

# Helicobacter pylori infection and its correlates among the patients of peptic perforation and gastric carcinoma

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## Research Article

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# Abstract

**Background:** Presence of *H. pylori* infection was found associated with peptic perforation and gastric carcinoma. Present study tried to estimate the prevalence of *H. pylori* infection in those patients and to find out the correlates of *H. pylori* infection.

**Methods:** After matching the inclusion and exclusion criteria, all cases of diagnosed peptic perforation and gastric carcinoma were taken for this prospective, single center, observational study.

**Results:** Among the study population, gastric carcinoma was found in higher age group; whereas peptic perforation was found in lower age group; male and female ratio was 2:1 in both groups of patient. Laborer and housewives were mostly affected in both cases. Gastric carcinoma was more prevalent in urban residents, opposite was seen in peptic perforation. Most patients in two groups had no previous co-morbid condition. Use of NSAIDs was found in high frequency in both groups. Most of the patients were chronic alcoholic and chronic smoker, and most of them had history of taking spicy foods more than twice in a week.

**Conclusions:** *H. pylori* infection was found in high frequency in both group of patients, and it was higher in peptic perforation. The study establishes the association of *H. pylori* with the gastric carcinoma and peptic perforation.

# Introduction

Peptic ulcer disease was a common problem since dawn of human civilization. This disease was believed to be caused by stress, dietary factors, and increased gastric acid secretion till as late as 1983, when Warren and Marshall identified the correlation between *Helicobacter pylori* infection and peptic ulcer<sup>1</sup>. Near half of the world population is affected by *H. Pylori*.<sup>2</sup> More than 95% of patients suffering from duodenal ulcers and about 70–80% of patients with gastric ulcers are *H. pylori* positive<sup>3</sup>. *Helicobacter Pylori*, name derived from its helix shape, is 3µm long with 0.5 µm in diameter gram negative bacteria which can also be seen by Giemsa stain, Haematoxyline-eosin stain, warren-starry siler stain, acridine orange stain and phase contrast microscopy. It can produce biofilms and can convert from spiral to coccoid form, which is non-culturable,<sup>4</sup> and gets transmitted by oral-oral or oral-fecal route. *H. pylori* infection was seen more frequently in patients with duodenal ulcer than gastric ulcer<sup>5</sup>. In early half of the 20th century, surgery was the only way to treat the patient of peptic ulcer disease. Invention of the H<sub>2</sub> Blocker and Proton pump inhibitor dramatically decreases the morbidity and mortality by these diseases. Surgery is now only indicated in peptic perforation cases. An untreated perforated peptic ulcer therefore has high mortality rate. Worldwide, Gastric cancer is considered the second most common cause of cancer-related deaths and it is fourth most common malignancy. Approximately 70% of them are found in less developed regions<sup>6</sup>.

H. Pylori colonize in the epithelial cells by burrowing the mucous lining of the stomach. It can sense the pH gradient of the mucosa, so it uses its flagella to reach the less acidic epithelium. It produces adhesions BabA and SubA, for binding the epithelial cell membrane. BabA binds with the Lewis b antigen, expressed on the stomach epithelial cell surface. This bindings are acid sensitive, and it can be reversed in increased acidic condition. Sab A binds with the sialyl-Lewis x antigen expressed on the gastric mucosa. H. Pylori can also neutralize the acid by producing urease, which degrades the urea into carbon di oxide and ammonia, which in turn neutralizes the acidic environment. H. Pylori breach the mucosal linings of stomach and duodenum by several other mechanisms, like, by producing ammonia, proteases, vacuolating cytotoxin A, and some phospholipases, which in turn causes chronic inflammation and gastritis as well as carcinoma. H. Pylori increase the COX2 by triggering an immune response through the helicobacter cysteine-rich proteins (Hcp) particularly HcpA, which causes inflammation and destruction of mucus membrane. Similarly, it causes duodenal ulcer by causing increased secretion of acid by stimulating the parietal cells of the fundus, through increased release of gastrin hormone from the antral G Cell. It also causes alterations in cell proteins such as adhesion proteins by inducing inflammation which in turn causes high levels of TNF- $\alpha$  and interleukin-6 secretion.

Screening for H. Pylori is not routinely recommended. Several diagnostic methods can be employed for the detection of H. pylori such as non-invasive tests, ie- i) Blood Antibody Test (serological tests which measures specific anti H. pylori, IgG and or IgA), ii) Stool Antigen Test, iii) Carbon Urea Breath test and some invasive tests such as bacterial culture, histopathological examination of biopsy specimen (Endoscopic biopsy with rapid urease test is the most recommended and accurate method) with different stains and assays for urease activity.<sup>3</sup>

In order to prevent the Gastric carcinoma and Peptic perforation, current study aims to detect the most common causative factors, and to establish the relationship with Helicobacter Pylori. This study is mainly intended to observe the prevalence of H. pylori in patients with peptic ulcer perforation and gastric carcinoma. Along with this other factors like type and location of ulcer, proportion of H. pylori infection in factors like smoking, alcohol, NSAID intake, diet, hypertension, diabetes mellitus, occupation were also studied.

Specific objectives of this study were – i) To study the demographic profile of the patients. ii) To estimate the prevalence of H. Pylori infection in patients of peptic perforation and gastric carcinoma. iii) To find out the correlates of H. Pylori infection.

## Methods

This was an institution based (single center) prospective, observational study conducted for 1 year (from 01/01/2019 to 31/12/2019). The study population comprised of 90 patients, satisfying the inclusion and exclusion criteria mentioned below. They were considered into the study at General Surgery Department of BSMCH, WB, India. After taking the Informed consent from the participants, data were collected using the proforma. The primary data for this study were the investigation reports of the patients. Considering

10% drop-out, the sample size was taken 45 in each group (viz peptic perforation group and Gastric carcinoma group). Inclusion criteria for the study was -Patients, more than 12 years of age, of both genders with diagnosis of peptic perforation or gastric carcinoma.

