

Does Every Patient with Symptomatic Gallstones Need Cholecystectomy?

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Submitted for Publication: 10-05-2023
Accepted for Publication: 02-10-2023

How to Cite: Cheema K, Azeem M, Anjum N, Raza A. Does Every Patient with Symptomatic Gallstones Need Cholecystectomy?. APMC 2024;18(1):59-63. DOI: 10.29054/APMC/2024.1363

ABSTRACT

Objective: The aim of this study is to identify the impact of preoperative clinical symptoms of biliary colic –whether classic, dyspeptic or atypical type- on operative or non-operative clinical outcome. **Study Design:** Prospective study. **Settings:** Department of Surgery, Sargodha Medical College, Sargodha Pakistan. **Duration:** 15-01-2016 to 01-12-2017. **Methods:** Randomize control trial. **Results:** 106 patients with cholelithiasis were evaluated, out of which 86.79% (n- 92) underwent cholecystectomy. 91.3% (n-84) were asymptomatic postoperatively. More than 50% patients presented with associated symptoms like GIRD/reflux, dyspepsia (n-57). Heartburn/reflux patients were unresolved postoperatively (P=0.03). Overall, 12.2% (n-13) of patients and 21.2% of patients with associated symptoms improve with medical treatment of peptic ulcer/H-pylori triple regimen therapy pre/postoperatively. **Conclusion:** Patients with symptomatic gall stone associated with atypical presentation, may benefit from PPI treatment or H. pylori testing before cholecystectomy.

Keywords: Gallstone colic, atypical biliary colic, heartburn, H-pylori, Ineffective cholecystectomy.

INTRODUCTION

Pakistan, up to 18% adults have gallstone, and 1 to 2% become symptomatic, and approximately 270,000 gall bladder operations performed each year.¹

Apart from biliary colic symptoms of gallstone, patients are usually referred for surgical consultation with other symptoms like heartburn, epigastric pain, bloating or other non-specific upper abdominal pain for symptomatic gallstone disease.

Upper gastrointestinal diseases like H-pylori infection, heartburn due to GERD, dyspepsia, bloating and other underlying diseases contributes unnecessary operation without good outcome i.e. relieving the symptom after operation.

So, it is important to differentiate biliary colic pain from the rest of upper gastrointestinal pain.^{2,3,4} Classically it is characterized by paroxysmal biliary colic after meal in right upper quadrant of abdomen associated with nausea and vomiting is the hallmark presentation to identify the symptomatic cholelithiasis.⁵ However, there might be atypical presentation as well. It's not uncommon that referred pain of chest due to gallstone disease is managed for cardiac disease initially. It's a common practice that

gallstone on ultrasound finding usually referred to surgeon regardless of symptoms.

Decision making in reliance on radiological finding without going through detail history and physical examination leads to unnecessary surgical operation with bleak outcome of persistent symptoms postoperatively.

About 38% patients have symptoms even after cholecystectomy due to multiple reasons like GERD, dyspepsia, gastritis or functional disturbances in association with gallstone colic or in isolation, and its implication on outcome, whether managed by operation or medical treatment.⁵

The aim of this study is to identify the impact of preoperative clinical symptoms of biliary colic –whether classic, dyspeptic or atypical type- on operative or non-operative clinical outcome.

METHODS

Approval for study was obtained from Ethical Research Committee of University of Sargodha. It's a prospective study from 2016 to 2017 for all those patients referred to surgical department of Sargodha Medical College with gallstone disease was carried out.

All patients included in this study were referred from by physician of tertiary care hospital, emergency department and hospitals of District Sargodha for evaluation and management and those patients were excluded for diagnostic and operative management if they fail to admit on schedule date or lost in follow up course of study.

Patient's demographics aspect, clinical evaluation, ultrasound findings, and operative outcomes were collected and analyzed. Patient were classified into three categories according to symptomatology- heartburn and bloating, gallstone colic and atypical biliary colic. The number of symptoms for each of three categories was calculated for each patient along with associated gallstone colic and atypical colic, associated biliary colic and dyspepsia, or associated atypical biliary colic and dyspeptic symptoms (Table 1).

