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Original Article

INCIDENCE OF CARCINOMA OF GALL BLADDER IN PATIENTS WITH CHOLELITHIASIS

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ABSTRACT:

Objective: To see the frequency of carcinoma of gallbladder in patients with Cholelithiasis and to determine other associated factors along with the stones.

Material and Methods: This descriptive study was carried out in the Department of Surgery, LUMHS, Jamshoro from June 2011 to December 2011. The study included patients who had cholecystectomies. The frequency of Cracinoma gallbladder was determined with the histopathological confirmation of all the operated cases. Preoperatively patient's laboratory investigations, radiological findings, ultrasound of gallbladder and biliary tree, oral cholecystography and hepatic ultrasound were done. Non-probability randomized sampling was used to select the patients. Informed consent was taken from patient before their inclusion in this study.

Results: During the study period, 138 patients underwent cholecystectomy as per inclusion criteria. The average age of patients was 49.3±7 years. Out of total 138 patients 97 were females and rest were males. Overall rate of frequency Carcinoma Gallbladder among study population was 10.86% (15 out of 138). The analysis of data showed that the most common risk factor associated with the wound carcinoma gallbladder was gall stones (100%), followed by the thick and irregular gallbladder wall(46.6%), accordingly.

Conclusion: High incidence of carcinoma gallbladder in cholecystectomy patients warrants the histopathological examination in all operated cases.

Key Words: Carcinoma gallbladder, frequency, Cholelithiasis

INTRODUCTION:

Carcinoma of gall bladder is uncommon malignancy having high mortality and low five year survival rates[1-2]. It is the fifth most common cancer of digestive tract and the commonest malignancy of the biliary tract. It has predilection of occurrence in in females and in the seventh decade of life[1, 3-4]. These epidemiological studies have suggested a marked variation in overall prevalence between different populations. Generally it can be concluded that majority of the patients belong to Western Caucasian, Hispanic, and Native American populations[4]. The highest incidence of carcinoma of gallbladder is in Chileans, American Indians, and in parts of North India where it accounts for as much as 9.1% of all the biliary tract diseases[3]. In Pakistan, although no authentic cancer registry data available but various published studies report the incidence of Gallbladder cancer higher than the Western data[5-7]. There are many risk factors associated with Ca. Gallbladder more common of them are; cholelithiasis, estrogen, calcified gallbladder wall, adenomatous Gallbladder polyps and obesity[8]. Cholelithiasis has been consistently recognized as one of the most important associated factor in the causation of the Ca gallbladder. Interestingly, this is noted that in over 60-95% of patients with gallbladder cancer, there are accompanying gall stones. The reported incidence of Ca gallbladder in cholecystectomies in Pakistan ranges from 6-28% in various studies[9-10]. Carcinoma of

gallbladder is usually diagnosed as an incidental histologic finding following cholecystectomy for gall stone disease[5]. The strong recommendation for patients with asymptomatic stones is expectant malignancy. By the time of discovery most of the cancers have invaded the liver directly[3]. The depth of the tumour and lymph node metastasis are important prognostic factors. The haematogenous metastases are more prominent in well or moderately differentiated tubular adenocarcinoma. Most of the carcinomas of gallbladder are adenocarcinomas, some are papillary and others are poorly differentiated to well differentiated infiltrating tumours, 5% are squamous cell carcinomas or have adenosquamous differentiation, a minority are carcinoid tumors[3].

This study was designed with objectives to see the frequency of carcinoma of gallbladder in patients with cholelithiasis and to determine other associated factors along with the stones.

MATERIAL AND METHODS:

It was a descriptive study, conducted in Department of Surgery, LUHMS, Jamshoro. All cholecystectomy specimens were included in the study, operated for cholelithiasis with cholecystitis during January 2011 to December 2011. During this period 138 cholecystectomy specimens were analyzed histologically. The diagnosis of gall stones and cholecystitis was confirmed with laboratory investigations, radiological findings, ultrasound of gallbladder and biliary tree, oral cholecystography and hepatic ultrasound. The diagnosed cases underwent surgery. Most underwent cholecystectomy, and few had biliary drainage or hepatic resection. Patient with preoperative diagnosis of Carcinoma Gallbladder and absence of cholelithiasis were excluded from the study. Patients were further on categorized according to the pre, intra and postoperative diagnosis of thyroid and the association was seen with the clinical and investigative findings. All the specimen were histologically analyzed and data of conformed Ca gall bladder cases was analyzed for age, gender, ultrasound findings, type of tumour, grade and stage. The data obtained were reviewed and results tabulated.

