

Clinical and Pathological Profile of Gallbladder Cancer (GBC) and Gallstone Disease (GSD) among the Patients Admitted in Tertiary Care Institute in Kolkata

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ABSTRACT

Background: Gall bladder cancer (GBC) is a common cancer in the northern and North-eastern States of India. The six cancer registries of the Indian Council of Medical Research (ICMR) show a 10 times lower incidence of GBC per 1 00 000 in South India compared with the North. The objective of present study was to assess the epidemiological and pathological profile of gallstone disease and GBC patients of Eastern India visiting tertiary care hospital of Kolkata.

Method: This cross-sectional observational study was conducted, over a period of 18 months, at a tertiary referral hospital of Kolkata. In this study, 66 gallstone disease patients and 24 gallbladder cancer patients who undergone surgery were included in the study after their written informed consent. Pathological profile, and staging and type of gallbladder cancer were collected.

Results: Male to female ratio was 1:2 & 1:3 for GSD and GBC respectively. We found that nearly half (45.4%) GSD patients were in the age group of 21-40 years and more than half (58.6%) GBC patients were in age group of 41-60 years. Majority had multiple stones (57.6%) and cholesterol stones were most common (59.1%). Out of 24 GBC patients, nearly one-third (33.3%) had stage II cancer and only 12.5% patients had stage IV cancer. More than one-fourth (29.2%) GBC patients had poorly differentiated carcinoma.

Conclusion: The results of this study reaffirm that female gender and patients in fourth decade are strong predisposing factor for GSD and GBC. Large population based multicentric analytical study is further warranted.

Keywords: Gallstone disease, gallbladder carcinoma, tertiary care institute, Kolkata, India

ABSTRAK

Latar belakang: Kanker kantung empedu (KKE) adalah keganasan yang banyak dijumpai di bagian utara dan timur laut India. Enam registri kanker the Indian Council of Medical Research (ICMR) menunjukkan insidens kanker kantung empedu 10 kali lebih rendah per 100.000 penduduk di India bagian selatan dibandingkan utara. Tujuan studi ini adalah untuk melihat profil epidemiologis dan patologis pasien dengan penyakit batu empedu (PBE) dan KKE di India bagian Timur yang datang ke rumah sakit tersier di Kolkata.

Metode: Studi potong lintang ini dilaksanakan selama periode 18 bulan pada rumah sakit rujukan tersier di Kolkata. Pada studi ini, 66 pasien dengan PBE dan 24 pasien dengan KKE yang menjalani operasi diikutsertakan setelah mendapatkan persetujuan tertulis. Data yang diambil adalah profil patologis, stadium, dan tipe kanker kantung empedu.

Hasil: Rasio pria dan wanita adalah 1:2 dan 1:3 untuk PBE dan KKE secara berturut-turut. Kami menemukan bahwa hampir setengah (45,4%) pasien PBE ada pada kelompok usia 21-40 tahun dan lebih dari setengah (58,6%) pasien KKE ada pada kelompok usia 41-60 tahun. Mayoritas memiliki batu multipel (57,6%) dan batu kolesterol adalah yang tersering (59,1%). Dari 24 pasien KKE, satu pertiganya (33,3%) mengalami kanker stadium II dan hanya 12,5% yang mengalami kanker stadium IV. Lebih dari satu perempat (29,2%) pasien KKE memiliki karsinoma yang berdiferensiasi buruk.

Simpulan: Hasil studi ini memperkuat bahwa jenis kelamin wanita dan usia dekade keempat adalah faktor predisposisi PBE dan KKE. Dibutuhkan penelitian analitik multisenter pada populasi yang lebih besar di kemudian hari.

