

A Descriptive Study on the Risk of CA Gall Bladder in Patients with Cholelithiasis

ZUNAIR MUSHTAQ¹, ALJASIA KALSOOM², AYESHA²

¹Medical officer, Department of Medicine, CMH Medical and Dental College, Lahore

²WMO, Department of Medicine, Faisalabad Medical University

³WMO, Department of Medicine, Faisalabad Medical University

Correspondence to: Dr. Zunair Mushtaq, Email: zunairmushtaqujjar@gmail.com Cell No 03367268556

ABSTRACT

Objective: The aim of our research was frequency determination in the patients of gall bladder experiencing the cholelithiasis surgery.

Material and Methods: The research was descriptive by design and the duration of this study was from January, 2017 to December, 2019 in Mayo hospital, Lahore. We included two hundred cholelithiasis patients who experienced cholecystectomy in the setting of our research. We included both male and female having the incidence of cholelithiasis, which was diagnosed through clinical manifestations and ultrasonography. Uniform process was adopted for every patient including history, investigations, physical examination and treatment and documented every information on a specified proforma.

Results: In the total research sample patients were processed through gall bladder stone disease surgery, gall bladder carcinoma was observed in 8 cases (4%). The range of the age was from 35 – 70 years. Mean age was observed in female and male respectively 50 (+5.3) and 56 (+ 2) years. Ratio of female to male three to one. On the basis of USG, we observed 3 cases (37.50%) having an advanced disease in addition to the carcinoma as a pre-operative sign.

Conclusion: Gall bladder carcinoma frequency in our sample was higher in comparison to the population of western research studies. Dominance of female number was observed than males facing the subject issue. USG can possibly cause the miss malignant lesions; therefore, all the specimen of gall bladder is to undergo histopathology. While, in the un-suspected patients experiencing laparoscopic cholecystectomy, gall bladder gentle handling becomes critical to evade any port site implantation that results by bile spillage.

Keywords: Gall bladder, Carcinoma, Cholelithiasis, Laparoscopy, Cholecystectomy.

INTRODUCTION

Gall bladder carcinoma among the 5th repeated reason of the digestive tract cancer and also a common biliary tract malignancy. The affected proportion of females is three times higher than the males. Gall bladder carcinoma peak incidence is seen in the 6th and 7th life decade. Instead of diagnostic advancements and improvised methods of surgery, its diagnosis is still delayed and also poor prognosis, incidental diagnosis is an exception in the early life after cholelithiasis cholecystectomy. Overall survival which is reported worldwide is five percent [1]. Difference is significant in the geographical incidence specifically in the sub-continent also noticed high. The incidence of gall bladder carcinoma in the subjects of USA was observed as 2.5 / 100,000 and in United Kingdom observed as 1.5 / 100,000. The range of gall bladder carcinoma in Pakistan was observed in the range of 1.15% – 11%. The factor of exact etiology is still not known; whereas, presence of gall stones was noticed in the range of 75% – 90% in the known gall bladder carcinoma series. However, risk factor of twenty years for the cancer development in the gall stones patients is below 0.5 percent for the whole population and in risk groups it is 1.5 percent. Gall bladder cancer development risk is high in the symptomatic patients than asymptomatic patients of gall stones. There is an association of the large stones (3 cm) to tenfold increased cancer risk [2]. There are few of the other factors of risk such as calcified porcelain (gall bladder), sessile polyps (> 10 mm), sclerosing cholangitis, choledochal cysts, carcinogens exposure (nitrosamines & AZ toluene)

and typhoid carriers. Most common histological type is adenocarcinoma in 80% cases of carcinoma of gall bladder. Other associated lesions such as, squamous carcinoma, non-differentiated carcinoma (6%), Aden squamous carcinoma, sarcoma, carcinoid tumors, lymphomas and melanoma were also observed. An in-time gall bladder cancer diagnosis is rare to achieve due to the indistinguishable signs of gall bladder carcinoma linked to the cholelithiasis and cholecystitis. These associated factors include abdominal discomfort, pain in the right upper quadrant, vomiting and nausea. Jaundice, anorexia, weight loss, abdominal mass and ascites are involved but less involvement is observed [3]. Diagnosis cannot be made on the laboratory results, marked biliary tract advances, accuracy of the imaging diagnostic was also not satisfying in the case of cancer. The correctness was documented in 8.6% pre-operative diagnoses cases. Through USG thickened, irregular wall of gall bladder wall or gall bladder mass replacing can be seen that may possibly be a positive but at the same time false outcome. Only available cure is possible through surgery. Unfortunately, in the number of cases the patients have gone beyond surgical resection when they were diagnosed for the first time having a poor prognosis. We planned a well-structured research for the assistance of the demographic assessment in our country's risky population. These is a need for the establishment of protocols and policies to diagnose the incidence early as the disease is very aggressive.

