



Prospective Study of 50 Patient of Cholelithiasis with Dyspeptic Symptoms: The Need of Upper Esophagogastrroduodenoscopy Prior to Surgery and Effect of Cholecystectomy on Symptomatic Relief

Authors

Dr Nitin Borle¹, Dr Shraddha Bhone²

¹Assistant Professor, ²Senior Registrar

K.B.Bhabha Municipal General Hospital, Bandra, Mumbai

Corresponding Author

Dr Nitin Borle

Assistant Professor K.B.Bhabha Municipal General Hospital, Bandra, Mumbai

Abstract

Introduction: Cholelithiasis forms approximately 98% of symptomatic gall bladder disease and affects 10% of population in developed countries. The incidence of gall stone in third world has been steadily increasing and this has been attributed to the westernization of dietary habits. Cholecystitis is common pathological condition that is frequently diagnosed in majority of patients who come to outpatient department with history of abdominal pain and dyspepsia. Cholecystectomy is usually indicated in symptomatic patients having cholelithiasis. Many times there are gastrointestinal symptoms which may be erroneously attributed to presence of gallstones found incidentally at ultrasound. Majority of such patients continue to have similar symptoms even after undergoing cholecystectomy. The post-operative continuation of symptoms attributed to cholelithiasis was such a common occurrence so as to compel some authors to observe that 'cholecystectomy has little or no effect in curing the unpleasant symptoms of flatulent dyspepsia.

With these facts in mind we conducted a study consisting of patients with cholelithiasis who fulfilled the criteria as laid down for the study. The purpose of this study was to determine the pre-operative incidence of flatulent dyspepsia in patients with gallstones and the effect of cholecystectomy alone on these symptoms.

Aims and Objectives:

1. To study age and sex wise distribution and clinical presentations of gall stone disease with dyspepsia.
2. To find out necessity of oesphagogastrroduodenoscopy prior to cholecystectomy.
3. To find out the incidence of acid peptic disease in patient of cholelithiasis.
4. To study relief of symptom after cholecystectomy in patient who had undergone preoperative oesphagogastrroduodenoscopy.
5. To study the effect of various addictions on acid peptic disease in post cholecystectomy patients.

Materials and Methods: A prospective study of 50 cases was carried out at public hospital Mumbai over a period of 2 years. 50 patient of documented gall bladder pathology with dyspepsia and open or laparoscopic cholecystectomy done on them were studied. The study was approved by institutional ethical committee. Patients above 20 years of age and presenting to a tertiary care center with sign and symptoms of cholelithiasis and calculus cholecystitis were included in the study oesphagogastrroduodenoscopy was done

pre and post cholecystectomy. Patients who have asymptomatic gall stones, pregnant females and immunocompromised and Patients having any other clinical abdominal pathology were excluded from the study.

A detailed history was taken in all patients. Detailed clinical examination was done. Patients were managed according to set protocol. Postoperative course in the ward with regards to drain if kept, and removal of sutures and presence of complication if any were noted. Data was analyzed using approved statistical methods.

