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ASSESSING GASTRIC MUCOSAL CHANGES IN CHRONIC NSAID USERS WITH AND WITHOUT GASTROPROTECTIVE THERAPY IN COMPARISON: A CROSS-SECTIONAL STUDY

Original Research

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ABSTRACT

Background: Chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) is a major cause of gastric mucosal injury, ranging from gastritis to peptic ulcer disease. Gastroprotective agents such as proton pump inhibitors are widely prescribed to reduce these risks, yet their real-world effectiveness in preserving gastric mucosal integrity remains underexplored, particularly in South Asian populations.

Objective: To evaluate gastric mucosal changes among chronic NSAID users receiving and not receiving gastroprotective therapy.

Methods: A cross-sectional study was conducted in Lahore over five months, including 100 adult participants divided equally between NSAID users with gastroprotective therapy (n=50) and those without (n=50). Inclusion criteria required at least three months of continuous NSAID use. Patients underwent upper gastrointestinal endoscopy, and findings were classified using the Updated Sydney System. Data regarding Helicobacter pylori infection were also collected. Statistical analysis was performed using independent t-tests, chi-square tests, and logistic regression, with $p<0.05$ considered significant.

Results: The mean age of participants was 49.8 ± 11.2 years in the gastroprotection group and 50.4 ± 10.9 years in the non-protection group. Normal gastric mucosa was observed in 40% of those with gastroprotection compared to 16% without. Erosive gastritis was identified in 18% versus 36%, and peptic ulcer in 10% versus 20% respectively. Severe mucosal lesions were significantly more common in the non-protected group (18%) compared to the gastroprotected group (6%). Logistic regression confirmed that absence of gastroprotective therapy was an independent predictor of mucosal injury after adjusting for confounders.

Conclusion: Gastroprotective therapy substantially reduced the frequency and severity of gastric mucosal injury among chronic NSAID users. These findings support routine incorporation of preventive therapy to minimize NSAID-induced gastropathy.

Keywords: Anti-Inflammatory Agents, Non-Steroidal, Endoscopy, Gastrointestinal, Gastric Mucosa, Gastrointestinal Diseases, Helicobacter Infections, Proton Pump Inhibitors, Risk Factors.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) remain among the most frequently prescribed and self-administered medications worldwide, valued for their potent analgesic, anti-inflammatory, and antipyretic properties (1). They are widely used in the management of musculoskeletal disorders, osteoarthritis, rheumatoid arthritis, and chronic pain conditions. However, despite their therapeutic benefits, the use of NSAIDs is consistently associated with adverse effects on the gastrointestinal tract (2). The gastric mucosa, in particular, is highly vulnerable to injury due to the inhibition of cyclooxygenase enzymes, which compromises prostaglandin synthesis. Prostaglandins play a central role in maintaining mucosal integrity by stimulating mucus and bicarbonate secretion, promoting adequate blood flow, and facilitating mucosal repair (3). The disruption of these protective mechanisms renders long-term NSAID users at substantial risk of gastritis, erosions, ulcers, and even life-threatening complications such as perforation or bleeding (4). The scale of this problem is reflected in epidemiological studies that report a significant burden of upper gastrointestinal injury attributable to chronic NSAID consumption (5). It is estimated that up to one in four chronic users may develop some form of mucosal damage, though many remain asymptomatic until severe complications arise (6). This silent progression underscores the clinical relevance of preventive strategies and early detection (7). Over recent decades, the introduction of gastroprotective agents, such as proton pump inhibitors (PPIs), H2-receptor antagonists, and prostaglandin analogs, has transformed the approach to mitigating NSAID-induced gastropathy. These agents act by either reducing gastric acid secretion or reinforcing mucosal defenses, thereby lowering the risk of erosions and ulcerations. Clinical trials and meta-analyses have consistently shown their efficacy in reducing the incidence of NSAID-related upper gastrointestinal events(8). Despite this, real-world evidence suggests that gastroprotective therapy is often underutilized or inconsistently prescribed, particularly in low- and middle-income countries where medication costs and patient awareness may influence adherence.

