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Clinicopathological Profile of Gallbladder Cancer at a Tertiary Cancer Centre in Northern India; A Continuing Challenge.

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Abstract

Background: *This study aims to evaluate the demographic and clinicopathological profile of patients with gallbladder cancer. The prognosis of gallbladder cancer is poor due to the aggressive tumor biology, late presentation, complicated anatomic position, and advanced stage at diagnosis. Locally advanced and metastatic disease is treated with palliative chemotherapy.*

Methods: *A retrospective study was carried out in Savera Cancer & Multispeciality Hospital, Patna from January 2020 to December 2020. Total one hundred (n=100) confirmed cases of gall bladder cancer patients' data were analyzed retrospectively.*

Results: *This study reveals majority of the patients were female 66. From rural areas 78 gall bladder cancer cases were reported and 22 cases from urban areas. Ultrasonography (USG) of the whole abdomen was advised in 71 and PET CT Scan was in 51 cases of gallbladder cancer and considered to be the promising tool (PET-CT) in the staging of GBC. Death rate reported in 54 patients due to disease progression. 66.54% of patients clinically presented with gallbladder cancer in advanced stage (Stage IV), 19.35% patients at Stage III, only 2 % in Stage II and none in Stage I.*

Conclusions: *In this study female patients are at higher risk of developing gallbladder cancer compared to males. Majority of the patients clinically presented at a very late stage. Tier two/ three cities i.e. Bihar & Uttar Pradesh needs to conduct multicentric and randomized clinical trials. Treatment of gallbladder cancer is still a continuing challenge in India especially eastern and northern India.*

Keywords: *Gallbladder cancer, Jaundice, Adenocarcinoma, Endoscopic retrograde cholangiopancreatography stenting.*

Introduction:

Gallbladder cancer was first described in 1777 **[**1**]**. Even more than 200 years later, delayed diagnosis and the absence of effective treatment for many patients remain typical features of this disease **[**2**]**. The majority of gallbladder cancer (65%) occurs in developing countries **[**3**]**. In India, the incidence of GBC is 10 times higher in North India compared to the southern Indian states [8.9/100,000 population (Delhi) vs. 0.8/100,000 population (Chennai)].

The objective of this study was performed to check the clinicopathological profile of gallbladder cancer patients. Gallbladder cancer doesn't usually cause signs or symptoms until later in the course of the disease when the tumor is large and/or has spread. But sometimes symptoms can appear sooner i.e. abdominal pain, weight loss, nausea or vomiting, jaundice and ascites mostly in an advanced stage of the disease **[**4**]**.

The primary disease grows rapidly with local invasion into the liver and with distant spread to lymph nodes. It is often detected late, due to which management can be challenging. Despite routine use of computed tomography and ultrasonography for detection is often considered for a detailed assessment of the anatomic behavior of these tumors **[**5, 6**]**.

Certain tumor markers such as (CA 19-9, CEA and AFP are associated with hepatobiliary pathologies, including both benign and malignant ones **[**7,8**]**. Histopathological evaluation of gallbladder specimens is an important step in the confirmation of clinical and radiological diagnoses **[**9**]**. Adenocarcinoma is the most common histologic type, accounting for 98% of all gallbladder tumors, two-thirds of which are moderately/poorly differentiated. The remaining common histopathological variants include papillary, mucinous, squamous, and adenosquamous subtypes **[**10**]**.

Complete surgical resection remains the only potentially curative treatment for primary adenocarcinoma of the gallbladder **[**11**]**. National Comprehensive Cancer Network has provided two options for gallbladder cancer treatment: single-agent therapy, which is fluoropyrimidine or gemcitabine-based treatment, and multiagents regimen, which includes oxaliplatin, cisplatin, and capecitabine **[**12, 13, 14**]**.

The metastatic cancer of the gallbladder continues to frustrate the treating oncologists around the world.

Methods:

This was a retrospective and observational study carried out from the data available in the Medical Record Department of Savera Cancer & Multispeciality Hospital. Total (n=100)

confirmed cases of gallbladder cancer patients enrolled in this study from January 2020 to December 2020. All patients and participants were informed of the study and gave voluntary, signed informed consent. The data set consisted of patient information on GBC registered from January 2020 to December 2020. Patient personal details have been kept confidential. All cases were retrospectively analyzed for gender, age, clinical presentations, radiological & histological findings, TNM stage at diagnosis, and treatment (surgery, chemotherapy & palliative) received by the patient, overall survival, etc. The Eastern Cooperative Oncology Group (ECOG) status scale was used in this study to describe a patient's level of functioning in terms of their ability to self-care, daily activity and physical ability (working, walking, etc). Telephonic follow-ups are done to know the survival status of the patients.

Histologically confirmed and radiologically diagnosed cases of gallbladder cancer were included in this study. Descriptive data analyses were transferred and calculated in an excel sheet this is not a funded study.