The Exclusion Criteria were like-i) Patients with unconfirmed diagnosis and presence of any other suspected pathology was excluded from the study. ii) Previously diagnosed and treated patients of peptic ulcer disease, due to *H. Pylori*. iii) Non operable, clinically unfit patients for operations. iv) Patient or Legally Acceptable Representative's unwillingness to participate in the study.

A total of 90 cases (45 each for benign peptic perforation & 45 for diagnosed/suspected gastric carcinoma), presenting with acute perforation of duodenum/stomach and diagnosed/suspected gastric carcinoma during this study period, were considered. In Cases of perforation, after resuscitation, the cases were subjected to emergency exploratory laparotomy. The exact site of perforation were identified, biopsy was taken from the ulcer margin at 2–3 sites and the tissue was sent for *H. pylori* culture and histopathological examination. In patients with suspected/diagnosed gastric carcinoma, endoscopic evaluation done and biopsy was also taken. The collected data was explored by descriptive statistics like mean, standard deviation and proportion. Data visualisation was done by using various tables and charts. Inferential statistical tests e.g. 'unpaired t-test' and 'chi-square test' etc were used for establishing relationship between the variables. The level of significance was set at 5% for all comparisons.

## Results

Study Population:

The study population included 90 patients with diagnosis of peptic perforation or gastric carcinoma (Table1).

### Table1: Demographic distribution of Patients

	Carcinoma N=45	Perforation N=45	p. overall
<b>Age in Years - Mean (SD)</b>	50.8 (5.72)	34.7 (7.84)	<0.001
<b>sex:</b>			1.000
Female	13 (28.9%)	13 (28.9%)	
Male	32 (71.1%)	32 (71.1%)	
<b>Religion:</b>			1.000
Hindu	33 (73.3%)	32 (71.1%)	
Muslim	12 (26.7%)	13 (28.9%)	
<b>Occupation:</b>			0.274
Businessman	6 (13.3%)	4 (8.89%)	
Farmer	8 (17.8%)	9 (20.0%)	
Govt Employee	5 (11.1%)	3 (6.67%)	
Housewife	8 (17.8%)	9 (20.0%)	
Laborer	11 (24.4%)	12 (26.7%)	
Private job	7 (15.6%)	3 (6.67%)	
Student	0 (0.00%)	5 (11.1%)	
<b>Literacy:</b>			0.475
Illiterate	14 (31.1%)	10 (22.2%)	
Literate	31 (68.9%)	35 (77.8%)	
<b>Marital status:</b>			0.005
Married	43 (95.6%)	32 (71.1%)	
Unmarried	2 (4.44%)	13 (28.9%)	
<b>Residence:</b>			0.003
Rural	16 (35.6%)	31 (68.9%)	
Urban	29 (64.4%)	14 (31.1%)	
<b>Age between two groups was compared using Student's independent t-test. Rest of the parameters were compared using Chi- Square test. Level of significance was 0.05.</b>			

Table 1 shows that most of the patients were male and belongs to Hindu religion. Age of gastric carcinoma group was significantly higher (Mean = 50.8 years, SD = 5.72) than peptic perforation group (Mean = 34.7 years, SD = 7.84). Evidently most of the participants from carcinoma group were married (95.6%) in comparison with perforation group (71.1%). Interestingly, carcinoma group had more urban population (64.4%) than perforation group (31.1%) and the difference was statistically significant (p value=0.003).

Distribution of age in two groups:

We analysed the age distribution in two groups using a density plot (Figure 1). As depicted in the figure and described in Table 1 also, prevalence of gastric carcinoma is more in higher age group.

Site of Perforations:

As shown in the Figure 2, among 45 patients of peptic perforation, 66.7% cases were presented with duodenal perforation and 33.3% with gastric perforation.

The presence of free gas under diaphragm in perforation at two different sites, were analysed using a bar diagram (Figure 3).As depicted in the figure,the frequency was higher in gastric (2 out of 15, 13.3%) perforation than duodenal (0.00%) perforation group ( $p\text{ value} = 0.10$ ,Fisher'sExact test).

Co-morbidities associated with two groups of patients

Table 2 shows most of the patients in perforation group (77.8%) did not have any co-morbidities. Most common associated medical conditions were related to cardiovascular or endocrine origin.

<b>Co-morbidities:</b>	Carcinoma N=45	Perforation N=45
Without associated co-morbidities	24 (53.3%)	35 (77.8%)
Arthritis	4 (8.89%)	2 (4.44%)
Coronary Artery Disease (CAD)	2 (4.44%)	1 (2.22%)
Diabetes Mellitus (DM)	4 (8.89%)	3 (6.67%)
DM and CAD	2 (4.44%)	1 (2.22%)
Hypertension (HTN)	7 (15.6%)	2 (4.44%)
HTN and CAD	0 (0.00%)	1 (2.22%)
HTN and DM and CAD	2 (4.44%)	1 (2.22%)

Table2: Distribution of two groups according to the presence of Co-morbidities

History of NSAIDs use in two groups:

We analysed the relation of use of NSAIDs in two groups using a bar diagram (Figure 4A). As depicted in the figure, the frequency was higher in gastric carcinoma group (22.2%) than peptic perforation group (13.3%). The difference was not statistically significant ( $p$  value = 0.408, Chi-square test).

Food habit in two groups:

We analysed the possible association of frequency of spicy food per week in two groups using a bar diagram (Figure 6). As depicted in the figure, the frequency was higher in gastric carcinoma group (44.4% thrice weekly and 13.3% more than that) than peptic perforation group (55.60% twice a week). Although, the difference was not statistically significant ( $p$  value = 0.435, Chi-square test).

