Post cholecystectomy biliary gastritis and H. pylori infection

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Background: Post cholecystectomy abdominal pain is a significant problem in a group of patients with gall stone surgery. The pathogenesis of post cholecystectomy dyspepsia is still poorly understood and yet difficult to ascertain. H. Pylori have been associated with significant number of the cases with gastritis, gastric ulcer, duodenal ulcer and other gastro -duodenal disorders. Hence, post cholecystectomy biliary gastritis associated with H. pylori infection might be a major aetiological factor. This study aims to evaluate the association of bile reflux gastritis, the presence of H. pylori and dyspeptic symptoms in post choecystectomized patients.

Patients and Methods: This is a prospective non-randomized study carried out on 68 patients with post cholecystectomy dyspeptic symptoms during 2 years period through September 2002 to October 2004 in Tribhuvan University Teaching Hospital at the Department of Surgery.

Results: Two hundred and thirty eight patients who were having cholelithiasis and underwent cholecystectomy were prospectively studied non-randomized way. Out of 238, 68 (28.57%) patients presented with upper abdominal pain, belching water brass with or without nausea and vomiting. So only 68 cases were included in the study. Of 68 patients, dyspeptic symptoms were more common in Bile reflux positive group (BR +)and H. pylori infection was seen in 38% (14/36) when compared with Bile Reflux negative (BR-) patients 13.75 %(4/32), which was statistically significant. Biliary gastritis was found on 32, more over reflux esophagitis in 3 cases, duodenal ulcer in 1 case was also found on BR (-) group. H. Pylori were positive on 18 cases detected by endoscopic biopsy by giemsa stain, 14 in BR (+) and 4 in (BR-) group.

Conclusion: This study suggests that excessive bile reflux may be responsible for persistence of symptoms after cholecystectomy by causing gastric mucosal damage and that biliary gastritis might be a significant problem associated with H.pylori infection in our context.

Introduction

Cholecystectomy is associated with an increase in the incidence of gastritis and may contribute to the post-cholecystectomy syndrome [1]. Patients that underwent cholecystectomy for symptomatic gallstone may have still dyspeptic symptoms. Gastric mucosal changes related to bile reflux (BR) are the cause for this if other gastrointestinal pathologic lesions are eliminated. Gastric alkaline episodes after cholecystectomy especially in symptomatic patients are suggested to be related with these symptoms [2, 3].

The aim of this prospective study was to investigate the rates of BRGastritis, H.pylori infection and dyspeptic symptoms in cholecystectomized patients. A search for postoperative H.pylori status and the relation between BR and gastric mucosal changes were evaluated.

Patients and methods

Between September 2002 to October 2004, 238 patients who were having cholelthiasis and underwent cholecystectomy were prospectively studied non-randomized way. Informed consent was taken from the patients to enter in the study group according to principle of Helsinki declaration, 1975. Out of 238, 68 (28.57%) patients presented with upper abdominal pain, belching water brass with or without nausea and vomiting. So only 68 cases were included in the study. After an overnight fast the patient underwent endoscopy with Olympus GIF Q21 gastrodudenoscope, the only premedication used was local anaesthetic (2% Xylociane Viscus). Before insufflations of stomach, all resting gastric juice was aspirated through a polyethylene catheter and pH determined immediately. The endoscope was assessed for the presence of erythema, hyperemia, and friability; changes were graded on a 0 to 3 scales. Biliary gastritis was defined as bile stained gastric mucosa with congestion, hyperemia, and oedema with or with our duodenogastric reflux. An OGD (Oesophagogastrodudenoscopy) was performed on those 68 patients to find out the cause and 2 or more antral biopsy were taken within 5 cm of the pylorus in all cases. The extent

of gastritis was assessed according to Whitestead classification system [4], in addition, the histological assessment was examined for fovelar hyperplasia, oedema in the lamina propia, capillary congestion and acute and chronic inflammatory cells. Cases were divided into (BR+) and (BR-) according to the endoscopic evidence of dudenogastric reflux or bile reflux.