Results:

A total of 100 cases with gallbladder cancer were identified retrospectively from the database of a cancer hospital. The majority of the gallbladder cancer case (n=78 patients) were reported from rural areas and 22 reported from urban areas of Bihar. Out of 100, 66 female and 34 male patients were diagnosed with gallbladder cancer. The mean age is 57.33. Table 1 illustrates the age-wise distribution of gallbladder cancer cases. The most common clinical presentations reported in patients with gallbladder cancer were a pain in the abdomen 87, vomiting 29, anorexia 28, past/ current history of jaundice 34, past/ current history of GB stone in 32, Ascites in 67 patients out of 100 in Stage 3 and
4. In this study gallbladder cancer patients were categorized as per ECOG performance status. Table 2 depicts the number of gallbladder cancer patients who fall in between Grade 0 – 5.

The majority of the gallbladder cancer patients (n=59) clinically presented lately and falls into Stage 3 and 4 diseases. Rest 29 patients in stage 2b and 11 patients in stage 1. Radiologically total of 57 patients was diagnosed. PET CT Scan performed in 51 patients and USG whole abdomen in 71 patients (71%). MRI had advised in only one case. Tumor markers i.e. CA19.9, CEA and AFP have not a very significant role in the diagnosis of GBC. Table 3 depicts the number of gallbladder cancer cases that went through the tumor markers.

Table 4 illustrates the clinicopathological profile of patients. Under microscope 100 gallbladder cancer cases were diagnosed pathologically. Adenocarcinoma (81/100) is the

most common finding under microscope whereas squamous cell carcinoma (8/100) of GB is the least. Poorly differentiated adenocarcinoma was the predominant histology seen in 63% of cases.

Interventional biliary drainage including Endoscopic retrograde cholangiopancreatography and Percutaneous Transhepatic Biliary Drainage stenting was done in 26 patients, chemotherapy was given in 59 patients and 18 patients received palliative treatment. The death rate due to disease progression was observed in 54 patients, 16 patients are on follow-ups and 16 are lost to follow-ups. Overall survival was reported in only 16/100 (16%) patients. The prognosis of the GBC is very poor due to delayed diagnosis and treatment.

Discussion:

The majority of gallbladder cancer patients (n=78) were from rural areas means closest proximity to the river Ganges and 22 cases were reported from urban areas. Richa Madhwai and et al had also shown a higher incidence of gallbladder cancer cases reported in rural areas especially closest to the river Ganges **[**15**]**. Our study data revealed that female patients were more exposed to gallbladder cancer whereas male patients were less. A recent study by Randi et al also supported this statement that Indo - Gangetic regions have the highest number of gallbladder cancer cases compared to the west, especially in females **[**16**]**. Other predisposing factors were sedentary lifestyles, presence of heavy metals in water (i.e. arsenic, lead) consumption, obesity, consumption of chickpeas etc **[**17, 18, 19, 20,**]**.

Ambiguous symptoms often delay the diagnosis and treatment of gallbladder cancer, contributing to its overall progression and poor outcome **[**21**]**. Patients with gallbladder cancer may present with several non-specific complaints like stomachache, anorexia, nausea, jaundice and ascites in the advanced stage **[**22**]**. In this study, 32% of cases of gallbladder cancer were associated with the past or present history of gall stones. Zantoski et al also demonstrated a strong association between gallstones and gallbladder cancer, suggesting that it is the most important risk factor **[**23**]**. Ultrasonography (US) has been widely used for the peri-operative staging of gallbladder cancer. It looks like a hypoechoic mass with or without GB wall calcifications **[**24**]**. The overall accuracy rate of 91.9% has been reported in differentiating neoplastic from non-neoplastic masses **[**20**]**.

Mitake et al also had shown the effectiveness of USG in the determination of the extent of tumor invasion and diagnosis of gallbladder cancer **[**25**]**. In our study multi-modality imaging scans USG and PET CT was advised in 71% of patients (n=71) and PET CT alone in 51% of patients (n=51) in the advanced stage to rule out the extent of disease. Faiq et al

believed that PET/CT can be a useful modality for staging and restaging of gallbladder cancer. Also useful in treatment response assessment, and maybe a viable alternative to MRI in patients in the assessment of local invasion with post-procedural metallic stent placement **[**26**]**.

Adenocarcinoma was the most common finding (81/100) under microscope whereas squamous cell carcinoma was only 8/100. Moderately and poorly differentiated carcinoma was the predominant histology seen in 81% of cases. Rajveer Hundal and et al found adenocarcinoma is the most frequent histologic type, accounting for 98% of all gallbladder tumors; two-thirds of these are moderately or poorly differentiated **[**27**]**.

The current study demonstrated that CA 19.9, CEA and AFP values increase as the tumor burden increases. Sachan et al in their analysis found CA19.9 is useful but the same was not true for CEA levels. Thus the role of tumor markers in GBC is not well established **[**28**]**.

Conclusion:

The majority of gallbladder cancer patients clinically presented at a very late stage. The pathology of this disease is very complex. In our study, ultrasonography whole abdomen was advised in the early stage and PET CT in the advanced stage was found to be effective in the treatment planning of this disease. Tier two/ three cities i.e. Bihar & Uttar Pradesh needs to conduct multicentric and randomized clinical trials. Treatment of gallbladder cancer is still a continuing challenge in eastern and northern India.