Results: Majority of patients suffering with gall stones were in the age group of 31 – 40 yrs (46%) followed by 41 – 50 yrs (26%). Females were predominantly affected with a M:F ratio of 1:6. Most common presenting complaints were found to be abdominal pain (100%); vomiting (20%), fever (12%) and h/o jaundice (6%). Abdominal tenderness was present in 10 (20%) patients. On ultrasound 43 (86%) patients had features of chronic calculus cholecystitis while 7 (14%) patients had acute calculus cholecystitis. Common bile duct was normal in majority of the patients (94%) while only 3 patients (6%) had a dilated common bile duct. All patients had undergone preoperative oesphagogastroduodenoscopy out of which 5 (10%) patients had gastritis and 3 (6%) patients had peptic ulcer. 42 (84%) patients had a normal oesphagogastroduodenoscopy. All patients once again had undergone oesphagogastroduodenoscopy on postoperative day 15. The findings were normal in 37 (74%) patients while gastritis and peptic ulcers were seen in 10 (20%) and 3 (6%) patients respectively. 41 (82%) patients had got relieved of pain post operatively whereas 37 (74%) patients got relieved of dyspepsia. In our study of 50 cases, 5 patients were addicted to smoking, alcohol or both. Pain relief and resolution of dyspepsia was suboptimal in patients addicted to smoking or alcohol. Pain relief was not achieved in 57% males and 11% females. Dyspepsia was relieved in 71% males and 18% females. As the age advances there were less chances of pain relief and resolution of dyspepsia. Abnormal preoperative or postoperative OGDscopy was associated with fewer chances of relief of pain and resolution of dyspepsia after cholecystectomy. Finally in this study 30% patients were not relieved of their symptoms out of which 14% patients were having pain and dyspepsia, 12% and 4% patients were having dyspepsia and pain respectively.

Conclusion: Due to the high incidence of simultaneous disease of the upper gastrointestinal disease we believe that routine preoperative oesphagogastroduodenoscopy is indicated before elective surgical treatment of cholelithiasis.

Keywords: Cholelithiasis, Cholecystectomy, Dyspepsia, Pain relief.

Introduction

Cholelithiasis forms approximately 98% of symptomatic gall bladder disease and affects 10% of population in developed countries^[1]. cholecystitis is common pathological condition that is frequently diagnosed in majority of patients who come to outpatient department with history of abdominal pain and dyspepsia^[2]. These days we have been diagnosing more and more cases of calculus cholecystitis. It does not always mean incidence of calculus cholecystitis has gone up. The increased hospital registration of this disease may be attributed to various causes, like increased awareness of disease in public, increased health consciousness, easily approachable hospital services and easily available diagnostic facilities. Important advances in the field of imaging have led to better evaluation of intra abdominal

pathology. These include non invasive modalities like ultrasonography and computed tomography scan of abdomen, and invasive modalities like endoscopy and choledochoscopy^[3]. With these invasive and non-invasive techniques early and accurate diagnosis is possible. Cholecystectomy for gall stone disease has become one of common major general surgical procedure performed in an institute^[4]. The incidence of gall stone in third world has been steadily increasing and this has been attributed to the westernization of dietary habits. This disease is extensively dealt in western literature but the data is always pertinent to western population. We lack specific data regarding profile of the disease in India. Disease pattern in Northern India has been similar to that in the west. Comparative information on gall stone disease in south India is relatively less.

Although it is commonly thought that the typical patient with gallstones is a 'fat, flatulent, female in their forties and fifties', the relationship between gallstones and flatulent dyspepsia is far from certain. On the one hand it has been increasingly realized that cholecystectomy fails to relieve these symptoms in a proportion of patients up to the extent that Maingot (1956) could write that 'cholecystectomy has little or no effect in curing the unpleasant symptoms of flatulent dyspepsia' [5]. Similar symptoms occur frequently in patients with a normal gallbladder; in fact Price (1963) found that in women between 50 and 70 years there is equal incidence of these symptoms in those with a normal and those with an abnormal cholecystogram [6].

Materials and Methods

A prospective study of 50 cases was carried out at a public hospital in Mumbai over a period of 2 years. 50 patient of documented gall bladder pathology with dyspepsia and open or laparoscopic cholecystectomy done on them were studied. The study was approved by institutional ethical committee

Inclusion criteria

1. All patients with calculus cholecystitis (acute or chronic) and dyspepsia.
2. Age group more than 20 years.
3. Oesphagogastroduodenoscopy done pre and post cholecystectomy.

Exclusion criteria

1. Patients who have asymptomatic gall stones.
2. Pregnant females.
3. Immunocompromised patients and those having any other clinical abdominal pathology.