Patients with common bile duct stones, previous gastric surgery and a history of any type of pathology of digestive tract were excluded in the study. Biopsy specimens were fixed in buffered 12 hours formalin embedded in paraffin and stained with hematoxylin and eosin and were taken to search for *H. pylori* with the use of Giemsa method. These sections were examined by two teams of pathologists. Patients were followed up to three months. Dyspeptic symptoms were defined as epigastric pain and abdominal upset, belching problems, gastric distension, fullness, nausea and bilious vomiting.

Statistical analysis was done by using SPSS system version 10 using Mann Whitney U test and Fisher exact tests. P values less than 0.05 was considered significant.

Results

Over 2 year's period from September 2002 to October 2004, we evaluated the relationship of bile reflux with gastric mucosal changes by histopathological methods along with *H. pylori* status and dyspeptic symptoms in cholecystomized patients.

Table 1. Age and sex wise Group distribution of

Age group	Male	Female	Total
15-45	39	103	132
46-60	18	61	79
61>	5	22	27
TOTAL	**62**	**176**	**238**

Cholecystectomized patients

The total number of patients who underwent cholecystectomy was 238. Age wise there were 132(55%) patients below 45 years of age, 79(33.5%) between 46-60 years of age and 27(11.5%) above 61 years of age**.** There were 62 male and 176 female and the male to female ratio was 1: 3.52. (Table 1). Youngest age was 15 yr, oldest age being 82 yr; the mean age of the patients was 45 years, range being 15-80 years.

Table 2. Symptomatology Between BR + and BR - group.

Symptoms	NO	(BR+)	(BR-)	p value
Epigastric pain	68	36	32	0.37
Nausea	58	33	23	0.57
Bilious Vomiting	49	29	20	0.89
Retrostrnal pain	18	11	7	0.63
Water brass	12	7	5	0.59
Fatty intolerances	3	2	1	0.44

Symptomatologically, epigastric pain was the most frequent symptom on both BR +and BR - group, followed by in the descending order of nausea, bilious vomiting, retrosternal pain, waterbrash and fatty intolerance, however there was no statistically significant difference in the presenting symptoms between BR + and BR - group (Table 2).

Table 3. Age and sex wise incidence of Post cholecystectomy gastritis and Bile reflux**.**

AGE	BR +		BR -		Total			
	M	F	M	F	M	F		%
15-45	10	14	4	16	14	30	44	64
46-60	3	7	3	5	6	12	18	26
>60	1	3	1	1	2	4	6	9.0
Total	14	24	8	22	22	46	68	100

Detailed of the age and sex wise distribution of the post cholecystectomy biliary gastritis and bile reflux has been shown in Table 3. In the age group between 15-45 year there were 10 male and 14 females in the BR + and 4 males and 16 females in BR - groups. And altogether 14 male and 30 females comprising 44, that is a total of 64% in that age group followed by 26% in the age group between 46 to 60 years of age, where out of 18 in that age group 10 were having bile reflux. On the other hand, in the age group above 60, out of 6 patients, 4 had bile reflux.

Table 4. The relationship of BR and histological gastritis**.**

Variables	H.Gastritis positive(%)	H.Gastritis negative(%)	Total
BR +	30	6	36
	83.33	16.66	100
BR -	4	28	32
	12.5	87.5	100
Total	34	34	34
	50	50	100

$p<0.001$ OR= 31.67 (H. Gastritis= Histological gastritis)

Presence of large amounts of bile was associated with abnormal inflammatory gastric mucosa during endoscopy of 36 (52%) of the 68 patients with cholecystectomy within three months after the operation were studied. Histologically proven gastritis with positive H.pylori infection was present in 18/68 (26.47%) of these patients. Biliary gastritis was found on 36, reflux esophagitis in 3 cases, duodenal ulcer in 1 case in BR+ group. Histologically, gastritis was found in 68 of 238 (28.57%) of cholecystectomised patients, 36 in BR +, and 32 in BR - group (Table 4).