Other investigations include radiological imaging, upper GI Scope (EGD) and outcome of using different groups of medications including PPIs', H2 receptor antagonist, or cholecystectomy. If patients tested positive for Pylori on stool antigen, then response of triple regime was evaluated.

There was no definite protocol for patient regarding management, however individual patient underwent clinical decision like, in general, and patients with typical biliary colic symptoms proceeded with cholecystectomy, whereas those with associated gallstone colic with atypical symptoms tested for H-pylori, and those associated typical biliary colic and dyspepsia received PPI either before or after operation

Outcomes of patients were charted during follow-up with surgeon at 4 and 8 weeks post-operatively. Univariate and multivariable analyses were performed to evaluate clinical outcomes with significance set at $p < 0.05$. All statistical analyses were performed by using SAS 9.4 or Stata Version 12.

Table1: Presenting symptoms

Typical Gallstone Colic	Atypical Symptoms	Dyspepsia
Pain right upper abdomen	Discomfort in epigastrium	Epigastric abdominal pain
Pain after meal	Diarrhea	Left upper quadrant abdominal pain
Referred pain to back	Constipation	Heartburn
Nausea	weight loss	Reflux
Vomiting	pain in chest	Early satiety
	Regurgitation	Bloating
	Cough	Belching
	Pain lower abdomen	

RESULTS

In two years from 2016 to 2017, a total 106 patients were managed for symptomatic cholelithiasis. The demographic details and clinical characteristics are summarized in Table 2.

Table 2: Demographic and clinical presentations

Variables		Frequency (Percentage)
Age (Median Years)	35 (15 to 67)	
Sex	Male	92 (86.7%)
	Female	14 (13.20%)
BMI (Median)	27 (18 to 42)	
Referral Origin	Primary Care or Outside Hospital	71 (66.9%)
	Emergency or Urgent Care	31 (29.2%)
	Inpatient Referral	4 (3.7%)
Reason for Referral	Pain right upper abdomen	65 (61.3%)
	Pain epigastrium	12 (11.3%)
	Atypical pain (diffuse, left upper abdomen, back)	29 (27.35%)
	Atypical symptoms (i.e., nausea, bloating)	6 (5.6%)
Duration of symptoms	Acute (1 to less than 3 months)	44 (41.5%)
	Chronic (more than three months)	62 (68.4%)

The average age was 35 years, average BMI was 26, 93.3% (n=99) patients were belonging to Sargodha district, and 86.7% (n=87) were female. About 91.5% (n=97) had typical biliary pain, 20.7% (n=22) had atypical biliary symptoms and 44.3% (n=47) had dyspeptic symptomatology.

On their first presentation 20.7% (n=22) had associated with typical gallstone colic and atypical biliary colic, 43.3% (n=46) associated with typical gallstone colic and dyspepsia, and 11.3% (n=12) had associated atypical biliary colic with dyspepsia.

Of 106 patients underwent clinical evaluation for symptomatic gallstone, 86.7% (n=92) underwent cholecystectomy, among them 78.3% (n=83) had resolution of symptom after operation. All cholecystectomies started laparoscopically however 1.8% (n=2) end up with conversion to open. The individual predictors which not resolved after operation are given in Table 3.