Detailed history was taken in each case. Thorough Clinical examination and appropriate investigations were done. History included presenting complaints as regards to the mode of onset, duration and progress of symptoms which included pain in abdomen, presence of fever, nausea and vomiting, jaundice and flatulent

dyspepsia. Clinical examination included inspection of abdomen, palpation with due importance to presence of tenderness, guarding and rigidity, presence of palpable gall bladder and Murphy's sign. Per abdomen examination was carried out as per protocol. A thorough examination of other systems was also done for the identification and management of associated disease. Investigation include complete haemogram, liver function tests, Ultrasound abdomen, Pre and post operative Esophagogastroduodenoscopy, ERCP and CT abdomen was done when considered necessary. Management included drugs in the form antibiotics and surgical intervention. Postoperative course in regards to the removable of drain if it was kept postoperatively, and removal of sutures and presence of complication if any were noted. The purpose of this study was to determine the pre-operative incidence of flatulent dyspepsia in patients with gallstones and the effect of cholecystectomy alone on these symptoms. In order to try to define flatulent dyspepsia more exactly, it has been divided into nine individual symptoms as following:

Flatulence

- (1) Repeated belching.
- (2) Full-feeling after normal-sized meal.
- (3) Inability to finish a normal-sized meal.
- (4) Abdomen becomes blown-out so that clothes have to be loosened.

Dyspepsia after meals

- (5) Burning discomfort in the epigastrium.
- (6) Burning discomfort in the chest ('heartburn').
- (7) Bitter fluid regurgitating into the mouth.
- (8) Vomiting.
- (9) Nausea.

Some belching is normal so it is only considered significant if accompanied by one or more of the other symptoms. Inability to finish a normal-sized meal implies that the patient is hungry but feels full-up soon after starting a meal and this must be distinguished from true anorexia.

It was decided to consider a history of flatulent dyspepsia to be positive if two or more of the individual symptoms were regularly present up to the time of operation (provided they were not numbers 8 and 9 alone).

Results

In our study we have found that majority of patients suffering with gall stones were in the age group of 31 – 40 yrs (46%) followed by 41 – 50 yrs (26%).

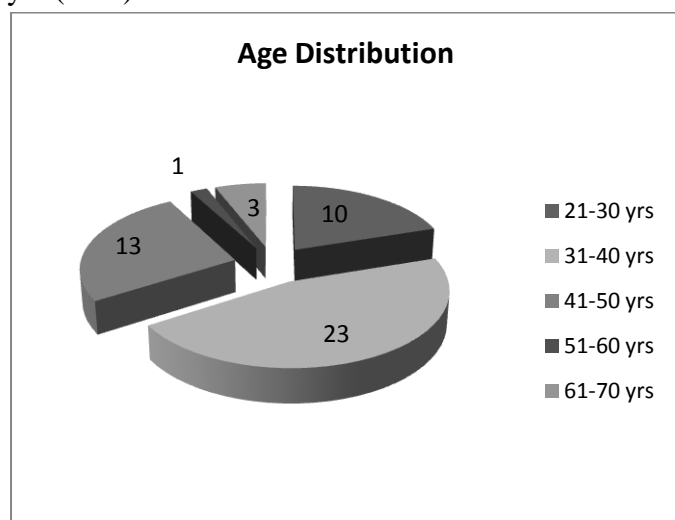


Figure. 1: Age wise distribution of gall stone disease.

43 out of 50 i.e. 86% patients with gall stone disease with dyspepsia were female. Male to female ratio was 1:6.