When we evaluated the relationship between BR + and gastritis it was seen that 83.33% (30/36) of BR + patients had histologically proven gastritis while only 12.5% (4/32) of BRG - patients had histologically proven gastritis, (Table 4). The difference was found to be statistically significant ($p<0.001$).

Table 5. The relationship of BR and H.Pylori.

Variables		H. Pylori (+)	H. Pylori (-)	Total
(BR+)	**n**	**14**	**22**	**36**
	%	38.88	61.12	100
BR(-)	**n**	**4**	**28**	**32**
	%	12.50	87.50	100
Total	**n**	**18**	**50**	**68**
	%	26.47	73.53	100

p<0.05 OR =24

There was statistically significant difference between BR and *H.pylori* status .In BR + group there was 38.8%(14/36) H. pylori positivity. On the other hand, in BR - group only 4/32 (12.50%) was having *H. pylori* positivity (Table 5). Overall *H. pylori* positivity was 26.47%(18/ 68), (Table5).

Table 6. Histological grading of Biliary Gastritis, Bile Reflux(BR) & H.Pylori Status

Histology	BR (+)	BR (-)	H.Pylori (+)	H.Pylori (-)
Acute Gastritis	5	4	2	1
Chronic Gastritis	18	17	5	1
Acute on chronic G.	10	11	7	2
Chronic Atrophic.G	3	-	-	-
Total	**36**	**32**	**14**	**4**

Histology vs. BR status p=0.69 Histology vs. H.pylori status p<0.05

BR was not present in other 32(47%) of the cholecystectomized patients. Histologically reported as chronic atrophic gastritis was found in three (8.33%) of these patients in BR (+) while others were having acute and chronic gastritis. (Table 6). Histologically chronic gastritis was more common in both BR + and BR - group 18/36 (50%), 17/32(53%) respectively. It was followed by acute on chronic gastritis in 18 and 17, acute gastritis in 5 and 4 and chronic atrophic gastritis in 3 and none in BR + and BR - group respectively in the descending order. However there was no statistically significant difference among histology and BR status (p=0.69). On the other hand, there was statistically significant difference seen *H.Pylori* status and different grades of histological gastritis (p< 0.05) Table 6.

Discussion

Cholecystectomy is the most common routine general surgical operation performed in our hospital. There were 458 of 2809 general surgical patients comprising 16.30% of the surgical procedures in our hospital in the period of 2 years through September 2002 to October 2004. Post cholecystectomy dyspepsia is significant problem in general population. There are very few literatures regarding the aetiophathogenesis of this disorder in particular with H. pylori study [2]. Cholecystectomy is associated with an increase in the incidence of gastritis and may contribute to the post-cholecystectomy syndrome[1]. It is shown that BRG is increased after cholecystectomy [3]. It may be due to the absence of reservoir function of gallbladder causing a more continuous flow of bile in the duodenum and abnormal antroduodenal motilities. In addition, fasting bile acid concentration in the bile produced by the liver is increased after cholecystectomy and also reflux of especially the glucoconjugated bile acids [5,6]. Bile acid is known to be harmful for gastric mucosa [9]. Previous studies brought out that duodenal reflux may damage the gastric mucosa and cause symptoms like epigastric pain, nausea and bilious vomiting [10].

BR is one of the important factors in gastritis etiology. The BR rate of 29%(68/238) in our cases with gastritis is found to be in accordance with the literature [3, 12, 14, 15]. The relation between BR occurrences with gastritis is statistically significant (p<0.01). Six months after surgical intervention a morphologic variation in the gastric mucosa with a decrease in parietal cells and a slight increase in gastrin cells was shown as a result of BR [8].

Some studies has shown that 64-68 % of patients had chronic superficial gastritis, and 12% had chronic atrophic gastritis after cholecystectomy [7, 15]. In the present study 51% (35/68) of the patients with gastritis had histological evidence of chronic gastritis and 31% (21/68) 13% (9/68) had acute gastritis, 30% (21/68) had acute on chronic gastritis and 4% (3/68) had atrophic gastritis, (Table 6) which is very similar to the results seen by others 6,7,8. However, as seen also in our study, Bile reflux does not always give rise to gastritis nor do patients with gastritis always have symptom[16].