Kata kunci: India, kanker kantung empedu, Kolkata, penyakit batu empedu, rumah sakit tersier

INTRODUCTION

Gallstone disease (GSD) is the most common cause of biliary tract disease and is the leading cause of inpatient admissions for gastrointestinal problems. The burden of GSD in the U.S. affects some 6.3 million men and 14.2 million women aged 20-74 years, marking it a most costly digestive disorder at an estimated \$6.5 billion annually.¹ Epidemiological studies have suggested a marked variation in overall prevalence between different populations.² In India too, the GSD is relatively common with an overall prevalence in the order of 10-20% and is predominantly a female disease.³ It has been recognized that gallstones and gallbladder cancer (GBC) are common in the gangetic belt comprising of Uttar Pradesh, Bihar, West Bengal, and Assam. States of South India do not have a high incidence of these diseases. Its occurrence has been found to be high in the adult population in the cities of Chandigarh and New Delhi in North India, which is interestingly seven times more frequent than in South India.⁴

It was observed that in United States white people of both males and females are being affected 50% more frequently than the black people. Mapuche Indians in Chile showed the highest incidence and mortality rate of GBC (12.5 in 100,000 in men and 27.5 in 100,000 in women) however, in Indians of New Mexico with an annual average rate of 9.0 in 100,000.⁵ Gallbladder

Carcinoma is the most common abdominal malignancy in India. According to recent data published by Indian Council of Medical Research, the highest incidence worldwide to the tune of in India, there is about 800,000 new cases of GBC (21.5 per 100,000) and 550,000 deaths per year. Northern India (Uttar Pradesh, Bihar, Orissa, West Bengal, and Assam) is a very high risk zone of GBC with incidence of 4.5 per 100,000 for men and 10.1 per 100,000 for women.⁶

Several risk factors had been identified for the development of GBC. These risk factors include female gender, ethnicity, geographical location, genetic predisposition, chronic infection, congenital developmental anomaly of biliary tract, etc. None of these risk factors provide any convincing fact for screening and early diagnosis of GBC.⁷ The most consistently implicated etiological factor in the development of GBC is gall stone disease (GSD) and chronic inflammation.⁸ Because bacterial colonization often accompanies chronic cholecystitis, bacteria have been proposed to play an important role in carcinogenesis.⁹ As the Gangetic Belt of India is a land of high incidence of both GSD and GBC, there may be some association between the two disease conditions.¹⁰ Thus, the aim of the present study was to study the epidemiological and pathological profile of GSD and GBC patients of Eastern India visiting tertiary care hospital of Kolkata.

METHOD

The study design is cross-sectional observational study. The study setting is in Department of General Surgery, Medical College Hospital, Kolkata, West-Bengal. This study was carried out in collaboration with Indian Statistical Institute, Kolkata. Study population is all patients admitted with suspicion of GSD or GBC in General Surgery Department fulfilling the eligibility criteria were included in the study. The inclusion criteria of the study were all patients who underwent laparoscopic or open or extended cholecystectomy with GSD or suspected GBC. The exclusion criteria are radiologically inoperable GBC and patients not willing for participating in study. The study duration is February 2018 to July 2019. Sample size and sampling technique: All patients admitted with suspicion of GSD or GBC during study period and fulfilling eligibility criteria were included in the study. Thus, 66 GSD patients and 24 GBC patients were studied.

Study procedure: Patients coming to OPD with signs and symptoms suggestive of GSD or GBC were admitted in the general surgery ward for further evaluation. They were clinically examined and investigated with transabdominal ultrasound initially and blood parameters like CA19-9, complete hemogram, liver function test, renal function test with electrolytes, blood coagulation profile. Then the GBC patients were subjected to further radiological investigations like MDCT abdomen to assess the tumor and nodal status. Operable patients were then taken for surgery and included in the study after written informed consent. Samples were collected from the patients after being histopathologically confirmed. Biopsy sample of the tumour tissue as well as normal adjacent tissue in case of GBC and GB wall tissue in case of GSD as well as clinic pathological data were collected with patient consent.

Ethical consideration: The study was approved by Institute Ethic Committee (IEC) from Medical College Hospital, Kolkata (Ref. no:MC/Kol/IEC/non-spons/08/01-2018 dated 03/02/2018) February 2018. Written informed consents were obtained from patients participating in the study after explaining the purpose of the study in local language. The confidentiality of the information were maintained during and after the study. The patients were given full freedom to withdraw at any point during the study. All provisions of the Declaration of Helsinki were followed in the study.

