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ORIGINAL ARTICLE

Association between non-steroidal anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori* infection on the incidence of peptic ulcers

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Abstract

Background: Peptic ulcer is defined as damage to the upper gastrointestinal mucosa resulting in ulcer formation that extends to the submucosal layer. *Helicobacter pylori* act by producing various enzymes to damage gastric defenses resulting in chronic inflammation while NSAIDs inhibit the COX-1 enzyme which has a toxic effect on membrane permeability in the gastrointestinal system. This study was conducted to determine the association between the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and *H. pylori* infection on the incidence of peptic ulcers.

Methods: This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Hospital, Makassar. The samples used patients aged ≥18 years, had an upper gastrointestinal tract endoscopy. Endoscopy results are used to diagnose gastrointestinal ulcers. *H. pylori* infection diagnosed based on histopathology. NSAID use identified through interviews. Chi-square test and logistic regression were used to analyze the data.

Results: This study involved 151 subjects, history of NSAIDs 135 subjects (89.4%) and H. pylori positive 45 subjects (29.8%). Significant association ($p < 0.05$) between NSAIDs and the incidence of duodenum and gastric ulcers. Significant association

(p<0.05) also found in subjects with positive *H. Pylori* with the incidence of gastric and peptic ulcers. The incidence of duodenal ulcer (odds ratio, 5.358; 95% CI, 1.162–24.700) and gastric ulcer (odds ratio, 6.343; 95% CI, 1.370–29.362) was found to be independently associated with NSAID use.

Conclusion: There is an association between NSAIDs and H. pylori infection and the incidence of gastrointestinal ulcers. NSAID use has been found to be an independent risk factor for the development of duodenal and gastric ulcers.

Keywords: *Helicobacter pylori*, NSAIDs, peptic ulcer, gastrointestinal ulcer

INTRODUCTION

Peptic ulcer is defined as damage to the upper gastrointestinal mucosa resulting in ulcer formation that extends to the submucosal layer.(1) Helicobacter pylori and NSAIDs are the two most common causes of peptic ulcers.(2) H. Pylori acts by producing various enzymes that can damage the defense of the stomach resulting in chronic inflammation.(3) At the same time NSAIDs through the mechanism of inhibiting the COX-1 enzyme which has a toxic effect on membrane permeability in the gastrointestinal system.(4)

NSAID users had a 20–30% prevalence of peptic ulcers, with gastric ulcers occurring almost six times more frequently than duodenal ulcers.(5) The prevalence of peptic ulcers due to H. Pylori infection was 60%, with a higher incidence of duodenal ulcers (66.9%) compared to gastric ulcers (48.5%).(6)

A previous study reported that among 754 patients, there were 472 with duodenal ulcers, 193 with gastric ulcers, and 89 with peptic ulcers. H. pylori infection was more common in patients with duodenal ulcers, and NSAID use was more common in patients with gastric ulcers.(7) We conducted a study on the effects of H. pylori and NSAIDs on the incidence of peptic ulcers because gastrointestinal ulcers remain a public health concern, particularly when complications arise in the form of gastrointestinal bleeding.

METHODS

This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar from December 2023 until the minimum sample size was reached. Our minimum sample size was 83 patients. The study sample was patients aged ≥18 years who underwent endoscopic examination of the upper gastrointestinal tract at the gastroenterology department and were diagnosed with peptic, duodenal, and gastric ulcers regardless of the degree of ulcer, degree of activity, and form (primary or recurrent).

Histopathologic techniques were used to diagnosis H. pylori from ulcer samples, and the results were documented. Through interviews, NSAID use was verified. The variety and length of NSAID use were not differentiated in this study. A logistic regression test and a Chi-square test were used to assess the data. If the p value for a statistical test was less than 0.05, the results were deemed significant.

The study was approved by the Ethics Committee for Biomedical Research on Humans at the Faculty of Medicine, Hasanuddin University, Makassar, Indonesia. Based on the letter of recommendation Number: 920/UN.4.6.4.5.31/PP36/2023 with protocol number: UH23110823.

RESULTS

There were 151 subjects who met the criteria; the mean age in this study was 55.8 ± 13.0 years. NSAID was found in 135 subjects (89.4%), infected with H. pylori 45 subjects (29.8%). Gastric ulcer 65 subjects (43%), duodenal ulcer 60 subjects (39.7%), and peptic ulcer 26 subjects (17.2%).