MATERIAL AND METHODS

The aim of our research was frequency determination in the patients of gall bladder experiencing the cholelithiasis surgery. The research was descriptive by design and it was completed in the time of two years starting from January, 2017 to December, 2019 in Mayo Hospital Lahore. We included two hundred cholelithiasis patients who experienced cholecystectomy in the setting of our research. We included both male and female having the incidence of cholelithiasis, which was diagnosed through clinical manifestations and ultrasonography. Uniform process was adopted for every patient including history, investigations, physical examination and treatment and documented every information on a specified proforma. Management of all the cases was carried out in surgical wards in the time of research study and documented every information that was helpful. Histopathological assessment was also carried out in all the patients and biopsy results was taken from department of pathology about the gall bladder cancer type, partial involvement of gall bladder and spread of the disease in terms of area of influence.

RESULTS

In the total research sample patients were processed through gall bladder stone disease surgery, gall bladder carcinoma was observed in 8 cases (4%) as shown in Table – I. The range of the age was from 35 – 70 years. Mean age was observed in female and male respectively 50 (+5.3) and 56 (+ 2) years. Ratio of female to male three to one. On the basis of USG, we observed 3 cases (37.50%) having an advanced disease in addition to the carcinoma as a pre-operative sign. LFTs were deranged in minority of the cases as shown in Table – II. Level of bilirubin was slightly raised in two patients and level of serum alkaline phosphatase was also increased in three cases (37.5%). Through USG three patients having an advanced disease presented carcinoma clue pre-operatively. Calculated tomography was carried out in only case having mass as revealed in the USG. Table – III reflects histo-pathological outcomes, various gall bladder parts involvement was observed. There were 04 fundus specimens (50%), 03 body cases (37.5%) and one case of gall bladder in the research sample (12.5%). Every case of cancer of gall bladder was adenocarcinomas and half of the cases (50%) were well defined. Confined mucosa growth was observed during 1st stage in two cases (25%) and only case (12.5%) was observed peri-muscular and muscular without any nodal involvement in the 2nd stage. We observed 3rd stage in 03 cases (37.5%) where tumor perforated was carried out by serosa and involvement of the lymph node was observed. At 4th stage two cases were observed having 01 inoperable growths (12.5%) because of an extensive invasion and second was observed in liver gut.

Table I: Age and Sex Distribution of Gall Bladder Carcinoma Cases

Age (Years)	Female	Male	Total	Percentage
31-40	1	0	1	12.5
41-50	1	0	1	12.5
51-60	3	2	5	62.5
61-70	1	0	1	12.5

Table II: Sign and Symptoms in Cases of Carcinoma of Gall Bladder

Clinical feature	Female	Male	Total	Percentage
Pain in upper quadrant	5	2	7	87.5
Dyspepsia	4	2	6	75
Nausea/ vomiting	3	2	5	62.5
Anorexia	3	2	5	62.5
Weight loss	2	1	3	37.5
Positive Murphy's sign	4	2	6	75

Table III: Ultrasound Findings in Carcinoma Of Gall Bladder Cases

Finding	Number	Percentage
Gall bladder wall thickness	2	66.66
Gall bladder mass	1	33.33

Table Iv: Histological Types and Grading of Gall Bladder carcinoma Cases

Type	Number / specimen	Percentage
Adenocarcinoma	8	100
Well differentiated	4	50
Moderately well differentiated	3	37.5
Poorly differentiated	1	12.5

