

RESEARCH ARTICLE

Is it Necessary to Submit Grossly Normal Looking Gall Bladder Specimens for Histopathological Examination?

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Abstract

Background: The objectives of the study were to: 1) determine the frequency of incidental malignancy in unsuspected/grossly normal looking gall bladders; 2) determine the frequency of malignancy in suspected/grossly abnormal looking gall bladders. **Materials and Methods:** This prospective, cross sectional study was carried out at a tertiary care hospital in Pakistan, during a four year period (Jan 2009-dec2012). All the cholecystectomy cases performed for gallstone diseases were examined initially by a surgeon and later on by a pathologist for macroscopic abnormalities and accordingly assigned to one of the three categories i.e. grossly normal, suspicious, abnormal/malignant. Frequency of incidental carcinoma in these categories was observed after receiving the final histopathology report. **Results:** A total of 426 patients underwent cholecystectomy for cholelithiasis, with a 1:4 male: female ratio. Mean age of the patients was 45 years with a range of 17-80 years. The frequency of incidental gallbladder carcinoma was found to be 0.70 % (n=3). All the cases of gallbladder carcinoma were associated with some macroscopic abnormality. Not a single case of incidental carcinoma gallbladder was diagnosed in 383 'macroscopically normal looking' gallbladders. **Conclusions:** Incidental finding of gall bladder cancer was not observed in any of macroscopically normal looking gall bladders and all the cases reported as carcinoma gallbladder had some gross abnormality that made them suspicious. We suggest histopathologic examination of only those gall bladders with some gross abnormality.

Keywords: Gallbladder neoplasm - gall bladder cancer - incidental finding - histopathological examination

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Introduction

Gall bladder carcinoma is a rare malignancy with great variation in overall incidence reported from different geographic areas. In a study by Kalita et al. (2013) from Delhi India reports the frequency of gall bladder carcinoma to be 0.6%, Ghimire et al. (2011) from Nepal reports it to be 1.28%, Tadashi Terada from Japan reports it to be 2.2%, Abdulsamad from Pakistan, (2005) reports it to be 1.15%. However from Pakistan few studies report quite high incidence of even up to 15.7% by Waseem et al. (2010).

Incidental finding of carcinoma in clinically non suspected gall bladder specimens is even more rare, with only 0.17% reported by Bazona et al. (2007), 0.37% by Bawahab et al. (2013), 0.99% by Mittel et al. (2010), and 1.28% by Ghimire et al. (2011).

For gall bladder diseases both open and laparoscopic cholecystectomy constitutes major bulk of the general surgical practice. At present all the gall bladder specimens are submitted for histopathological examination regardless of their gross appearance. This practice is in fact recommended by Report of working group of royal college

of pathologists (2005) and many authors (Shreshtha et al., 2010; Ghimire et al., 2011; Hamdani et al., 2012; Kalita et al., 2013).

In recent years results of many studies question this practice, and recommend selective submission of only those gall bladder specimens with some gross abnormality, in order to save time and workload on histopathology laboratory as well as cost effectiveness for patients. (Dix et al., 2003; Akyurek et al., 2004; Bazona et al., 2007; Darmas et al., 2007; Mittel et al., 2010; Almusalmi et al., 2011; Romero-Gonzalez et al., 2012; Bawahab et al., 2013). These studies report that there is no chance of missing incidental carcinoma, if only grossly abnormal looking gall bladders are submitted for histopathological examination. However most of these studies were retrospective analysis of histopathology laboratory records and patient files.

Keeping these controversies regarding selective submission of specimens, this study was conducted with objectives to: 1) Determine the frequency of incidental malignancy in unsuspected/grossly normal looking gall bladders. 2) Determine the frequency of malignancy in suspected/grossly abnormal looking gall bladders.

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Materials and Methods

This prospective study carried out over a four year period from January 2009 to December 2012 in department of surgery Kuwait and Mercy teaching hospitals Peshawar and Peshawar Medical college histopathology laboratory.

Sample size calculation

Incidental finding of carcinoma in clinically non suspected gall bladder specimens is reported to be 0.17% by Bazoa et al. (2007), 0.37% by Bawahab et al. (2013), 0.99% by Mittel et al. (2010), 1.28% by Ghimire et al. (2011).

