



Gallbladder cancer in Eastern Province of Saudi Arabia: A retrospective cohort study



Mohammed Yousef Aldossary^{a,*}, Amal Ali Alayed^a, Samir S. Amr^b, Shareef Alqahtani^a, Mamdouh Alnahawi^a, Mohammed Saad Alqahtani^a

^a Department of General Surgery, Hepatobiliary Unit, King Fahad Specialist Hospital, Dammam, Saudi Arabia

^b Department of Pathology and Laboratory Medicine, King Fahad Specialist Hospital, Dammam, Saudi Arabia

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ABSTRACT

Background: There is paucity in the literature regarding gallbladder cancer in Saudi Arabia, possibly because it is not among the top 10 cancers diagnosed nationwide according to the Saudi Cancer Registry. Moreover, national or regional data on gallbladder cancer in Saudi Arabia have not been analyzed. The purpose of this study was to describe the presentation, disease stage, histology, and survival rates for gallbladder cancer in Saudi patients at a single institution between January 1, 2010 and December 31, 2017.

Materials and methods: This was a retrospective study of 76 patients who presented to our hospital between January 1, 2010 and December 31, 2017, with established diagnosis of gallbladder carcinoma. The diagnosis was made either histopathologically following simple laparoscopic cholecystectomy or biopsy from metastatic liver lesion in patients with gallbladder mass, or the high suspicion of gallbladder carcinoma based on incidental radiological findings. Presentation, disease stage, histology, and treatment modalities were analyzed using descriptive statistics and frequency distributions. Survival rates were analyzed and presented using Kaplan-Meier curves.

Results: Based on initial analyses the disease was more frequent among women (62.0%) than men (39.0%). Surgical resection was attempted in 40.8% patients. The average age at presentation and diagnosis of gallbladder carcinoma was 62.4 years. The disease had two peaks, one at 51.0 years and the other between 66.0 and 70.0 years. The median survival time for the overall at-risk patients was only 1.0 year, while for stage IVB patients was 7.2 months. Adenocarcinoma not otherwise specified (NOS) was the most common histopathology type (75.0%), with most patients presenting with stage IVB disease (75.0%). Gallbladder carcinoma was incidentally detected in 42.1%, including three cases (3.9%) diagnosed at our hospital.

Conclusions: Gallbladder cancer is a rare type of cancer in Saudi Arabia, and most patients are treated surgically, despite being mostly diagnosed at the advanced stage of the disease.

1. Introduction

Based on autopsy studies, gallbladder cancer (GBC)¹ is highly common among the biliary tract cancers, accounting for about 80.0%–90.0% of the biliary tract cancers globally, and is the third most common among the gastrointestinal cancers [1,2], with high prevalence in South America and South-east Asia [1]. However, there is significant regional and ethnic variability in the prevalence of GBC, with much lower prevalence in Europe and India [2]. In the Middle East, GBC is a rare neoplasm. It does not rank among the top 10 cancers in the Kingdom of Saudi Arabia (KSA), according to the Saudi Cancer Registry

[3].

The silent nature of GBC makes it difficult to diagnose. Besides, most symptoms (including abdominal pain, fever, nausea, and jaundice) can be attributed to other more common conditions, such as hepatitis, stones of the biliary tract, and pancreatitis [4]. GBC typically has a very poor prognosis with a 5-year survival rate of 29.0% for stage II and less than 2.0% for stage IVB [5]. The low survival rate is usually because of late presentation in most patients, with close to 37.0% of patients presenting with advanced stage disease (IVB) due to unspecific early symptoms [6].

The regional and ethnic variability in GBC prevalence in Saudi

* Corresponding author. Department of General Surgery, Hepatobiliary unit, Building 7, 2nd floor, King Fahad Specialist Hospital, Dammam, Saudi Arabia.
E-mail address: Dr.Mohd.Aldossary@gmail.com (M.Y. Aldossary).

¹ List of abbreviations: GBC, gallbladder cancer; KSA, Kingdom of Saudi Arabia; AJCC, the American Joint Committee on cancer.

Arabia is a potential cause for the continuing dearth in literature in this topic. Further, national and regional data on GBC in Saudi Arabia have not been analyzed. Even though it is not among the more prevalent cancer types, the difficulty in diagnosing GBC presents the need to understand this disease in the context of the Saudi population.

Being a referral hospital, patients either diagnosed or suspected to have GBC are referred to our hospital for highly advanced treatment. The purpose of this study was to describe the characteristics of GBC in Saudi patients at a single institution and provide insight into their clinical profile, disease stage, histology, and survival rates.

2. Materials and methods

2.1. Patients

Data on gallbladder carcinoma patients, treated at our hospital between January 1, 2010 and December 31, 2017 were obtained from the institution's database. Data on patient characteristics including age, presence of gallstones, diabetes, and hypertension were collected. Stage at diagnosis and other cancer characteristics were also included. The 7th edition of the American Joint Committee on cancer (AJCC) staging system was used for clinical and/or surgical (pathological) staging. In patients with incidental gallbladder carcinoma, pTNM values were based on the first pathological report. Patient treatment strategies were decided by a team of medical specialists and included surgical removal, chemotherapy, or palliative care if other options were not feasible. The study was approved by the Institutional Review Board of our hospital. We report the results of this analysis in accordance with the STROCCS reporting statements [7].