Data entry and analysis: Data was entered into Microsoft excel vs. 2016 (Microsoft, Redmond, WA, USA) and analyzed using STATA version 13 [Stata Corp LLC, 4905 Lakeway Drive, College Station, TX 77845, USA]. The patients in study were analyzed upon the age and sex distribution, presenting signs and symptoms like right upper quadrant pain, presence of lump, weight loss, jaundice, history of addictions, comorbidities, tumor grading, staging, survival after operation using descriptive statistics. Variables were summarized by proportions and 95% confidence intervals.

RESULTS

In this study, we studied 66 gall stone disease patients and 24 gall bladder cancer patients during the study period. The study sample consisted of 33.3% males and 66.7% females. The ratio of male : female was 1:2. We have found that 30 (45.4%) out of 66 patients were in the age group of 21-40 years, followed by 26 (39.4%) in the age group of 41-60 years. Most of the patients were non-smoker (84.8%) and non-alcoholic (97%). Nearly half of the patients (48.5%) were having complaints for less than 6 months duration (Table 1).

Table 1. Socio-demographic characteristics of gall stone disease (GSD) patients (n = 66)

Variable	n (%)
Gender	
Male	22 (33.3)
Female	44 (66.7)
Age (year)	
21-40	30 (45.4)
41-60	26 (39.4)
61-80	10 (15.2)
Smoking habit	
Smoking	10 (15.2)
Non-smoking	56 (84.8)
Alcohol consumption	
Alcoholic	2 (3)
Non-alcoholic	64 (97)
Diabetes	
Yes	11 (16.7)
No	55 (83.3)
Duration of complaints	
< 6 months	32 (48.5)
6 months-1 year	19 (28.8)
1 year-18 months	7 (10.6)
> 18 months	8 (12.1)

Out of 66 GSD patients, majority (71.2%) of the patients had normal gall bladder anatomy. Majority of patient (59.1%) had cholesterol type of gall stone (Table 2).

Table 2. Distribution of gallstone disease (GSD) patients according to pathological features (n = 66)

Variable	n (%)
Gallbladder wall anatomy	
Normal	47 (71.2)
Abnormal	19 (28.8)
Cholesterosis	
Present	29 (44)
Absent	37 (56)
Types of stones	
Cholesterol	39 (59.1)
Mixed	16 (24.2)
Pigmented	11 (16.8)
No of stones	
One stone	4 (6.0)
Two stones	24 (36.4)
Multiple stones	38 (57.6)

Out of 24 gallbladder cancer patients, most of them (87.5%) were female and more than half (58.3%) belonged to 41-60 years of age group. In our study, we had 29% cases of poorly differentiated adenocarcinoma and 33% cases of carcinoma other than adenocarcinoma. In our study population, we found only 13% cases presenting in stage I disease and >50% cases in Stage III & IV, suggesting that GBC is a late presenting disease with a poor prognosis (Table 3 & Figure 1).

Table 3. Distribution of gallbladder cancer (GBC) patients clinico-demographic characteristics (n = 24)

Variable	n (%)
Gender	
Male	3(12.5)
Female	21(87.5)
Age (year)	
21-40	2 (8.3)
41-60	14 (58.3)
61-80	8(33.3)
Stage of cancer	
I	6 (25)
II	8 (33.3)
III B	7 (29.2)
IV B	3 (12.5)
Grade of cancer	
Well differentiated adenocarcinoma	5 (20.8)
Moderately differentiated adenocarcinoma	4 (16.7)
Poorly differentiated adenocarcinoma	7 (29.2)
Others	8 (33.3)