History of alcohol consumption in two groups:

We analysed the possible association of alcohol use in two groups using a bar diagram (Figure 4B). As depicted in the figure, the frequency was quite high in both the groups - gastric carcinoma group (60.00%) and peptic perforation group (57.8%). The difference was not statistically significant ( $p$  value = 1.00, Chi-square test).

History of smoking in two groups:

We analyzed the possible association of smoking in two groups using a bar diagram (Figure 4C). As depicted in the figure, the frequency was quite high in both the groups - gastric carcinoma group (71.10%) and peptic perforation group (62.20%). The difference was not statistically significant ( $p$  value = 0.50, Chi-square test).

Effect of alcohol and smoking in two groups:

Figure 5 demonstrates the effect of both smoking and alcohol in a Double-decker plot. It shows in alcoholic patients, occurrence of carcinoma and perforation is almost similar if the subject is also a smoker. Whereas, in non-alcoholic patients, occurrence of carcinoma is higher than perforation.

Rapid Urease Test in two groups:

We analysed the possible association of H. pylori association with rapid Urease Test in two groups using a mosaic plot (Figure 7). As depicted in the figure, the frequency of Positive result was lower in gastric carcinoma group (64.40%) than peptic perforation group (82.20%). The difference was not statistically significant ( $p$  value = 0.09, Chi-square test). High associations prove the fact that H. pylori might have a role to play in gastric carcinoma also.

## Discussion

Distribution of Age of Patients in Two Group:

Current study reveals that gastric perforation was taken place in lower age group (Table 1 and Fig 1), with mean age is 34.7 years, and gastric carcinoma was taken place in higher age group people, with mean age is 50.8 years.

Distribution of two groups according to the Sex of the Patients:

Distribution of male and female is equal in two groups, and male is affected more than female, the male and female ratio is almost 2:1 (Table 1), which is not statistically significant.

Distribution of two groups according to the Religion of the Patients:

Current study reveals that (Table 1), most of the patients suffering from gastric cancer and perforated ulcer were Hindu (73% in case of gastric cancer and 71% in case of perforation). The findings are not statistically significant. The religion of the people lived in the service area of the hospital is Hindu, and it is probably influenced the result. Very few previous studies were evaluated about that fact, so it is an unique finding of the current study.

Distribution of two groups according to the Occupation of the Patients:

Current study reveals that (Table 1), the patients, who were laborer by occupation was the most affected individuals in both groups, though gastric cancer and peptic perforation is not a said occupational hazard of laborers but it was in the higher note due to the poor food habits, food timing, and hygiene. The second most common affected patients were housewives, and it was a known fact that Indian especially Bengali housewives didn't maintain healthy food timing, probably due to the enormous work pressure on them. Irregular meal time leads to H. Pylori infection and also gastritis, gastric ulcer and gastric carcinoma<sup>7</sup>.

Distribution of two groups according to the Literacy Rates, Marital Status and Residency of the Patients:

We analyzed that (Table 1), most of the affected persons in two groups were literate. The findings were not statistically significant. Married persons were the commonest sufferer in two groups. Urban residents (64.4%) were more sufferer of the gastric carcinoma, where rural population was more suffered from the peptic perforation. The observation is statistically significant. Married people, especially women skipped their meal and invited the H. Pylori infection as well as gastritis, and resultant cancer and perforation.<sup>7</sup> B. Smith et al<sup>8</sup> conducted a study on Morocco, and they found a large number of patients suffering from gastric carcinoma were belongs from the urban population. They suggested that, the excess availability of processed foods, environmental pollution in urban area, made people prone to the gastric cancer.

Distribution of Peptic Perforation Patients according to the Site of Perforation (N = 45)

The study reveals that, 66.7% cases of perforation taken place in duodenum, and rest of the cases in stomach (Figure 2) K. Byacodi et al<sup>9</sup> observed the similar result, though frequency of duodenal perforation (53.4%) was bit lower than current study.

### Distribution of two groups according to the presence of Co- morbidities

Co-morbidities associated with patients of gastric carcinoma and peptic perforation causes increase morbidity, mortality and long hospital stay, and increases postoperative complications. Current study reveals (Table 2), that 77.8% patient presented with peptic perforation and 53.3% patients presented with gastric carcinoma had no co- morbidities. The incidence is lower in Perforation Group patients, due to the lower age group of the patients. The most co- morbidities associated with two groups were the cardio-diabetic diseases. The findings are not statistically significant. M. Unver et al<sup>10</sup> found, respiratory diseases were the most common co-morbidities present with peptic perforation patients. W. Wang et al<sup>11</sup> found 23% patients of gastric carcinoma had no co-morbidities. The frequency was much lower in comparison with the findings of current study, but the most common co-morbidity was cardio-diabetic diseases.

### Distribution of two groups According to the Use of NSAIDs

Current study analyzed (Figure 4A), that, 22% patients of Carcinoma Group and 13% patients of Perforation Group had the history of NSAIDs consumption. The findings are not statistically significant. A. Soll et al<sup>12</sup> found almost 48% of peptic perforation patients took long standing NSAIDs. They also suggested that the frequency was higher with the high age group. M. Drini et al<sup>13</sup> and R. Russel et al<sup>14</sup> also found the higher frequency of use of NSAIDs in patients of peptic perforation. The findings were clearly opposes the finding of current study. W. Wang et al<sup>15</sup> found lower frequency of use of NSAIDs in patients with gastric cancer, which supports the finding of our study. X. Huang et al<sup>16</sup> also found the inverse correlations. The study findings strongly support the finding of current study.

