Original article

Association of Helicobacter Pylori with Peptic Ulcer Perforation

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Abstract

Background: Helicobacter pylori is found in more than 90% cases of peptic ulcer. This study examines the possibility of association of Helicobacter pylori in perforated peptic ulcer disease and its relation to persisting ulcer as well as the influence of other risk factors; namely: smoking, alcohol, current non-steroidal anti inflammatory drugs (NSAIDs) and steroid use.

Materials and Methods: In this prospective study, total of 50 cases of peptic ulcer perforation admitted in College of Medical Sciences and Teaching Hospital, Bharatpur, Nepal were selected on the basis of the non-probability (purposive) sampling method. All patients who presented with suspected peptic ulcer perforation were included in the study and the perforations were repaired by Modified Graham's Patch and were given triple therapy postoperatively. The age, sex, incidence, mode of presentation, precipitating factors, association with the risk factors and postoperative complications were all evaluated and compared.

Results: Of 50 patients studied, the age ranged from 17 to 75 years, mean age being 40.1 years with the peak incidence in the 3rd and 5th decades of life showing a male dominance (92%). H. pylori was seen in ulcer edge biopsy in 29 patients (58%). Most common clinical presentation was pain abdomen, the most common signs of perforation were tenderness, rebound tenderness and absent bowel sounds. The mean duration of stay in hospital in H. pylori positive patients was 12.07±8.15 days as compared with 11.1±5.12 days in H. pylori negative patients. The incidence of peptic ulcer perforation was higher in the patients consuming alcohol (64%) than smokers (48%), followed by NSAIDs user (22%). 20% of the patients with delayed presentation developed complications postoperatively. Perforated peptic ulcer was repaired by Modified Graham's Patch Repair, followed by anti H. pylori therapy in all of them.

Conclusion: Peptic ulcer perforation is quite common among the patients with peptic ulcer disease with history of chronic smoking, alcoholism and analgesic intake, more commonly in males. There is association of H. pylori in 58% of patients with peptic ulcer perforation.

Key Words: Anti H. pylori treatment, duodenal ulcer, modified Graham's patch repair, peptic ulcer perforation

Introduction

Peptic ulcer is one of the most common maladies that affects the mankind in the under developed and developing countries.[1] It is a heterogenic disease, with multiple factors involved in its genesis, most often diagnosed in middle aged to older adults, but may become evident in young adult life. Male to Female ratio for young adult is about 3:1 and for gastric ulcer is around 1.5:2.1.[2]

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Helicobacter pylori (H. pylori) plays a crucial role in pathogenesis of peptic ulcer. '*Helicobacter pylori*' was rediscovered in 1982 by two Australian scientists, Robin Warren and Barry J. Marshall as a causative factor for ulcer.[3] However, the association between H. pylori and perforated peptic ulcer is less well defined. Some of the studies show significant association between peptic ulcer perforation and H. pylori, especially with recurrent perforation.[4,5] In spite of modern progress in the management, perforation of peptic ulcer is the most common and life-threatening complication of peptic ulcer disease. It may occur in a patient with previous history of ulcer disease or it may happen without any prior symptoms. The sudden release of gastric or duodenal content into the peritoneal cavity through a perforation can lead to a sequence of events which, if not properly managed, is likely to cause death.[6] The perforated peptic ulcer can be repaired by simple closure, Graham's omental patch or Celine Jones repair with pedicle omental patch.[7] A meta-analysis of 5 RCTs (n= 401 patients) has confirmed that eradication of H. pylori significantly reduces the incidence of ulcer recurrence at 8 weeks (relative risk= RR 2.97; 95% CI 1.06–8.29).[8] A 2013 Cochrane review showed that eradication rates using a standard triple regimen (PPI + clarithromycin + amoxicillin) increased with longer duration of treatment (e.g. 14 days compared to 7 or 10 days).[9]

In Nepal, peptic ulcer perforation is quiet often a case of emergency surgery. Therefore, this endeavor has been considered to study the association of H. pylori and peptic ulcer perforation along with the basis of management of perforated peptic ulcer in future, thereby decreasing the morbidity and mortality.