Table 3: Unresolved symptoms following cholecystectomy (OR -Odd Ratio)

Presenting Symptoms	Frequency	OR	P-Value
Pain Right Upper abdomen	86 (81.1%)	2.6 (0.9-7.2)	0.13
pain after meal	74 (69.81%)	1.8 (0.9-3.6)	0.27
Nausea/vomiting	61 (57.5%)	2.1 (1.0-3.2)	0.03
Pain epigastrium	37 (34.9%)	2.2 (1.0-3.5)	0.04
Pain Left Upper abdomen	8 (7.54%)	2.9 (1.2-6.3)	0.02
Referred pain to back	40 (37.7%)	1.4 (0.8-2.1)	0.31
Regurgitation/ Heartburn	16 (15.09%)	2.9 (1.1-5.0)	0.009
Reflux	11 (10.3%)	2.9 (0.4-3.5)	0.27
Bloating	7 (6.6%)	1.4 (0.4-4.1)	0.68
Flatulence	4 (3.7%)	11.0 (0.6-122.3)	0.05
Belching	3 (2.8%)	2.6 (0.3-21.7)	0.4
Diarrhea	8 (7.5%)	3.7 (1.6-5.2)	0.005
Constipation	6 (5.6%)	2.7 (1.0-4.4)	0.04
Weight loss	5 (4.7%)	0.5 (0.3-2.9)	0.45
Pain lower abdominal	3 (2.8%)	2.4 (0.9-6.0)	0.09
Chest pain	4 (3.7%)	2.9 (0.7-6.7)	0.22
Associated typical & atypical biliary symptoms	22 (20.7%)	1.9 (1.4-5.1)	0.003
Combined typical biliary & dyspepsia symptoms	46 (43.3%)	2.1 (1.7-4.1)	0.02
Combined atypical biliary & dyspepsia symptoms	15 (14.1%)	2.9 (1.8-7.2)	0.0001

The predictors of symptomatology which were not resolved after operation include preoperatively vomiting/nausea (p= 0.04), pain in upper abdomen (p=0.03), pain left side of upper abdomen (p=0.02), heartburn (p=0.007), diarrhea (p=0.005), associated typical and atypical biliary symptoms (p=0.002), similarly combined typical gallstone colic and dyspeptic symptoms (p=0.02). We reinforce by comparing predictors of resolved and unresolved symptoms after operation as shown in table-3. As a whole, patients presented with associated symptoms of atypical or dyspepsia showed increase odds ratio postoperatively of having persistent pain, it is observed that patients without typical gallstone complaints were at highest risk of OR 3.1 (P= 0.0001) Table 4.

Table 4: Odd ratio of operation (cholecystectomy), resolved vs. unresolved symptoms postoperatively

Presenting symptoms Unresolved n	Frequency	Cholecystectomy (n = 92)	Performed Postoperative symptom resolution (83)	Post-operative symptoms (n=09)
Pain Right Upper abdomen	86 (81.1%)	6.2 (4.3-10.2, p < 0.0001)	0.7 (0.5-2.3, p ¼ 0.43)	2.6 (0.9-7.2, p= 0.13)
pain after meal	74 (69.81%)	2.6 (2.1-3.6, p < 0.0002)	0.8 (0.4-1.6, p= 0.41)	1.8 (0.9-3.6, p= 0.27)

