ORIGINAL ARTICLE

IS HISTOPATHOLOGICAL EXAMINATION OF EVERY SURGICALLY RESECTED GALLBLADDER FOR SYMPTOMATIC GALLSTONES REALLY NECESSARY? A REVIEW OF 644 PATIENTS IN ISLAMABAD, PAKISTAN

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ABSTRACT

Background: Cholecystectomy done for symptomatic gallstones, is the most common elective surgical procedure. Histological examination of every gallbladder specimen is often questioned since the incidence of these conditions is very low and varies from country to country.

Objective: To ascertain the necessity of gallbladder pathological examination based on frequency of malignant and premalignant gall bladder disease among resected specimens.

Study Design: Cross Sectional study.

Place and Duration of Study: Department of Pathology, Fauji Foundation Hospital Rawalpindi. Duration of study was 8 months.

Material and Methods: Data of only those gallbladder specimens was included in the study who had a preoperative diagnosis of gallstones using ultrasonography (USG). Data was computed on Statistical Package for Social Sciences (SPSS Version 21). Data was analyzed using software and interpreted in the form of frequencies and percentages.

Results: A total of six hundred and forty-four samples were analyzed. Most specimens received belonged to patients of 41-60 years age group. There was predominance of specimens from female subjects (96.3%). Most common pathological diagnosis was chronic cholecystitis 79.2%.One case of gallbladder adenocarcinoma was identified. Sample identified was of an elderly woman (75 years). Specimen had gross increase in wall thickness, ulceration and exophytic growth. pT2 was the tumor stage.

Conclusion: The frequency of incidental gallbladder carcinoma is very low among our population. It was only seen in one old woman. Diagnosis of gall bladder carcinoma is rare. Carcinoma occurs with gross features suggestive of malignancy. Old age patient's sample should always be checked. We do not prefer routine histological examination of every specimen and therefore, advocate a selective approach in pathology referrals from surgeons.

Key words: *cholecystectomy; gallbladder; gallstones; pathological examination.*

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INTRODUCTION

Incidence of gall stones is on the rise due to sedentary life style and obesity epidemic[1]. The incidence varies among different parts of the world. It is lowest in Black African (less than 5%) and highest in American Indian (64-73%)[2]. In India incidence is around 10-22% while 11% in Pakistan[2,3]. Gallstones can present in the form of complications like acute or chronic cholecystitis, pancreatitis, biliary tract infections, mucocele etc[4]. Risk factors for gall stones include, increasing age, female gender, pregnancy, obesity, ethnic background, family history. Apart from these, there are numerous modifiable risk factors which include rapid weight loss, drugs like somtatostatin analogues, oral contraceptive pills, biliary tract infections, cirrhosis, metabolic syndrome etc[2,5]. Treatment options include laparoscopic or open cholecystectomy. Natural Orifice Transluminal Endoscopic Surgery (NOTES) and robotic surgery are among the newer techniques of cholecystectomy[6,7]. Bile salts treatment can be used in cholesterol stones but not in pigment bile stones[5]. After resection of gallbladder, pathological examination is warranted to detect any carcinoma in situ or carcinoma gall bladder. Large gall stones are a risk factor for developing carcinoma gall bladder. Incidence of carcinoma gallbladder in Pakistan is 11/100,000 while in India it is 22/100,000. Moreover, prognosis of advanced carcinoma gallbladder is poor with surgery as the only option of cure[8].

The approach of surgeons for pathology referral of resected gallbladder specimens for symptomatic gallstones is not guided

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by local data/ guidelines. Some surgeons selectively refer samples, referring only those specimens where either history or gross features are suggestive of malignancy[9]. Others send all specimens for histology examination. In Pakistan, healthcare facilities are poor. Patients bear the cost of healthcare themselves. Furthermore, an unnecessary referral of gallbladder specimen might put extra burden on limited resources. Various studies have reported gall bladder carcinoma only in macroscopically suspicious specimens and recommended a selective approach for histology examination[10,12]. Thus, we have designed this study to find the patterns of pathological lesions in gallbladder specimens resected for symptomatic gall stones and define local policy that whether routine pathological examination of carcinoma gallbladder is warranted or not. Currently the policy of the institute is to send all gallbladder specimens for histological examination.

