

## Prevalence of Helicobacter Pylori Infection in Patients with Perforated Duodenal Ulcer: A Hospital-based Study.

Subhash Bhardwaj, Gousia Rahim

Department of Pathology, Govt. Medical College, Jammu, Jammu and Kashmir, India

**Abstract :** Peptic ulcer disease remains the most common cause of gastroduodenal perforation. Among peptic ulcers, it is the duodenal ulcer which commonly perforates. Pyloroduodenal perforation occurs 6-8 times more often than gastric perforations. It is believed that *Helicobacter pylori* plays an important role in the causation of peptic ulcer. However, its role in duodenal ulcer perforation has not been investigated extensively and the results are conflicting. To determine the prevalence of *H. pylori* in patients with perforated duodenal ulcer. All the patients admitted over a period of one year with the diagnosis of perforated duodenal ulcer formed the study material. Biopsies taken from all the patients were processed and stained with hematoxylin and eosin and modified Giemsa. Histopathological changes and presence of *H. pylori* was noted. Seventy five cases of perforated duodenal ulcer were identified. Sixty nine biopsies showed active chronic inflammatory reaction and 5 showed acute inflammation. One biopsy showed an adenocarcinoma. Thirty eight biopsies out of 75 (50.66%) were positive for *H. pylori*.

**Conclusion:** Our study showed the presence of *H. pylori* in a considerable number of patients, emphasizing the fact that eradication of *H. Pylori*, in addition to other treatment modalities, is important in the treatment of perforated duodenal ulcers.

### INTRODUCTION

Peptic ulcer disease remains the most common cause of gastroduodenal perforation<sup>1</sup>. Among peptic ulcers, it is the duodenal ulcer which commonly perforates. Pyloroduodenal perforation occurs 6-8 times more often than gastric perforations<sup>2</sup>. The duodenal ulcer perforations occur in all parts of the world in different age groups, with various food habits, environmental and other factors like consumption of tobacco, alcohol and drugs (especially NSAIDs), as most probable causes<sup>3</sup>.

Infection with *H. pylori*, a spiral shaped bacterium mostly found in gastric and duodenal mucosa, has been clearly implicated in the development of gastric and duodenal ulcers.<sup>4</sup> Recent studies have identified *H. pylori* as one of the most important causative agents of duodenal ulcer perforation and it has been isolated from the duodenal biopsy taken from the ulcer sites<sup>5,6</sup>. The explanation of how *H. pylori* can cause duodenal ulcer perforation has been found in the phenomenon of duodenal gastric metaplasia. Although normal duodenal mucosa cannot be infected by *H. pylori*, the gastric metaplasia in the duodenum is commonly infected with these microorganisms. This results in duodenitis which is almost certainly a precursor of duodenal ulcer formation and subsequent perforation<sup>7</sup>.

This study was undertaken with intent to see prevalence of *H. pylori* in perforated duodenal ulcers.

### MATERIALS AND METHODS

This study was undertaken in post graduate department of Pathology, Government Medical College, Jammu. All the patients with suspected perforated duodenal ulcer who were admitted to the hospital over a period of 1 year were enrolled for the study after taking informed consent. The diagnosis of these patients was made by history, clinical examination and radiological examination and was confirmed at laparotomy.

Exclusion criteria included patients already on *H. pylori*

eradication therapy, patients with traumatic perforation and patients who refused to give consent for participation in the study. On admission a detailed and thorough clinical examination was done and the patients were subjected to relevant laboratory investigations. The patients were then subjected to surgery. The perforation site was identified and biopsies were taken from the site of perforation. The biopsy material was immediately fixed in 10% buffered formalin solution. The material was then processed and stained with hematoxylin and eosin and special stains such as modified Giemsa. Microscopic examination of the stained sections was done and *H. pylori* organisms were searched for under high power and oil immersion lenses.

### RESULTS

During our study period 75 cases of perforated duodenal ulcer were identified. The maximum number of the patients was in the age group of 31-40 years (Table 1) and majority (92%) of the patients were males (Figure 1). In most of the cases (96%), perforation was identified in the first part of duodenum. Only 4% patients had a pyloroantral perforation (Table 2).