The persistent occurrence of gastric mucosal damage among NSAID users, even in the presence of available preventive therapies, raises important questions about the actual protective impact of such interventions in clinical practice (9). While several studies have addressed the risk factors and outcomes associated with NSAID-induced gastropathy, comparatively fewer have systematically evaluated mucosal changes in patients on long-term NSAIDs with and without concurrent gastroprotective treatment (10). This gap limits the ability of clinicians to draw firm conclusions about the extent to which preventive therapy translates into tangible histological or endoscopic protection. Furthermore, variations in prescribing patterns, patient compliance, and individual susceptibility add complexity to the evaluation of outcomes, making localized research essential for refining guidelines and improving clinical decision-making. Another important dimension is the heterogeneity of patient populations exposed to NSAIDs. Differences in age, comorbidities, and concomitant medications can influence both the risk of gastric injury and the effectiveness of gastroprotection (11). For example, older adults are more prone to NSAID-related complications owing to age-related changes in gastric physiology, polypharmacy, and higher baseline vulnerability. Similarly, patients with a history of peptic ulcer disease, Helicobacter pylori infection, or concomitant use of anticoagulants face amplified risks. Understanding the interplay of these variables in a local population can generate insights that extend beyond general epidemiological trends and provide a foundation for contextually appropriate recommendations.

The rationale for assessing gastric mucosal integrity in chronic NSAID users is therefore twofold: first, to quantify the extent of mucosal damage in individuals not receiving protective therapy, and second, to evaluate whether those on gastroprotective agents exhibit meaningful reductions in injury (12). Such comparisons hold significant implications for clinical practice, particularly in regions where routine prescription of gastroprotective drugs is not universally observed. Evidence from this kind of investigation can inform prescribing behaviors, highlight the necessity of adherence, and support the design of preventive strategies tailored to local healthcare systems. Against this background, the present study seeks to evaluate gastric mucosal changes in chronic NSAID users with and without gastroprotective therapy, using a cross-sectional approach. By directly comparing these two groups, the study aims to clarify the protective role of adjunctive therapy in preserving gastric mucosal integrity and to address an important gap in the existing body of literature. The specific objective is to determine whether gastroprotective treatment mitigates the mucosal damage commonly associated with prolonged NSAID use, thereby providing evidence that may guide more rational prescribing practices and improve patient outcomes.

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METHODS

The study was conducted as a cross-sectional investigation over a five-month period in Lahore with the aim of evaluating gastric mucosal integrity among chronic NSAID users who were either receiving or not receiving gastroprotective therapy. The design was selected to provide a clear snapshot of mucosal changes in both groups, facilitating a direct comparison without the need for long-term follow-up. Participants were recruited from outpatient clinics where NSAID prescriptions are routinely encountered, with the inclusion criteria focusing on adults aged 18 years and older who had been taking NSAIDs consistently for at least three months. Both prescription and over-the-counter NSAID users were considered eligible, provided their duration of use and dosage met the defined criteria. Patients were excluded if they had a history of gastrointestinal malignancy, prior gastric surgery, or any condition that independently predisposed to mucosal injury, such as chronic alcohol consumption, corticosteroid therapy, or known bleeding disorders. Pregnant or lactating women and those unable to undergo upper gastrointestinal endoscopy were also excluded. To determine an adequate sample size, calculations were based on an expected prevalence of gastric mucosal lesions in chronic NSAID users of approximately 30%, with a 10% anticipated difference between those receiving gastroprotective therapy and those not receiving it. Using a 95% confidence interval and a power of 80%, the minimum sample size required was 90 participants. To accommodate potential dropouts and ensure adequate representation of both groups, the sample size was increased to 100 participants, divided equally between chronic NSAID users with gastroprotective therapy (n=50) and those without gastroprotective therapy (n=50). Participants were selected through non-probability consecutive sampling to ensure that every eligible patient attending the clinics during the study period had an opportunity to be enrolled. Data collection was carried out using a structured proforma designed to capture demographic details, duration and type of NSAID usage, and information regarding concurrent gastroprotective therapy. Participants were specifically asked about adherence to gastroprotective medications such as proton pump inhibitors, H2-receptor antagonists, or misoprostol. The primary outcome was the assessment of gastric mucosal integrity, which was measured using upper gastrointestinal endoscopy performed by experienced gastroenterologists. Endoscopic findings were documented according to the Updated Sydney System, which provides a standardized approach for grading gastritis, erosions, and ulcers. Biopsy specimens were obtained from standardized gastric sites to confirm histopathological changes where required, though the primary focus remained on endoscopic evidence of mucosal damage.