Material and Method

This was a hospital based prospective study conducted in 50 patients, in the Department of General Surgery, College of Medical Science, Bharatpur for a period 12 months from September 2012 to August 2013 after getting ethical clearance from Institutional Review Committee. All patients who presented in surgery casualty undergoing surgery for peptic ulcer perforation were included in the study and the perforations were repaired by Modified Graham's Patch. Exclusion criteria were: patients who did not give a consent, previous gastrectomy or vagotomy and presence of large ulcer requiring gastrectomy. During admission, blood for qualitative detection of antibodies to H. pylori was taken and during surgery, biopsy of the ulcer margin was taken for Giemsa Staining and Rapid Urease Test. Patients were classified into two groups- H. pylori positive and H. pylori negative based on the above findings. Patients with two of three tests positive for H. pylori were classified as H. pylori positive.[17] The age, sex, incidence, mode of presentation, precipitating factors, association with the risk factor and postoperative complications were all evaluated and compared. Postoperatively triple therapy was started once the patient was started on oral diet.

Follow up was done at 6-8 weeks postoperatively. During follow-up, upper gastrointestinal endoscopy was done and biopsy was taken from antral region for the confirmation of H. pylori.

Result

Peak incidence was seen in two age groups. First peak was seen in 21-30 years age group (n= 11), and the other was seen between 41-50

years (n= 11). Mean age of presentation was 40.1±15.53 years, ranging from 17 to 75 years. Mean age of patients in H. pylori negative group was 40.05±16.07 years whereas that in H. pylori positive group was 40.14±15.42 years. Most cases of Peptic ulcer perforation were males (92%), with only few cases females (8%). In H. pylori positive group (n= 29), 93.1% were male (n= 27) and 6.9% were female (n= 2), whereas in H. pylori negative group (n= 21), 90.5% were male (n= 19) and 9.5% were female (n= 2). In H. pylori positive group (n= 28), 62.1% of patients (n= 18) consumed alcohol, whereas in H. pylori negative group (n= 21), 66.7% of patients (n= 14) consumed alcohol but this is statistically insignificant. Among the study population (n= 50), 78% of the patients (n= 39) denies the history of intake of non steroid anti inflammatory drugs. Only 22% of cases (n= 11) consumed non steroid anti inflammatory drugs. In H. pylori positive group, 51.7% were smoker (n= 15) and 48.3% were non-smoker (n= 14), whereas in H. pylori negative group, 42.9% are smoker (n= 9) and 57.1% are non-smoker (n= 12) which is not significant statistically. Only 1 patient (2%) had history of intake of steroid among the study population. Most common clinical presentations were: pain abdomen in all (100%), abdominal distension in 47 (94%), vomiting in 38 (76%) and fever in 18 patients (36%). On examination; tenderness (100%), guarding (98%), rigidity (98%) were present in almost all the cases. Bowel sound was not audible in any cases and liver dullness on percussion was obliterated in 88% of cases. Out of 50 patients, 58% of the cases (n= 29) were positive for H. pylori and remaining 42% of cases (n= 21) were negative for H. pylori. In H. pylori positive cases (n= 29), Giemsa stain showed H. pylori in 29 cases, rapid Urease test (RUT) showed H. pylori in 26 cases and antibody confirmed H. pylori in 22 cases. The sensitivity, specificity and accuracy of RUT were 89.65%, 90.47% and 90% respectively whereas those of antibody test were 75.86%, 80.95% and 78% respectively.

Most commonly peptic ulcer was perforated in the 1st part of duodenum in its anterior wall 94% (n= 47), and in gastric antrum 6% (n= 3). Perforation size range from 0.1 to 1.5 cm with mean size of 0.66 cm. Maximum perforations (60%) sized 0.6-1.0 cm. Perforations of size more than 1 cm were only 6% (n= 3). Among 50 cases, 80% (n= 40) didn't develop any complication whereas 20% developed. Wound infection was seen in 8% (n= 4) patients, bronchopneumonia developed in 6% (n= 3) patients. One patient developed burst abdomen and 1 patient had renal failure. One patient died on the 4th postoperative day who presented after 72 hours of symptoms and he developed multiple organ dysfunction syndrome and severe sepsis. The rate of complication increased as the duration of hospital stay increased. It was also seen that as the size of perforation increased, there was also increase in the rate of complications. All patients (n= 3) who had perforation size more than 1 cm and 7 patients with perforation sized more than 0.6 cm developed complication and this is statistically significant. Complication was seen more in longer duration of pain, 62.5% (n= 5) in patients who presented after 48-72 hours of pain and 100% (n= 2) who presented after 72 hours of pain. Complications were absent in 96% patients (n= 24) who presented within 24 hours of pain. Thus, complication was significantly associated with longer duration of pain or later presentation to Emergency room. After 8 weeks, 12% (n= 6)