MATERIAL AND METHODS

A case series study was conducted in 2016 in the department of Histopathology, Foundation University Medical College, Islamabad from Jan till Oct 2016. Ethical approval was taken from the institute's ethical and review board (No. 215/FF/FUMC/ERC). All consecutive samples received in the laboratory with clinical diagnosis of symptomatic gallstones were included. All the specimens were stored in 10% formalin and were sent for histopathological examination. Hematoxylin and Eosin staining was done. Poorly fixed specimens, referred cases or pre-operative diagnosis of cancer cases were not included in the study. Slides were reviewed and diagnosed by at least one fellow pathologist of the department. The data was collected by the investigators with the help of Self-Administered Proforma sheet. Data was put in Statistical Package for Social Sciences Version 21. Data analysis was done. Descriptive statistics were assessed on variables.

RESULTS

The study sample consisted of 644 patients. The age of the patients was divided into 5 groups. 389 (60.4 %) patients were between the ages of 41-60 years, 126 (19.6%) patients were between the ages of 61-80 years whereas 107 (16.6%) were between 21-40 years and 14 (2.2%) were less than 20 years old. These findings are given in table 1.

Out of 644, 620 (96.3%) of the study participants were females and 24 (3.7%) were males. Male to female ratio was 1:26 showing a female preponderence. The findings are shown in figure 1.

Table 1: Age group of the participants:

Age Group	Distribution Percentage
1. Less than 20 years	2.17%
2. 21-40 years	16.61%
3. 41-60 years	60.4%
4. 61-80 years	19.57%
5. More than 80 years	1.24%

It was found out that the majority of the participants had dyspepsia (44.72%), pain in hypochondrium 239 (37.1%) and

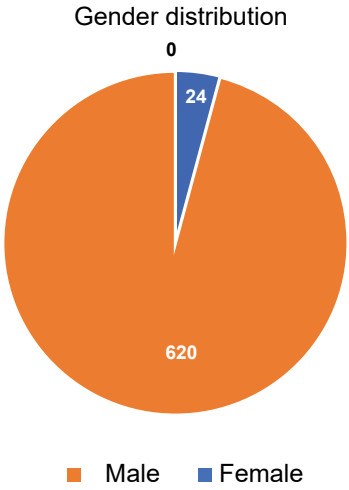

Figure 1: Gender distribution of the participants.

Table 2: Frequency and percentage of main presenting complaints of patients:

	Presenting complaint	n (%)
1	Dyspepsia	288 (44.72%)
2	Pain in right hypochondrium	239 (37.11%)
3	Pain abdomen and vomiting	89 (13.8%)
4	Abdominal discomfort	6 (0.93%)
5	Fever	6 (0.93%)
6	Others	16 (2.48%)
	Total	644 (100%)

pain along with vomiting 89 (13.8%) as presenting complaint. These findings are given in table 2.

Different patterns of histopathological lesions were found in the reports, chronic cholecystitis being the most common accounting for 515 (79.96%) of all the cases. Acute cholecystitis was found in 80 (12.42%) patients, chronic cholecystitis with cholesterosis were in 26 (4.0%) and xanthogranulomatous cholecystitis in 26 (4%) patients. There was just one case of adenocarcinoma in our sample. These findings are given in table 3.

When the received gallbladders were opened carefully, gallstones were present in 592 (91.9%) of the patients whereas no gallstones were found in 52 (8.1%) of the patients.

Gross focal lesions were noted down in 11 (1.7%) patients. Most of the gross focal lesions were found in adenocarcinoma (1), xanthogranulomatous cholecystitis (2) and follicular cholecystitis (1).