RESULTS:

Out of 138 cases, (70.2%) patients were females and rest (39.8%) were males. The average age of the patient was 49.3±7. The most common presenting complaint was pain in the epigastrium (64%), followed by the complaint of dyspepsia in 72(52 %) cases. In study population nausea /vomiting was noted in 66 (48%) cases, fever in 47 (34%) cases, pain in the right upper quadrant 50 (36%), clinical jaundice in 23(17%), weight loss in 12 (8.6%) cases. The Murphy sign was positive in 117 (85%) cases. (Table-1).

Out of total study population of 138 patients 15 (10.86%)were histopathlogicaly diagnosed to have the Ca Gall bladder. Out of 15 diagnosed patients 2 were categorized as having pre-operative suspicion of Ca Gallbladder. 7 patients had intro-operative suspicion of Ca. and 6 patients had no suspicion of Ca gallbladder only the histopathology of the gallbladder specimen proved the diagnosis. (Table 2). Out of the 15 Ca gallbladder confirmed patients further correlation with other factors showed that presence of thickened of irregular gallbladder wall, presence of polyp and porta hepatics lymph nodes raised the clinical suspicion of the Ca peroperatively. Table2.

On ultrasound examination all diagnosed cases of Ca gallbladder showed gallstones with thickened wall in 7 (46.6%) cases and dilated common bile duct in 1 (6.66%) of cases. Hepatomegaly was seen in 2 patients (13.3%). Most of the gall stones (46.6%)were

TABLE 1:
SIGN & SYMPTOMS IN STUDY POPULATION

	Sign & Symptom	No of Patients	Percentage
1	Pain epigastrium	89	64
2	Dyspepsia	72	52
3	Nausea & Vomiting	66	48
4	Fever	47	34
5	Pain Right hypochondrium	50	36
6	Weight loss	12	8.6
7	Jaundice	23	17
8	Positive Murphy Sign	117	85

TABLE 2:
SUSPICION OF CARCINOMA GALLBLADDER AT VARIOUS STAGES

			Ultrasound findings			Surgical findings	
	No of pts	**Mean age**	**Gall stones**	**Thick walled GB**	**Irregular walled GB**	**Polyp**	**Palpable LN at porta hepatis**
Pre-Operatively suspicious	2	43.7	2	1	2	0	1
Per-operatively suspicious	7	42.9	7	5	2	3	4
Unsuspected	6	56.2	6	1	1	1	0

TABLE 3:
ULTRASONOGRAPHIC AND HISTOPATHOLOGICAL FEATURES OF DIAGNOSED CASES

Variables		
Ultrasound Findings	**No of Patients**	**Percentage**
Thick walled GB	7	46.6
Gall stones	15	100
Hepatomegaly	2	13.3
Dilated common bile duct	1	6.6
Enlarged LN	1	6.6
Sites of Gall Stones		
Fundus	7	46.6
Body	5	33.3
Neck	1	6.6
Entire GB	2	13.3
Histopathological findings		
Tumor grade		
Undifferentiated	1	6.6
Poorly differentiated	1	6.6
Moderately differentiated	5	33.3
Well Differentiated	8	53.3
Tumour Size		
pT1	8	53.3
pT2	4	26.6
pT3	3	20

in fundus followed by body (33.3%) and 1 patient had stone in neck of gall bladder. Most patients had histopathologicaly well differentiated tumours (53.3%) followed by moderately differentiated and only 2 patients had poorly differentiated and undifferentiated tumour Table 3.

