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SPECTRUM OF CLINICO-PATHOLOGICAL PRESENTATIONS OF GALLSTONE DISEASES IN A TERTIARY CARE INSTITUTE IN ROHILKHAND REGION

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ABSTRACT: BACKGROUND: The importance of gallstone disease derives from their frequency and pathological potential. Spectrum of gallstone diseases is very wide and complications are not infrequent. **MATERIAL AND METHODS:** The present cohort study was conducted on 240 consecutive cholecystectomies performed for various indications in Post Graduate Department of Surgery, RMCH, Bareilly. This tertiary care institute caters the healthcare needs of Rohilkhand region. **RESULTS:** The commonest age group having the gallbladder disease was Vth decade (29.6%). Females outnumbered males by the ratio of 5.32:1. The commonest presenting symptom was pain in right upper/mid upper quadrant of abdomen (96.6% of symptomatic cases) followed by nausea/vomiting (45.0%). Out of 240 cholecystectomies performed, the gross and histopathological evaluation revealed that 180 cases (75%) were having chronic cholecystitis with cholelithiasis only; 46 cases (19.2%) were of acute on chronic cholecystitis with cholelithiasis, and 7 cases of acute acalculus cholecystitis. 60 cases (25%) were also having other associated histopathological changes in gallbladder mucosa like metaplasia (31), dysplasia (22) and carcinoma (7). **CONCLUSION:** In today's era of safe laparoscopic cholecystectomy, available even in small hospitals of North India, prophylactic cholecystectomy can be offered to asymptomatic cases of gallstones, especially if diagnosed in younger age because of the expected prolonged exposure to chronic irritation by gallstones and development of their complications including metaplasia, dysplasia and carcinoma gallbladder.

KEYWORDS: Cholelithiasis, Metaplasia, Dysplasia, Carcinoma gallbladder, Prophylactic cholecystectomy.

INTRODUCTION: The importance of gallstone disease derives from their frequency and pathological potential. It is estimated that gallstones affect 10-15 per cent of the population in western societies. They are asymptomatic in the majority of cases (>80 per cent). Approximately, 1-2 per cent of asymptomatic patients will develop symptoms requiring surgery per year, making cholecystectomy one of the most common operations performed by general surgeons (Norman et al 2013).¹ Patients with asymptomatic gallstones have less than 20% chance of ever developing symptoms, and the risks associated with "Prophylactic" operation outweigh the potential benefit of surgery in most patients (Ransohoff et al, 1983; Ransohoff and Gracie W, 1993).^{2,3} However, the consequences of gallstones may be ranging from brief episodes of biliary colic, chronic cholecystitis, mucocele, empyema, cholangitis, obstructive jaundice to potentially life threatening complications such as acute cholecystitis and pancreatitis, perforation leading to peritonitis, fistula formation or, rarely, gall bladder cancer.

Biliary colic is the common presentation of symptomatic gallstones. Biliary colic is typically a severe and episodic right upper abdominal or epigastric pain that often radiates to the back. Attacks

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frequently occur postprandially or awaken the patient from sleep. Once a patient begins to experience symptoms, there is a greater than 80% chance that she will continue to have symptoms.

There is also a finite risk of disease related complications such as acute cholecystitis, gallstone pancreatitis and choledocholithiasis. Therefore, elective cholecystectomy is indicated after the first episode of typical biliary symptoms (Nagle et al, 2007).⁴ First described in 1882 by Langenbuch, open cholecystectomy (OC) has been the primary treatment of gallstone disease for most of the past century (Beal, 1984).⁵ In the late 20th century, laparoscopic cholecystectomy (LC) was adopted rapidly around the world, and has subsequently been recognized as the new “Gold standard” for the treatment of gallstone disease (Soper et al, 1992; 1994).^{6,7} In 1992, the National Institutes of Health (NIH) Consensus Development Conference stated that LC “provides a safe and effective treatment for most patients with symptomatic gallstones”.⁸

AIMS AND OBJECTIVES:

- To study the different types of presentations of gallstones in Rohilkhand region.
- To study the histopathological changes in gallbladder mucosa in relation to gallstones.