### Distribution of two groups according to the History of Alcohol Consumption

Frequency of Alcohol consumption was high in both the groups in the current study (Figure 4B). 60% patients of carcinoma group and 57% patients of perforation group had history of alcohol consumption. The findings are not statistically significant.

### Distribution of two groups according to the History of Smoking

Frequency of smoking was also high in both the group of patients (Figure 4C),. 71.10% patients of carcinoma group had positive history of smoking and 62.20% patients of perforation group had positive history. The findings were not statistically significant. We also analyzed that frequency of gastric carcinoma and peptic perforation was similar, when patient taken alcohol and smoking in combination.

### Distribution of two groups according to the food habit

We analyzed the possible association of frequency of spicy food per week in two groups using a bar diagram (Figure 6). As depicted in the figure, the frequency was higher in gastric carcinoma group (44.4% thrice weekly and 13.3% more than that) than peptic perforation group (55.60% twice a week). Although,

the difference was not statistically significant. YH Chen et al<sup>17</sup> Suggested in their meta analysis that there was positive co- relations between spicy food and gastric carcinoma. Yusefi et al<sup>18</sup> suggested spicy food is one of the prime risk factors for gastric carcinoma. X. J. Cheng et al<sup>19</sup> observed salt and salt-preserved foods as well as smoked foods, processed, grilled (broiled) and barbecued (charbroiled) animal meats are probably causes of gastric cancer.

A. S. B. Albaqawi et al<sup>20</sup> conducted a study on Arar, Saudi Arabia, and they found 57% patients suffering from peptic perforation had history of taking spicy food twice or more than twice a week, which strongly supports the current study, though the frequency was much lower in the current study. M. N. Satynarayana<sup>21</sup> observed high frequency association of capsaicin intake and peptic perforation. Capsaicin is a base product of spicy and streetfoods.

#### Distribution of two groups according to the result of Rapid Urease Test

Current study reveals (Figure 7), that rapid urease test, indicator of H. Pylori infection, was positive in 64.5% patients of carcinoma and 82% patients of peptic perforation. Though the differences were not statistically significant, but the high frequency association proves that H. Pylori is a great risk factor both for peptic perforation and gastric cancer. The result was supported by large number of previous studies. Plenty of study suggested the fact that, H. Pylori is a causative organism of the gastric cancer.<sup>22</sup> V. Herrera et al,<sup>23</sup> also supported the findings of current study. N. Uemura et al<sup>24</sup> found somehow different result in their study, only 2.9% H. Pylori infected patient developed gastric cancer. The findings are strongly opposes the current study finding.

Perez et al<sup>25</sup>, also had similar findings and strongly support the view of the current study, that the Helicobacter Pylori infection had strong relation with peptic perforation and eradication of which can prevent gastric cancer, as well as peptic perforation.

To conclude, out 90 patients, 45 patients of Gastric carcinoma and 45 patients of peptic perforation was selected after applying proper inclusion and exclusion criteria. Among the two groups, gastric carcinoma found in higher age group; where peptic perforation found in lower age group; male and female ratio is 2:1 in both groups of patient. Hindu patients were prevalent in both the groups. Laborer and housewives were mostly affected in both cases.

Gastric carcinoma and peptic perforation found in high frequency in married persons. Urban residents were more sufferer of gastric carcinoma, vice versa in peptic perforation. Duodenal ulcer is the commonest site for perforations. Most patients in two groups had no previous co-morbid condition. Use of NSAIDs was found in high frequency in both groups. Most of the patients were chronic alcoholic and chronic smoker, and most of them had history of taking spicy foods more than twice in a week. H. Pylori found in high frequency in both group of patients, and it was higher in peptic perforation, which establish the association of H. Pylori with the gastric carcinoma and peptic perforation.

## Declarations

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*Conflict of interest:* The authors declare that they have no competing interests.

*Ethical approval:* Obtained from the Institutional Ethics Committee, BSMCH, Bankura, West Bengal, India. Approval letter (Memo No.BSMC/Aca/15 dt 02.01.18) is available for review by the editor of the journal. Written consents from individual patients were also obtained. Written informed consent for participation in the study was obtained where participants were children (under 16 years old) from their parent or guardian.

