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Is There an Endoscopic and Prognostic Difference between Bleeding Post-NSAID Bulbar Ulcers and Non-NSAID Bulbar Ulcers?

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Abstract

Background: Digestive toxicity caused by non-steroidal anti-inflammatory drugs (NSAIDs) is common and can be severe, particularly when leading to peptic ulcer hemorrhage. This study aimed to compare the endoscopic and prognostic characteristics of post-NSAID bleeding bulbar ulcers with non-NSAID bulbar ulcers. **Methods:** We conducted a retrospective, descriptive, and analytical study over a 25-month period in the Gastroenterology Department of Hassan II University Hospital of Fez. All cases of upper gastrointestinal bleeding due to bulbar ulcers were included. Patients were divided into two groups: those with NSAID exposure (Group A) and those without (Group B). Endoscopic and prognostic profiles were compared. **Results:** A total of 102 cases were included. NSAID use was documented in 40 patients (40.8%). Male predominance was observed in both groups. The mean age was 54.8 years in Group A and 52.7 years in Group B. No significant differences were found in hemoglobin levels, need for surgery, rebleeding rates, or transfusion requirements. Forrest stage III classification was observed in 54% of Group A versus 66.7% of Group B ($p = 0.69$). Multiple ulcers were more frequent in Group A (37.5% vs. 22.5%; $p = 0.004$). Endoscopic treatment was required in 35% of Group A versus 5% of Group B ($p = 0.03$). *Helicobacter pylori* infection was more common in NSAID users (80% vs. 50%; $p = 0.054$). **Conclusion:** Post-NSAID bulbar ulcers were more likely to be multiple and to require endoscopic treatment compared with non-NSAID bulbar ulcers, highlighting the severity of NSAID-related digestive bleeding. The coexistence of *H. pylori* infection and NSAID use further increased ulcer risk.

Keywords

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), Duodenal Bulbar Ulcer, Upper Gastrointestinal Bleeding, Endoscopic Findings, Prognosis, *Helicobacter pylori*

1. Introduction

A peptic ulcer is defined as a mucosal defect greater than 5 mm in diameter that develops within the lining of the stomach or duodenum. Various etiological factors may contribute to the occurrence of peptic ulcer disease, with *Helicobacter pylori* infection and the use of non-steroidal anti-inflammatory drugs (NSAIDs) representing the two principal causes [1]. Other less common causes of peptic ulcers are classified as *H. pylori*-negative and NSAID-negative ulcers. These include gastrinoma (Zollinger-Ellison syndrome), gastric malignancies such as adenocarcinoma and lymphoma, Crohn's disease, eosinophilic gastroenteritis, viral infections, Behçet's disease, acute stress, and mucosal ischemia [2].

The duodenal bulb is a common site for ulcer development, and hemorrhagic bulbar ulcers represent a frequent and potentially life-threatening condition. Although both NSAID and non-NSAID etiologies contribute to ulcerogenesis, little data exists comparing their clinical, endoscopic, and prognostic differences in the Moroccan population.

The objective of this study was to evaluate whether post-NSAID bleeding bulbar ulcers differ from non-NSAID bulbar ulcers in terms of endoscopic features and clinical outcomes.

2. Methods

Study design and setting:

We conducted a retrospective, descriptive, and analytical study at the Department of Hepato-Gastroenterology, Hassan II University Hospital of Fez, Morocco, over a 25-month period.

Patient selection:

All patients admitted with upper gastrointestinal bleeding due to duodenal bulbar ulcers confirmed by endoscopy were eligible. Patients were classified into:

- **Group A:** patients with a history of NSAID use prior to bleeding.
- **Group B:** patients without NSAID exposure.

Included agents were conventional NSAIDs (ibuprofen, diclofenac, naproxen, ketoprofen, indomethacin, aspirin ≥325 mg/day) as well as selective COX-2 inhibitors (celecoxib, etoricoxib, etc.). Low-dose aspirin (<325 mg/day) prescribed for antiplatelet therapy was not considered as NSAID exposure.

