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Original Article

CLINICOPATHOLOGICAL FEATURES AND OUTCOMES OF GALLBLADDER CANCER IN SOUTHERN PAKISTAN

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ABSTRACT:

Background: Gallbladder (GB) cancer is not an uncommon cancer, however, has a geographical variation in incidence. Data on the presenting features and outcome are sparse from our part of the world. Hence, a retrospective analysis was undertaken to study the features.

Patients and Methods: Adult patients diagnosed to have carcinoma of GB and admitted to two different University Hospitals in southern Pakistan between Nov 1998 and Sept 2003 were the subjects of the study.

Results: One-hundred and eleven patients were diagnosed to have GB cancer, however, only 59 had biopsy-proven disease, and are the subjects of the study.. There were 40 females and 19 males. The mean age was 53 ± 11.3 years. Fifty-five patients had adenocarcinoma and 4 had squamous cell carcinoma. Liver functions were deranged in a significant majority of patients; 34% had an SGPT more than 2 times the upper limit of the normal, 65% patients presented with an elevated serum bilirubin level, 80% presented with a high alkaline phosphatase, and 96% had a low albumin. 25% patients presented with acute renal failure. The median survival for the entire group was 10.2 months.

Conclusion: Patients with GB carcinoma present with advanced stage disease. A vast majority of patients had abnormal liver or renal functions at the time of diagnosis precluding meaningful palliative treatment

Key words: Gall bladder cancer, advanced disease, Prognostic factors

INTRODUCTION:

Gall bladder (GB) cancer is not an uncommon cancer and accounts for 3.6% of all cancers in females in Pakistan[1,2] The only curative treatment is complete resection of the gall bladder along with the tumor, however, most of the patients present with advanced stage disease[3,4]. The treatment at this stage is either palliative chemotherapy or best supportive care. The outcomes are dismal and the median survival is 4-6 months. Data on the presenting features and outcome of such cases are sparse from our part of the world[5-8]. The purpose of this study was to report the clinicopathological features and outcomes of patients who present with GB cancer in southern part of Pakistan.

PATIENTS AND METHODS:

A retrospective analysis was undertaken to study the clinico-pathological features and outcomes of consecutive patients presenting with gall bladder cancer. Adult patients diagnosed to have carcinoma of GB and admitted to one of the two university hospitals in south of Pakistan over a 5-year period were the subjects of the study. The information was extracted on to pre-designed questionnaires, and the data were analyzed using SPSS. The results on the laboratory parameters are expressed as mean ± S.D. The method of Kaplan and Meier was used to estimate the survival.

RESULTS:

A total of 111 records were available, of whom 59 had a biopsy-proven diagnosis and are the subjects of this study. There were 40 females and 19 males. The mean age was 53 ± 11.3 years. Clinical presentation was as follows: pain in the right hypochondrium 68%, jaundice 60%, nausea 45%, anorexia 38%, encephalopathy 16%. (Please see table 1 for details of presenting symptoms and signs). Laboratory features at presentation were as follows: Hemoglobin 11.07 gm/dl, TLC 14.9 x 10^9/L, platelets 322 x 10^9/l, creatinine 1.3 mg/dl, SGPT 74.9 IU/L, SGOT 102.7 IU/L, alkaline phosphate 409 IU/L, bilirubin 9.8 mg/dl, LDH 675 IU/L, albumin 2.3 gm/dl. (Table 2).

The mode of tissue diagnosis was either using a fine needle aspiration, n = 23; core biopsy, n = 3; or open biopsy/excision, n = 33). 55 had adenocarcinoma and 4 had squamous cell carcinoma. Survival data were available for all patients. The overall survival was calculated from the time of diagnosis to either death, or the last follow up. The median survival for the entire group was 10.2 months (Figure 1).

DISCUSSION:

Gallbladder cancer is the most common malignancy of the biliary tract. Regional variations occur in incidence around the globe[9]. For example, in Pakistan, it is the most common cancer of gastrointestinal origin in women. According to a study conducted in the southern city of Karachi, gall bladder cancer accounts for 7.8% of all cancers in females[10]. The incidence is also high in some parts of India[6] Gallstones seem to be an important risk factor[11]. The majority of patients have a history of cholelithiasis[12,13]. Ultrasound is usually the initial radiological procedure and helps to analyze in distinguishing between gall bladder cancer from benign conditions of the gall bladder[14].

The majority of reports suggest that the gallbladder carcinoma is two to six times more common in women and the incidence peaks in the seventh decade of life.

We compared demographic features of our patients with other published reports. In our series the female to male ratio was approximately 2:1 and the mean age at the time of diagnosis was 53 years. The age and sex distributions are very similar to the local data as well as to the patients from other developing countries [15-17] However, they were younger than the patients seen in North America and the Europe, where the incidence peaks in the seventh decade of life[18].