DISCUSSION

Our study cohort comprised of a large sample. The importance of routine examination of every gallbladder specimen was

Table 3. Histology of the resected specimen as mentioned in report:

	Histopathological Diagnosis	**n (%)**
1	Chronic cholecystitis	515 (79.96%)
2	Acute on chronic cholecystitis	80 (12.42%)
3	Xanthogranulomatous cholecystitis	26 (4%)
4	Empyema	9 (1.4%)
5	Follicular cholecystitis	4 (0.6%)
6	Chronic cholecystitis with cholesterosis	2 (0.4%)
7	Adenocarcinoma gallbladder	1 (0.2%)
8	Atrophic gallbladder	1 (0.2%)
9	Acute suppurative cholecystitis	1 (0.2%)
10	Gangrenous cholecystitis	1 (0.2%)
11	Focal low-grade dysplasia	1 (0.2%)
12	Adenomatous hyperplasia	1 (0.2%)
13	Chronic cholecystitis with adenomyoma	1 (0.2%)
14	Acute on chronic cholecystitis with empyema	1 (0.2%)
	Total	644 (100%)

evaluated for the detection of gallbladder carcinoma. Previously conducted study in Jamshoro Pakistan included only 220 patients[9]. Moreover, the catchment area of affiliated hospital is large with patients referred from Northern areas, Khyber Pakhtunkhaw province and northern Punjab. Hence, the cohort comprised of various ethnicities of Pakistan. There was female predominance in study sample for all age groups. Most samples were from women of 41-60 years age group. This was followed by samples from women of 61-80 years of age. The male to female ratio was 1: 26. This is more than 1:7 reported by Siddiqui et al[9]. It is believed that female sex hormones and pregnancy causes an increased incidence of gall stones among women especially after post-menopause, the gap between men and women decreases[2]. However, in our sample the gap remained high among both genders. Though gallbladder diseases are more common in females but one of the reasons for female predominance is institutional policy which basically caters for families of retired army personnel. We observed twenty cases of gallstones among less than 20 years age group.

The incidence of incidental gallbladder carcinoma in cholecystectomy samples is around 1%[13]. In our sample size it was 0.2% which is much less than that reported. The one case identified as gallbladder carcinoma had gross ulceration, increased gallbladder wall thickness and exophytic growth. The sample belonged to an elderly woman i.e. 75 years old who underwent cholecystectomy for symptomatic gallstones. Only in this sample, incidental gallbladder carcinoma was identified. Pathological staging of tumor was pT2 Nx Mx. It is believed that simple cholecystectomy offers radical cure in all T1a cases while in T1b stage extended cholecystectomy may be warranted[14]. Hence, diagnosis of T1a stage cancer which may exist without gross lesions does not change clinical decisions. T1b stage is the one where neoplastic cells have invaded muscularis propria. In cases with stage T2 or more there is a role of post-operative adjuvant chemotherapy[14],therefore, a selective approach is needed over routine examination. A similar research showed that macroscopic abnormalities and increased wall thickness were seen among gallbladder carcinoma cases, justifying a selective approach to reduce cost as well as human workload[15]. The enormous pressure lies on the pathology department including the excessive use of resources and time. However, the results are only applicable to the population under study or in our clinical setting atleast. More researches should be performed to clear the views about adopting this new selective approach.

CONCLUSION

Based on results from this study we conclude a very low prevalence of incidental gallbladder carcinoma i.e. 0.2% which is much less than reported elsewhere. Time and resources can be spent more efficiently on better things. Literature suggests that carcinoma without any gross lesions are usually T1a tumors which are cured by simple cholecystectomy. Moreover, specimen of females with old age should be sent for histopathological examination. Hence, a selective approach towards sending gallbladder specimens is justified and an evidenced based approach.

RECOMMENDATIONS

More researches should be performed to reach a conclusive policy. Specimens of old age should never be discarded without proper examination as carcinoma tends to target old age. There

is a need to decide the age limit and those lying in these limits should only be subjected to histopathology, this can only be achieved by thorough research.

AUTHORS' CONTRIBUTION

Muhammad Saad: Manuscript writing.
Usman Ali: Manuscript writing.
Urooj Aamir: Result interpretation.
Omair Ali Khan: Data collection.
Muhammad Asad Khan: Data collection, interpretation and methodology.
Faiza Kazi: Data collection.

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