2.2. Study design

Closed cohort and case study designs were employed. The occurrence of death among the same group of patients at various points of time over the 7-year study interval was reviewed, and the end point occurrence was correlated with patients' demographic characteristics, co-morbidities, operative procedures, and related factors.

2.3. Statistical analysis

Univariate frequency tables and charts were used alongside cross-tabulations to understand the presentations of various cancer-related symptoms and outcomes as well as the administration of various treatment modalities. Survival analysis was performed using the Kaplan-Meier method to assess overall survival rate, and determine the effectiveness of surgical treatment in survival. The log-rank Chi square test was used to compare relative survival rates between patients who underwent a resection and those who did not undergo any procedure. The survival rate was defined as the percentage of patients still alive at the end of the study period of 5-year after censoring had been accounted for.

3. Results

3.1. Patient characteristics

A total of 76 patients with GBC were included in the study. The average age at presentation and diagnosis was 62.4 years (range 38–82 years). The disease was most prevalent at 55 years of age and the most patients with GBC were 66–70 years old (Table 1). Further, most patients with GBC were female (n = 47, 62.0%). Only three patients (3.9%) were diagnosed at our hospital, all being incidental cases. The remainder of cases were referrals from other hospitals either upon suspicion of GBC (n = 44, 57.9%) or were incidental cases sent for further investigation and management (n = 29, 38.2%) (Table 2).

Using the obesity classifications of the Center of Disease and

Table 1
Descriptive statistics for patient data.

Descriptive statistic	BMI	Age at diagnosis
Mean	29.3	62.4
Standard Error	1.1	1.3
Median	27.4	62.5
Mode	24.5	55
Standard Deviation	9.5	10.9
Kurtosis	4.2	−0.6
Skewness	1.5	−0.2
Range	57	44
Minimum	14.7	38
Maximum	71.7	82
Count	76	76
Confidence Level (95.0%)	2.2	2.5

Control, 38.7% of the patients were either underweight or had normal weight, with 21.0% being overweight and 42.1% classified as obese. The body mass index (BMI) of the patients ranged between 14.7 kg/m², and 71.7 kg/m² with a mean of 29.3 kg/m². Overall 50.0% (n = 38) of patients were diabetic and 50% suffered hypertension. Most patients (84.0%) were non-smokers.

3.2. Clinicopathologic findings

The chief complaint by most patients (n = 64, 84.0%) was right upper quadrant pain. Only 3.0% of patients reported both right upper quadrant and epigastric pain as their first symptom. The primary clinical diagnosis was biliary colic in 43.4% of patients followed by acute cholecystitis (31.6%). 51.3% (n = 39) of the patients presented with jaundice. Gallstones were present in 75.0% (n = 57) patients of which 57.9% had multiple small gallstones less than 1.0 cm in size (57.9%) (Table 2).

On imaging, 50.0% of the incidental cases were of metastatic gallbladder cancer. However, 36.8% of patients showed no pre-op incidental findings except gallstones. Table 2 gives a complete list of imaging findings in patients enrolled in this study.

The tumor was considered inoperable in 42.1% (n = 32) of patients since metastatic gallbladder cancer was found incidentally on imaging; hence, no definite diagnosis was reached. GBC was confirmed by frozen biopsy in 11.8% of patients intraoperatively, while 9.2% of patients had metastatic GBC. Table 2 shows the complete list of final diagnoses for the 76 enrolled patients. Lymphadenectomy during surgery was performed in only 24 patients. Bile duct excision and port site excision were not performed in most patients either due to unresectable metastatic disease, the presence of gallbladder mass or incidental finding of GBC after laparoscopic cholecystectomy with evidence of metastatic disease (Table 2).

The cancer was pathologically diagnosed in only 39.0% of patients. In the other 61.0%, clinical staging was employed due to unresectability. Overall most patients were classified as stage IVB, based on the AJCC staging system for gallbladder carcinoma (Table 2). Only 3.9% of the patients were diagnosed at stage I of the disease. Adenocarcinoma not otherwise specified (NOS) was the most common histopathology type (75.0%) followed by papillary adenocarcinoma (9.2%) and mucinous adenocarcinoma (3.9%). Carcinosarcoma was the pathological diagnosis in 3.9% of the patients.

As presented in detail in Table 2, 10.5% of the patients suffered recurrence of the cancer after surgical resection with disease-free margin. Fifty percent of the recurrent cases were diagnosed as stage II disease, while the remaining 50.0% as stage IVB cancer. No recurrence was reported in 18.4% of patients, while 71.1% of patients were either diagnosed with unresectable tumor or became censored.

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