TABLE 1
SYMPTOMS AND SIGNS AT PRESENTATION

Symptoms		Signs	
• Pain in RHC	68%	Jaundice	62%%
• Jaundice	60%	Mass in RHC	48%
• Nausea	45%	Tenderness	42%
• Anorexia	38%	Pallor	37%
• Encephalopathy	16%		

TABLE 2
SELECTED LABORATORY FEATURES AT PRESENTATION

Haemoglobin	11.07 gm/dl	(6.8 – 14.2)	<10 gm/dl	25%
Total Leukocyte Count	14.9 x 10^9/l	(5.5 – 74)	>20 x 10^9/l	18%
Platelets	322 x 10^9/l	(66 – 592)	>400 x 10^9/l	20%
Serum Creatinine	1.29 mg/dl	(0.5 – 8.8)	>1.1 mg/dl	25%
Serum Bilirubin	9.83 mg/dl	(0.3 – 30.3)	>1 mg/dl	65%
SGPT	74.9 IU/L	(8-450)	>2 xULN	34%
SGOT	102.67 IU/L	(23 – 223)	>2 x ULN	42%
Alkaline Phosphatase	409 IU/L	(60 – 1691)	>ULN	80%
Serum Lactate Dehydrogenase	675 IU/L	(upto 548)	> ULN	40%
Serum Total Protein	6.65 gm/dl	(3.9 – 8.5)	< 5.0 gm/dl	30%
Serum Albumin	2.33 gm/dl	(1.1-3.6)	< 3.5 gm/dl	96%

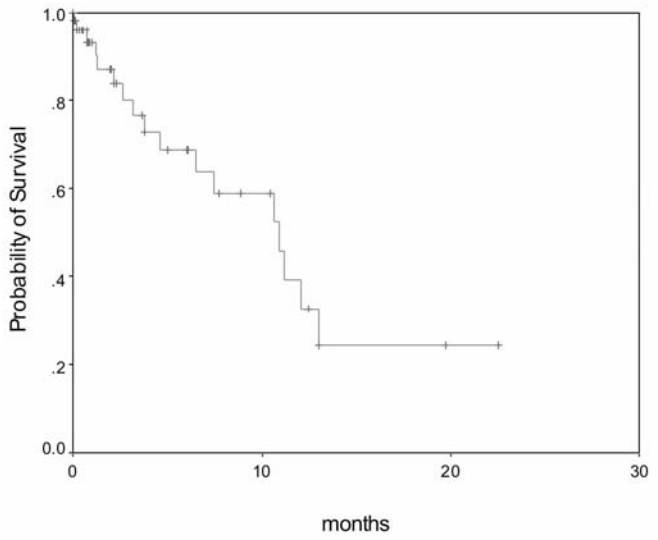
The clinical features of our patients are similar to other published reports. The most common presenting symptom is abdominal pain. Almost half of the patients had jaundice at the time of diagnosis and many had nausea, anorexia, and weight loss[5,13,15]

Between 10–20% of gallbladder cancers are discovered incidentally on pathological examination of the gallbladders removed for cholelithiasis. Although advanced cases can be diagnosed on ultrasonography or computed tomography (CT) scans, there are no specific tests available to make an early diagnosis. Hence, the majority of patients present with locally advanced or metastatic disease and only 10-30% of the tumors are surgically resectable at the time of presentation[3]. In our series too, vast majority of patients had distant metastasis at the time of diagnosis.

Fifty-two out of the total of the suspected 111 patients during

FIGURE 1

OVERALL SURVIVAL IN MONTHS



the period of study did not have the histo-pathological diagnosis and were excluded from the analysis. These patients had radiological evidence of either a mass or metastases indicating the advanced nature of the disease. The patients presented either in a state of poor performance status, or hepatic or renal failure, either preventing an invasive intervention by the treating physician, or such a procedure could not be performed because of patient-refusal. A separate analysis showed that significantly more patients who were encephalopathic, had obstructive jaundice, or had tenderness in the right hypochondrium did not have a tissue diagnosis.

Despite significant advances in surgical techniques, and better supportive care, the prognosis of patients with gallbladder cancer has not improved. The disease carries an extremely poor prognosis and the median survival of patients with unresectable disease is approximately 6 months or less. Chemotherapy and radiation are purely palliative, and a significant number of patients are not candidates by the time the diagnosis is established. In our series, the overall median survival was 10.2 months, which is consistent with what has been reported from the area and Japan[7,19].

There are several limitations of this study. First of all, owing to the retrospective nature of data collection, complete data including long-term survival data were not available of all the patients. However, survival data up until the last follow up were available on all patients, and the outcomes were not substantially different from what has been reported from the region. Secondly, data on tumor staging is not available. Several patients were diagnosed on abdominal CT scans and/or ultrasound scans, and a complete staging workup with a Chest X-ray and/or a CT scan of the chest was not available. However, almost all the patients presented with either locally advanced or metastatic disease within the abdomen, as evidenced by the CT scan of the abdomen or by per-operative findings. Thirdly, the data on the tumor markers, especially CA 19.9 are not reported. The test was not available for the better part of the study in the laboratories of the two hospitals, and was not routinely performed. CA 19.9 is a glycopeptide, which is not very specific for the malignancies of pancreatico-biliary tract. If elevated, it can be used to assess response to treatment and/or progression of the disease. However, in this particular study, we have not attempted to study the response to treatment. Only a very few patient received systemic palliative treatment.

In conclusion, carcinoma of the gallbladder has remained a uniformly fatal neoplasm. The reasons being: late presentation, early spread, a high propensity to seed the peritoneal surfaces and a lack of effective systemic therapy. Like elsewhere, in Pakistan, patients with GB carcinoma present at an advanced stage of disease.

CONCLUSION:

Patients with GB carcinoma present with advanced stage disease. A vast majority of patients had abnormal liver or renal functions at the time of diagnosis precluding meaningful palliative treatment

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