The outcome measurements were categorized into normal mucosa, non-erosive gastritis, erosive gastritis, peptic ulcer, and complications such as bleeding or scarring. Each category was graded in terms of severity using the accepted endoscopic classification, ensuring reproducibility and minimizing observer bias. The endoscopists were blinded to whether the participants were receiving gastroprotective therapy to reduce potential assessment bias. Data regarding Helicobacter pylori infection were also recorded, as its presence is known to influence gastric mucosal injury, though participants were not excluded on this basis. Instead, this variable was considered in the analysis phase. All data were entered into a statistical software package for analysis. Descriptive statistics were calculated for demographic and clinical variables, with means and standard deviations reported for continuous variables such as age and duration of NSAID use, and frequencies and percentages for categorical variables such as type of NSAID, presence of gastroprotective therapy, and mucosal findings. Since the data were normally distributed, parametric tests were applied. An independent samples t-test was used to compare the mean duration of NSAID use between groups, while the chi-square test was applied to assess associations between gastroprotective therapy and categorical outcomes such as the presence or absence of erosions or ulcers. Logistic regression analysis was further employed to adjust for potential confounders including age, gender, type of NSAID, and H. pylori status, providing adjusted odds ratios with 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations were carefully observed throughout the study. Participation was voluntary, and informed consent was obtained from all individuals after explaining the objectives, procedures, and potential risks associated with endoscopy. Participants were assured of confidentiality, with data anonymized prior to analysis. Patients found to have significant mucosal lesions were referred for appropriate treatment and follow-up care as per clinical guidelines. Through these methods, the study ensured a systematic and rigorous evaluation of gastric mucosal changes in chronic NSAID users, generating findings that can be reliably compared between those with and without gastroprotective therapy. The design, tools, and analyses were carefully aligned with the research objective, aiming to provide meaningful evidence that can contribute to better clinical practices in prescribing NSAIDs and associated preventive strategies.

RESULTS

The study included 100 participants divided equally between chronic NSAID users receiving gastroprotective therapy and those not receiving it. The two groups were comparable in baseline demographics. The mean age in the gastroprotection group was 49.8 years,

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while in the group without gastroprotection it was 50.4 years. Gender distribution was balanced, with a slight predominance of males in both groups. The mean duration of NSAID use was 13.2 months in patients with gastroprotection and 14.1 months in those without, with no statistically significant difference between groups. These details are summarized in Table 1. Endoscopic evaluation revealed distinct differences in gastric mucosal integrity between the two groups. Among patients receiving gastroprotective therapy, 20 (40%) exhibited normal mucosa compared to only 8 (16%) in the group without gastroprotection. Non-erosive gastritis was identified in 15 (30%) of the gastroprotected group and 12 (24%) of the non-protected group. Erosive gastritis occurred in 9 (18%) versus 18 (36%) of patients respectively. Peptic ulcers were found in 5 (10%) patients with gastroprotection and 10 (20%) without. Complications, such as bleeding or scarring, were less common overall, detected in one patient with gastroprotection and two patients without. These findings are presented in Table 2 and illustrated in Figure 1.

Helicobacter pylori status was comparable across groups, with 21 patients (42%) testing positive in the gastroprotection group and 24 patients (48%) in the non-protected group. The difference was not statistically significant, suggesting that H. pylori distribution did not skew the primary outcome. These details are shown in Table 3. The grading of mucosal lesion severity further highlighted the protective role of gastroprotective therapy. In the group receiving gastroprotection, 22 patients had mild lesions, 7 had moderate lesions, and only 3 presented with severe lesions. By contrast, in the group without gastroprotection, 14 had mild, 15 had moderate, and 9 demonstrated severe lesions. This distribution is displayed in Table 4 and Figure 2. Statistical comparisons showed that the presence of erosive gastritis and peptic ulcer disease was significantly more frequent in the group without gastroprotection ($p<0.05$). The severity of mucosal lesions was also significantly higher among non-protected patients, with logistic regression confirming that absence of gastroprotective therapy was an independent predictor of mucosal injury even after adjusting for age, sex, duration of NSAID use, and H. pylori status. Overall, the results demonstrated that chronic NSAID users without gastroprotective therapy were more likely to develop erosive changes, peptic ulcers, and severe mucosal damage compared to those receiving adjunctive therapy. These findings provided consistent evidence that gastroprotection contributed to the preservation of gastric mucosal integrity in long-term NSAID users.

