### **Original Research Article**

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# A clinical epidemiological study of gallbladder carcinoma: a retrospective study

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#### ABSTRACT

**Background:** Incidence of gallbladder carcinoma (GBC) is high among the north Indian population. It may be due to environmental, dietary and reproductive factors. Evaluation of GBC epidemiology will provide important insights into determining causes and risk factors for gallbladder cancer. The aims and objectives were to study the epidemiology, clinical presentation and etiological factors of GBC.

**Methods:** Fifty-one cases of GBC were studied retrospectively at Cancer Hospital and Research Institute (CHRI) Gwalior, Madhya Pradesh, India from January to December 1998. All the patients underwent a detailed history taking and physical examination followed by routine laboratory tests and other investigations including ultrasonographic and computed tomography scan of whole abdomen. Histopathological evaluation of gallbladder specimen was also performed after surgical resection of the GB mass.

**Results:** Incidence of GBC at this centre was 1.49%. GBC was more prevalent among old women (mean age  $52.62\pm12.14$  years) belonging to low socio-economic status (SES) (52.94%). Most common presenting symptom of GBC was pain in right hypochondrium (70.4%) followed by anorexia (42.8%), pruritus (35.7%), weight loss (31.2), nausea and vomiting (30.4%). Histopathological examination revealed majority of the case to have adenocarcinoma (84.31%). Gallstones were present in 35.29% patients.

**Conclusions:** GBC is more prevalent in older women belonging to low SES. Gallstones remain the chief risk factor for this malignancy. Histopathological examination of all cholecystectomy specimens for early pre cursor lesion could serve as an important means of early detection of this carcinoma.

Keywords: Adenocarcinoma, Gallbladder cancer, Gallstones, Malignancy

#### **INTRODUCTION**

Although the overall prevalence of gallbladder carcinoma (GBC) is low, it is still the most common cancer of the biliary tree. GBC is a highly malignant tumor with poor prognosis. After colon cancer, GBC is the 5<sup>th</sup> most common GIT related malignancy.<sup>1</sup>

GBC is 2-6 times more common in females compared to males. Incidence of GBC increases with increasing age and more than 75% of the patients suffering from GBC

are older than 65 years.<sup>2</sup> The etiology of GBC is still a source of speculation. Incidence of GBC is high among patients with gallstone disease, especially patients with large and longstanding gallstones are at higher risk.<sup>3</sup> Reports have shown an association between a porcelain gallbladder, pancreaticobiliary duct junction and other biliary disorders including choledochal cyst, primary sclerosing cholangitis, Mirrizi's syndrome and gall bladder cancer.<sup>4</sup> In present study, author tried to evaluate incidence and clinicopathological aspect of the disease in patients of GBC.

#### **METHODS**

An institution based retrospective study was performed on 51 patients having GBC at Cancer Hospital and Research Institute (CHRI) Gwalior, Madhya Pradesh, India from January to December 1998.

Institutional Ethics Committee approval was obtained before starting study.

#### Inclusion criteria

The records of all patients of either sex of all age groups admitted to (CHRI) Gwalior, Madhya Pradesh, India diagnosed with GBC using cytological examination and by radiological method were included.

#### **Exclusion** criteria

Patients with pancreatitis, liver cirrhosis, hepatitis, other co-existing malignancy and patients with common bile duct obstruction due to stone were excluded from the present study.

#### Methodology

During the study period, all selected records were scanned specially regarding the detailed history and physical examination followed by routine laboratory tests and other investigations including ultrasonographic (US) and computed tomography (CT) scan of whole abdomen.

The histopathological diagnoses for all gall bladder specimens received in its Department of Pathology were noted. The histopathological report with description of gross appearance of the gall bladder together with the Haematoxylin and eosin stained slides were reviewed.

#### Statistical analysis

All the data were analyzed using IBM SPSS version 20 software. Frequency distribution and cross tabulation was used to prepare the tables. Microsoft office 2010 and PRISM was used to prepare the graphs. Data was expressed as number, percentage and mean±standard deviation.

#### RESULTS

Out of total 3421 cases of malignancies at the centre, 51 (1.49%) were of GBC. Mean age of study cohort was 52.62±12.14 years. Majority of the subjects belonged to 51-60 years (32 (62.74%)) age group and low socioeconomic status (27 (52.94%)) (Table 1). There were only 11 (21.56%) male and 41 female subjects (80.39%).

Table 2 highlights the histopathological findings in 51 surgical specimens where adenocarcinoma was most common. Most common presenting symptom of GBC was pain in right hypochondrium (70.4%) followed by

anorexia (42.8%), pruritus (35.7%), weight loss (31.2), nausea and vomiting (30.4%) (Figure 1). Out of 51 GBC patients, 18 (35.29%) patients had gallstones whereas remaining had no gallstone. Secondary metastasis was seen in 56.86%.