The symptoms of clinical status named as post-cholecystectomy syndrome seen in cholecystectomized patients are defined as nausea, epigastric discomfort, burning pain, bilious vomiting, belching and feeling of fullness, indigestion, flatulence and eructation. Etiopathogenesis has not been classified yet but BR may play a significant role in the postcholecystectomy syndrome [3, 10, 11, 13, 14, 17, 18]. Dyspeptic symptoms disappear only in 46% of the patients who underwent cholecystectomy [19].

The description if *H. pylori* in 1963 have spawned the entire new body of medicine[25]. *H pylori* are gram-negative rods that have the ability to colonize and infect the stomach. The bacteria survive within the mucous layer that covers the gastric surface epithelium and the upper portions of the gastric foveolae. The infection usually is acquired during childhood. Once the organism has been acquired, has passed through the mucous layer, and has become established at the luminal surface of the stomach, an intense inflammatory response of the underlying tissue develops [26].

The presence of *H pylori* always is associated with tissue damage and the histological finding of both an active and chronic gastritis. H.pylori causes most of the histologic gastritis, peptic ulcers and predisposing factor in gastric carcinomas [(7)]. H. Pylori colonization of the stomach does not appear to be normal phenomenon; description of these bacteria goes back to 100 years. The method of transmission is suspected to be faeco-oral; its prevalence is 10% in 20s to 50% in 50-69[8]. In contrast, H pylori and histologic gastritis develop at early age and with much greater frequency in developing countries [21]. It has been estimated that 80%of

people in developing countries are infected during childhood [22] Regarding the incidence few studies have been carried out in Nepal, Thapa found *H. pylori* seropositivity in 74% patients with dyspepsia[21]. Similarly in another study Adhikari Showed *H. Pylori* infection and seropositivity in 76% and 78% in Giemsa stain [21]. In our own study also *H. pylori* was prevalent in 59% among 307 consecutive cases in our prospective study [24].

The data regarding the role of *H. pylori* infection in patients with bile reflux are conflicting. *Zullo et al found the* overall *H. pylori* infection rate in their study was 62%, with no difference between patients with (59.7%) and without (64%) endoscopic bile reflux [20]. This study focuses on the role of *H. pylori* in gastric pathology of patients who had undergone cholecystectomy. *Abayli et al* after cholecystectomy demonstrated Helicobacter-like organisms in 18 samples out of 22 past cholecystectomy specimens by three different histopathologic methods[21]. In the present study 68 patients underwent upper gastrointestinal endoscopy, and at least 3 biopsy specimens were taken in the antrum, incisura angularis, and in the gastric body. The presence of bile reflux in gastric fluid at endoscopic examination was recorded. The overall *H. pylori* infection rate was 26.5%, with significant difference between patients with (38.9%) and without BR (12.5 %) ($p < 0.05$). This study found that *H. pylori* infection is frequent in cholecystectomized patients, even in the presence of endoscopic bile reflux. Bile reflux seems to act synergistically with *H. pylori* infection on gastric pathology. However we could not perform preoperative endoscopic evaluation on those patients who had postoperative biliary gastritis.

In conclusion, this prospective study suggests that excessive BR may be responsible for persistence of symptoms after cholecystectomy by causing gastric mucosal damage and we found the association with *H. pylori* infection. In order to distinguish from the other causes of post-cholecystectomy syndrome, patients with dyspeptic symptoms in the follow-up period, they should be evaluated by endoscopic evaluation for BR related gastric mucosal changes and *H. pylori* examination in the gastric biopsy. However to better understand the association of BR and *H.Pylori* infection, further prospective study in the large cohort of patients is required to assess preoperative BR and *H. pylori* status and to compare subsequently in postoperative period those develop postoperative dyspepsia after cholecystectomy.

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