Epidemiology of Gallbladder Cancer in North India - a Radiological Descriptive Study

Shivi Mohini[1], Akash Agarwal[2]

ABSTRACT

Introduction: Gallbladder cancer (GBC) is one of the commonest cancers in North India. Despite the high incidence, very little data is available of the staging distribution of GBC in this region. We aimed at getting a snapshot of the distribution of GBC at a single high volume centre.

Material and Methods: One hundred and forty seven patients who were evaluated between 1st July 2017 and 31st October 2018 for staging of GBC, were included in this study. Radiological staging was done according to the AJCC TNM 8th edition using a standardized reporting format.

Results: Majority of patients were females (70%). Fundus of GB was the most common site of tumor (39.4%) and liver (76.8%) was the most common adjacent organ involved as well as the most common site of metastatic disease (36%). Only 42 (28.5%) patients had non-metastatic disease. Biliary obstruction was present in 63 (42.8%) patients, with majority being type 2 hilar blocks (65%). Loco-regional nodal involvement was present in 87.1% patients, station 12 nodal involvement being most common (76.1%).

Conclusion: This is the first study to describe the distribution of GBC stages in the high incidence region of North India. This should provide information for future research and funding for GBC related research.

Keywords: Epidemiology, Gallbladder Cancer, Radiological Descriptive Study

INTRODUCTION

Gallbladder cancer (GBC) is one of the common cancers of the gastrointestinal tract. It is also one of the commonest cancers in females in North India. A large number of patients with GBC present with advanced disease, with very poor prognosis.[1] The primary reason for this is the lack of symptoms in the early stages of the disease. Even when present, the symptoms are non-specific and can be confused with other benign conditions.

Like other cancers, staging of GBC is by clinical examination and radiology. An ultrasound of the abdomen is generally the first radiological investigation. However, the most frequently used and informative imaging is a triphasic CT scan of the abdomen and pelvis. This provides both the local extent of disease as well as its distant spread.[2] MRI and PET CT scans are infrequently used; generally limited in cases of equivocal findings on CT scans.[3]

Despite North India having a huge burden of GBC, there is no study till date that describes the stage distribution of GBC in this geographic area. This baseline data is important to establish a picture of the stage distribution of GBC. This will be useful in planning future research, both for investigators and funding agencies, so that most pertinent problems are addressed on priority. There is a lack of local/regional cancer databases and collecting data from individual departments and hospitals is neither feasible nor is it accurate. At present, getting staging information from radiology services presents the best, though imperfect, alternative. This study was an attempt to establish the distribution of GBC at a single high volume center.

MATERIAL AND METHODS

We reviewed the scans of patients of suspected gallbladder cancer, which were performed, between 1st July 2017 and 31st October 2018, in the radiology services of SRMS Functional Imaging and Medical Centre. In all, 147 patients were identified for our study.

All patients underwent a triphasic contrast enhanced CT (CECT) scan of the abdomen and pelvis. Additional thoracic imaging was done, if clinically indicated.

Triple-phase CT was performed on a PET-CT scanner (Biograph Mct Flow 64-3R, Siemens). Initial 10 mm contiguous, noncontrast axial sections of the whole abdomen were obtained. 1.5ml/kg body weight of nonionic iodinated contrast was then injected at a rate of 5 mL/sec using a pressure injector.

Scanning was performed using a pitch of 1.5:1, a scanning time of 0.5 sec/rotation, table speed of 7.5 mm/rotation, 250-300 mAs, and 120 kVp. Using a bolus-triggered technique by placing the cursor in the aorta at L1/L2 level and setting the threshold at 50 H, early hepatic artery phase images were obtained in a craniocaudal direction. Late arterial and porto-venous phase images were obtained in a caudocranial direction with a scan delay of 40 sec after initiation of contrast injection. Images were acquired in both phases in a single breath-hold with a slice thickness of 2.5 mm and a reconstruction interval of 1.0 mm. The rest of the abdomen and pelvis were then scanned in the axial mode by taking

[1]Consultant, Department of Radiodiagnosis, SRMS Functional Imaging and Diagnostic Centre, Gomti Nagar, Lucknow, [2]Associate Professor, Dept. of Surg Oncology, Dr. RMLIMS, Lucknow, India

Corresponding author: Dr. Akash Agarwal, Room No 31, Department of Surgical Oncology, 2nd Floor, Academic Block, Dr. RML Institute of Medical Sciences, Vibhuti Khand, Gomti Nagar, Lucknow-226010, India

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10-mm-thick sections.

All cases were reported according to a standardized synoptic reporting format, which allowed clinical staging according to the American Joint Committee on Cancer (AJCC) 8th edition TNM staging criteria.[4] Apart from the lesion in the gallbladder, the planes of the lesion with adjacent liver, pylorus and 1st part of duodenum and colon were evaluated for T staging.

For nodal staging, nodes along the hepatoduodenal ligament (station 12), along common hepatic a. (station 8) and the retropancreatic nodes (station 13) were evaluated. Enhancing nodes with short axis diameter greater than 10mm, loss of fatty hilum, round> oval were considered to be involved.