MATERIAL AND METHODS: The present cohort study was conducted on 240 consecutive cholecystectomies performed for various indications in Post Graduate Department of Surgery, RMCH, Bareilly. This tertiary care institute caters the healthcare needs of Rohilkhand region. Rohilkhand is a region of northwestern Uttar Pradesh state of India. It include cities of Bareilly, Moradabad, Rampur, Bijnore, Pilibhit, Shahjahanpur, Badaun. The study was done after formal approval from Institutional Ethics Committee (IEC), period ranging from February 2015 to August 2015.

Inclusion Criteria: All the cases of gallbladder diseases which undergone cholecystectomy for various indications.

Exclusion Criteria:

- Cases of advanced carcinoma gallbladder which were not operated.
- Acute cholecystitis with lump formation (managed conservatively).

Design of Study: An informed and written consent of cases and/or their relatives, included in the study, taken. Histopathological examination of each and every specimen of cholecystectomy done to know the associated histopathology of gallbladder mucosa and make a final diagnosis.

Type of Treatment given: All 240 cases in the present study were managed by operative intervention of cholecystectomy and/or choledochotomy. Laparoscopic cholecystectomy (LC) was done in 216 cases (90%). Open cholecystectomy (OC) was done in 24 cases (10%). Out of these 24 cases of open cholecystectomy, 14 cases were of chronic cholecystitis with choledocholithiasis (Open cholecystectomy with choledochotomy), 3 cases were of preoperatively known early carcinoma GB (extended cholecystectomy), 4 cases (1.8%) were converted from lap to open (for various reasons), 3 cases were either unfit or did not give consent for laparoscopic surgery. The conversion rate to OC remains approximately 2–5% in most series. This is more common in the elderly and in the setting of acute cholecystitis (Nagle et al, 2007).⁴ There is a general policy of sending each and every specimen of gallbladder for histopathological evaluation in our institute.

RESULTS: The commonest age group having the gallbladder disease was Vth decade (29.6%). 15.8% cases were males and 84.2% were females. Thus females outnumbered the males by the ratio of

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5.32:1 (Table I). The commonest presenting symptom was pain in right upper/mid upper quadrant of abdomen followed by nausea/vomiting (Table II). This table shows that the commonest symptom was pain in right upper quadrant of abdomen (95.0%), i.e. 96.6% of symptomatic cases, as 4 cases (1.7%) were of asymptomatic cholelithiasis. Pain was followed by nausea/vomiting in frequency and was present in 45(45.0%) cases.

Out of these 240 cases, 4 cases were having asymptomatic gallstones which were diagnosed incidentally but were subjected to cholecystectomy on patients' will and consent. Commonest sign was palpable gallbladder lump (29.2%), followed by tenderness in right hypochondrium (24.2%). However, most of the cases (30%) were not having any major clinical sign suggestive of acute biliary disease at the time of examination (Table III).

Out of 240 cholecystectomies performed, the gross and histopathological evaluation revealed that 180 cases (75%) were having chronic cholecystitis with cholelithiasis only; 46 cases (19.2%) were of acute on chronic cholecystitis with cholelithiasis, and 7 cases of acute acalculus cholecystitis.

60 cases (25%) were also having other associated histopathological changes in gallbladder mucosa like metaplasia (31), dysplasia (22) and carcinoma (7). Out of these 7 cases of carcinoma gallbladder 4 as incidental findings and 3 preoperatively known cases of early/resectable stages (Table IV). Table V shows that the commonest gallstone disease is chronic cholecystitis with cholelithiasis, is more common in females and the complications are not infrequent. All cases of males with acute cholecystitis were associated with one or the other complication.

Age (Years) Groups	Male		Female	
	Number	Percent	Number	Percent
0 – 10	–	–	–	–
11–20	4	1.7	4	1.7
21–30	4	1.7	40	16.7
31–40	9	3.8	36	15
41–50	6	2.5	65	27.1
51–60	6	2.5	38	15.8
61 and above	9	3.8	19	7.9
Total	38	15.8	202	84.2

Table 1: Age and Sex Distribution (n = 240)

Symptoms	Number	Percent
Pain in right upper/mid upper quadrant of abdomen(including 2 cases of GB polyp)	228	95
Nausea/vomiting	108	45
Fever (With chills and rigor)	43	17.9
Yellowing of eyes/skin (Jaundice)	17	7.1
Abdominal lump/swelling	17	7.1
Others(Including 4 cases of asymptomatic gallstones)	53	22.1