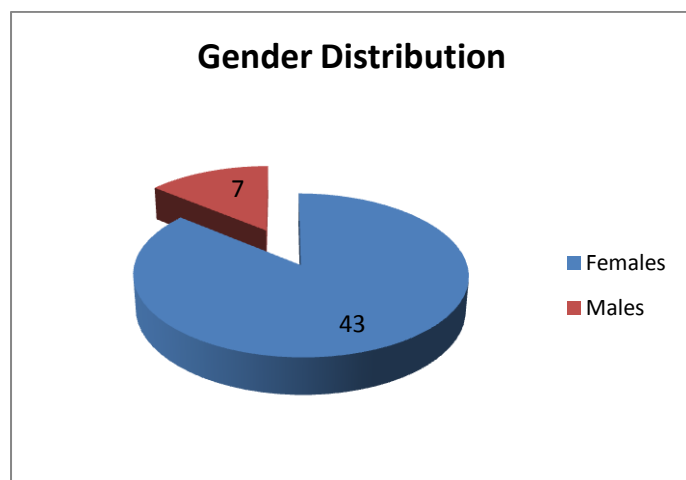


Figure. 2: Gender distribution of gall stone disease.

All the patients with gall stone disease and dyspepsia presented with pain in abdomen (100%), followed by vomiting 20%. 3 patients were having obstructive jaundice due to common bile duct (CBD) calculus; these patients had undergone endoscopic retrograde pancreaticochoangiography (ERCP) with CBD stenting prior to cholecystectomy.

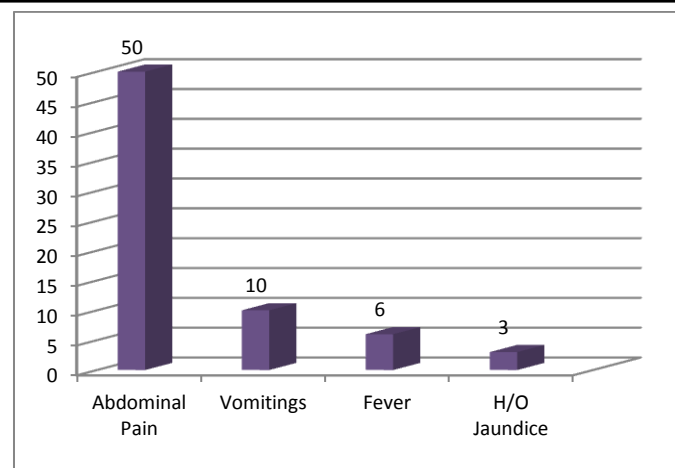


Figure. 3: Symptom wise distribution of gall stone disease

In our study, 10 out of 50 (20%) patients presented with abdominal tenderness. No patients had presented with abdominal guarding or distension.

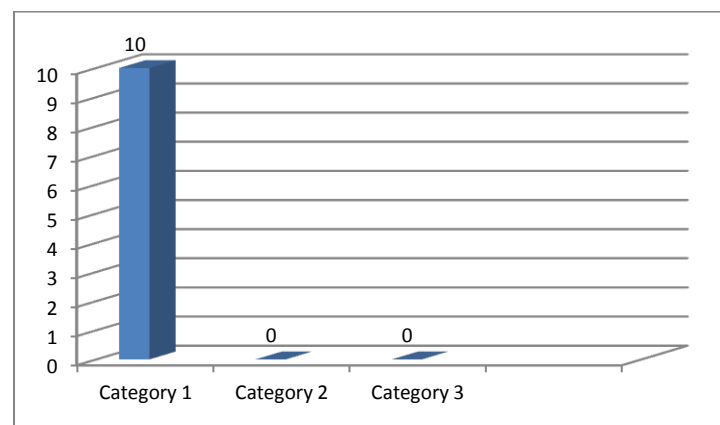


Figure 4: Abdominal sign wise distribution of gall stone disease.

In our study, 7 out of 50 patients who had undergone cholecystectomy were having acute calculus cholecystitis, rest were having chronic calculus cholecystitis.

Table 1: Ultrasound finding in gall stone disease

GALL BLADDER	NO. OF PATIENTS	PERCENTAGE
Acute Calculus cholecystitis	7	14%
Chronic Calculus cholecystitis	43	86%
Total	50	100%

3 out of 50 patients had dilated CBD on ultrasonography of abdomen which was due to CBD calculus for which ERCP with CBD stenting was done with ductal clearance.