Dose and duration of NSAID: When available, dose and duration were recorded and classified as occasional use (<7 days), regular use (≥7 consecutive days), or chronic use (>1 month).

Time frame before bleeding: Only drug intake within 7 days prior to the bleeding episode was considered relevant exposure; earlier intake was excluded.

Inclusion criteria:

- ✓ Patients admitted with upper gastrointestinal bleeding confirmed by endoscopy as originating from duodenal bulbar ulcers.
- ✓ Age ≥ 18 years.
- ✓ Availability of complete clinical records, including medication history, allowing assessment of NSAID exposure.

Exclusion criteria:

- ✓ Patients with bleeding ulcers located outside the duodenal bulb.
- ✓ Cases where the bleeding source was non-ulcerative (e.g., varices, Mallory-Weiss tear, malignancy).
- ✓ Patients with incomplete or missing medical records regarding drug history.
- ✓ Recurrent admissions of the same patient during the study period (only the first episode was included).

Data collection:

Data included demographics, clinical presentation, hemoglobin levels, endoscopic findings (number of ulcers, Forrest classification), need for endoscopic or surgical intervention, transfusion requirements, rebleeding rates, and *Helicobacter pylori* (HP) status.

Statistical analysis:

Comparisons between groups were performed using univariate tests because of the relatively limited sample size, which precluded robust multivariate modeling. The primary objective of the study was descriptive, aiming to highlight potential clinical and endoscopic differences between NSAID-related and non-NSAID bulbar ulcers rather than to establish independent predictors. Therefore, univariate analyses were considered appropriate for the scope and statistical power of this study.

3. Results (Table 1)

a. Demographic and clinical characteristics:

A total of 102 patients were included, of whom 40 (40.8%) reported NSAID use prior to bleeding. There was a male predominance in both groups, with mean ages of 54.8 years (Group A) and 52.7 years (Group B).

b. Endoscopic findings:

- Forrest stage III ulcers were observed in 54% of Group A versus 66.7% of Group B ($p = 0.69$).
- Multiple ulcers were more frequent in Group A (37.5% vs. 22.5%; $p = 0.004$).

c. Prognostic outcomes:

- Endoscopic therapy was required in 35% of Group A compared with 5% of Group B ($p = 0.03$).
- No significant differences were observed between groups regarding baseline hemoglobin, surgical intervention, transfusion requirements, or rebleeding

rates.

- HP positivity was higher in NSAID users (80% vs. 50%; p = 0.054).

Table 1. Comparison between NSAID-related and non-NSAID bulbar ulcers.

Factors	NSAID-bulbar ulcers (A) (n = 40)	Non-NSAID bulbar ulcers (B) (n = 62)	p-value
Average age (years)	54.8	52.7	0.81
Sex ratio W/M	2	1.8	0.74
Hemoglobin level (g/dL)	8.1	8.4	0.89
Need for blood transfusion %	18	19	1.2
HP status (%)	80	50	0.054
Forrest III (%)	57.5	66.9	0.69
Multiple lesions (%)	37.5	22.5	0.004
Endoscopic treatment (%)	35	5	0.03
Recurrence of bleeding (%)	10	7	0.22

4. Discussion

Our findings indicate that post-NSAID bulbar ulcers carry a higher risk of multiplicity and often necessitate endoscopic intervention compared to non-NSAID ulcers. This aligns with previous observations that NSAID-induced ulcers tend to be deeper, more extensive, and more prone to complications, as these drugs compromise mucosal defenses through direct COX inhibition.

Chronic NSAID use is also well recognized to elevate the risk of severe upper gastrointestinal adverse drug reactions, including peptic ulcer disease and bleeding [3]. Moreover, recent clinical-endoscopic studies have reinforced the notion that NSAID-related gastroduodenal lesions are particularly serious and frequently require therapeutic endoscopic management [4]. Finally, endoscopic detection of ulcers serves as a valid surrogate marker of impending gastrointestinal complications in NSAID users [5].