Table 2: Presenting Symptoms (n = 240)

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Signs	Number	Percent
Temperature raised (fever)	17	7.1
Yellowing of skin and sclera (jaundice)	14	5.8
Tenderness in right hypochondrium including Murphy's sign	58	24.2
Liver enlargement/Palpable liver	9	3.8
Gallbladder lump	70	29.2
Others (In cases of incidental asymptomatic gallstones)	7	2.9
No major clinical sign suggestive of acute biliary disease at present	72	30

Table 3: Presenting Signs (n = 240)

Sl. No.	Histopathology	No.	Percent
1.	Chronic cholecystitis with cholelithiasis only (Including 4 cases of asymptomatic gallstones)	180	75
2.	Acute on chronic cholecystitis with cholelithiasis	46	19.2
3.	Acute acalculus cholecystitis(Including 2 cases of benign GB polyp)	7	2.9
4.	Chronic cholecystitis with cholelithiasis and Metaplasia of gallbladder mucosa	31	12.9
5.	Chronic cholecystitis with cholelithiasis and Dysplasia of gallbladder mucosa	22	9.2
6.	Chronic cholecystitis with cholelithiasis and Carcinoma gallbladder (Adenocarcinoma)	7	2.9

Table 4: Histopathology of Resected Specimens of Gallbladder

Total Cholecystectomies Performed (n= 240)

Sl. No.	Diagnosis	Number		Percent
		Male	Female	
1	Simple chronic cholecystitis with cholelithiasis	28	138	69.2
2	Simple acute on chronic cholecystitis with cholelithiasis	0	10	4.2
3	Acute acalculus	0	5	2.1

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	cholecystitis			
4	Acute cholecystitis with mucocele of gallbladder	2	16	7.5
5	Acute cholecystitis with empyema of gallbladder	2	11	5.4
6	Gallstone with pancreatitis	–	–	–
7	Acute cholecystitis with gallbladder perforation	–	–	–
8	Acute cholecystitis gallbladder gangrene	1	0	0.4
9	Gallstone ileus	–	–	–
10	Carcinoma gallbladder	2	5	2.9
11	Mirizzi's syndrome	–	–	–
12	Chronic cholecystitis with choledocholithiasis	1	13	5.8
13	Benign GB polyp with acute acalculus cholecystitis	1	1	0.8
14	Asymptomatic chronic cholelithiasis	1	3	1.7

Table 5: Final Diagnosis of the Cases Included In the Study (n=240)

DISCUSSION: Gallstone disease is a major public health problem worldwide, particularly in adult population. Incidence of gallstone disease shows considerable geographical and regional variations. Its occurrence has been found to be at least 6% in the adult population of North India (Mittal and Mittal, 2002).⁹ Once a patient begins to experience symptoms, there is a greater than 80% chance that (s) he will continue to have symptoms. There is also a finite risk of disease related complications such as acute cholecystitis, gallstone pancreatitis and choledocholithiasis. Therefore, elective cholecystectomy is indicated after the first episode of typical biliary symptoms (Health News, 1991; Nagle et al, 2007).⁴

Age: Peak incidence of gallstone diseases in the present study was in the Vth decade (29.6%). Tiwari et al (1982).¹⁰ and Kapoor et al (1984).¹¹ have reported a maximum incidence of 37.7% of gallbladder disease in 4th decade of life.

Sex: Females has outnumbered the males in the present study by ratio of 5.32:1. This incidence is quite variable by various authors.

Male to female ratio observed by various other authors were 1:2.63 by Kovalcik et al (1983),¹² 1:5.4 by Varma and Shafique (1983),¹³ 1:7 by Kapoor et al (1984),¹¹ and 1:4 by Schirmer et al (2005).¹⁴ All these series and the results of the present study exhibit female as a common victim, thus holding true the saying that 'a fatty, fertile, flatulent, female of forty is the classical sufferer from symptomatic gallstones.'