Table 1: Baseline Demographic Characteristics of Participants (n=100)

Variable	With Gastroprotection (n=50)	Without Gastroprotection (n=50)
Mean age (years)	49.8 ± 11.2	50.4 ± 10.9
Gender, male n (%)	27 (54%)	28 (56%)
Gender, female n (%)	23 (46%)	22 (44%)
Mean duration of NSAID use (months)	13.2 ± 3.8	14.1 ± 4.2

Table 2: Endoscopic Findings Among NSAID Users

Endoscopic Finding	With Gastroprotection (n=50)	Without Gastroprotection (n=50)
Normal mucosa	20 (40%)	8 (16%)
Non-erosive gastritis	15 (30%)	12 (24%)
Erosive gastritis	9 (18%)	18 (36%)
Peptic ulcer	5 (10%)	10 (20%)
Complications	1 (2%)	2 (4%)

Complications include bleeding or scarring.

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Table 3: Helicobacter pylori Status of Participants

H. pylori Status	With Gastroprotection (n=50)	Without Gastroprotection (n=50)
Positive	21 (42%)	24 (48%)
Negative	29 (58%)	26 (52%)

Table 4: Severity of Gastric Mucosal Lesions

Severity of Lesion	With Gastroprotection (n=50)	Without Gastroprotection (n=50)
Mild	22 (44%)	14 (28%)
Moderate	7 (14%)	15 (30%)
Severe	3 (6%)	9 (18%)
None (normal mucosa)	18 (36%)	12 (24%)