Table 2: Common bile duct findings in our study

CBD	NO. OF PATIENTS	PERCENTAGE
Normal	47	94%
Dilated	3	6%
Total	50	100%

All our patients with calculus cholecystitis had undergone oesphagogastroduodenoscopy (OGDscopy), out of which 5 patients were having gastritis and 3 patients were having peptic ulcer.

Table 3: Preoperative Esophagogastroduodenoscopy findings

PRE OP OGD SCOPY	NO. OF PATIENTS	PERCENTAGE
GASTRITIS	5	10%
PEPTIC ULCER	3	6%
NORMAL	42	84%
TOTAL	50	100%

All the 50 patients, were undergone OGDscopy on post operative day 15. It showed that incidence of gastritis in postcholecystectomy patient was 20% i.e. 10% increase than preoperative incidence. The peptic ulcer incidence remained same i.e. 6%.

Table 4: Postoperative OGDscopy findings

POST-OP OGD SCOPY	NO. OF PATIENTS	PERCENTAGE
Gastritis	10	20%
Peptic Ulcer	3	6%
Normal	37	74%
Total	50	100%

In our study of 50 cases, 41 (82%) patients had got relieved of pain post operatively whereas 37 (74%) patients got relieved of dyspepsia.

Table 5: Post cholecystectomy outcome

OUTCOME	PAI N	%	DYSPEPSI A	%
Relieved	41	82%	37	74%
Not Relieved	9	18%	13	26%
Total	50	100%	50	100%

Out of 50 cases, 5 patients were addicted to smoking, alcohol or both. 50% of smokers were not relieved of pain and 66% of patients who were

addicted to both were not relieved of pain, as compared to 13% of patients not addicted.

Table 6 Relationship between Pain and Addiction

ADDICTION		PAIN		NO.O F PATIE NTS
		RELE VIED	NOT RELE VIED	
Addict ion	Smoker	1	1	2
	Alcoholic	0	0	0
	Smoker + Alcoholic	1	2	3
No Addiction		39	6	45
Total		41	9	50

In our study of 50 cases, 5 patients were addicted to smoking, alcohol or both. All (100%) patients who were addicted to both were not relieved of dyspepsia, as compared to 20% who were not addicted.

Table 7: Relationship between Dyspepsia and Addiction.

ADDICTION		DYSPEPSIA		NO.OF PATIENTS
		RELEVIED	NOT RELEVIED	
Addiction	Smoker	2	0	2
	Alcoholic	0	0	0
	Smoker + Alcoholic	0	3	3
No Addiction		35	10	45
Total		37	13	50

An analysis of pain relief according to gender revealed that 4 out of 7 male patients (57%) were not relieved of pain as compared to 11% of female.

Table 8: Pain relief in Male and Female

SEX	PAIN		TOTAL NO.OF PATIENTS
	RELIE VED	NOT RELIEVE D	
MALE	3	4	7
FEMALE	38	5	43
TOTAL OUTCOME	41	9	50

In our study, 5 out of 7 male patients (71%) were not relieved of dyspepsia as compared to 18% of female.

Table 9 : Dyspepsia relief in Male and Female

SEX	DYSPEPSIA		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
MALE	2	5	7
FEMALE	35	8	43
TOTAL OUTCOME	37	13	50

33% of patients in age group 61 – 70 yrs were not relieved of pain postoperatively, followed by 21% of patients were between age group 31 – 40 yrs.

Table 10: Age wise distribution of pain relief

AGE	PAIN		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
21-30	9	1	10
31-40	18	5	23
41-50	11	2	13
51-60	1	0	1
61-70	2	1	3
TOTAL OUTCOME	41	9	50

66% of patients in age group 61 – 70 yrs were not relieved of dyspepsia postoperatively, followed by 20% of patients were between age group 21 – 30 yrs.