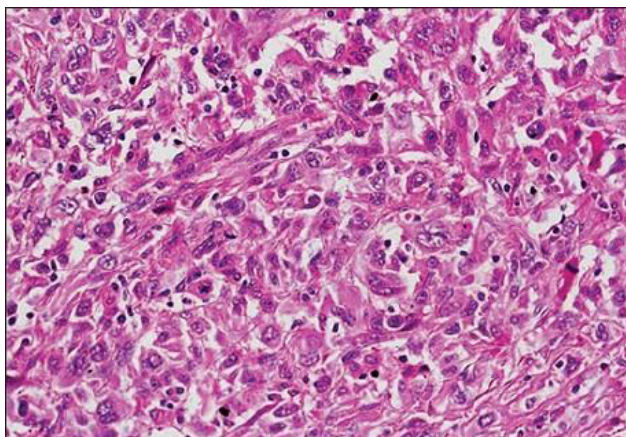


Figure 1. Histopathological picture of gallbladder adenocarcinoma (GBC)

DISCUSSION

The purpose of this study was to study the epidemiological and pathological characteristics of patients undergoing surgery for GSD or GBC. In this study 66 patients of operated gallstone disease and 24 patients of operated GBC were included between January 2018 and July 2019. In our study, gallstone disease had a female preponderance with female-male ratio of 2:1, which is similar to findings reported by Pradhan SB et al, Palermo M et al, Palapatti A et al, in which women are almost twice as likely as men to form stones; the gap narrows following menopause.^{11,12,13} In this study, majority were non-smoker (84.8%) and non-alcoholic (97%). Nearly half of the patients (48.5%) were having complaints for less than 6 months duration. Our findings were supported by Joshi HN et al in their study done in Nepal.¹⁴ We found that out of 66 GSD patients, majority (71.2%) of the patients had normal gall bladder anatomy. Majority of patient (59.1%) had cholesterol type of gall stone and nearly half (57.6%) were having multiple gall stones. Similarly, Rao KS et al in their study found that 63% patients had cholesterol type stone and 80% had multiple gall stones.³ It is a known fact that diabetic mellitus and insulin resistance are predisposing risk factors for development of gallstone disease. In our study, we got 16.7% patients to be known diabetic and were on treatment for the same.

In our study, gallbladder carcinoma also showed female preponderance with female-male ratio of 7:1, which is more than the worldwide population that have been reported of approximately 3:1 female-male ratio.⁷ This difference may be due to small sample size of the present study. The incidence of GBC increases with age and reaches a peak by seventh decade. In our study GBC was most commonly found in the 41-60 years age group and approximately 70% of cases were above 50 years of age. The mean age was 54 years which was similar to study done in Uttarakhand by Gupta A et al.¹⁰ In our evaluation of stages of GBC; 33% of the patients (8 out of 24 patients) were in stage II, while 29% (7 out of 24 patients) were having stage IIIB. Only 25% (6 out of 24 patients) presented in stage I disease, suggesting GBC to be a disease of advanced presentation. Whereas, Gupta A et al and Rawla P et al in their studies reported that majority of patients belonged to advanced stage (stage III & IV) of cancer.^{10,15} This difference may be due to variation in geographical distribution or difference in sample size of the studies. Over 80% of GBC are adenocarcinomas arising from fundus (60%), followed

by body and neck. In our study, we found 71% of the GBC of adenocarcinoma variety, corroborating with the other studies.^{16,17}

The strength of our study was we studied the staging as well as histopathological features of GSD and GBC patients. Our study has some inherent limitations like small sample size and geographically limited catchment area of the patients enrolled. Another limitation was lack of application of statistical tests in view of small sample size of the study.

CONCLUSION

The present hospital-based study showed a higher percentage of both GSD and GBC is associated with female gender. Majority of GSD patients belonged to 21-40 years of age group, whereas GBC is found to be a disease of post forty age group. Majority of GSD patients had cholesterol type of gall stone and had multiple gall stones. Majority of gallbladder carcinoma pathologically were well differentiated adenocarcinoma and around one-third patients belonged to advanced stage of cancer. A broader population-based study, taking into consideration multiple other risk factors for GSD and GBC is warranted to provide more accurate information regarding the predominant regional factors associated with GSD and GBC.

Conflict of interest: None to declare

Source of funding: Nil

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