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## Figures

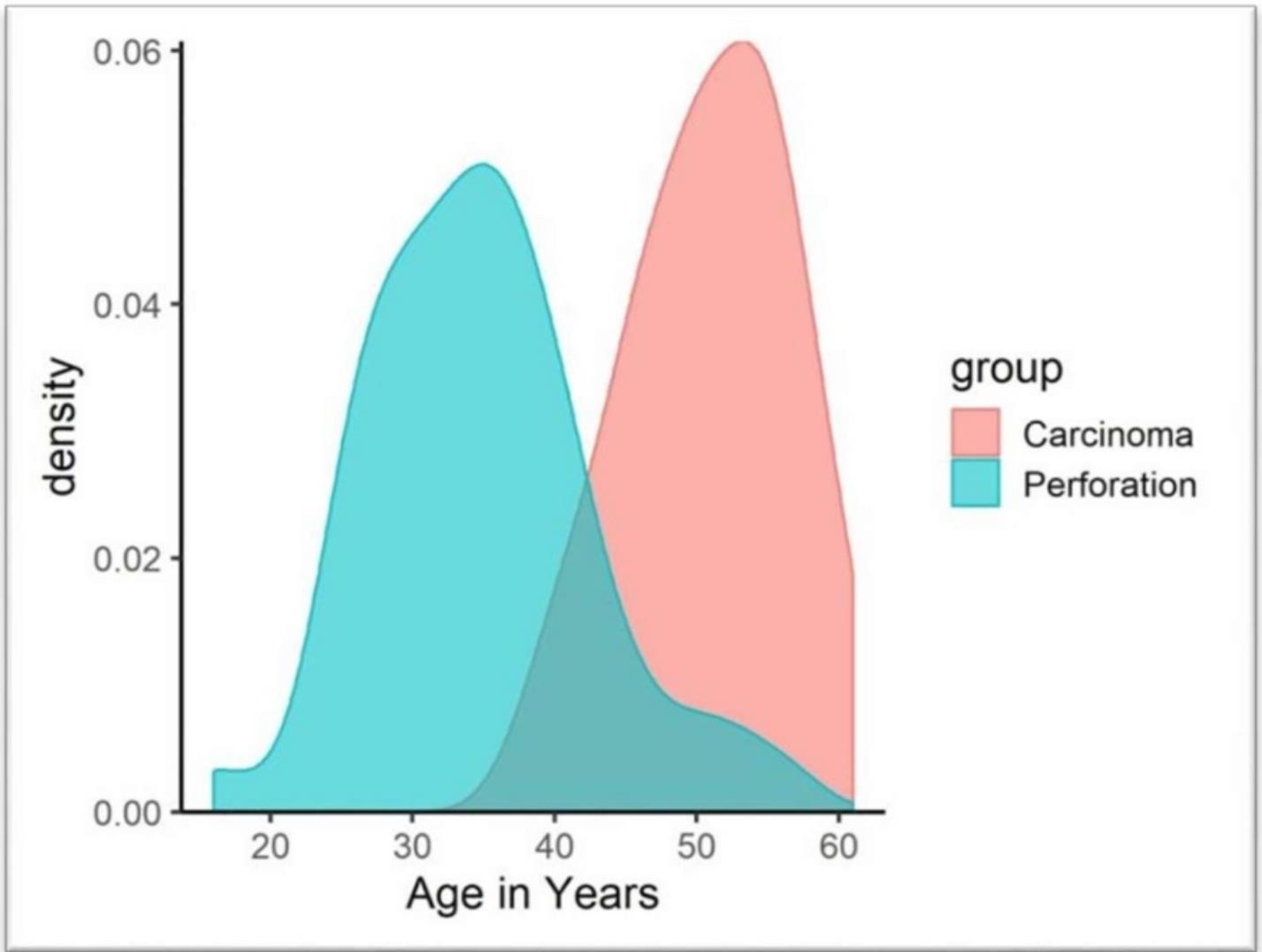
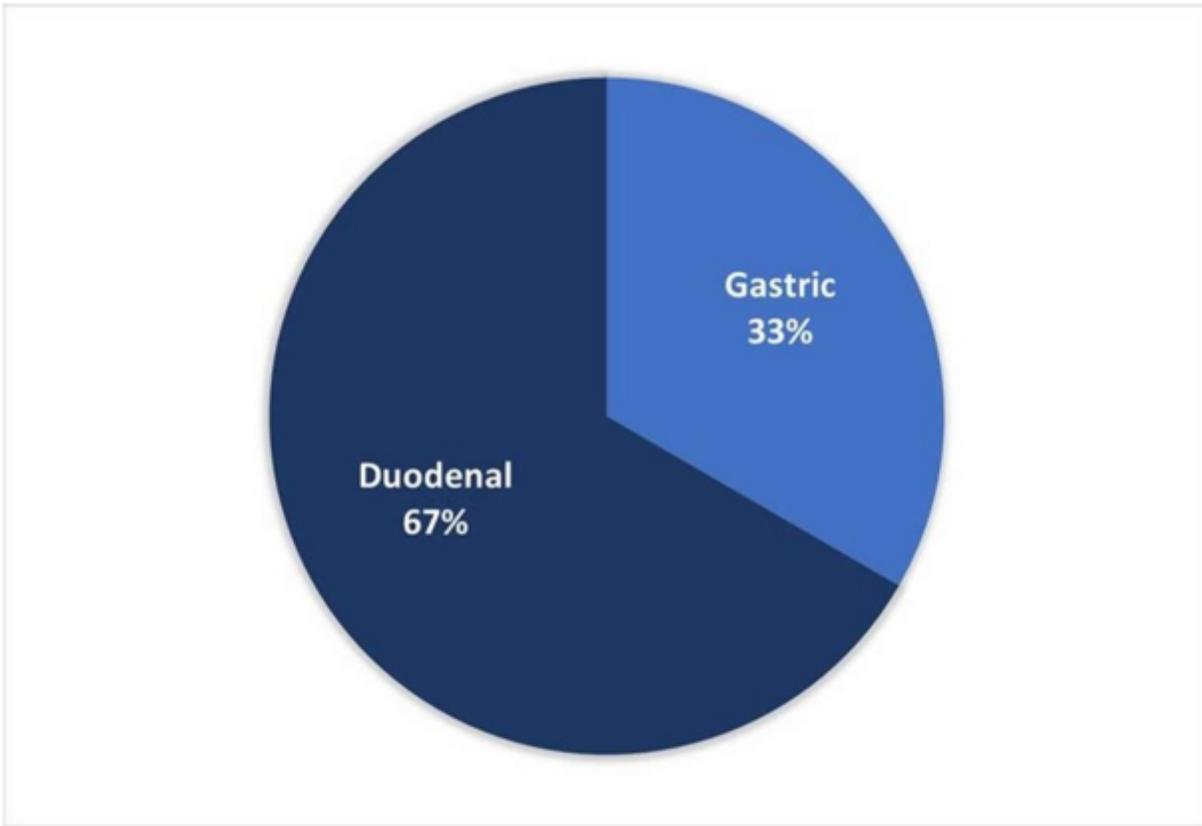