For evaluation of metastatic disease, whole of the abdomen was evaluated with emphasis to the most common sites: liver, interaortocaval nodes (level 16b1), peritoneal, mesenteric and omental nodules, and the presence of ascites.

RESULTS

In the period 1st July 2017 to 31st October 2018, a total of 147 triphasic CECT scans were performed for staging of suspected GBC. All patient scans were reported according to a standardized reporting format that included comprehensive, detailed and objective information for staging.

Of the 147 patients, 104 were females and 43 were males. The male to female ratio was 1:2.41. The median age of the patients was 55 years (range: 28-81 years).

We evaluated the location of the disease in gallbladder. The most common site of disease was the fundus of GB. The disease was present in 34 (23.1%) patients only in the fundus and in 24 (16.3%) patients, in the fundus and body of GB. Thirty-two (21%) patients had disease arising from the neck of GB, 18 (12.2%) patients had disease arising from body of GB and the GB was diffusely involved in 31 (21%) patients. Ten patients (6.8%) were those who were evaluated post-simple cholecystectomy for incidental GBC.

Disease limited to the gallbladder was seen in only 25 (17.0%) patients. Contiguous liver involvement was the most common adjacent organ involvement and was seen in 113 (76.8%) cases. However, isolated liver involvement was seen in only 27 patients. Colonic involvement/infiltration was seen in 43 (29.2%) cases, with isolated colonic involvement seen in only 2 patients. Similarly, distal stomach and 1st part of duodenum involvement was seen in 61 (41.4%) patients, with only 2 patients having isolated duodenal involvement. Biliary tree obstruction was seen in 63 (42.8%) patients, with only 5 patients having isolated biliary obstruction, without involvement of any other adjacent structures. A detailed description of the adjacent organ involvement is shown in Table 1.

Biliary obstruction was present in 63 patients. We used the Bismuth Corelette classification of hilar blocks to stratify blocks. Eighteen (12.2%) patients had type 1 block, 41 (65%) patients had type 2 blocks, 3 (4.7%) patients had a type 3a block and 1 (1.5%) patient has an isolated block in the left biliary system. Of the patients with type 1 block, 5 were benign- 4 due to CBD calculus disease, 1 patient had a lower end common bile duct benign biliary stricture. Thirteen patients had malignant type 1 block.

			Number	%
T stage	T1-2		25	17.0
	T3	Liver	27	18.3
		Duodenum	2	1.3
		Colon	2	1.3
		Biliary tract	5	3.4
		Liver + 1 adj	40	27.2
	T4		46	31.2
N stage	N0		19	12.9
	N1	Station 12	23	15.6
		Station 8	4	2.7
		Station 13	5	3.4
		Station 12+8	29	19.7
		Station 12+13	9	6.1
		Station 8+13	2	1.3
		All	51	34.6
M stage	M0		42	28.5
	M1	Liver only	18	12.2
		Station 16b1 only	20	13.6
		Omentum only	4	2.7
		Peritoneum only	5	3.4
		Ascites	6	4.0
		2 sites	30	20.4
		=>3 sites	22	14.9

Table-1: TNM distribution of GBC

Stage	T stage	N stage	M stage	No (%)
I	T1	N0	M0	4 (2.7)
IIA	T2a	N0	M0	
IIB	T2b	N0	M0	
IIIA	T3	N0	M0	5 (3.4)
IIIB	T1-3	N1	M0	24 (16.3)
IVA	T4	N0-1	M0	9 (6.1)
IVB	any T	N2	M0	105
	any T	any N	M1	(71.4)

Table-2: TNM staging of GBC

Type of block		Number	%
I		18	28.5
	Benign	5	7.9
	Malignant	13	20.6
II		41	65.0
III		3	4.7
Isolated Left block		1	1.5

Table-3: Distribution of biliary obstruction according to Bismith Corelette classification

Regional nodal disease was evaluated in nodal stations 8, 12 and 13. No regional lymphadenopathy was identified in 19 (12.9%) patients. All three stations, 8, 12 and 13, were involved in 51 (34.6%) patients.

Significant nodes in station 12 (76.1%) were identified in 112 patients. Of these, 23 patients had nodal involvement only in the HDL. Station 13 nodes were involved in 67 (45.5%) patients, of which this was the only station of involved nodes in 5 patients. Similarly, station 8 nodes were involved in 86

(58.5%) patients. However, this was the only site of regional nodal disease in 4 patients. The various regional nodal distributions are shown in table 1.

Forty-two patients (28.5%) had non-metastatic disease. Seventy-one percent (105) patients had metastatic disease. Of these, 53(36%) patients had liver metastases. Omental nodules were present in 26 (17.6%) patients, while peritoneal spread was present in 31 (21%). Ascites was present in 27 (18.3%) patients and station 16b1 nodes were present in 50 patients. Five patients had lung lesions and 6 had adnexal lesions, which were suspicious for metastases.

Single site of metastasis was found in 53 (36%) patients. Thirty patients (22.4%) had metastasis to 2 sub-sites while 22 (14.9%) patients had metastases to more than 2 sites. The distribution of sites of metastatic disease is shown in table 1.