Table 1: Age Distribution

Age group	No. of patients (n = 75)	Percentage (%)
0 - 10	Nil	Nil
11 - 20	3	4
21 - 30	6	8
31 - 40	32	42.6
41 - 50	18	24
51 - 60	9	12
61 - 70	6	8
71 - 80	1	1.33

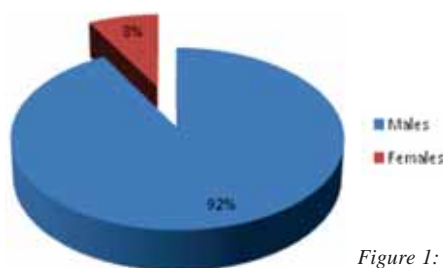


Figure 1: Sex Distribution

**Correspondence:** Dr. Gousia Rahim, A-4, Sector 2, Pocket 3, Chhani Himmat, Jammu, J&K, India e-mail: gousiarather@gmail.com  
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Table 2: Sites of Perforation

Site of perforation	No. of cases	Percentage (%)
First part of duodenum	72	96
Pyloroantral	3	4
Total	75	100

Hematoxylin and eosin stained sections were examined from all the biopsy specimens (Table 3). Sixty nine biopsies (92%) showed active chronic inflammatory reaction (acute as well as chronic inflammation) in the ulcerated mucosa and submucosa. Out of these 69 biopsies, 36 were positive for *H. pylori*. Out of the 5 biopsies which showed acute inflammatory changes, two were *H. pylori* positive. The presence of *H. pylori* in the sections was confirmed by modified Giemsa stain.

Table 3: Histopathological Changes

S.No.	Type of histopathological changes	No. of patients (n = 75)	Helicobacter pylori positive cases
1.	Acute inflammation	5 (6.66%)	2 (40%)
2.	Active chronic inflammation	69 (92%)	36 (52.17%)
3.	Adenocarcinoma	1 (1.33%)	Nil

In one patient who presented with symptoms of duodenal ulcer perforation, the duodenal biopsy showed an adenocarcinoma, but it was negative for *H. pylori*.

Thirty eight out of the total 75 patients (50.66%) were *H. pylori* positive. The maximum number of such patients was in the age group of 31 – 40 years (Table 4).

Table 4: Relation of Age to the Presence of Helicobacter Pylori

Age group	No. of patients n=75	No. of Helicobacter pylori positive patients
0 – 10	Nil	Nil
11 – 20	3 (4%)	0
21 – 30	6 (8%)	2 (33.33%)
31 – 40	32 (42.6%)	23 (71.87%)
41 – 50	18 (24%)	10 (55.55%)
51 – 60	9 (12%)	3 (33.33%)
61 – 70	6 (8%)	0
71 – 80	1 (1.33%)	0

## DISCUSSION

Since the time when gram negative urease producing bacteria were cultured from gastric antrum of patients with peptic ulcer disease, considerable interest has been aroused about the role of *H. pylori* in peptic ulcer disease. It is believed that *H. pylori* plays an important role in the causation of peptic ulcer. However, its role in duodenal ulcer perforation has not been investigated extensively and the results are conflicting. The aim of this study was to determine the prevalence of *H. pylori* infection in patients with perforated duodenal ulcer.

In our study, the maximum number of patients was in the age group of 31-40 years. Our findings are comparable to those of Hannan et al, who found majority of the patients to be in the same age group<sup>7</sup>; however Coogan et al found it to be more frequent in middle aged and elderly individuals<sup>8</sup>. Most of the patients in our study were males similar to other studies where majority of the patients were reported to be males<sup>9,10</sup>.

Duodenum is the most common site of ulcer perforation<sup>11</sup>. In

96% of our cases the perforation was seen in the first part of duodenum on the anterior wall.

Data regarding prevalence of *H. pylori* infection is conflicting and shows a wide variation from 0 to 92% which could be due to the different population groups studied in the past. Many studies have documented a high prevalence of *H. pylori* infection in patients with duodenal ulcer perforation<sup>12,13</sup>. In the present study prevalence of *H. pylori* was 50.66%. However, many workers are of the opinion that *H. pylori* is not significantly associated with perforated duodenal ulcer. Kate et al in their study of 202 patients found that prevalence of *H. pylori* in patients with perforated duodenal ulcer was not significantly different from that in controls<sup>14</sup>.

In our study, 69 patients showed active chronic inflammatory reaction out of which 52.17% were *H. pylori* positive. Out of the 5 patients who showed acute inflammation, two were *H. pylori* positive. In one of the patients who presented with symptoms of duodenal ulcer perforation, the duodenal biopsy showed an adenocarcinoma but it was negative for *H. pylori*. Ananthkrishnan and Kate have reported that infection with *H. pylori* is the cause of type B chronic active gastritis, the initial factor in the pathogenesis of majority of peptic ulcer disease, a factor which leads to gastric adenocarcinoma and is significantly associated with gastric B cell mucosa associated lymphoid tissue (MALT) lymphoma<sup>15</sup>.