Nausea/vomiting	61 (57.5%)	2.7 (1.8-4.1, p < 0.0005)	0.6 (0.5-1.3, p= 0.09)	2.1 (1.0-3.2, p= 0.03)
Pain epigastrium	37 (34.9%)	0.7 (0.3-0.9, p < 0.0001)	0.7 (0.4-1.5, p = 0.2)	2.2 (1.0-3.5, p = 0.04)
Pain Left Upper abdomen	8 (7.54%)	0.1 (0.06-0.3, p < 0.0001)	0.3 (0.1-0.8, p = 0.003)	2.9 (1.2-6.3, p= 0.02)
Referred pain to back	40 (37.7%)	1.3 (0.8-2.4, p= 0.19)	0.5 (0.4-1.1, p =0.12)	1.4 (0.8-2.1, p= 0.31)
Regurgitation / Heartburn	16 (15.19%)	0.5 (0.2-0.8, p < 0.0007)	0.4 (0.3-0.7, p= 0.0004)	2.9(1.1-5.0, p= 0.009)
Reflux	11 (10.3%)	0.7 (0.08-4.2, p= 0.62)	NA	2.9 (0.4-3.5, p =0.27)
Bloating	7 (6.6%)	0.4 (0.2-0.7, p < 0.0001)	1.4 (0.2-3.4, p= 0.98)	1.4 (0.4-4.1, p= 0.68)
Flatulence	4 (3.7%)	0.2 (0.01-0.9, p < 0.0001)	0.2 (0.03-1.0, p= 0.005)	11.0 (0.6-122.3, p=0.05)
Belching	3 (2.8%)	0.2 (0.03-0.5, p < 0.001)	0.2 (0.03-3.0, p= 0.15)	2.6 (0.3-21.7, p= 0.4)
Diarrhea	8 (7.5%)	0.5 (0.3-0.7, p = 0.02)	0.5 (0.4-1.4, p = 0.1)	3.7 (1.6-5.2, p = 0.005)
Constipation	6 (5.6%)	0.3 (0.3-0.9, p < 0.009)	0.7 (0.3-2.6, p < 0.43)	2.7 (1.0-4.4, p < 0.04)
Weight loss	5 (4.7%)	0.7 (0.4-1.7, p < 0.30)	1.9 (0.3-11.5, p < 0.56)	0.5 (0.3-2.9, p < 0.45)
Pain lower abdominal	3 (2.8%)	0.3 (0.1-0.8, p < 0.0001)	0.4 (0.2-1.2, p < 0.05)	2.4 (0.9-6.0, p < 0.09)
Chest pain	4 (3.7%)	0.6 (0.3-1.4, p = 0.15)	0.5 (0.2-2.1, p = 0.30)	2.9 (0.7-6.7, p = 0.22)
Associated typical & atypical biliary symptoms	22 (20.7%)	0.5 (0.3-0.7, p < 0.0001)	0.7 (0.4-1.3, p = 0.19)	1.9 (1.4-5.1, p = 0.003)
Combined typical biliary & dyspepsia symptoms	46 (43.3%)	0.5 (0.4-0.8, p < 0.002)	0.5 (0.3-0.9, p < 0.01)	2.1 (1.7-4.1, p < 0.02)
Combined atypical biliary & dyspepsia symptoms	15 (14.1%)	0.3 (0.2-0.5, p < 0.001)	0.4 (0.3-0.9, p < 0.007)	2.9 (1.8-7.2, p < 0.0001)

However, patients who were referred without typical biliary complaints were at highest risk, OR 3.3 (1.6-5.9, p < 0.001), (Table 3).

Patients with atypical biliary colic before operation particularly, was significant. Combined persistent heartburn, the most common unresolved symptom after

operation on both univariate (OR = 2.4, 1.3-6.1, $p < 0.02$) and multivariable analysis (OR=2.4, 1.4-4.9, $p < 0.04$).

Patients who remained dyspeptic even after operation (n=16), 41.5% (n=43) get resolution of symptoms with medical therapy with PPI or H-pylori eradication triple regime.

Nine patient who remained symptomatic even after surgical or medical management, had persistent dyspepsia with epigastric pain, were referred back to medical specialist for further medical workup.

25% patients (n=26) suspected preoperatively of having symptoms of gastritis rather than gallstone colic were tested for Pylori. Of these, 38% (n=10) found positive for Pylori, and 58% positive patients get relieved of symptoms after taking triple regime therapy. This makes 6.1% of total cohort and avoided operation in these cases after a follow up for one year.

Among 106 patients, 21.2% (n=24) improved after taking medical treatment suffering with atypical or dyspeptic symptoms with gallstone disease before or after operation. Medical treatment consists of either PPI or H-Pylori eradication therapy.

Among 14 patients who were managed non-operatively with medical therapy, 64.2% (n=9) relieved their symptoms. The rest of these patients were not offered surgery and referred back to medical specialist.

