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Original Article

Role of Helicobacter Pylori Infection and Nonsteroidal Anti-Inflammatory Drug Use in Bleeding Peptic Ulcers

Zainab Irshad[1], Muhammad Sajjad Khan[2], Kamran[3], Muhammad Sohail[4*], Muhammad Fahim[5], Sundus Naeem[4], Salman Ur Rashid[4] and Syeda Rubina Gillani[6]

[1]Khyber Medical College, Peshawar, Pakistan
[2]Primary Health Services, Bannu, Pakistan
[3]Primary Health Services, Charsadda, Pakistan
[4]Primary Health Services, Mardan, Pakistan
[5]Medical Teaching Institution, Mardan Medical Complex, Mardan , Pakistan
[6]Primary Health Services, Nowshera, Pakistan

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***Corresponding Author:**
Muhammad Sohail
Primary Health Services, Mardan, Pakistan
drsohailgastro@gmail.com

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ABSTRACT

Most peptic ulcers and their complications are caused by Helicobacter pylori and nonsteroidal anti-inflammatory drugs (NSAIDs). **Objective:** To characterize the bleeding peptic ulcers features. **Methods:** This prospective study was carried out on 124 cases in the Department of Gastroenterology, Lady Reading Hospital in collaboration with Pharmacology Unit of Khyber Medical University, Peshawar from July 2018 to June 2020. All the patients were categorized into four groups: Positive H. pylori and no NSAID history (Group I), Positive H. pylori and NSAID use (Group-II), Negative H. pylori and NSAID user (Group-III), and Negative H. pylori and no NSAID history (Group-IV). Data analysis was carried out in SPSS version 26. **Results:** Of the total 124 cases, the prevalence of positive and negative H. pylori infection was 77.4% (n=96) and 22.6% (n=28) respectively. The number of patients in group I, II, III, and IV patients were 80 (64.5%), 16 (12.9%), 17 (13.7%), and 11 (8.9%) respectively. The incidence of NSAID users were 33 (26.6%) patients, out of which 18 used on daily basis and 15 on demand. Those in groups I and IV were substantially younger than groups II and III and they had less comorbid disorders than patients in group I. **Conclusion:** The present study concluded that about 26.6% of patients with bleeding ulcers took NSAIDs, meaning that low-dose aspirin will cause bleeding ulcers as will NSAID use on-demand.

INTRODUCTION

Helicobacter pylori and nonsteroidal anti-inflammatory medication (NSAID) are the most major risk factors in the pathophysiology of peptic ulcer disease and ulcer bleeding [1]. Those infected with H. pylori have a slightly higher risk of peptic ulcer bleeding, while patients using NSAIDs have an approximately fivefold greater risk [2]. A previous study investigated the bleeding peptic ulcer patients taking NSAIDs to compare with matched control and found that H. pylori infections was reported in 16% patients of bleeding peptic ulcer with NSAIDs users. Another study reported that the incidence of H. pylori negative ulcers was 8.8% [3]. Numerous investigations reported that peptic ulcers patients who are infected with H pylori and who are being treated with NSAIDs are more likely to develop H pylori negative ulcers [4, 5]. Non-bleeding ulcers have been shown to be less likely to be infected by H pylori than bleeding ulcers [6, 7]. Researchers studying Helicobacter pylori and nonsteroidal anti-inflammatory medications (NSAIDs) in the context of peptic ulcer disease have reached conflicting conclusions regarding their potential

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roles in the etiology of peptic ulcer disease [8, 9]. However, in multiple epidemiological studies of NSAID-treated individuals, H pylori infection reduced the frequency of peptic ulcer illness compared to those without it [10]. Randomized controlled clinical trials have also yielded conflicting results, studies that examine the eradicating effect of the H. Pylori infection and NSAID users on ulcer healing and their risk of developing peptic ulcers [11]. The incidence of negative H. pylori infectious ulcers is limited in the absence of NSAID use [12].

