes		
Gender	**Count**	**%**	**Count**	**%**	**P value**
Female	45	49.45	18	62.07	0.236
Male	46	50.55	11	37.93	
Total	91	100	29	100	

Gender-Based Comparison and Risk of Acute Interstitial Nephritis

Analysis of gender distribution showed no statistically significant association with acute interstitial nephritis (AIN) (p = 0.236). In the non-AIN group (n = 91), males (50.6%, n = 46) and females (49.5%, n = 45) were nearly equally represented. Among patients with AIN (n = 29), females comprised a larger share (62.1%, n = 18) compared to males (37.9%, n = 11). While this indicates a slight female predominance, the absence of statistical significance suggests that gender is not a major determinant of AIN risk in the context of proton pump inhibitor (PPI) exposure. These findings support the view that renal monitoring in chronic PPI users should be applied uniformly across both sexes.

Graph-7: Gender-Based Comparison and Risk of Acute Interstitial Nephritis

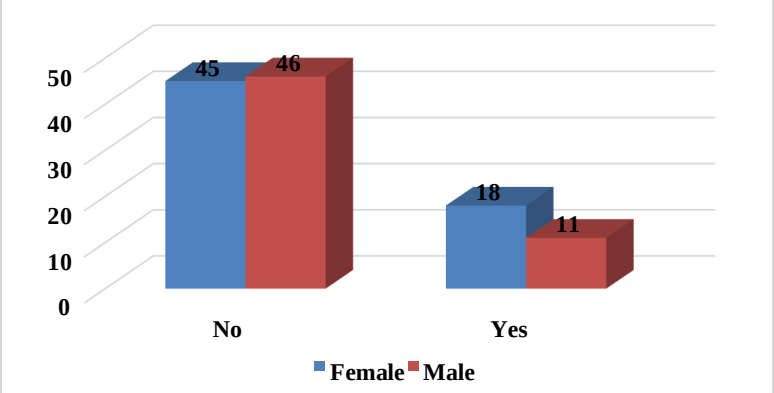


Table 8: COMPARISON OF PPI TYPE CAUSING AIN

	AIN				
	N	o	Y	es	
PPI Type	**Count**	**%**	**Count**	**%**	**P value**
Esomeprazole	16	17.58	8	27.59	0.058
Lansoprazole	31	34.07	3	10.34	
Omeprazole	23	25.27	12	41.38	
Pantoprazole	21	23.08	6	20.69	
Total	91	100	29	100	

PPI Type and Its Association with Acute Interstitial Nephritis

Comparison of individual proton pump inhibitors (PPIs) with the occurrence of acute interstitial nephritis (AIN) demonstrated a near-significant association (p = 0.058), indicating a possible relationship that merits further investigation. Among participants without AIN (n = 91), PPI use was distributed as esomeprazole in 17.6% (n = 16), lansoprazole in 34.1% (n = 31), omeprazole in 25.3% (n = 23), and pantoprazole in 23.1% (n = 21). In contrast, among patients diagnosed with AIN (n = 29), omeprazole accounted for the largest share at 41.4% (n = 12), followed by esomeprazole at 27.6% (n = 8), pantoprazole at 20.7% (n = 6), and lansoprazole at 10.3% (n = 3). Although statistical significance was not achieved, the relatively higher proportion of omeprazole use in the AIN group suggests the possibility of agent-specific nephrotoxic effects. These observations highlight the importance of larger, prospective studies to clarify whether certain PPIs pose greater renal risks, with potential implications for prescribing practices and long-term risk stratification.

Graph-8: Comparison of PPI Type causing AIN

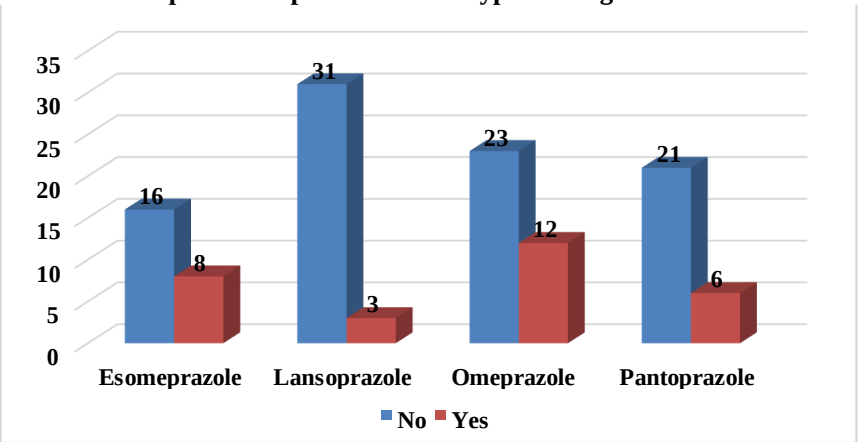


TABLE 9: COMPARISON OF DURATION OF PPI USE IN AIN

	AIN				
	N o		Y es		
Duration of PPI Use	**Count**	**%**	**Count**	**%**	**P value**
2 weeks - 1 month	22	24.18	3	10.34	0.013
1 month – 3 months	21	23.08	7	24.14	
3 months – 6 months	25	27.47	3	10.34	
>6 months	23	25.27	16	55.17	
Total	91	100	29	100	