Table 1. Subjects' characteristics.

Variabel	n (151)	%
Sex		
Male	88	58.3
Female	63	41.7
Age	57.17 + 13.01	
History of NSAID		
Yes	135	89.4
No	16	10.6
H. Pylori infection		
Yes	45	29.8
No	106	70.2
NSAID + H. Pylori		
Yes	40	26.5
No	111	73.5
Ulcer Location		
Gaster	65	43.0
Duodenum	60	39.7
Peptic	26	17.2

NSAID: *Nonsteroidal Anti-inflammatory Drugs*, HP: *Helicobacter pylori*;

Based on the location of gastrointestinal ulcers, subjects with a history of NSAIDs and positive H. pylori had the most duodenal ulcers at 35% (21/60), and negative H. pylori was found in gastric ulcers at 76.9% (50/65). Subjects without a history of NSAIDs with positive H. pylori found in duodenal ulcers were 5% (3/60), and negative H. pylori found in duodenal ulcers were 10% (6/10).

Table 2. Prevalence of gastrointestinal ulcers based on etiology and ulcer locations.

Variables	GU	DU	PU	Total
	n (%)	n (%)	n (%)	
NSAID (+)/ HP (+)	13 (20)	21 (35)	6 (23.1)	40
NSAID (+) /HP (-)	50 (76.9)	30 (65)	15 (57.7)	95
NSAID (-) /HP (+)	0 (0)	3 (5)	2 (7.7)	5
NSAID (-) /HP (-)	2 (3.1)	6 (10)	3 (11.5)	11
Total	65	60	26	**151**

NSAID: *Nonsteroidal Anti-inflammatory Drugs*, HP: *Helicobacter pylori*; GU: *Gastric Ulcers*; DU: *Duodenal Ulcers*; PU: *Peptic Ulcers.*

This study analyzed the relationship between NSAIDs and *H. pylori* with gastrointestinal ulcers. Gastric ulcers were found in 63 subjects (41.7%) with a history of NSAIDs and 13 subjects (8.6%) with positive *H. pylori*. Duodenal ulcers were found in 58 subjects (38.4%) with a history of NSAIDs and 13 (8.6%) with positive *H. pylori*. Peptic ulcers were found in 26 subjects (17.2%) with a history of NSAIDs and 3 (2%) with positive *H. pylori*. This study found a significant ($p<0.05$) correlation between Gastric and duodenal ulcers with NSAID. Subjects with gastric and peptic ulcers who confirmed positive for H. pylori also had significant results ($p<0.05$).

Table 3. Association between NSAIDs and H. pylori with gastrointestinal ulcers

Variables		NSAID			*H. pylori*		
		(+)	(-)	p*	(+)	(-)	p*
Gastric Ulcer	Yes	63	2	**0.009**	13	52	**0.022**
	No	72	14		32	54	
Duodenal ulcer	Yes	58	2	**0.019**	13	47	0.076
	No	77	14		32	59	
Peptic ulcer	Yes	26	0	0.054	3	23	**0.025**
	No	109	16		42	83	

*Chi square ($p<0.05$)

NSAID: *Nonsteroidal Anti-inflammatory Drugs*

Patients with History of NSAID had a higher risk of duodenal ulcer (OR, 5.358; 95% CI, 1.16–24.70; p<0.05) and gastric ulcers (OR, 6.343; 95% CI, 1.37–29.36; p<0.05) in multivariate analysis (Table 4).

Table 4. Multivariate analysis of NSAIDs and H. pylori on the incidence of gastrointestinal ulcers

variables	p	Odds ratio	95% CI.	
Gastric Ulcer				
NSAID	0.018	6.343	1.370	29.362
H. pylori	0.022	0.411	0.192	0.881
Duodenal Ulcer				
NSAID	0.031	5.358	1.162	24.700
H. pylori	0.077	0.503	0.235	1.077
Peptic Ulcer				
NSAID	0.998	3789.2	0.000	0.000
H. pylori	0.034	0.254	0.072	0.901