The pathogenic mechanism of *H. pylori* responsible for ulcer formation, though outside the purview of this article, is quite an interesting one. The role of *H. pylori* as a gastric pathogen is dependent on virulence factors and pathogenic mechanisms. Virulence factors are those that allow *H. pylori* to survive in the hostile environment of the gastric lumen which includes its spiral shape, motility, adaptive enzymes, proteins and its ability to adhere to gastric mucosal cells and mucus<sup>16</sup>. Pathogenic mechanisms are those that lead either directly to disruption of the gastric mucosal barrier including its toxins like Vac A and Cag A and mediators of inflammation<sup>17</sup>.

The spiral shape and flagella of the organism allow efficient motility in the mucus and in the gastric juice. The enzyme urease by breaking down urea in the gastric juice appears to generate enough bicarbonate and ammonium ions around the organism to allow its safe passage through the gastric acid barrier to reach the protective mucous layer<sup>18</sup>. Once within the gastric mucus, *H. pylori* is able to attach itself to phospholipids such as phosphatidyl ethanolamine, sialylated glycoproteins such as ganglioside monosialic 3 (GM3), and Lewis B antigens present in persons with blood group O<sup>19,20</sup>. Once attached to the mucus layer and the mucosa, *H. pylori* secretes soluble proteases and phospholipase, which may be harmful to both the integrity of the mucus layer and the underlying cells<sup>21</sup>.

One of the most important aspects of *H. pylori* pathogenicity is the “vacuolating cytotoxin” which is expressed in nearly all patients with *H. pylori* associated duodenal ulcer. The marker for cytotoxin is a gene for the cytotoxin protein called Vac A. A second protein at 127kDa is called cytotoxin-associated gene A or Cag A. Cag A is a marker for the vacuolating toxin effect and the gene for Cag A is only present when Vac A cytotoxin effect is present. The organisms have been classified into type I organisms which have Cag A and Vac A which are more ulcerogenic and type II

organisms that lack Cag A and do not produce cytotoxins<sup>22</sup>. Antibodies to the toxin are present in nearly all duodenal ulcer patients. This is one of the factors which determine that all patients with *H. pylori* do not have duodenal ulcer disease<sup>17</sup>.

Recently, a novel virulence factor, duodenal ulcer promoting gene A (dup A), has been identified and found to be associated with disease in some populations. In a recent meta-analysis of 2358 patients from around the world, it was found that in 48%, dup A was associated with duodenal ulcer<sup>23</sup>. In another study from India, it was reported that the prevalence of dup A was significantly greater among strains isolated from patients with duodenal ulcer than from patients with non-ulcer dyspepsia in this population. The authors suggested that dup A can be considered a biomarker for duodenal ulcer patients in India<sup>24</sup>.

There is a conflict in the literature regarding *H. pylori* infection being the primary cause of duodenal ulceration or a secondary factor interfering in the long term healing of the ulcer. A recent publication put forth the point of view of two groups of workers in this field. According to one group of workers, *H. pylori* infection plays an important role in perforated duodenal ulcer and eradication is recommended in all infected patients following simple closure to prevent ulcer relapse. The other group was of the opinion that the primary cause of duodenal ulceration was acid secretion along with reduced mucosal resistance; however there was no doubt about the value of *H. pylori* eradication in the long term healing of duodenal ulcers<sup>17</sup>.

## CONCLUSION

Our study showed the presence of *H. pylori* in a considerable number of patients, emphasizing the fact that eradication of *H. Pylori*, in addition to other treatment modalities, is important in the treatment of perforated duodenal ulcers.

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## ERRATUM

**ARTICLE** entitled “*Ten Most Effective Coping Strategies in Spouses of Critically Ill Patients*” by Rizwan Ahmad Khan published in the **October - December, 2015 issue** on **page 211** contains an abstract which has been printed by mistake. The original article doesn't contain any abstract and it is published as ‘**Brief Communication**’.

**The abstract may be taken as deleted.**

Wrong inclusion of this abstract is highly regretted. The corrected version as per original is printed again and is given as an insert in the **APRIL-JUNE 2016, VOL. 29, issue no 2**.

*Editor, JIMSA*

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