Association Between Duration of PPI Use and acute interstitial nephritis

Analysis of the association between proton pump inhibitor (PPI) exposure duration and acute interstitial nephritis (AIN) revealed a statistically significant relationship (p = 0.013). Among participants without AIN (n = 91), treatment duration was fairly evenly distributed: 24.2% (n = 22) had used PPIs for 2 weeks to 1 month, 23.1% (n = 21) for 1–3 months, 27.5% (n = 25) for 3–6 months, and 25.3% (n = 23) for more than 6 months. In contrast, among patients with AIN (n = 29), more than half (55.2%, n = 16) reported PPI use exceeding 6 months. Shorter exposure was less common, with 24.1% (n = 7) on 1–3 months of therapy, and only 10.3% (n = 3 each) using PPIs for 2 weeks to 1 month or 3–6 months. These results suggest that prolonged PPI therapy, especially beyond six months, substantially increases the likelihood of AIN. The findings underscore the importance of regular renal function monitoring in long-term users and highlight the need for judicious prescribing to reduce the risk of drug-induced nephrotoxicity.

Graph-9: Comparison of Duration of PPI Use in AIN

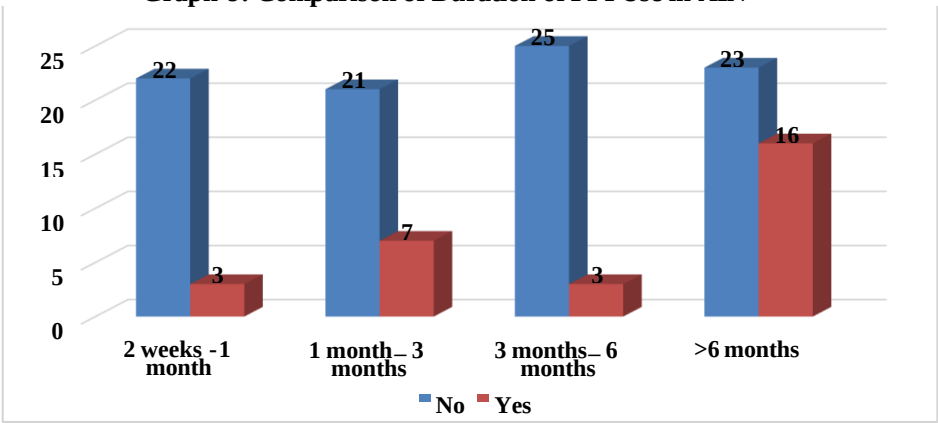


Table-10: OUTCOME IN PATIENT WITH ACUTE INTERSTITIAL NEPHRITIS (n=29)

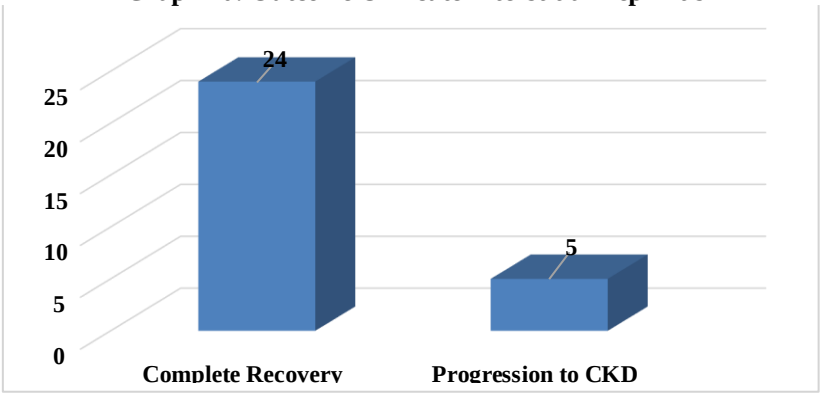
Outcome	No. of Patients	Percentage

Complete Recovery	24	82.75
Progression to CKD	5	17.24
Total	29	100

Outcome in patient with Acute Interstitial Nephritis

Among the 29 participants assessed for dialysis-related outcomes, 82.75% (n=24) demonstrated complete recovery of renal function, while 17.24% (n=5) progressed to chronic kidney disease (CKD). These figures reflect a full outcome capture within this subgroup and suggest that the majority of patients achieved favorable renal recovery following appropriate management. However, the persistence of renal dysfunction in a significant minority underscores the heterogeneity in clinical response, potentially reflective of the severity or duration of renal injury. This variability may be influenced by long-term proton pump inhibitor (PPI) use or additional comorbid factors and polypharmacy (e.g cytochrome inhibitors). The findings emphasize the need for prompt identification and timely intervention in individuals at risk, with the goal of mitigating irreversible renal damage and reducing the burden of progression to CKD.

