

# AGE AND GENDER RELATED FREQUENCY OF CANCER IN CHRONIC CHOLELITHIASIS

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## ABSTRACT

- Objective* To find out age and gender related frequency of cancer of the gall bladder in patients with chronic cholelithiasis.
- Study design* Descriptive case series.
- Place & Duration of study* PNS Shifa Hospital Karachi for a period of 12 months.
- Methodology* A total of 153 patients were inducted in the study who were suffering from chronic cholelithiasis and carcinoma (Ca) gall bladder. The diagnosis was confirmed by various laboratory and radiological methods. After surgical intervention the positive cases were referred to the oncologist who monitored and assessed them accordingly;
- Results* Twenty-four patients had Ca Gall bladder. The youngest patient was 40 years of age and oldest of 70 years with an average age 54.8 years. The male to female ratio was 1:2. Preoperative diagnosis was made only in 4 patients. Frequency of carcinoma gall bladder peaked after 60 years in males while in females it peaked after 40 years.
- Conclusions* Although chronic cholelithiasis is predominantly a female disease but if present in males then chances of cancer is higher especially after the age of 60 years.
- Key words* Carcinoma gall bladder, Cholelithiasis, Biliary tract.

## INTRODUCTION:

Carcinoma of the gall bladder (Ca GB) is relatively uncommon, but a very lethal disease. Gall bladder cancer constitutes 3-4% of all malignant lesions. It holds 5<sup>th</sup> place amongst the tumors of digestive system and first among the biliary tract tumors. Despite the advances in imaging and diagnostic techniques, a correct preoperative diagnosis of Ca GB at curable stage is made in less than 10% of patients and curative resection is possible in only one fourth. Cholelithiasis is one of the important etiological factors implicated in causation

of Ca GB.<sup>1</sup> A significantly higher incidence of Ca GB has been observed in patient population with a traditionally high incidence of gall stones or in persons harboring gall stones for longer duration. Two to 4 percent predilection for elderly patients with female to male ratio of 3:12 is reported. When younger patients are affected the prognosis is even worse. Despite modern diagnostic techniques, better pre and post operative care and more aggressive surgical approach, the disease still has rapidly aggressive course.

The early stage of the disease is silent, presentation is non-specific and that is why it is diagnosed late. Even in developed countries where facilities of radical surgery are available, 60- 90% of these tumors are wide spread at the time of diagnosis. The best chance of cure of Ca gall bladder is its diagnosis in early stages. Ultrasound is of great help in early pre operative diagnosis of the

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Ca gall bladder. Gall bladder specimens sent routinely for histopathological examination reveal malignancy in about 1-2% cases. It is therefore recommended that every gall bladder removed should be opened, any suspicious lesion be examined histopathologically by taking frozen sections<sup>2</sup>

The etiology of this tumor is complex, but there is a strong association with gall stones. Symptoms of GB malignancy are usually masked by chronic cholecystitis and therefore most of the patients present in advanced stage and therefore even with radical resection, 50% of patients have positive margins. Favorable results can be predicted in incidentally discovered gall bladder cancer. Carcinoma has been reported in the age group of 11-15 years but the majority of patients fall in between 50-70 years of age. The incidence of gallbladder carcinoma is less than 1% of all malignancies in Great Britain while overall incidence is 1-2% in patients undergoing surgery on biliary tract.<sup>3</sup> Gall bladder carcinoma carries a high mortality and a low five year survival rate (<2.1%).<sup>1-3</sup> Although uncommon in the West,<sup>4</sup> a high frequency (6-8%) of this malignancy has been reported from Pakistan.<sup>5-7</sup> In spite of high frequency and grave mortality, risk factors for this disease have not been clearly understood.<sup>4</sup> This study was conducted to find out frequency of Ca GB in patients with cholelithiasis so as to maintain a registry which will help in planning strategies to deal with the condition.

#### **METHODOLOGY:**

The study was carried out in the navy established hospital PNS Shifa. The study was spanned over a period of one year. The patients attended the hospital belonged to the armed forces, the transferred cases from other parts of the province, and the civilian population. The age ranged from 10 years to 80 years. The diagnosis 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. Frozen section was provided by the pathology department of PNS Shifa and surgery planned accordingly. The data was collected from the statistics officer and the follow up visits were advised for the assessment of the operative procedure and then for review of oncologist of the hospital. Follow-up data was obtained from patients records.

#### **RESULTS:**

The data of a total of 153 patients was studied for gallbladder calculous and malignancies. Amongst these females were 88.23% (135 patients) as compared to 11.77% (18 patients) males. Most of the patients were older than 30 years of age and the disease frequency

peaked after 30 years of age in both males and females with calculous cholecystitis. The age incidence for carcinoma gallbladder in males peaked after the age of 60 years and after 40 years in females. Twenty-four patients had Ca gall bladder. The youngest patient was 40 years of age and oldest 70 years with an average age 54.8 years. The male to female ratio was 1:2. Preoperative diagnosis was made only in 4 patients.