DISCUSSION

Gall bladder carcinoma is amongst the list of aggressive diseases which is diagnosed at very late stage, progresses rapidly, dismal outcomes and reoccurrence is early [4]. There is an association of cholelithiasis and gallbladder carcinoma with different rate of incidence in the various populations because of involved factors such as stone size, lifestyle, diet, hepatobiliary anomalies, chronic bacterial infections and pollutants of the environment [5]. In the present literature the patients in the range of 0.3% - 2.85% experience cholecystectomy because of the presumed diagnosis of gallbladder carcinoma [6]. Gall bladder carcinoma proportion detected in the cases who underwent cholelithiasis cholecystectomy were 04% as observed in this research, this incidence is high as observed in the literature of the west [7]. Contrary to that, few of the research studies held in Pakistan also report high proportions such as six and eleven percent in gallbladder carcinoma patients [8]. These large-scale variations of frequencies can be attributed to various size of the sample population and varying environment and geographical factors. Samad (2005) states a frequency of 1.15%, almost same as observed by the western research studies [9]. Gall bladder carcinoma occurrence in Pakistan in the early age is dominant in the females (50 years' average age); whereas, in the seventy above cases of western countries. Gall bladder carcinoma is a dominant female disease. However, male to female's proportions are different in the region to region analysis [10]. We observed a three to one ratio of female to male. Same as other international research outcomes. No typical features of the clinical observations have been observed in the cases of gallbladder carcinoma [11]. Chronic or acute syndromes were observed in ninety percent of the cholecystitis cases. Major signs as observed in our research were pain of right upper quadrant, nausea, dyspepsia, weight loss and vomiting with the common most sign as a positive Murphy.

Global outcomes are matching to our research that presents the unchanged incidence of this fatal disease [12]. Huguet KL (2005), states that an irregular alkaline phosphatase serum and gamma glutamyl transferase may be increased in jaundice absence. We observed level of alkaline phosphatase serum enhanced in 03 cases (37.50%) and raised value of serum bilirubin was observed in 2 cases (25%) with a value of not above 2.5 mg/dl and in the noncitric patients [13]. Which speaks for the supportive role of clinical observations. No satisfactory diagnosis was observed in the advanced imaging of biliary tract. Advance disease pattern may be tracked through USG in the seventy percent of the cases; whereas, trans abdominal ultrasound sensitivity for the detection of the early disease onset was varying. Another better option instead of USG is CT scan, having low sensitivity for the lymph node metastasis detection [14]. Both CT and US scan may be unsuccessful to reflect omental in filtration, gastrointestinal and peritoneal deposits. Our research suspected 37.50% cases through sonography; whereas, no assistance was provided in 62.50% cases. Many other areas of the country also reported the same. The reason behind may be the restricted skill level [15]. Current hepato-biliary surgery improvements have highlighted the early specific diagnosis importance, that needs multi-disciplinary strategy in case of an emergence with dedicated equipment. Nanty percent of the cases may be accurate diagnosed through ultrasound guided fine needle aspiration cytology for the gall bladder carcinoma assessment [16]. Percutaneous transhepatic cholecystostomy and endoscopic ultrasonography are latest instruments for an in-time diagnosis of gallbladder carcinoma with an emphasized utilization need. Cholangiography, Color Doppler ultrasonography and dynamic magnetic resonance imaging preoperative use for the differentiation of benign from malignant disease is linked to success proportions and degrees. There is a need of the more refined method that leads to an even better pre-operative malignancy future diagnosis [17]. An incidental diagnosis was 03 cases (37.50%) through histopathological reports; this frequency is high in comparison to the already available literature. Careful and routine intra-operative specimen assessment can diagnose carcinoma of gallbladder with a specificity (93%) and sensitivity (79%) [18]. During surgery we found five suspected cases of gallbladder carcinoma which was later confirmed through histopathological reports (62.50%). A careful and curative management was not possible because of the developed disease stage and scarcity of the treatment facilities [19]. We advise to the patients of gallbladder carcinoma for the patients of endemic areas having signs of gall stones to be confident and encouraged for the cholecystectomy experience to reduce and avoid malignant change risk and improve the rate of their survival through an early diagnostic [20]. Small population size was a limitation of the research so care is mandatory in the interpretation of the research outcomes.

CONCLUSION

Gall bladder carcinoma frequency in our sample was higher in comparison to the population of western research studies. Dominance of female number was observed than

males facing the subject issue. USG can possibly cause the miss malignant lesions; therefore, all the specimen of gall bladder is to undergo histopathology. While, in the unsuspected patients experiencing laparoscopic cholecystectomy, gall bladder gentle handling becomes critical to evade any port site implantation that results by bile spillage.