Using this prevalence of 1% with a precision of 1%, and a significance level of 95%, the sample size was calculated using the standard WHO recommended formula:

$$n = z^2 \frac{p(1-p)}{d^2}$$

This gives a sample size of 382 for this study.

All the open and laparoscopic cholecystectomy specimens were included in the study. Pediatric age group, gall bladders removed as part of any other surgical procedure or cases with pre-operative diagnosis/strong suspicion of malignancy were excluded from the study.

Each gall bladder specimen was initially sectioned

and thoroughly examined by the operating surgeon and his findings recorded on a proforma. The specimens were then fixed in ten percent buffered formalin and sent to histopathology lab. The pathologist would then examine the specimen and record her findings on the same proforma. Both the surgeon and the pathologist would assign the case into one of the three categories; A) grossly normal looking (gall bladder specimen with no mucosal ulceration/irregularity, mass, polyp, localized or generalized wall thickness) B) grossly suspicious looking (gall bladder specimen with some mucosal ulceration/irregularity, or generalized wall thickness) C) grossly malignant looking (gall bladder specimen with marked mucosal ulceration/irregularity, a definitive mass, polyp, localized wall thickness).

For category- A cases standard three sections from fundus, body and neck were submitted, while for category -B and C additional sections were taken from the suspicious areas. Microscopy was performed and findings recorded on the proforma.

Results

Total 426 cholecystectomy specimens were examined. Majority of the specimen were from female patients (n=342, 80%). Male to female ratio of 1:4 was observed. Mean age of the patients was 45 years with a range of

Table 1. Gross Findings of Surgeon and Pathologist in Specimens Operated for Gall Stones

Macroscopic Findings	Surgeon	Pathologist
Total number of Macroscopically normal looking allbladders	384	395
Total number of Macroscopically suspicious looking gallbladder	26	16
Total number of Macroscopically abnormal looking gallbladders	16	15
Total Number of Cases	426	426

Table 2. Final Histopathology Breakup of the Gall Bladder Specimens Assigned to Different Categories on Gross Examination by Surgeon

Final histopathology breakup	Macroscopically Normal looking (384)	Macroscopically Suspicious looking (26)	Macroscopically abnormal looking (16)	Total (426)
Normal	3	0	0	3 (0.7%)
Chronic Cholecystitis	346	16	5	367 (86.15%)
Chronic Cholecystitis with Cholesterolosis	12	1	1	14 (3.28%)
Acute Cholecystitis	18	8	2	28 (6.57%)
Acute Cholecystitis Empyema, Gangrenous	5	1	1	7 (1.64%)
Benign Polyp	0	0	3	3 (0.7%)
Adenomyoma	0	0	1	1 (0.23%)
Primary adenocarcinoma	0	0	3	3 (0.7%)

Table 3. Details of Patients with a Histopathological Diagnosis of Gallbladder Carcinoma

	Age	Sex	Gallbladder ultrasound	Surgery	Macroscopic Findings by pathologist and surgeon	Gross features	Pathology	TNM Stage
1	65	Female	Acute cholecystitis	Laparoscopic converted to open cholecystectomy	Abnormal looking	1 cm Polyp at fundus	Adeno carcinoma	T1
2	40	Female	Chronic cholecystitis	Open cholecystectomy	Abnormal looking	1.5 cm growth at fundus	Adeno carcinoma	T2
3	60	Male	Chronic Cholecystitis	Laparoscopic cholecystectomy	Abnormal looking	Generalized thickness of wall	Adeno carcinoma	T3

Table 4. Studies Against the Selective Submission of Gall Bladder Specimens

Author	Year of study	Place of study	Type of study	Frequency of incidental carcinoma in clinically unsuspected cases	Gross findings of the incidental carcinoma cases
Kalita et al	2013	Dehli ,India	Prospective	18/4115 (0.44%)	“· 8 cases with localized thickness of gall bladder wall ·10 cases with generalized thickness of gall bladder wall”
Hamdani et al	2012	Calcutta india	Retrospective/ prospective	7/13876 (3.5%)	“· 3 cases had polypoidal mass ·2 cases had localized thickness of gall bladder wall ·2 cases had mucosal irregularities”
Ghimire et al	2011	Nepal	Retrospective	10/783 (1.28%)	“· 2 cases had polypoidal mass ·1 case had Thick wall ·7 cases had no gross abnormality”
Shreshtha et al	2010	Nepal	Retrospective	9/668 (0.15%)	“· 5 Cases had growth ·2 had irregular mucosa ·1 case was a contracted gall bladder ·1 case had thick fibrosed wall”

17-80years.