#### **DISCUSSION:**

Cancer of gall bladder has always been associated with an unfavorable prognosis.<sup>8,9,10</sup> Recent improvements in diagnostic modalities, a better knowledge of the natural history of gallbladder cancer and its mode of spread, and reports of long term survival after resection of bile duct carcinoma have induced several authors to advocate radical surgical treatment of gallbladder cancer in an attempt to prolong survival. This report based on 153 patients of gallbladder stones treated by cholecystectomy, biliary drainage and hepatic resection shows no differences in patients survival compared with other reports.

Gallbladder malignancies are still diagnosed too late. Carcinoma of the gallbladder is rare as compared to the incidence of chronic calculous cholecystitis and is usually confirmed only at postoperative histopathologic examination. All the patients who developed carcinoma of the gallbladder had chronic calculus cholecystitis. A total of 8 patients developed carcinoma of the gallbladder out of 153 patients with presenting chronic calculous cholecystitis. Therefore the risk of developing Ca gallbladder in patients with chronic calculous cholecystitis is 0.053%.

The post operative follow-up showed a significant decrease in the incidence of bile duct cancer 10 or more years after cholecystectomy and concluded that long persistent gallstones play a significant role in development of gallbladder cancer. Increased incidence of gallbladder cancer in the elderly has been observed. However there was a significant difference of age between the male and female patients of gallbladder cancer. The male patients of Ca gallbladder were older than 60 years where as female patients were older than 30 years. Therefore the risk of developing Ca gallbladder in patients with chronic calculous cholecystitis is far more in female patients at a younger age as compared to the male patients. Thus the sex of the patient may also be an important factor along with age in the development of gallbladder cancer. The findings of formation of gallbladder cancer and its relation to chronic calculous cholecystitis led to previous reports showing the association of long-persisting cholecystitis.<sup>11,12</sup>

Most of the patients of Ca gallbladder were detected

at a later stage because gallbladder carcinoma grows silently and remains undetected at an early stage. Therefore Ca gallbladder has been observed as a fatal disease and remains a disease of the elderly and might just be termed as a male or female disease. A radical and aggressive approach is needed for potentially curative surgery but offers a chance only if it is detected at an early stage.<sup>9,10,13,14</sup> Therefore the diagnosis of an unsuspected early tumor stage is very important and may lead to best prognosis. Among Chile population and Czechoslovakians the risk of gallbladder cancer was seven times more among patients with stones than those without stone. Mean age in the current study was 59 years for males, and 53 years for females with a peak frequency in the sixth decade of life and more than 86% of the patients were under 60 years of age.<sup>4</sup> Carcinoma of the gall bladder is a disease of poor prognosis. Most patients present late and at this stage only palliative treatment is possible.

The incidence of carcinomas in the cholecystectomies performed for any reason was 13.7% in our study. Bhurgri et al in 1995 reported an incidence of 6.39%. The incidence is 1.21% in the Western literature. The male to female ratio was 1:2 in our study. It was 1:5 in Bhurgri et al 1995 study and 1:3 in the study of Carty and Johnson. Male to female ratio was 1:6 in one study.<sup>2</sup> Ca of the GB is the most common malignant tumor of biliary tract and particularly high incidence is observed in Chile and Japan. In Pakistan GB malignancy occurs at an early age and more common in females. Behavior of this malignancy in our population seems to be similar to those ethnic groups who have higher incidence of Ca GB like in American Indians and Hispanics. The incidence of this disease in earlier Pakistani studies has been reported as 2.7% and 6.6%.<sup>15,16</sup> Most western studies have reported higher incidence of Ca GB in 6<sup>th</sup> and 7<sup>th</sup> decade of life and it appears to rise with age. Nadler and Masberry have reported that GB malignancy is a disease of elderly females with cholelithiasis. The peak incidence in Chinese population is in 6<sup>th</sup> and 7<sup>th</sup> decade. GB malignancy is predominantly a disease of females, however there is a regional variation in female to male ratio from 1:1.1 to 4:1 in the world literature. Female to male ratio is even high in those areas where the gall bladder disease and GB Ca is rare as in Uganda. The ratio was 2.5:1 in an Italian study. Female to male ratio has been reported to be 3:1 in Pakistan. In a local study female to male ratio has been reported as 1.5:1. Only Smithies has presented a small series of Ca GB where it was more common in males.

#### CONCLUSIONS:

The risk of development of Ca gallbladder due to long persisting gallstones is low but once developed proves fatal. Cholecystectomy has been observed as a very

successful treatment of chronic calculous cholecystitis. It has also been observed although the incidence of chronic calculous cholecystitis was low in male patients but frequency of Ca GB was higher in males within the age range of 50 – 70 years.

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