Among 92 patients underwent cholecystectomy, 8.3% (n=7) had not resolved pain after operation, whom 42.8% (n =3) were H. pylori positive and 66% (n =2) treated and symptoms resolute after taking triple regime therapy.

The odds ratio for H-pylori in pre-operative compared with postoperatively was 2.3 (96% CI 1.2-3.9, $p < 0.02$).

DISCUSSION

It still a dilemma for a surgeon whether patient with gallstones and atypical symptomatology should be offered operation or not. Patients with atypical or dyspeptic symptoms like reflux/retrosternal burning are usually complaining same symptoms postoperatively if not properly evaluated preoperatively. However, majority of patients presents with typical gallstone colic of RUQ abdominal pain particularly after taking meal, while history of atypical symptoms or dyspepsia with gallstone should alert the surgeon for any other underlying pathologies which may need other management rather than operation.^{1,5,6} So it is essential to evaluate such patients preoperatively to reach a surgical decision. It has been seen that among junior consultants, only 21% diagnosed biliary colic accurately⁶. Particularly dyspepsia is the most commonly misdiagnosed in 40% of patients⁶. Similarly atypical symptoms attributed to

gallstone colic is important, as H-pylori infection is the commonest cause with similar presentation.^{7,8}

As with advent and convenience for laparoscopic approach, the low threshold of surgeon has been seen with increased rate of cholecystectomies.^{2,6}

“Ineffective cholecystectomies” term is coined where patient complaint persistent symptoms after operation. In a systemic review and meta-analysis by Latenstein *et al.* it has been seen that gallstone disease associated with upper GI disturbance predict ineffective cholecystectomies without resolution of symptoms.^{5,9}

Patients particularly female with long standing upper abdominal pain with cholelithiasis experience continuous pain after operation^{2,9}. In our study it has been seen that 20% of patients with atypical or dyspepsia had improvement in symptoms with medical treatment for heartburn/Pylori pre-operatively or after operation.

The medical management improve symptoms in 61% pre or post-operative cases and about every third patient with Pylori infection get benefit of eradication therapy and avoided operation. However, Pylori infection is a potential etiologic factor in most cases of atypical gallstone disease.^{10,11} So any patient with atypical or dyspeptic symptomatology should be thoroughly evaluated to avoid unnecessary operation.⁹

Our study is limited to Sargodha Division area and people with higher incidence of dyspepsia and atypical symptoms are seen in study of Lubna *et al.*¹²

In follow-up, difficulties noted in regard of patients visit to hospital or no response on telephone or patient went to seek medical advice from other institution. As already explained in exclusion criteria, such non-responded patient excluded from our study.

Being a tertiary care teaching hospital, the medical history, evaluation and documentation including negative systemic review with thoroughness by the trainee maybe existed. Variation may exist among attending surgeons but outcome of this limited study showed that no major complications has been noted except a few cases with abdominal pain for readmission with this volume of cases.

CONCLUSION

Association of gallstone disease with atypical biliary colic or dyspepsia are usually end up with ineffective cholecystectomies.

If we follow a protocol to subject such patients with H-pylori testing and proton pump inhibitor before operation, they might get benefit of it.

A comprehensive approach is necessary for early identification and management for such patients having gallstone disease with H-pylori infection, reflux or gastritis preoperatively for better outcome and reduce ineffective cholecystectomies

A thorough clinical evaluation to diagnose and manage such cases with medical therapy may avoid unnecessary surgery with its potential complications and financial loss of patient.

LIMITATIONS

Being in periphery and lack of education, patients contact and follow-up causes problems regarding outcome of the operative procedure.

SUGGESTIONS / RECOMMENDATIONS

Before proceeding cholecystectomy, rule out other causes of pain in upper abdomen in atypical presentation of cholelithiasis patients

CONFLICT OF INTEREST / DISCLOSURE

All authors do not have any financial or personal conflicts of interest to disclose.

ACKNOWLEDGEMENTS

I do recognize the efforts of Dr. Azeem, for guiding, collection and tabulating the data.

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