Majority of the specimens on macroscopic examinations were normal looking (category-A), followed by suspicious looking (category-B), and then abnormal looking (category-C) respectively. There was some difference in surgeon and gross observations however to the patients benefit surgeon's threshold for suspicious category was lower as compared to pathologist. (See Table 1)

Not a single case of malignancy was detected in grossly normal and suspicious looking categories (category-A and B). The final diagnosis on microscopy of these two groups is given in Table 2.

Out of 426 case 0.70% (n=3) turned out to be incidental gall bladder carcinomas. All were primary adenocarcinoma. These three cases showed gross abnormalities in the form of a mass, polyp and significant wall thickness so they were assigned to category- C by the surgeon as well as the pathologist (Table 3).

Discussion

Gall bladder carcinoma although is a rare malignancy but usually detected in late stage with a dismal prognosis. The overall incidence reported by various studies is variable ranging from 0.6% by Kalita et al. (2013) to 13.7% by Asadullah et al. (2003)

Incidental finding of carcinoma in clinically non suspected gall bladder specimens is even more rare 0.1% reported by Bazoa et al. (2007), 0.37% by Bawahab et al. (2013), 0.99% by Mittel et al. (2010) 1.28% by Ghimire et al. (2011). In present study the incidence of incidental gallbladder carcinoma was found to be 0.70% which is comparable to the studies from different parts of the world.

All the three cases of carcinoma gall bladder in our study were assigned to category- C (i.e. grossly abnormal looking) .One case had a mass in gall bladder, one case had a polyp and one case had a generalized significant thickening of the wall. These findings prompted the suspicion of malignancy on gross examination. Hence we suggest that gross examination has 100% sensitivity

in picking the gall bladder malignancies.

Many authors have reported that the gallbladder specimens that turn out to be malignant always have some gross abnormality in the form of mass polyp localized or generalized wall thickness or mucosal ulceration and irregularities. These studies support the selective submission of only those gall bladders that are grossly abnormal/suspicious looking for histopathologic examination in order to avoid extra burden on histopathology laboratory. (Dix et al., 2003; Akyurek et al., 2004; Bazoa et al., 2007; Darmas et al., 2007; Mittel et al., 2010; Almusalmi et al., 2011; Romero-Gonzalez et al., 2012; Bawahab et al., 2013).

Yet there are studies suggesting that the practice of submitting every gallbladder specimen for microscopic examination regardless of its gross appearance is safer than the selective submission. As with this practice clinically unsuspected gall bladder malignancies that are not picked up by ultrasound or intraoperative examination of the specimen will not be missed. However it is an interesting observation that most of these authors report a definitive gross abnormality in the cases diagnosed as cancer. For example one prospective study by Kalita et al. (2013) reports 25 gall bladder carcinoma cases out of total 4115 cases. Eighteen of these carcinoma cases were clinically unsuspected incidental carcinomas. Gross findings of these 18 cases showed diffuse thickening of gallbladder wall in 8 cases and a localized growth in 10 cases. Gross findings from few other such studies are listed in Table 4.

Since most of these studies are retrospective analysis of surgical and laboratory records and there is high chance that the specimens may not have been examined with that diligence as they would have been if the surgeon knew that the decision lies solely on his examination of the specimen whether to label it as normal or suspicious. As was the case in our study surgeons threshold for the suspicious category was lower and he put more cases in suspicious looking category as compared to pathologist. Even the slightest wall thickness or mucosal irregularity was not missed by the surgeon.

These authors suggest that the cases grossly presenting as subtle mucosal abnormalities can be easily missed by an inexperienced or casual observer (Kalita et al., 2013). However the cases which are usually missed on macroscopic examination due to subtle mucosal abnormalities usually turn out to be early cancers (stage Tis) which are successfully treated by cholecystectomy alone and no further treatment is necessary. This is the key point behind considering selective examination of gallbladder specimens. (Almusalmani et al., 2011)

In conclusion, selective submission for microscopy of only those gall bladder specimens that look abnormal on gross examination is less likely to jeopardize the diagnosis of incidental carcinoma in clinically unsuspected cases. This practice will also decrease the work load of busy histopathology laboratories.

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