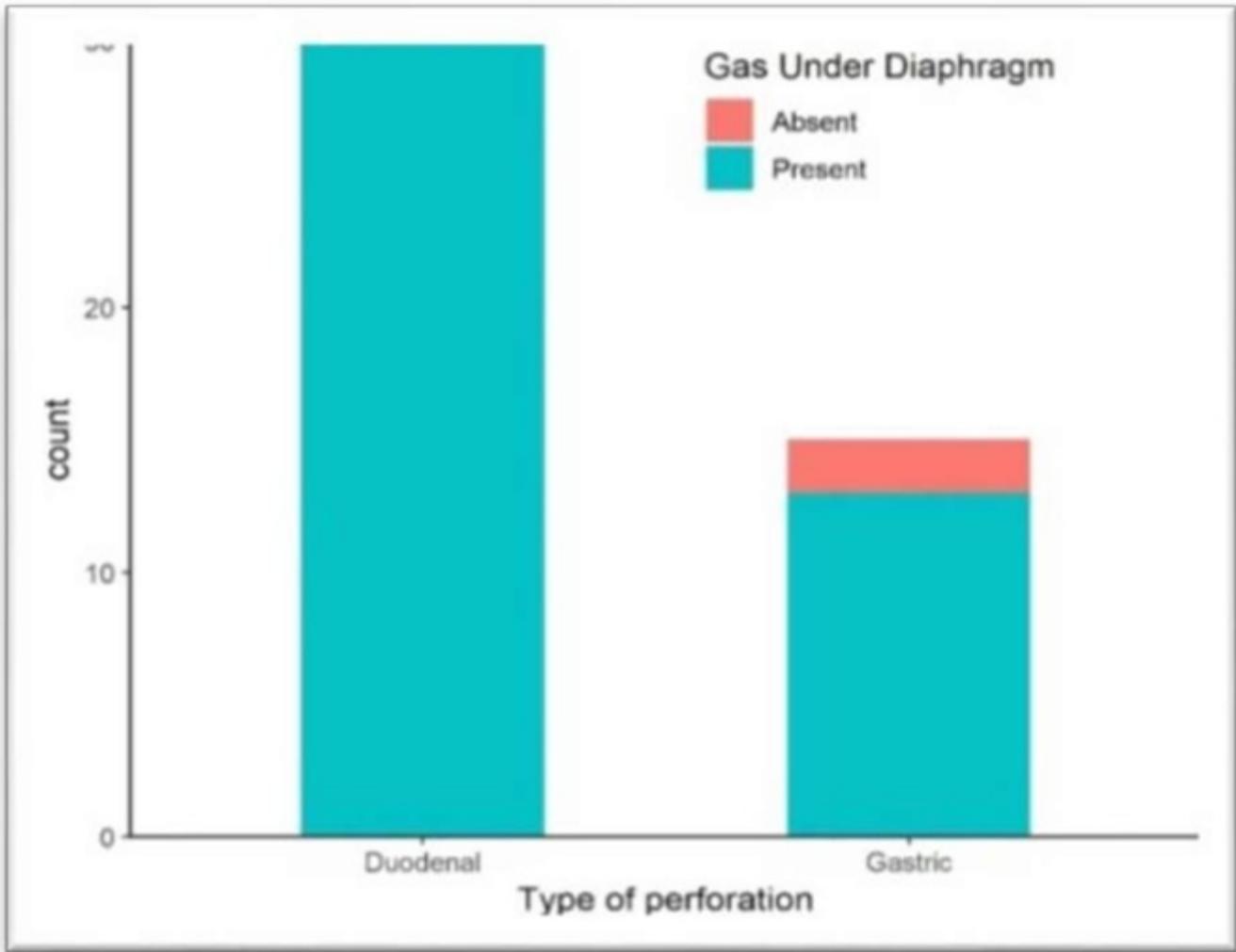
Figure 1

Comparison of Ages in Gastric Carcinoma and Gastric Perforation Patients



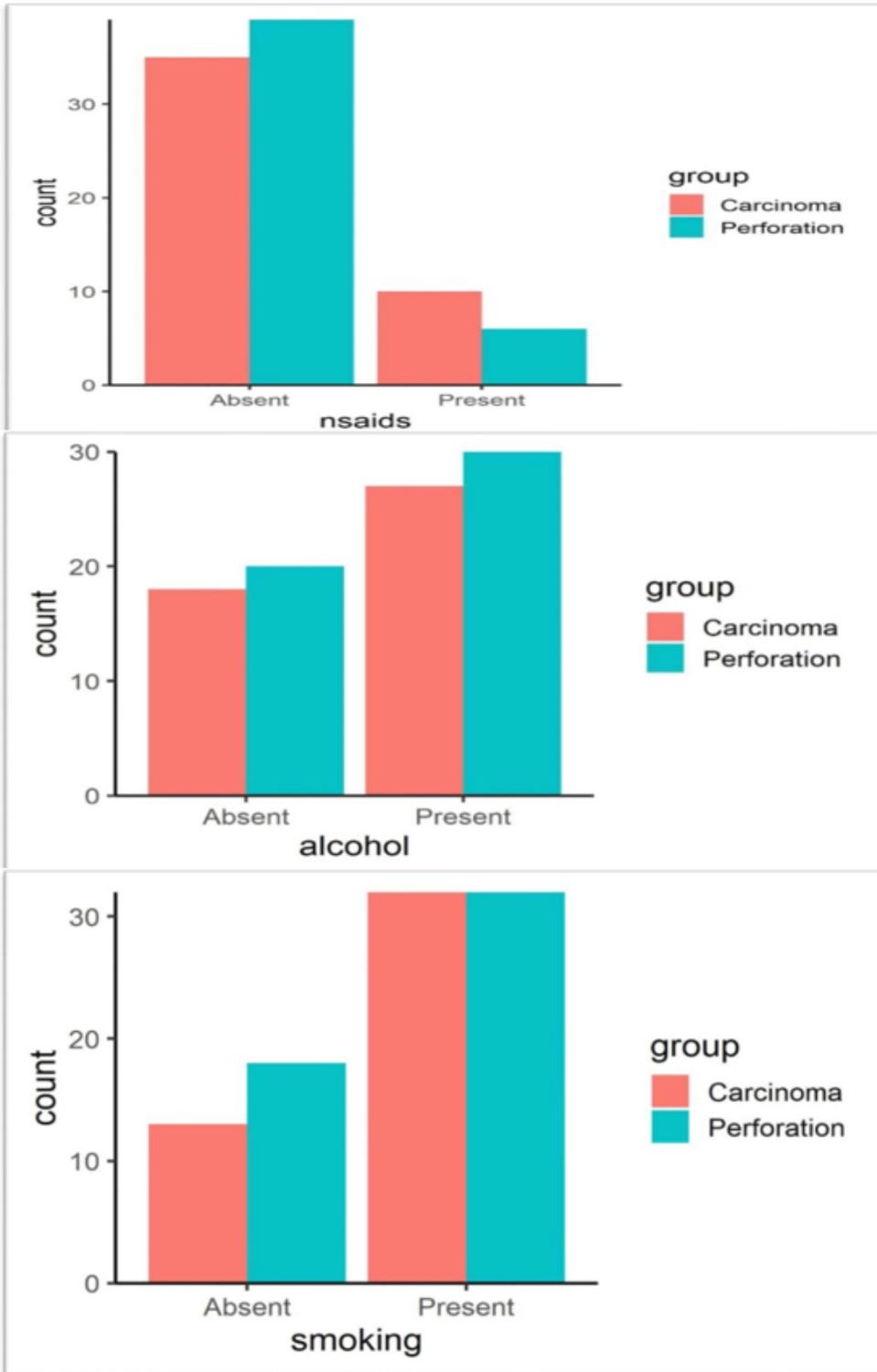
**Figure 2**

Distribution of Peptic