Graph 10: Outcome Of Acute Interstitial Nephritis



DISCUSSION

This retrospective observational study conducted at Sree Balaji Medical College and Hospital, Chennai, examined the possible association between long-term proton pump inhibitor (PPI) therapy and acute interstitial nephritis (AIN). A cohort of 120 patients with chronic PPI exposure was analyzed to assess demographic factors, type and duration of PPI use, clinical features, and renal outcomes. Although a definitive statistical link between overall PPI use and AIN incidence was not demonstrated ($p > 0.05$), several clinically meaningful patterns >.

Age Distribution and AIN Susceptibility

Over half of the study population was above 50 years of age; however, the highest proportion of AIN cases (34.5%) occurred among patients aged 31–40 years. This age-related association was statistically significant ($p = 0.034$). These findings diverge from studies such as Muriithi et al., which reported greater AIN prevalence in older adults due to comorbidities, age-related renal changes, and polypharmacy [5]. Similarly, Xie et al. identified higher renal risks in elderly veterans on PPIs [6]. In contrast, our results may reflect prescribing trends in India, where younger adults are often placed on empirical PPI therapy for nonspecific dyspepsia [7,8]. This suggests that middle-aged patients, in addition to the elderly, may warrant closer renal surveillance during long-term PPI treatment [3,9].

Gender Distribution

The gender distribution was nearly equal (52.5% female), with no statistically significant association between sex and AIN ($p = 0.236$). However, women accounted for 62.1% of AIN cases, indicating a slight female predominance. Similar to our findings, Blank et al. in New Zealand and Geevasinga et al. in Australia reported no gender-specific predisposition to PPI-induced AIN [3,10]. The higher proportion of female cases in our study may reflect increased healthcare utilization or higher prevalence of GERD among women [13]. Taken together, the evidence suggests that gender is not an independent determinant of PPI-related AIN risk [11,12].

Type of PPI and AIN Risk

When analyzed by drug type, omeprazole accounted for 41.4% of AIN cases, followed by lansoprazole (10.3%). Although the association between PPI type and AIN did not reach significance ($p = 0.058$), the predominance of omeprazole is noteworthy. This aligns with the first report of omeprazole-induced AIN by Ruffenach et al. in 1992 [7]. Conversely, studies by Xie et al. and Blank et al. suggest higher relative risks with lansoprazole and esomeprazole compared to omeprazole [6,9]. Geevasinga et al., however, argued for a class effect, implicating all PPIs equally [3]. The predominance of omeprazole in our cohort likely reflects local prescribing preferences, given its affordability and widespread availability in India [13]. The near-significant p-value indicates that larger studies are needed to determine whether risk varies between PPI agents or is class-wide.

Duration of PPI Use and Renal Outcomes

Prolonged PPI exposure (>6 months) was significantly associated with AIN (p = 0.013), with more than half (55.2%) of AIN cases linked to extended therapy. This supports global evidence that chronic use increases nephrotoxicity risk. Xie et al. reported a 1.5–2-fold higher risk of AIN and CKD in long-term users [6], while Blank et al. observed a fivefold increase in risk among current users, particularly with longer treatment durations [10]. Similarly, Canadian cohort studies identified PPI use beyond 30 days as a significant risk factor [11]. Our smaller sample size (n = 120) may explain why overall incidence did not reach statistical significance despite alignment with international trends. The high prevalence of long-term PPI use (75% of our participants >1 month) reflects prescribing practices in India, where empirical and unsupervised use is common [7,14].

Strengths and Limitations

This study adds valuable Indian data to the global literature on PPI-induced nephrotoxicity and highlights demographic and prescribing patterns that differ from Western cohorts. Strengths include multi-departmental data collection, use of a structured proforma, and inclusion of biochemical and imaging markers in AIN diagnosis.

Limitations include its retrospective design, modest sample size, and reliance on clinical and radiological criteria rather than universal biopsy confirmation. While renal biopsy remains the diagnostic gold standard, practical limitations restricted its application to select cases. The near-significant findings regarding PPI type also suggest the need for larger, prospective cohorts to clarify agent-specific risks. Additionally, unmeasured confounders such as undocumented over-the-counter drug use or genetic predisposition could not be accounted for.

Future Directions

Future research should focus on prospective, multicenter studies with larger populations and routine renal biopsies to strengthen diagnostic accuracy. Comparative analyses with H2-blocker users, as reported by Klatte et al., may help delineate PPI-specific risks [15]. Exploration of genetic factors or metabolic variations in the Indian population could also explain the younger age susceptibility observed in our cohort [12,13]. Finally, research into non-invasive biomarkers for early AIN detection could reduce reliance on biopsy while ensuring timely intervention.

CONCLUSION

This study highlights the potential nephrotoxic risks associated with long-term PPI therapy. Although causality could not be definitively established, significant associations were observed with prolonged use (>6 months) and suggestive trends with PPI type. The findings emphasize the importance of rational prescribing, regular renal monitoring in chronic users, and greater clinician awareness in India, where PPI overuse is widespread. Early recognition and prompt withdrawal of the offending drug remain crucial to preventing irreversible renal damage and improving patient outcomes.

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