Table 11 Age wise distribution of dyspepsia relief

AGE	DYSPEPSIA		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
21-30	5	5	10
31-40	19	4	23
41-50	11	2	13
51-60	1	0	1
61-70	1	2	3
TOTAL OUTCOME	37	13	50

Preoperatively 8 patients were having gastritis and peptic ulcer on Esophagogastroduodenoscopy out of which 6 patients (75%) were not relieved of pain postoperatively as compared to 3 out of 42 (7%) patients having normal Esophagogastroduodenoscopy findings.

Table 12 Relationship between Pre op OGDscopy findings and Pain

PRE OP OGDSCOPY	PAIN		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
GASTRITIS	2	3	5
PEPTIC ULCER	0	3	3
NORMAL	39	3	42
TOTAL OUTCOME	41	9	50

Preoperatively 8 patients were having gastritis and peptic ulcer on Esophagogastroduodenoscopy out of which, none relieved of dyspepsia. However 12% of patients having normal preoperative Esophagogastroduodenoscopy were not relieved of dyspepsia postoperatively.

Table 13: Relationship between Pre op OGDscopy findings and dyspepsia

PRE OP OGDSCOPY	DYSPEPSIA		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
GASTRITIS	0	5	5
PEPTIC ULCER	0	3	3
NORMAL	37	5	42
TOTAL OUTCOME	37	13	50

Postoperatively 13 patients were having gastritis and peptic ulcer on Esophagogastroduodenoscopy out of which 7 patients (53%) were not relieved of pain postoperatively as compared to 2 out of 37 (5%) patients having normal Esophagogastroduodenoscopy findings.

Table 14: Relationship between Post op OGDscopy findings and pain

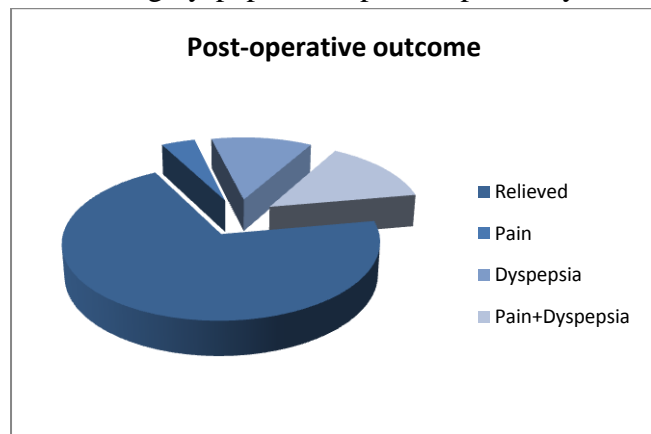
POST OP OGDSCOPY	PAIN		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
GASTRITIS	6	4	10
PEPTIC ULCER	0	3	3
NORMAL	35	2	37
TOTAL OUTCOME	41	9	50

Postoperatively 13 patients were having gastritis and peptic ulcer on Esophagogastroduodenoscopy out of which, none relieved of dyspepsia patients. However all patients (37) having normal postoperative Esophagogastroduodenoscopy were relieved of dyspepsia postoperatively.

Table 15: Relationship between Post op OGDscopy findings and dyspepsia.

POST OP OGDSCOPY	DYSPEPSIA		TOTAL NO.OF PATIENTS
	RELIEVED	NOT RELIEVED	
GASTRITIS	0	10	10
PEPTIC ULCER	0	3	3
NORMAL	37	0	37
TOTAL OUTCOME	37	12	50

In our study 30% patients were not relieved of their symptoms out of which 14% patients were having pain and dyspepsia, 12% and 4% patients were having dyspepsia and pain respectively.