METHODS

This prospective study was carried out on 124 cases in the Department of Gastroenterology, Lady Reading Hospital in collaboration with Pharmacology Unit of Khyber Medical University, Peshawar from July 2018 to June 2020. All the patients were categorized into four groups: Positive H. pylori and no NSAID history (Group I), Positive H. pylori and NSAID use (Group-II), Negative H. pylori and NSAID user (Group-III), and Negative H. pylori and no NSAID history (Group-IV) as shown in table 1. WHO software for sample size calculation was used by taking 95% confidence interval, 5% margin of error, and prevalence of H pylori infection and NSAID use in patients with peptic-ulcer bleeding 8.8% [3]. The sample size was 124. Patients with a history of H pylori eradication and an antibiotic or anti-ulcer drug had been taken in the past 3-4 weeks or a gastric surgery history were excluded. Hemodynamically unstable patient undergone through upper endoscopy for hemocliping and pure ethanol injection in order to stop active bleeding. Follow-up endoscopy was performed 48 hours after emergency endoscopy and hemostasis was confirmed. A rapid urease test was used for the confirmation of H. pylori and those with negative H. pylori underwent 13C-urea breath test 1 day after endoscopy during follow-up. Patient's members were thoroughly questioned about their NSAID usage. Daily usage of NSAIDs was defined as consistent ingestion during a 4-week period. Informed consent was obtained before phospholipid determination. The prevalence of non-NSAID ulcers and non- H. Pylori infection was matched to the prevalence of H. pylori and NSAID-related ulcers. A comparison was made for comorbid illnesses and ulcer locations of the individuals. Both the serology and 13C-urea breath tests are used to assess H pylori status. If either test is positive, the patient is considered positive for H pylori. Smoking was assessed through interviews as a potential confounding factor. Statistical analyses (SPSS version 26.0) was used for data analysis. We compared the incidence of ulcers caused by H pylori or NSAIDs with those not caused by H pylori or NSAIDs. The coexisting diseases of the patients and the location of the ulcers were compared. Analysis of variances or the χ-squared test were used as statistical methods. P <0.05 was considered statistically significant.

Categories	NSAIDs and H. Pylori status
Group-I	Positive H. pylori and no NSAID history
Group-II	Positive H. pylori and NSAID user
Group-III	Negative H. pylori and NSAID user
Group-IV	Negative H. pylori and no NSAID history

Table 1: Patients categorization in different groups

RESULTS

Of the total 124 cases, the prevalence of positive and negative H. pylori infection was 77.4% (n=96) and 22.6% (n=28) respectively. The frequency of patients in different groups I, II, III, and IV patients were 80 (64.5%), 16 (12.9%), 17 (13.7%), and 11 (8.9%) respectively. The incidence of NSAID users were 33 (26.6%) patients, out of which 18 used on daily basis and 15 on demand. Those in groups I and IV were substantially younger than groups II and III and they had less comorbid disorders than patients in group I. Endoscopic examination indicated atrophic changes in 9 individuals in Group IV, indicating a previous H. pylori infection, and these atrophic alterations continued during bleeding. The number of patients in different groups are shown in Table 2.

Groups	N (%)
I	80 (64.5%)
II	16 (12.9%)
III	17 (13.7%)
IV	11 (8.9%)
Total	124 (100%)

Table 2: Patient's distribution in different groups

Majority of the patients in Group IV had significant co-morbidities. The incidence of positive and negative H. pylori is depicted in Figure 1.

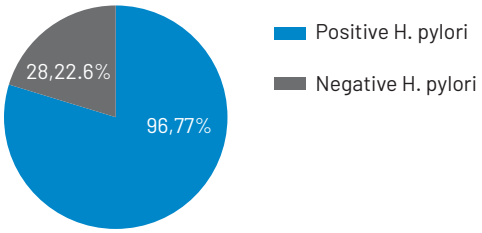

Figure 1: Incidence of Positive and Negative H. Pylori

Infection with Helicobacter Pylori and use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients are compared in Table 3.