Perforation Patients according to the Site of Perforation



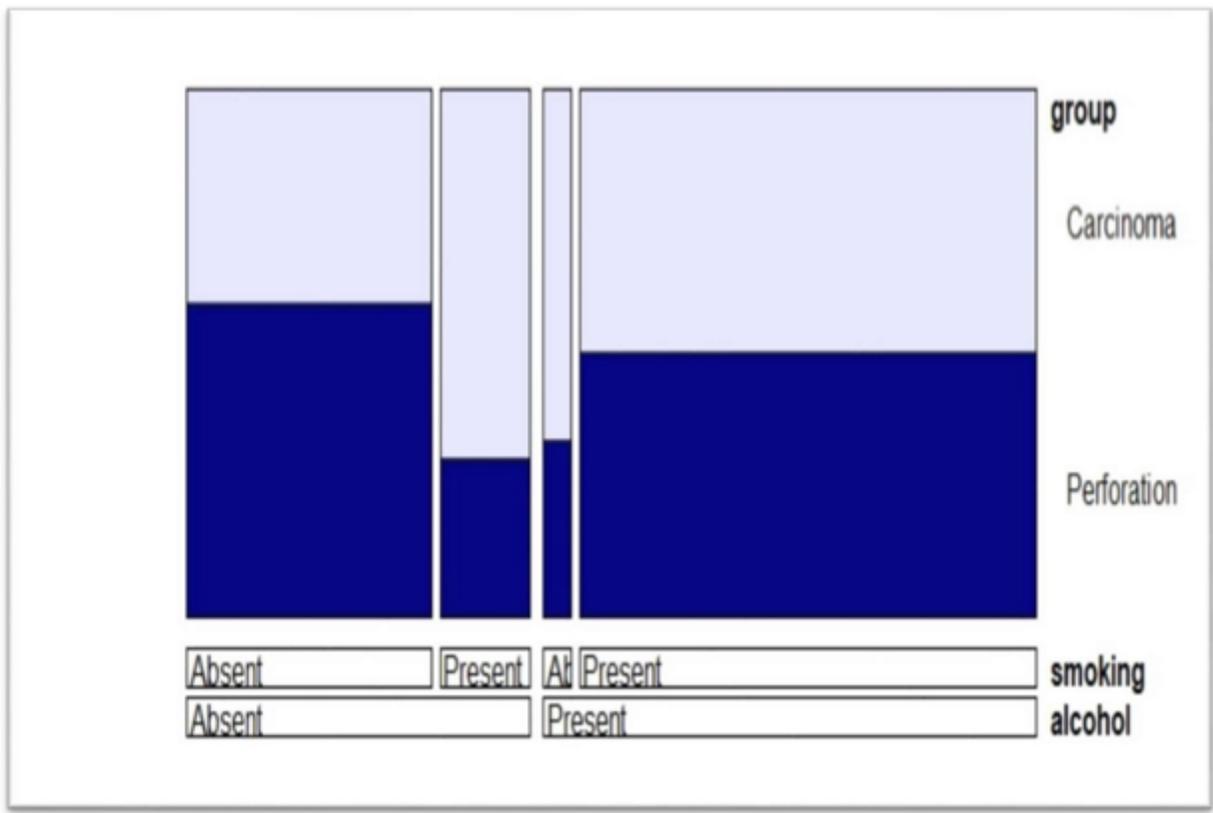
**Figure 3**

Distribution of Peptic Perforation Patients according to the Presence of free Gas under Diaphragm