**Figure 5:** Postoperative symptomatic outcome.

Discussion

50 consecutive patients who have undergone cholecystectomies in a tertiary care public hospital were included in this study. Most Patients with calculus cholecystitis were in the age group of 31 – 40 years. In western population maximum incidence is noted in age group of 50 – 59 years [7]. Age range in present study was 20 – 77 yrs. The gall stone disease is uncommon in first two decades of life. In India Rattan et al have reported 6 years old with non hemolytic gall stones [8]. Youngest reported infant with gall stones in worldwide is being 41 days old by as reported by Morales et al [9]. In our study females were affected predominantly with a F:M ratio being 6.2:1. In western literature this ratio varies from 2:1 to 4:1. Raza et al [10] reported female to male ratio 5:1, while Ghosh et al reported it to be 6:1 [11]. The analysis of symptomatology of the patients revealed that 100% of patients presented with pain in abdomen. Common site of pain was right hypochondrium and in majority of patients' pain was dull aching, intermittent and non radiating. In some patients abdominal pain radiated to back. Singh et al [12] and Wani et al [13] reported pain in right hypochondrium with radiation to back as the commonest presenting complaint. Ghosh et al have noticed pain in epigastric region in 66% of patients [11]. Endoscopy done in these patients showed that 10 % and 20% patients were having preoperatively and postoperative gastritis respectively. Farsakh et al reported that endoscopic gastritis developed in 50% after surgery compared with 30% before surgery [14]. Atilla Soren et al reported 55% gastritis in post-cholecystectomy patients [15]. Incidence of peptic ulcer was same in preoperative as well as postoperative patients (6%). 26% patients were not relieved of dyspeptic symptoms. In their study Johnson et al reported that 30% patients were not relieved of dyspeptic symptoms after cholecystectomy [16]. These results are similar to those of Rhind & Watson (1968) who found that 70% of such patients were cured or improved by operation [17]. Goldsmith (1957)

found that only twenty-three out of 114 patients (20%) were completely symptom-free, the remainder being generally improved ^[18]. Bodvall (1964) found that one-third of his patients had postoperative flatulent dyspepsia ^[19].

In present study post cholecystectomy pain was present in 18% of patients. Gui G P et al reported post cholecystectomy pain in 30% of patients. Middelfart HV et al found post cholecystectomy pain in 20 – 30 % patients ^[20].

The cholecystectomy is accompanied by an alkaline shift of gastric pH. There is much experimental and clinical evidence that cholecystectomy increases incidence of duodenogastric reflux ^[21]. It is widely recognized that duodenogastric reflux is an important factor in pathogenesis or symptomatology of several upper gastrointestinal disorders like gastritis, peptic ulcer and oesophagitis ^[22]. Loss of reservoir function of gall bladder in cholecystectomised patients causes increase in duodenogastric reflux, due to a constant supply of bile in to the duodenum, even when fasting ^[23]. Another possibility is that the pyloric mechanism may be impaired in patients after cholecystectomy with subsequent pyloric incompetence. There is clinical and experimental evidence that regurgitation of duodenal juice and bile into the stomach is capable of damaging the gastric mucosa and cause symptoms ^[24]. The composition of bile refluxing in to the stomach is altered after cholecystectomy to a composition that is more damaging to gastric mucosa ^[25].

Overall our findings were in conformity with the studies carried out by various authors who have undertaken similar studies.

Conclusion

Due to the high incidence of simultaneous disease of the upper gastrointestinal disease we believe that routine preoperative gastroscopy is indicated before elective surgical treatment of cholelithiasis, however cholecystectomy remains the corner stone for treatment of cholelithiasis. Patients who have an abnormal oesphagogastroduodenoscopy

should be counseled about the possibility of suboptimal pain relief after cholecystectomy.