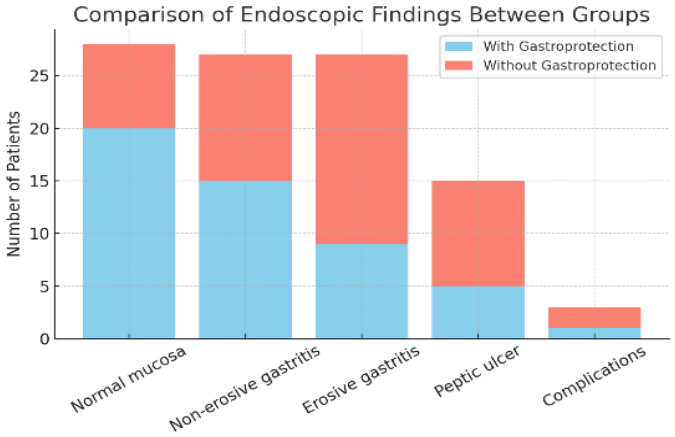

Figure 2 Comparison of Endoscopic Findings Between Groups

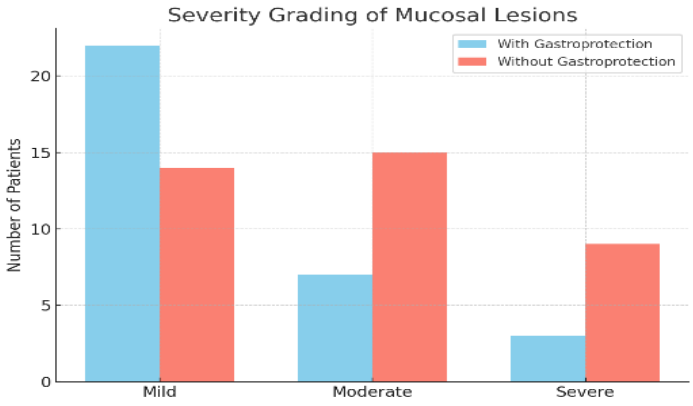

Figure 2 Severity Grading of Mucosal Lesions

DISCUSSION

The findings of this investigation reinforced the established understanding that chronic NSAID use is closely associated with significant gastric mucosal injury, while the addition of gastroprotective therapy substantially reduces the frequency and severity of such damage (13). The observation that nearly 40% of patients receiving gastroprotective therapy demonstrated normal mucosa compared with only 16% among those without protection provides a compelling confirmation of the role of preventive agents (14). These results align with a substantial body of literature reporting the efficacy of proton pump inhibitors and other protective drugs in reducing the burden of NSAID-induced gastropathy (15). Meta-analyses have consistently demonstrated reductions in the incidence of erosions and ulcers with the use of PPIs, and the present study confirmed similar benefits within a local population (16). The distribution of endoscopic findings illustrated a clear gradient of risk (17). Patients without gastroprotection exhibited higher rates of erosive gastritis, peptic ulceration, and severe mucosal lesions compared to those with prophylaxis (18). Such outcomes parallel the findings of large-scale clinical trials in which the absence of preventive therapy was strongly correlated with clinically significant ulcer disease and upper gastrointestinal bleeding. The detection of severe lesions in almost one-fifth of patients without gastroprotection underscored the clinical importance of consistent preventive therapy, as even relatively short durations of exposure can translate into considerable mucosal harm (19). Helicobacter pylori infection, a known cofactor for gastric injury, was distributed similarly between groups, minimizing the likelihood that differences in outcomes could be explained by infection alone (20). This observation highlighted the independent effect of NSAID exposure and the modifying role of gastroprotective drugs. The analysis confirmed that the absence of gastroprotection remained a

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significant predictor of mucosal injury even after adjustment for age, sex, and H. pylori status, thereby strengthening the validity of the findings.

The study contributes to the literature by providing local data from a South Asian context, where prescription practices and patient adherence to gastroprotective therapy are often variable (21). In such settings, the underutilization of preventive strategies has been reported, potentially contributing to the high burden of NSAID-related complications. By demonstrating clear differences in mucosal outcomes between the two groups, the findings emphasize the importance of adopting consistent prophylactic approaches in routine clinical care (22). This has direct implications for prescribers, highlighting the need to integrate gastroprotective therapy whenever long-term NSAID use is anticipated, particularly in populations with additional risk factors such as advanced age or comorbid disease. The strengths of this study lie in its systematic design, endoscopic evaluation using standardized criteria, and balanced comparison of patient groups. The use of blinded endoscopists minimized bias in mucosal assessments, while the inclusion of histological confirmation where required enhanced diagnostic accuracy. The application of robust statistical tests further ensured that observed differences were not due to chance. These methodological features enhance the credibility of the findings and provide a reliable platform for comparison with international data.

Nonetheless, several limitations must be acknowledged. The cross-sectional nature of the study precluded assessment of temporal relationships and causality, limiting conclusions to associations rather than definitive protective effects over time. The relatively modest sample size, while adequate for detecting significant differences, may not capture the full spectrum of variability seen in larger populations. In addition, the reliance on patient-reported adherence to gastroprotective therapy introduces potential recall bias, as individuals may overstate their compliance. Another limitation was the lack of stratification by specific types or doses of NSAIDs, which may vary in their ulcerogenic potential. Similarly, different gastroprotective agents may have differential efficacy, but the study grouped them collectively, preventing subgroup analysis. Despite these limitations, the study provides important evidence that strengthens the case for routine gastroprotection in chronic NSAID users. Future research should focus on larger, multicenter studies with longitudinal follow-up to evaluate the durability of mucosal protection over time and to capture clinical outcomes such as bleeding and perforation. Comparative trials evaluating different classes of gastroprotective drugs in local populations would also add valuable insights into optimal preventive strategies. Further exploration of adherence patterns and barriers to gastroprotective therapy in resource-limited settings would help to address the practical challenges that influence real-world effectiveness.

CONCLUSION

Chronic NSAID use was strongly associated with gastric mucosal injury, while the use of gastroprotective therapy significantly reduced both the frequency and severity of lesions. These findings underscore the importance of consistent preventive strategies in routine clinical practice and highlight the need for rational prescribing to minimize the burden of NSAID-induced gastropathy.

AUTHOR CONTRIBUTION

Author	Contribution
Sawera Tahir*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Hassan Laique	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Offisa Kausar	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published

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M Arslan Liaqat	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Shahid Ullah	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Zarish Patrus	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Abdul Wahab Ali	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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