of the patients didn't come for follow up while 88% (n= 44) patients presented to surgery outpatient clinic. In H. pylori positive group (n= 29), 6.9% of patient (n= 2) failed to follow up in surgery outpatient clinic whereas in H. pylori negative group (n= 21), 19.04% of patients (n= 4) failed to follow up. During follow-up, upper gastrointestinal endoscopy was done and biopsy taken from gastric antrum which revealed H. pylori in 1 patient who was again prescribed triple therapy. But, recurrence and H. pylori infection were statistically insignificant

Graph: Age distribution in comparison with H. pylori status

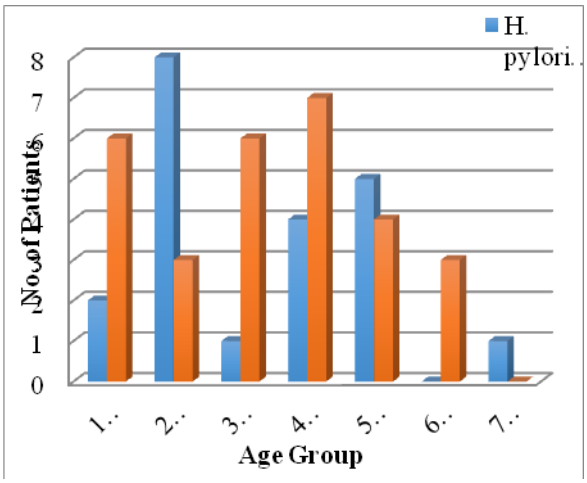


Table 1: Signs and symptoms of peritonitis in comparison with H. pylori

Signs and Symptoms	H. pylori		p-value
	Negative	Positive	
Vomiting	13	25	0.047
Fever	7	11	0.738
Distension	21	26	0.128
Guarding	20	29	0.235
Rigidity	20	29	0.235
Obliteration of liver dullness	19	25	0.647
Shock	3	7	0.39

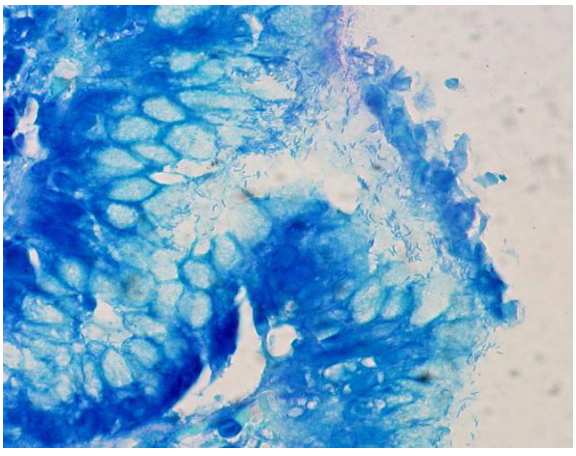
Table 2: Complications in patients with peptic ulcer perforation

Complications	No. of Patients	Percent
None	40	80.0
Bronchopneumonia	3	6.0
Burst abdomen	1	2.0
Death	1	2.0
Renal failure	1	2.0
Wound infection	4	8.0
Total	50	100.0

Table 3: Complication in relation with H. pylori

Complication	H. pylori		Total
	Negative	Positive	
No	17	23	40
Yes	4	6	10
Total	21	29	50
p = 0.886			

Figure: H. pylori on Giemsa staining



Discussion

Peptic ulcer perforation is one of the major surgical emergencies. The optimal surgical treatment for perforated duodenal ulcer has been controversial. Simple repair has been the most

commonly performed procedure since its popularization by Graham in 1937. However, long-term follow-up of patients who underwent simple repair reveals a high incidence of ulcer relapse. Now, it is advocated that simple repair followed by H. pylori eradication therapy for positive cases is the ideal management to be followed.[10]