DISCUSSION :

Carcinoma Gallbladder is rare but aggressive tumour of GIT carrying low five year survival rate and high mortality rates. The aggressiveness and high mortality can be linked with the fact that due to imprecise clinical presentation, it is usually diagnosed late. By the time diagnosis is established tumour has already spread locally making its resection and subsequent treatment difficult. The other important factor in its delayed diagnosis is co-existing cholelithiasis which usually diverts clinical diagnosis to the cholecysititis instead of Gallbladder carcinoma. The gallstones have been found to be one of the most common and most frequent causative factor for Ca Gallbladder.

The western literature review revealed that 0.3% to 2.85% of the patients who underwent cholecystectomy for presumed benign disease were found to have carcinomas of gall bladder[11-12]. In contrast to this, some local studies have reported that 4% to 12% of the patients undergoing cholecystectomy for cholelithiasis had gall bladder carcinoma[13-15]. There are some studies which even acclaim incidence of upto 28%. This high frequency of co-incidental occurrence of the Ca gallbladder with cholelithiasis warrants mandatory histopathological analysis of all the cholecystectomy specimens. In our patient population the frequency of the Ca gallbladder in was found to be 15 patients (10.86%). The finding in our study is in upper range of the reported range. There are some studies which claim to have very low frequency of the Ca gallbladder occurrence accompanying the cholelithiasis[16]. The probable reasons for high incidence in our study population could be; smaller patient cohort, higher incidence in the region from which patient population was selected or inadequate clinical evaluation pre-surgically.

The analysis of presenting sign and symptoms of the study population showed most common presenting complaint was pain in the epigastrium (64%), followed by the complaint of dyspepsia in 72(52 %) cases. In study population nausea /vomiting was noted in 66 (48%) cases, fever in 47 (34%) cases, pain in the right upper quadrant 50 (36%), clinical jaundice in 23(17%), weight loss in 12 (8.6%) cases. The Murphy sign was positive in 117 (85%) cases. (Table-1). Our findings are in concordance with published study of Naqvi et al[10]. These sign and symptoms are not specific for Ca Gallbladder but are more frequently described with cholecysitits. More aggressive symptoms like anorexia, weight loss and jaundice were seen in a very small portion of our study population (8-17%). This could be a reason that on clinical grounds only negligible proportion of patients are suspected to have carcinoma. Another reason for missing the pre and peroperative diagnosis could be that most of our patients were in pT1-pT2 stages. Small eraly lesion can easily be missed if careful evaluation is not done on investigative modalities.

The association of diagnosed patients with other pre and per-operative findings revealed presence of the gall stones in 100% of the patients. The reported literature shows this association to be in range of 60-98%[11, 16-17]. This strong association proves the presumed notion that longstanding chronic inflammation by cholelithiasis plays a role in carcinogenesis.

Despite marked advances in biliary tract imaging, diagnostic accuracy is not satisfactory in cases of gall bladder carcinomas. Abdominal ultrasonography is a valuable screening imaging modality for carcinoma of the biliary tract. Gall bladder carcinoma can be recognized by a polypoid mass or focal thickening of the gall bladder wall. Preoperative ultrasonographic evaluation can more readily detect polypoid mucosal lesions of the gall bladder than flat lesions and those greater than 1 cm in diameter have been associated with malignancy. Ultrasonography may detect advanced disease in upto 70% of the cases, but the sensitivity of trans-abdominal ultrasound in detecting early disease is variable. In our study population ultrasound examination of all of the 138 cases was done. After presence of gall stones in 100% of diagnosed cases the next most frequent finding was thickened wall in 7 (46.6%) cases and dilated common bile duct in 1 (6.66%) of cases. Hepatomegaly was seen in 2 patients (13.3%). Most of the gall stones (46.6%)were in fundus followed by body (33.3%) and 1 patient had stone in neck of gall bladder. Almost similar findings are reported in study done by Malik et al[18].

CONCLUSION:

Carcinoma of gallbladder is asymptomatic in the early stages. Present study and studies published previously highlight the importance of careful gross and histopathologic evaluation of gallbladders removed. The frequency of carcinoma of gallbladder seems to be quite common in our region.

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