REFERENCES

- Hundal, R. and E.A. Shaffer, Gallbladder cancer: epidemiology and outcome. *Clinical epidemiology*, 2014. 6: p. 99.
- Ethun, C.G., et al., A novel pathology-based preoperative risk score to predict locoregional residual and distant disease and survival for incidental gallbladder cancer: a 10-institution study from the US Extrahepatic Biliary Malignancy Consortium. *Annals of surgical oncology*, 2017. 24(5): p. 1343-1350.
- Torre, L.A., et al., Worldwide burden of and trends in mortality from gallbladder and other biliary tract cancers. *Clinical Gastroenterology and Hepatology*, 2018. 16(3): p. 427-437.
- Mhatre, S., et al., Common genetic variation and risk of gallbladder cancer in India: a case-control genome-wide association study. *The Lancet Oncology*, 2017. 18(4): p. 535-544.
- Andrea, C. and A. Enzo, Cholesterol gallstones larger than 3 cm appear to be associated with gallbladder cancer: identification of a high risk group of patients that could benefit from preventive cholecystectomy. *Annals of surgery*, 2016. 263(3): p. e56.
- Goetze, T.O., Gallbladder carcinoma: prognostic factors and therapeutic options. *World journal of gastroenterology*, 2015. 21(43): p. 12211.
- Koshiol, J., et al., Salmonella enterica serovar Typhi and gallbladder cancer: a case-control study and meta-analysis. *Cancer medicine*, 2016. 5(11): p. 3310-3235.
- Kanthan, R., et al., Gallbladder cancer in the 21st century. *Journal of oncology*, 2015. 2015.
- Rakić, M., et al., Gallbladder cancer. *Hepatobiliary surgery and nutrition*, 2014. 3(5): p. 221.
- Larsson, S.C., E.L. Giovannucci, and A. Wolk, Sweetened beverage consumption and risk of biliary tract and gallbladder cancer in a prospective study. *Journal of the National Cancer Institute*, 2016. 108(10): p. djw125.
- Le, M.D., et al., Is gallbladder cancer decreasing in view of increasing laparoscopic cholecystectomy? *Annals of hepatology*, 2016. 10(3): p. 306-314.
- Lepage, C., et al., Survival in patients with primary liver cancer, gallbladder and extrahepatic biliary tract cancer and pancreatic cancer in Europe 1999-2007: results of EURO-CARE-5. *European Journal of Cancer*, 2015. 51(15): p. 2169-2178.
- Espinoza, J.A., et al., The inflammatory inception of gallbladder cancer. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*, 2016. 1865(2): p. 245-254.
- Go, S.-I., et al., Is There a Role for Adjuvant Therapy in R0 Resected Gallbladder Cancer?: A Propensity Score-Matched Analysis. *Cancer research and treatment: official journal of Korean Cancer Association*, 2016. 48(4): p. 1274.
- Shindoh, J., et al., Tumor location is a strong predictor of tumor progression and survival in T2 gallbladder cancer: an international multicenter study. *Annals of surgery*, 2015. 261(4): p. 733.
- Aune, D. and L.J. Vatten, Diabetes mellitus and the risk of gallbladder disease: A systematic review and meta-analysis of prospective studies. *Journal of diabetes and its complications*, 2016. 30(2): p. 368-373.
- Kagohara, L.T., et al., Global and gene-specific DNA methylation pattern discriminates cholecystitis from gallbladder cancer patients in Chile. *Future Oncology*, 2015. 11(2): p. 233-249.
- Ben-Josef, E., et al., SWOG S0809: a phase II intergroup trial of adjuvant capecitabine and gemcitabine followed by radiotherapy and concurrent capecitabine in extrahepatic cholangiocarcinoma and gallbladder carcinoma. *Journal of clinical oncology*, 2015. 33(24): p. 2617.
- Koshiol, J., et al., Association of aflatoxin and gallbladder cancer. *Gastroenterology*, 2017. 153(2): p. 488-494. e1.
- van Rappard, D.F., et al., Gallbladder and the risk of polyps and carcinoma in metachromatic leukodystrophy. *Neurology*, 2016. 87(1): p. 103-111.