Conflict of Interest: None

References

1. Maram ES, Linos DA, Thistle JL, Linos A, O'Fallon WM, Kurland LT. The incidence of cholelithiasis and cholecystitis in Rochester, Minn, 1950 through 1969. Arch Intern Med. 1990 Sep;150(9):1833
2. Portincasa P, Moschetta A, Petruzzelli M, Palasciano G, Di Ciaula A, Pezzolla A. Gallstone disease: Symptoms and diagnosis of gallbladder stones. Best Pract Res Clin Gastroenterol. 2006;20(6):1017-29.
3. Birtwhistle RV, Sauerbrei EE. Ultrasonography in the Diagnosis of Gallbladder Disease. Canadian Family Physician. 1983;29:1621-1625.
4. Luman W, Adams WH, Nixon SN, et al. Incidence of persistent symptoms after laparoscopic cholecystectomy: a prospective study. Gut. 1996;39(6):863-866.
5. Maingot R. (1956) Cholecystectomy. In: Operative Surgery (Ed. By C. Rob & R. Smith), 1stedn, Vol. 2, p. 390. Butterworth, London.
6. Price W.H. (1963) Gallbladder dyspepsia. British Medical Journal, 2, 138.
7. Chuttani PN. Cholelithiasis in India. Proceedings of the third world congress of gastroenterology, vol 4, Tokyo Bassel Karger, 1996, PP 163.
8. Ratan KN, Sodhi D et al: Gall stones in children (non hemolytic). Indian J Med Science, 1995, 49,32 – 34.
9. Morales D et al: Acute cholecystitis and cholelithiasis in a 41 day old newborn. British journal of surgery 1995: 82: 13.
10. Raza MH, Khan MA et al: Gall stone disease. Indian journal of Surgery 1990, 52(9), 415 – 20.

11. Ghosh S.K, Das K.N, Dose D et al: Aetiopathogenesis of chronic cholecystitis in Gangetic West Bengal. A study of 300 cases: Indian Journal of Surgery 1995; 57: 313-315.
12. Singh A, Bagga SPS et al: gall bladder disease – an analytical report of 250 cases. Indian Medical Association 1989, 87,253 – 56.
13. Wani NA, Khan ZA et al: Experiences with calculus biliary tract surgery. Indian Journal of Surgery 1995, 57, 181-86.
14. Abu Farsakh NA, Stietieh M, Abu Farsakh FA. The postcholecystectomy syndrome. A role for duodenogastric reflux. J ClinGastroenterol. Apr 1996; 22(3): 197-201.
15. Atilla Soran, Nilufer Erverdi, Cavit Col: Effect of cholecystectomy on duodenogastric reflux, gastric mucosa and serum gastric level.
16. A G Johnson: Cholecystectomy and gallstone dyspepsia, Clinical and physiological study of a symptom complex. Annals of the Royal Collage of Surgeons of England, 1975, vol 56.
17. Rhind J.A. & Watson L. (1968) Gallstone dyspepsia. British medical Journal, 1, 32
18. Goldsmith HJ. The results of cholecystectomy. Guys Hosp Rep. 1957;106(2):80-91.
19. Bodvall b. Late results following cholecystectomy in 1930 cases and special studies on postoperative biliary distress. Acta chir scand suppl. 1964;325:suppl 329–329:1
20. HV Middelfart, J. U. Kristensen, C. N. Laursen, N. Qvist, L. Hojgaard, P. Funch-jensen, H. Kehlet: Pain and Dyspepsia after Elective and Acute Cholecystectomy.
21. Warshaw AL. Bile gastritis without prior gastric surgery. Contributing role of cholecystectomy. Am J Surg 1979; 137: 527-531.
22. Svenson J, Gelin J, Svanik J. Gallstones, cholecystectomy and duodenogastric reflux of bile acid . Scand J Gastroenterol 1986;21 :181-187.
23. Wilson P, Jamieson JR, Hinder RA, Anselmino M, Perdakis G, Ueda RK, DeMeester TR . Pathologic duodenogastric reflux associated with persistence of symptom after cholecystectomy. Surgery. 1995 Apr;117(4):421-8.
24. Yazicioglu N, Gonenc U, Karaoglu AO, et al. Histopathologic changes in gastric and duodenal mucosa in patients with cholecystectomy. Turkish J Gastroenterol 1994; 5: 386-389
25. Ritchie WP. Bile acids and reflux related clinical disorders of the gastric mucosa. Surgery 1977; 82: 192-198.