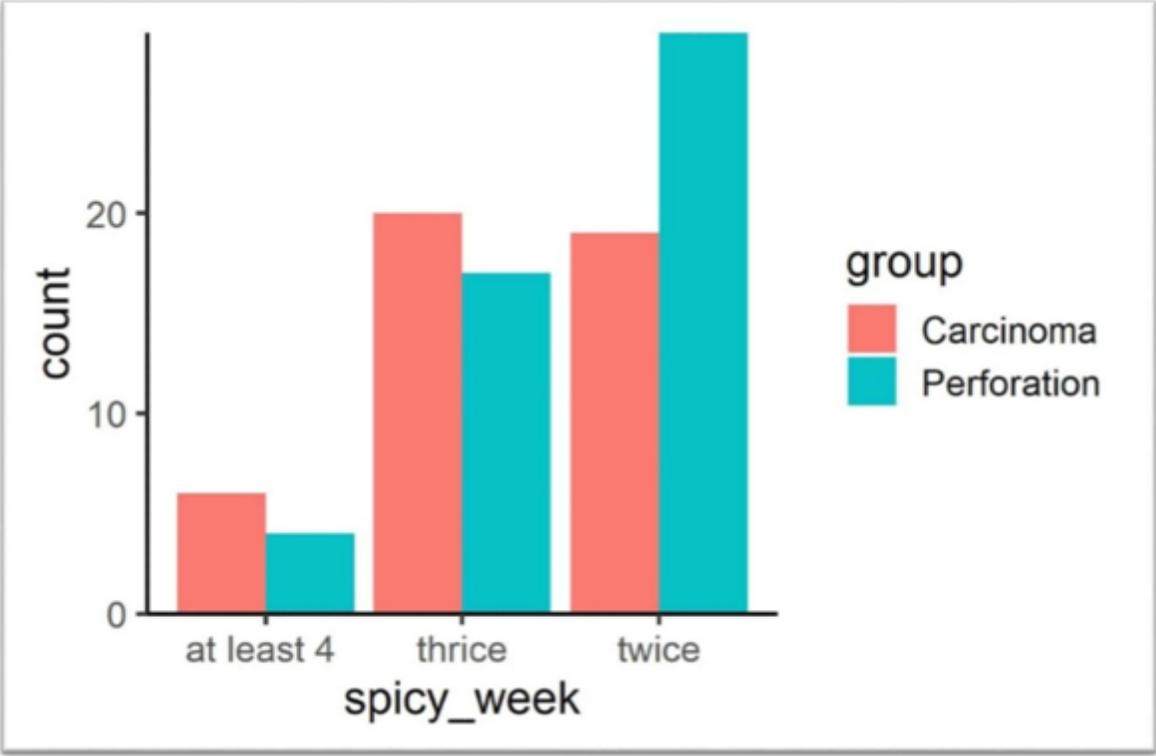


**Figure 4**

A: Distribution of two groups According to the Use of NSAIDs. B: Distribution of two groups According to the Consumption of Alcohol. C: Distribution of two groups According to the Habit of Smoking



**Figure 5**  
 Distribution of two groups according to the habit of smoking and consumption of alcohol



**Figure 6**  
 Page 17/18

Distribution of two groups According to the Frequency of Spicy food per wee

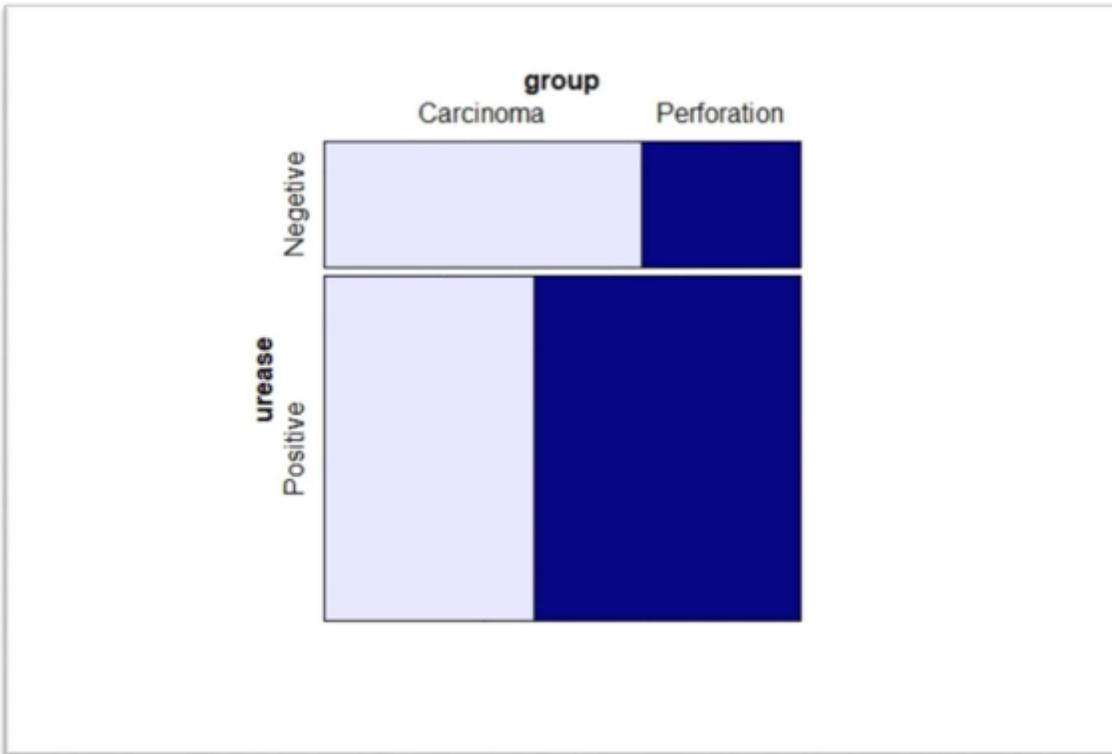


Figure 7

Distribution of two groups According to the Result of Rapid Urease Test