A 2025 Korean review highlights that prolonged NSAID use notably contributes to peptic ulcer disease (PUD) and severe complications such as bleeding or perforation. The pathogenesis involves inhibition of cyclooxygenase (COX) enzymes and direct mucosal damage, impairing gastro-protective defenses. Importantly, it emphasizes that ulcers resulting from NSAID use often require potent acid-suppressive agents or endoscopic treatment [6]. This dovetails with our study's finding of increased need for endoscopic intervention in NSAID-exposed patients, reinforcing the notion of deeper and more extensive mucosal injury in this group. The same review also underscores the importance of preventive strategies: proton pump inhibitors (PPIs) and newly emerging potassium-competitive acid blockers are promising for prophylaxis and treatment. Moreover, *Helicobacter pylori* eradication is particularly crucial in patients taking NSAIDs due to the

synergistic risk for ulcer development [6].

Although foundational, earlier studies have established the credibility of endoscopic ulcers as a surrogate marker for NSAID-induced mucosal damage. A 2013 evaluation concluded that detection of endoscopic ulcers reliably indicates increased risk of future severe gastrointestinal harm, validating their use as an endpoint in both research and clinical practice [5].

Contemporary evidence: Recent large-scale and meta-analytic data reinforce the association between NSAID exposure and clinically significant GI bleeding. A 2024 meta-analysis showed that combining NSAIDs with anticoagulants doubles the risk of gastrointestinal bleeding compared with anticoagulant monotherapy, underscoring the additive hazard of NSAIDs in high-risk regimens [7]. Gutnliver In a 2024 nationwide real-world cohort of rheumatoid arthritis patients on long-term NSAIDs, the incidence of upper/lower GI bleeding remained substantial and gastroprotective strategies (PPI, rebamipide, DA-9601) showed comparable protection—highlighting the persistent baseline risk in chronic NSAID users despite prophylaxis [8]. Additionally, contemporary reviews and updates continue to identify NSAID use (particularly at higher doses or in older adults) as a key modifiable risk factor for non-variceal upper GI bleeding, aligning with our findings on ulcer severity [9].

This study has several limitations. First, its retrospective design may have introduced information and selection biases. Second, the assessment of NSAID exposure relied in part on patient or family reporting, which raises the possibility of recall bias, particularly for over-the-counter medications not documented in medical records. Finally, the modest sample size limited the statistical power of the analyses and may have restricted the ability to perform more comprehensive multivariate modeling.

5. Conclusions

In this retrospective study, we demonstrated that post-NSAID bulbar ulcers are more frequently multiple and significantly more likely to require endoscopic therapy compared with non-NSAID ulcers. While baseline clinical and prognostic parameters such as hemoglobin levels, transfusion requirements, surgical intervention, and rebleeding rates did not differ between the two groups, our findings highlight the distinct endoscopic severity of NSAID-related ulcers.

These results are consistent with previous literature indicating that NSAID-induced ulcers are often deeper, more extensive, and associated with higher morbidity. The synergistic presence of *Helicobacter pylori* infection further amplifies the risk of ulceration in NSAID users, emphasizing the importance of systematic screening and eradication strategies in this population.

Preventive approaches, including the cautious prescription of NSAIDs, routine gastroprotection with proton pump inhibitors, and emerging alternatives such as potassium-competitive acid blockers, remain critical to reducing the burden of ulcer complications. From a clinical standpoint, early endoscopic evaluation plays

a pivotal role in identifying high-risk lesions and guiding timely therapeutic intervention.

Overall, our study reinforces the need for vigilant risk stratification and comprehensive management strategies in patients exposed to NSAIDs, particularly in regions with a high prevalence of *H. pylori* infection. Further prospective studies with larger cohorts are warranted to refine preventive algorithms and optimize patient outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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