The stage distribution according to the AJCC TNM system is shown in table 2. As can be seen, the vast majority of patients had advanced or metastatic disease.

DISCUSSION

Gallbladder cancer is an uncommon cancer in the West, but has a high incidence in North India.[5] Due to the low incidence in the developed world, there is scarcity of data, which elaborates on the different stages on GBC, especially from high incidence region.

Imaging by CT scanning is the most important step in the workup for management of GBC. Triphasic CT scan has been shown to have a high sensitivity and specificity for staging GBC and deciding resectibility as compared to ultrasound examination.[2] The role of MRI of the liver is limited to defining doubtful lesions in the liver and for patients with biliary tree involvement.[3] The role of PET-CT is still undefined, with evidence to support its use in incidental GBC. However, its use is limited by low rate of detection of occult metastases.[6]

There was a female preponderance in our patients. This is consistent with the gender distribution across most studies of GBC. The median age of these patients was 55 years, which is similar to previous publications, which show that the sixth decade is the most common age group for GBC.

The fundus and body were the most common sites of disease in the gallbladder as described in literature.[7] Our data showed a greater than reported incidence of tumor arising from the neck of GB (21% versus 10% in literature).[7] Also almost a third of our patients showed diffuse involvement of GB wall abnormality. This is peculiar and may be responsible for a greater proportion of patients presenting with advanced locoregional disease. Liver invasion was the most common adjacent visceral organ invasion. Duodenum and colon were the next most commonly involved adjacent organs.

Biliary tree involvement clinically evident as obstructive jaundice, has been shown to be associated with poor prognosis, largely owing to the unresectable nature of this involvement. Some biliary system involvement, however, may be due to benign conditions- calculi or benign strictures. We found that 8% of our patients had benign biliary block, all of them presenting with a block distal to the biliary confluence. Of the malignant type 1 biliary blocks, the cause was compression/infiltration by GB mass in 6(46%) patients and due to nodal disease in 7 (54%) patients.

Most biliary blocks (71%), were found to involve the biliary confluence and causing the separation of the left and right systems or were also involving the right secondary confluence as well. The majority was due to GB mass (40 patients) rather than nodal involvement, which was responsible in only 4 patients. These patients carry a higher risk of unresectability, and would be candidates for percutaneous approach for biliary decompression.

Thus, it is important to evaluate the level and cause of biliary block as well as the cause of obstructive jaundice. Merely, the presence of jaundice may not necessarily mean malignant infiltration and unresectability.

Nodal disease is one of the most important prognostic criteria in GBC. Nodal disease evaluation must include imaging of nodal stations 8 (common hepatic a.), 12 (hepatoduodenal) and 13 (retropancreatic nodes) for local staging and other non regional nodes- mesenteric interaortocaval (16b1) and para-aortic nodes. Though the detection of nodal involvement may not be very accurate on CT scan, it remains the standard modality for diagnosis of nodal spread.[8]

Our data shows that a more than three fourth of patients had loco-regional nodal involvement. The most common involvement was of the first level of drainage, the nodes along the hepatoduodenal ligament (76%). Common hepatic a. nodes were the next most common nodal station involvement followed by the retropancreatic nodal station. This emphasizes the need for complete nodal clearance of these regions in patients of GBC in order to achieve R0 resection.

Non-regional nodal involvement (station 16b1) is considered to be metastatic disease. This was seen in almost a third of our patients. Non-regional nodal spread in the absence of other sites of metastases was found in 20 patients. Agrawal et, al. found that 28% patients had non regional nodal metastases in the absence of other visceral or surface metastases.[9-10] Thus, this reinforces the need for a detailed evaluation of station 12b1 nodes, even in the absence of other sites of metastases.

Liver was the most common site of metastatic disease in as many as 113 patients (76.8%). However, majority of patients had metastases to 2 or more intra-abdominal sites.

This is the first occasion when an epidemiological study of the distribution of stage of disease has been conducted in a high incidence area. This study will provide a foundation of future epidemiological and clinical research.

This study is not without its limitations. The radiological stage might not correlate with the actual pathological staging. The major risk is of overstaging, especially in patients with early stage disease who might turn out to have advanced disease at the time of surgical exploration. There also exists, a risk of understaging. However, features of advanced disease, especially with the presence of evidence of metastases in 2 or more sites in more than half of patients with metastatic disease provides almost unequivocal evidence of correct staging. Thus, the risk of understaging remains less likely.

We have not considered ancillary investigations that were performed in some of these patients. However, we would like to emphasize that as discussed in the preceding sections, there exists very little role of MRI or PET-CT in providing additional management changing information.

Also, this study was done in a single radiological service in a high incidence area. The data might not necessarily apply to other geographic or socioeconomic populations.

CONCLUSION

We have performed this study to demonstrate the distribution of disease and different stages of GBC in one of the highest incidence regions of the world. This radiological study provides one of the best ways to describe the presentation of disease. This study should provide starting blocks for numerous other studies and also identify thrust areas for research in the pathophysiology and management of GBC. There is also an urgent need to establish regional hospital based GBC databases and registries to aid in research and funding.

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