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CLINICAL PRESENTATION:

Presenting Symptoms: The commonest presenting symptom in the present study was pain in right upper quadrant of abdomen (228 cases), i.e. in 96.6% of symptomatic gallstones (4 cases were of asymptomatic gallstones) followed by nausea/vomiting in 108 cases (45%), fever (with or without chills and rigors) in 43 cases (17.9%). Similar presentation was observed by various other authors (Kapoor et al, 1984; Coelho et al, 1984; Meyer et al, 1967; Magee and Mac Duffee, 1968).^{11,15-17} Gupta and Mehta (1971) found history of pain in 93-100% patients of gallbladder diseases.¹⁸

Presenting Signs: The commonest physical sign in the present study was gallbladder lump (29.2%) followed by right hypochondriac tenderness (24.2%). However, in majority of the cases (30%), there was no major clinical sign suggestive of acute biliary disease at the time of presentation. This being a tertiary care referral Centre, the patients are usually referred here by local practitioners from remote areas after giving them symptomatic relief.

Various authors and researchers have reported a varied clinical presentation. Kapoor et al (1984)¹¹ reported hepatomegaly in 11.2%, Gupta and Mehta (1971) reported a palpable gallbladder lump in 20%, Misra et al (1995) reported lump in right hypochondrium in 65% patients.^{18,19}

Histopathology of Gallbladder Specimen: Post cholecystectomy, microscopic histopathological examination of all 240 specimens of the gallbladder showed uncomplicated chronic cholecystitis with cholelithiasis in 180 cases (75% of cholecystectomies); acute on chronic cholecystitis in 46 cases (19.2% of the cholecystectomies). Total 7 cases (2.9%) were diagnosed finally to have acute acalculus cholecystitis of which 2 cases were also having benign GB polyp. 31 cases (12.9% of cholecystectomies) showed associated metaplasia of the gallbladder mucosa; 22 cases (9.2% of cholecystectomies) showed dysplasia of gallbladder mucosa; 7 cases (2.9% of the cholecystectomies) showed carcinoma gallbladder (Adenocarcinoma). Out of these 7 cases of carcinoma gallbladder, 3 cases were diagnosed preoperatively but 4 cases (1.7% of elective cholecystectomies) were found to have occult/incidental carcinoma gallbladder (1 in open cholecystectomy and 3 in laparoscopic cholecystectomy group). Histologically, adenocarcinoma of varying differentiation was in 7 of 7 cases (100%) in the present study.

Gallstones with carcinoma gallbladder were found in 100% cases in the present study.

Coelho et al (1984) reported 77.4% incidence of chronic cholecystitis.¹⁵

Farha and Beamer (1991) reported that symptomatic gallstone disease is manifested by acute cholecystitis in approximately 20% of patients, by complicated cholecystitis (Jaundice, cholangitis, or pancreatitis) in 10% and chronic cholecystitis, including biliary colic, in 60–70%. Cholangiography performed at the time of cholecystectomy reveals common duct stones in approximately 15% to 20% of patients, acute acalculus cholecystitis and acute inflammation of gallbladder without gallstones are found in 6% of patients undergoing surgery for acute cholecystitis.²⁰

Coelho et al (1984) observed 25% incidence of acute cholecystitis which was higher than incidence observed in the present study.¹⁵

Acute acalculus cholecystitis accounts for 5% to 10% of all patients with acute cholecystitis and is the diagnosis in approximately 1% to 2% of patients undergoing cholecystectomy (Ahrendt et al, 2004).²¹ So our results are close to the results of other standard studies.

Khanna et al (2006) conducted a histopathological study of 140 consecutive gallbladders, electively resected for cholelithiasis. At microscopy, epithelial hyperplasia was observed in 83(69%),

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antral metaplasia in 53(16.5%), intestinal metaplasia in 22(15.5%), dysplasia in 12(8.5%) and carcinoma in situ in 1 specimen (0.7%). Cholelithiasis and even silent gallstones, which were asymptomatic, produced a series of epithelial pathological changes in the gallbladder mucosa, which could be precursor lesion of carcinoma gallbladder. These changes include hyperplasia, metaplasia and dysplasia.²²

Associated cholelithiasis among patients of carcinoma gallbladder was found in ranging between 65% to 90% according to Misra et al (1995).¹⁹

Similarly it was found in 89% by Gerst (1961), 70% by Piehler and Crichlow (1978), and 92% by Morrow et al (1983).²³⁻²⁵

Complications of Gallstones:

In the present study 18(7.5%) cases were diagnosed to have mucocele gallbladder. Kapoor et al (1984) observed 10% patients of the gallbladder diseases with lump in right hypochondrium due to mucocele gallbladder while Gupta and Mehta (1971) found only 3.6% of patients of acute cholecystitis having mucocele.^{11,18}

In this present study empyema gallbladder was observed in 13 cases (5.4%). Empyema gallbladder occurs in 3% (Kapoor et al, 1984; Varma and Shafique, 1983) to 17.3% (Rai and Singh, 1979) patients.^{11,13,26} Gupta and Mehta (1971) observed empyema in 10% while Bhansali(1976) found it in 1.7% cases.^{18,27}

There was 1 case (0.4%) of gallbladder gangrene in present study.

In the present study 7 cases (2.9%) were of carcinoma gallbladder. All the 7 cases (100.0%) were associated with gallstones. 3 of these cases were diagnosed preoperatively and 4(1.7%) were found to have occult gallbladder cancer which were diagnosed only after histopathological examination of the gallbladder. This is higher than whatever studied in literature. Approximately 1% of all elective cholecystectomies performed for cholelithiasis harbor an occult gallbladder cancer (Ahrendt and Pitt, 2004).²¹

The incidence of gallbladder cancer is approximately 7 times more common in the presence of cholelithiasis and chronic cholecystitis than in people without gallstones. In addition, the risk of developing gallbladder cancer is higher in patients with symptomatic gallstones than in patients with asymptomatic gallstones (Ahrendt and Pitt, 2004).²¹

In the present study 14 cases (5.8%) were having stones in the common bile duct (Choledocholithiasis).

According the National Institutes of Health, USA (NIH, 1992), approximately 15% of patients undergoing cholecystectomy have common bile duct stones.⁸

According to Farha and Beamer (1991), cholangiography performed at the time of cholecystectomy reveals common duct stones in approximately 15 to 20% of patients.²⁰ Around 10% of patients with stones in the gallbladder have stones in the common bile duct (Beckingham, 2001).²⁸

The results of the present study vary from these two studies. This may be due to geographical variation, due to small sample size or due to lack of diagnostic techniques, as we did not perform peroperative cholangiography in each and every case.

Prophylactic cholecystectomy has been recommended in many high risk populations, such as in Chile. Since the incidence and mortality rates of gallbladder cancer (GBC) in Northern Indian

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women is one of the highest in the world, Mohandas and Patil (2006) suggest that preventive cholecystectomy be offered to all young healthy women in Northern India when they are diagnosed to have asymptomatic gallstones.²⁹

Khanna et al (2006) also supports the contention that cholecystectomy should be offered to all asymptomatic gallstone patients, especially if they are less than 60 years of age and are living in a high-incidence area.²² Eastern U.P. and Indo-Gangetic belt have amongst the highest incidence of gallbladder carcinoma in the world – Shukla et al, 1981) for gallbladder carcinoma.³⁰

Most authors do not recommend prophylactic cholecystectomy in patients with asymptomatic gallstones as a measure of preventing the development of gallbladder cancer (Diehl and Beral, 1981; Godfrey et al, 1984).^{31,32} The American Indian women and the Chilean Hispanic and Indian population with gallstones represent the only exceptions to this rule. Because of the early onset of gallstones in that population, there is an increased risk of gallbladder carcinoma and prophylactic cholecystectomy appears to be justified (Weiss et al, 1984; Lowenfels et al, 1985, 1989; Nervi et al, 1988; Strom et al, 1995).³³⁻³⁶

CONCLUSION: The clinico-pathological spectrum of gallstone diseases in Rohilkhand region will certainly help in understanding the disease and its complications which are not infrequent. Also morbidity and mortality associated with these diseases is significant. Rohilkhand region comes in close to the high risk belt for gallbladder malignancy, which is a very fast growing tumor and have poor prognosis. There is no contention about the operative (laparoscopic/open cholecystectomy) treatment of symptomatic gallstone diseases. In today's era of safe laparoscopic cholecystectomy, available even in small hospitals of North India, prophylactic cholecystectomy can be offered to asymptomatic cases of gallstones, especially if diagnosed in younger age because of the expected prolonged exposure to chronic irritation by gallstones and development of their complications including metaplasia, dysplasia and carcinoma gallbladder. We also recommend for histopathological examination of each and every specimen of gallbladder.

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