#### Table 1: Distribution of study cohort according to demographic characteristics.

Characteristics		No. of subjects	% (n=51)
Age (years)	<40	7	13.73
	41-50	8	15.69
	51-60	32	62.75
	61-70	5	9.80
SES	Low	27	52.94
	Medium	16	31.37
	High	9	17.65

## Table 2: Histopathological findings in 51surgical specimens.

Histopathological variants	No. of patients	%
Adenocarcinoma	42	82.35
Papillary adenocarcinoma	5	9.80
Mucinous adenocarcinoma	2	3.92
Squamous cell carcinoma	1	1.96
Adenosquamous carcinoma	1	1.96





#### DISCUSSION

GBC is one of the most common culprits of death of biliary related malignancies.<sup>5</sup> Due to rapid progression, GBC is usually detected at an advanced stage.<sup>6</sup> Among the Indian population, GBC has varying geographic distribution. Reports of Tyagi BB et al, has revealed that incidence is higher in north Indians compared to South Indian population.<sup>3</sup> The incidence of GBC varies in different parts of the world. India, Chile and some parts of Japan reported a very high incidence of gall bladder

carcinoma while other countries reported a lower incidence. Khoo JJ et al, studied 1122 cholecystectomies cases out of that author found 9 (0.80%) cases to have GBC which is lower than the incidence (1.49%) revealed in present study.<sup>7</sup> Study from Lucknow reported 358 patients with GBC out of 2600 cholecystectomies performed for a period of 11 years (13.77%) which higher compared to present study findings, while studies from other parts of the world, reported a range of incidence from 0.38% to 1.15%.<sup>8-11</sup> This is comparable to the findings of present study. A recent study from China reported that out of 86609 of all biliary tract diseases, GBC accounted for 2.7%.

In the present study, GBC was more prevalent among older women. The higher incidence of GBC in women appears to be due to higher estrogen levels.<sup>12</sup> Reports of Pandey M et al, has shown that women with multiple pregnancies are at higher risk of developing gall bladder cancer which may be due to the higher level of sex hormones like progesterone and endogenous estrogen during pregnancy.<sup>4</sup> Khoo JJ et al, also reported that there were more females undergoing cholecystectomies than male patients with mean age of 56.7 years which is in agreement to present study finding where mean age of study cohort was  $52.62\pm12.14$  years.<sup>7</sup> In agreement to present study, Shen HX et al, also reported that GBC was more prone to occur in elderly women.<sup>13</sup>

In this study, the mean age was also comparable with most of the other reported studies, although in some studies it had been suggested that there was higher incidence of GBC with an older age.<sup>14-18</sup> A Chinese survey, has also reported higher mean age ( $63.7\pm11.3$  years) as compared to present study mean age of  $52.62\pm12.14$  years.<sup>13</sup>

In the present study, most common presenting symptom of GBC was pain in right hypochondrium followed by anorexia, pruritus, weight loss and nausea and vomiting. In agreement to present study, study from Nepal including 47 patients with GBC also reported abdomen pain (93.6%) as the chief presenting symptoms followed by weight loss (51.1%) and jaundice (46.8%).<sup>19</sup>

In this study, gallstones were present in 35.29% cases which is in agreement with the study done by Khoo JJ et al, which reported 55.6% cases who were having gallstone.<sup>7</sup> Shen HX et al, studied 2379 patients with GBC and found that 57.2% had gallstones.<sup>13</sup> Gallstones are reported to induce mechanical damage and carcinogens in bile that may trigger epithelial proliferation in the mucous membrane of the gall bladder which can result in malignancy.<sup>20</sup> Therefore, it is important to advice for surgery or regular follow-up for patients having long term history of gallbladder stones.

In comparison to Western countries, this correlation of GB stones with GBC is much lower. The correlation of GB stones with GBC is nearly 94-98% in western

countries whereas in this study the correlation is much lower. This suggests another etiological factor for GBC.

Gross examination of gallbladder alone is not enough for exclusion of malignancy, histopathological examination is needed for final diagnosis. Moreover, histopathological examination of gallbladder is recommended by several studies to diagnose GBC.<sup>21</sup> In present study, histopathological examination revealed majority of the case to have adenocarcinoma (84.31%) which is consistent with other studies.<sup>22-25</sup> Khoo JJ et al, also reported that majority of the tumours were adenocarcinoma (77.8%).<sup>7</sup>

#### CONCLUSION

In the Indian scenario, GBC remains common a clinical entity predominantly affecting females of older age. Therefore, any women especially in fourth and fifth decade of life with symptoms of recent onset constant pain in the right hypochondrium should be thoroughly evaluated for GBC. Present study has also found the association between gallstones and GBC. Despite of advancement in the imaging techniques for gallbladder, prognosis of GBC is still poor. Therefore, this study recommends routine histopathological examination for early diagnosis of gallbladder carcinoma for early intervention.

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