There is no age limitation to peptic ulcer perforation. It has been reported even in 4 year child up to the extreme of age. In our study, peptic ulcer perforation was seen commonly in two age groups between 21-30 years and 41-50 years. This may be because these age groups are exposed to stress. The mean age of patient was 40 years. However, there was no any significant relation with age of peptic ulcer perforation and H. pylori infection. In study conducted by Aman et al, the peak incidence was seen in same age groups of 20-30 and 40-50 which is consistent with present study.[11] In study of 49 patients done by Keane et al, mean age of patient with peptic ulcer perforation was 50 years.[12]

In present study, there was male predominance with 92%. Only 8% were females, the Male : Female ratio being 11.5:1. Perforation is more common in males than females, because males were subjected to more stress and strain of life and female sex hormone offer some protection against perforation as claimed by Skovgaard et al[13] and Aman et al.[11] In study conducted by Keane et al, 89.9% were male and 10.1% were female with male to female ratio of 8.8:1.[12] The finding of present study is also consistent with findings of Aman et al[11] (9:1) and Palanivelu et al (12.3:1).[14]

In our study, 64% of the patients consumed alcohol, 22% has a history of intake of non steroidal anti-inflammatory drugs and 48% of patients were smokers and 2% were under steroid treatment. In the study conducted by Palanivelu et al, 72.5 % of patients were smokers, 70.2% consumed alcohol and 10% taking NSAIDS. [14] Similarly, Chalya et al, in his study found that 64.3% of patients were smokers, 85.7% consumed alcohol and 10.7% consumed NSAID.[15] Aman et al found that 40% of patients had history of NSAIDS intake, 8% steroid intake and 28% were smokers.[11]

In the present study, pain and tenderness was present in all the cases of duodenal ulcer perforation. Abdominal distension in 94%, vomiting in 76%, fever in 36% of the cases. Guarding and rigidity was present in 98% of cases. In all patients bowel sounds were absent. In the study conducted by Chalya et al, pain was present in 97.6%, distension in 76.2%, vomiting in 36.9%, fever in 21.4% and tenderness in 88.1% of the cases.[15]

In the present study, the mortality and morbidity increased whenever, perforations exceed 24 hours because of the peritoneal infection. 50% of patients presented before 24 hrs and 20% patients presented to hospital after 48 hours and the mortality and morbidity in patients who presented to hospital after 24 hours was found to be 57.1%.

In present study, 20% of patients developed complications, most commonly bronchopneumonia (30%) and wound infection (40%). Other complications were: burst abdomen and renal failure. Present study was consistent with Bertleff et al who reported bronchopneumonia (30%) and wound infection (17%).[16]

El-Nakeeb et al analyzed that when the time

interval between onset of acute symptoms and surgery was less than or equal to 24 hours, mortality rate is 12% and if more than 24 hours, the mortality rate is 21%.[17] The mortality risk for a patient who is operated on more than 24 hours after the onset of acute symptoms is 4.9 times that of a patient operated within 24 hours. In a study conducted by Chalya et al, 28.6% of patients presented before 24 hours and 35.7% after 48 hours.[15]

In present study, the sensitivity, specificity and accuracy of RUT were 89.65%, 90.47% and 90% respectively whereas those of antibody test were 75.86%, 80.95% and 78% respectively. In a study conducted by Pande et al, the sensitivity, specificity and accuracy of RUT are 88.6%, 94.4% and 91.3% respectively.[18] In study conducted by Graham et al, the sensitivity, specificity and accuracy of RUT are 94.4%, 87.6% and 91.1% respectively. [19]

Conclusion

A high frequency (58%) of H. pylori infection was evidenced in patients with perforated peptic ulcer in the present study comprising 50 patients. Therefore, all such patients should be treated by simple closure (Modified Graham's Patch Repair) and eradication of H. pylori; as disappearance of the organism prevents or at least decreases ulcer recurrence and ulcer perforation in patients with H. Pylori associated perforation after simple closure. Therefore, H. pylori treatment during the immediate post operative period is suggested. Risk factors viz. alcohol consumption, smoking, NSAIDs intake should be prevented.

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