NSAID: *Nonsteroidal Anti-inflammatory Drugs*

DISCUSSION

There were 151 subjects who fulfilled the criteria, the mean age of the study subjects was 55.8 ± 13.0 years. Male gender was 88 subjects (58.3%), female 63 subjects (41.7%). NSAID history was found in 135 subjects (89.4%), 45 subjects (29.8%) were infected with H. pylori. The same results were found by Djumhana et al, about the prevalence of NSAIDs and H. Pylori in Indonesia on the incidence of gastrointestinal ulcers, H. Pylori infection 15% and NSAIDs 87.5% (Table 1).[8]

Previous investigations performed by Hamid et al found the prevalence of peptic ulcers in patients who were taking NSAIDs and H. Pylori positive was most prevalent in duodenal ulcers, 67% (16/24). H. Pylori infection without a history of NASID was mostly found in duodenal ulcers 70% (123/175). History of NSAIDs with negative H. Pylori was most common in duodenal ulcers 46% (13/28).[9] Research by Kim et al. found a

significant reduction in blood flow through the gastric antral mucosa (as determined by a laser doppler flowmeter) in subjects taking NSAIDs and significantly associated with an increased risk of gastric ulcers. These results are similar to our study which found subjects taking NSAIDs with positive H. pylori in duodenal ulcers 35% (21/60) and negative H. pylori in gastric ulcers 76.9% (50/65). Subjects without a history of NSAIDs with positive H. pylori were found in duodenal ulcers 5% (3/60) and negative H. pylori were found in duodenal ulcers 10% (6/10) (Table 2).[10]

This study found that NSAIDs were significantly associated with gastric and duodenal ulcers ($p<0.05$) while Helicobacter pylori infection was associated with the incidence of gastric ulcers and peptic ulcers. These results also confirmed the most common causes of gastrointestinal ulcers, where NSAIDs and H. pylori are the two independent factors that play the most role in gastrointestinal ulcer disease (Table 3). Previously Salit et al in a retrospective study in Turkey reported NSAIDs were associated with the incidence of gastric and duodenal ulcers while H. pylori was significantly associated with the incidence of gastric ulcers.[11] A study by Taha et al reported that NSAIDs were significantly associated with gastric metaplasia, gastritis and duodenal ulceration.[12]

In multivariate analysis, NSAIDs were found to be an independent risk factor for gastric ulcer and duodenal ulcer (OR, 6.343: 5.358; 95% CI, respectively). This result is not much different from previous studies that reported NSAIDs as an independent risk factor for gastrointestinal ulcers (OR: 1.34; 95% CI) (Table 4).[13]

Different results were found for helicobacter pylori infection on the incidence of gastric ulcer and peptic ulcer (OR, 0.411: 0.254; 95%CI, respectively). Some factors that are thought to affect these results are (1). The small number of subjects detected helicobacter pylori, (2). The method of diagnosis of helicobacter pylori which only uses the histopathology method of biopsy, (3). This study was conducted at a tertiary healthcare facility where most of the subjects had received eradication therapy at the primary healthcare facility. The clinical implication of this study is the need for careful consideration and close monitoring in prescribing NSAIDs to avoid the occurrence of peptic ulcers and complications.

CONCLUSIONS

NSAIDs and H. pylori infection are linked to an increased risk of gastrointestinal ulcers. NSAID use has been found to be an independent risk factor for the development of duodenal and gastric ulcers.

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Ethics committee approval

The ethics committee of Hasanuddin University's Faculty of Medicine in Makassar, South Sulawesi, Indonesia, accepted this study. Drawing from recommendation letter 920/UN4.6.4.5.31/PP36/2023, protocol number UH23110823

Conflict of interest

Every author certifies that they have no financial relationships (such as stock ownership, equity holdings, consulting, patent/licensing arrangements, etc.) that might create a conflict of interest with regard to the submitted work.

Authors' contributions

MF (Concept, Design, Materials, Sources, Data Processing, Analysis and Interpretation, Search for Literature, Manuscript Writing). SHK stands for Concept, Design, Supervision, Analysis, and Literature Search. LP stands for Concept, Design, Supervision, Analysis, and Interpretation; Research and Literature. SB (Concept, Design, Supervision, Interpretation and Analysis, Search of Literature). FS: Concept, Design, Supervision, Interpretation and Analysis, Literature Search. AS stands for Idea, Design, Analysis and Interpretation, and Critical

Assessment. The text was drafted, revised, and its content assessed by all authors. Each of them has reviewed and approved the article, attesting to the veracity and integrity of the study findings. All authors have reviewed and approved the completed work.

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