Parameters	Group-I	Group-II	Group-III	Group-IV
N (%)	80 (64.5)	16 (12.9)	17 (13.7)	11 (8.9)
Mean age (yrs.)	56.4 ± 1.7	64.4 ± 3.6*	62.4 ± 4.4*	52.8 ± 3.9
Gender (M/F)	58/22	14/2	5/12*	9/2
Daily NSAIDs	–	11	7	–
On-Demand NSAIDs	–	4	7	–
Comorbidity N (%)	19 (23.8)	14 (87.5)**	15 (88.3)**	6 (54.5)**
Malignancy N	8	6	4	7
Mortality	2	0	3	0

Table 3: Helicobacter Pylori Infection comparison with

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nonsteroidal anti-inflammatory drugs(NSAIDs)users
*Statistically significant compared with group A or group D, P < 0.05
**Statistically significant compared with group A, P<0.05
Gastric antral mucosa (µg/mg) phospholipid concentrations in Table 4.

Variables	Control	Group-I	Group-III	Group-IV
Number	30	24	12	10
Phosphatidylcholine (PC)	5.14 ± 0.38	3.38 ± 0.4	3.10 ± 0.37	3.81 ± 0.28
Phosphatidylethanolamine (PE)	3.18 ± 0.31	2.02 ± 0.26	1.97 ± 0.31	2.21 ± 0.21
Sphingomyelin (SM)	0.41 ± 0.09	0.39 ± 0.07	0.41 ± 0.07	0.44 ± 0.12

Table 4: Gastric antral mucosa (µg/mg) phospholipid concentrations

DISCUSSION

The present study mainly focused on the contribution of the non-inflammatory steroid and Helicobacter pylori infection in peptic ulcer bleeding cases and reported that H pylori-infected NSAID users are about twice as likely as non-infected NSAID users to suffer bleeding ulcers. NSAIDs were used by about 26.6% of patients with bleeding ulcers, suggesting that both low-dose aspirin and NSAID usage on-demand will produce bleeding ulcers. NSAIDs uses and H. pylori infection are the most common causes of peptic ulcers. Numerous studies have found that NSAID users with H. pylori-negative peptic ulcers varied from 2% to 11% [13, 14]. H. pylori was found to be negative in 11% of stomach ulcers and 6% of duodenal ulcers in USA patients [15]. The incidence of H. pylori-negative peptic ulcers in the Malaysia States was 11% [16], whereas others reported 4.4% and 1.3%, respectively [17, 18]. Previous research has indicated that rising risk of H. pylori infection increases the peptic ulcer disease by three to four times [19]. In the five controlled investigations, no peptic ulcer disease was detected in patients with non- H pylori infection and NSAIDs non-users [20-22]. As a result, this is the real control sample for assessing any probable connection between NSAID usage and H pylori infection for the peptic-ulcer illness development. A matched control cases were compared with NSAIDs users H. pylori infected patients and found that sensitive analysis validated the magnitude of risk representing the peptic ulcer disease development indicated by synergism between risk factors. It has been proposed that bleeding ulcers are less likely to be associated with infectious H. pylori [23]. NSAID usage is the promising variable related to negative ulcer's bleeding with H. pylori [24]. According to the previous study conducted in Europe that approximately 4.1% cases had peptic bleeding ulcer with H. pylori and non-NASAIDs user [25]. Gastric atrophy is commonly related with H. pylori infection [26]. Duodenal ulcers were more prevalent in Group I and comorbid illness was the lowest as compared to others groups. These characteristics are common in H. pylori-related ulcers [27]. NSAIDs user displayed comparable features in groups II and III. Their average age was substantially older than that of group I or group II. Although duodenal ulcers were uncommon in groups II and III, the majority of patients in both groups had some concomitant illness. Based on the hydrophobicity, the gastric mucosa phospholipids play a vital part in the gastroduodenal epithelium's protective barrier function [28]. Previous research has revealed that H. pylori infection reduces phospholipid concentrations in the stomach mucosa [29, 30]. A previous investigation discovered that the stomach mucosa related phospholipid concentration reduced in H. pylori infection patients [30].

CONCLUSIONS

It has been concluded that H. pylori-infected NSAID users are almost twice as likely to develop bleeding ulcers as non-infected NSAID users. About 26.6% of patients with bleeding ulcers took NSAIDs, meaning that low-dose aspirin will cause bleeding ulcers as will NSAID use on-demand.

Conflicts of Interest

The authors declare no conflict of interest.

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