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References

1.Nevin JE, Moran TJ, Kay S, King R. Carcinoma of the gallbladder. Staging, treatment, and prognosis. Cancer. 1976 Jan; 37(1):141–8.

2.Perpetuo MDCMO, Valdivieso M, Heilbrun LK, Nelson RS, Connor T, Bodey GP. Natural history study of gallbladder cancer.A review of 36 years experience at M. D. Anderson hospital and tumor institute. Cancer. 1978 Jul; 42(1):330–5.

3.Shukla HS, Sirohi B, Behari A, Sharma A, Majumdar J, Ganguly M, et al. Indian

Council of Medical Research consensus document for the management of gall bladder cancer. Indian Journal of Medical and Paediatric Oncology. 2015 Apr; 36(02):79–84.

4.Eldon A. Shaffer. Gallbladder Cancer: The Basics. Gastroenterol Hepatol (N Y). 2008 Oct; 4(10): 737– 741.

5.Kapoor VK, Pradeep R, Haribhakti SP, Sikora SS, Kaushik SP. Early carcinoma of the gallbladder: An elusive disease. Journal of Surgical Oncology. 1996 Aug; 62(4):284–7.

6.Shaikh F, Awan O, Khan SA. 18F-FDG PET/CT Imaging of Gallbladder Adenocarcinoma - A Pictorial Review. Cureus. 2015 Aug 9;

7.Ono T, Komatsu M, Hoshino T, Ishii T, Fujii T, Oshima S, et al. Alpha-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9-producing gallbladder cancer. Journal of Gastroenterology. 1996 Oct; 31(5):742–6.

8.Vij U, and Baskaran. V Value of serum CEA and AFP in the diagnosis and prognosis of carcinoma gallbladder. Tropical Gastroenterology. 2001; 22:227–9.

9.Jayasundara J, de Silva W. Histological assessment of cholecystectomy specimens performed for symptomatic cholelithiasis: routine or selective? The Annals of the Royal College of Surgeons of England. 2013 Jul; 95(5):317–22.

10.Shaffer E, Hundal R. Gallbladder cancer: epidemiology and outcome. Clinical Epidemiology. 2014 Mar; 99.

11.Zhu AX, Hong TS, Hezel AF, Kooby DA. Current Management of Gallbladder Carcinoma. The Oncologist [Internet]. 2010 Feb 1 [cited 2019 Oct 19]; 15(2):168–81.

12.Bridgewater JA, Stubbs C, Primrose JN. BILCAP: A randomized clinical trial evaluating adjuvant chemotherapy with capecitabine compared to expectant treatment alone following curative surgery for biliary tract cancer. Journal of Clinical Oncology. 2011 May 20; 29(15_suppl):4125–5.

13.Ben-Josef E, Guthrie KA, El-Khoueiry AB, Corless CL, Zalupski MM, Lowy AM, et al. SWOG S0809: A Phase II Intergroup Trial of Adjuvant Capecitabine and Gemcitabine Followed by Radiotherapy and Concurrent Capecitabine in Extrahepatic Cholangiocarcinoma and Gallbladder Carcinoma. Journal of Clinical Oncology. 2015 Aug 20; 33(24):2617–22.

14.Valle J, Wasan H, Palmer DH, Cunningham D, Anthoney A, Maraveyas A, et al. Cisplatin plus Gemcitabine versus Gemcitabine for Biliary Tract Cancer. New England Journal of Medicine [Internet]. 2010 Apr 8 [cited 2020 Jan 27]; 362(14):1273–81.

15.Gupta S, Kori C, Kumar V, Misra S, Akhtar N. Epidemiological Study of Gallbladder Cancer Patients from North Indian Gangetic Planes—a High-Volume Centre's Experience. Journal of Gastrointestinal Cancer. 2015 Nov 19; 47(1):27–35.

16.Maram ES, Ludwig J, Kurland LT, Brian DD. Carcinoma of the gallbladder and extrahepaic biliary ducts in Rochester, Minnesota, 1935–19711. American Journal of Epidemiology. 1979 Feb; 109(2):152–7.

17.Nervi F, Duarte I, Gómez G, Rodríguez G, Pino GD, Ferrerio O, et al. Frequency of gallbladder cancer in chile, A high-risk area. International Journal of Cancer. 1988 May 15; 41(5):657–60.

18.W A Zatonski 1, A B Lowenfels, P Boyle, P Maisonneuve, H B Bueno de Mesquita, P Ghadirian, M Jain, K Przewozniak, P Baghurst, C J Moerman, A Simard, G R Howe, A J McMichael, C C Hsieh, A M Walker. Epidemiologic aspects of gallbladder cancer: a case-control study of the SEARCH Program of the International Agency for Research on Cancer.

19.Misra NC, Jaiswal MSD, Singh RV, Das B. Intrahepatic arterial infusion of combination of mitomycin-C and 5-fluorouracil in treatment of primary and metastatic liver carcinoma. Cancer. 1977 Apr; 39(4):1425–9.

20.BATRA Y, PAL S, DUTTA U, DESAI P, GARG PK, MAKHARIA G, et al. Gallbladder cancer in India: A dismal picture. Journal of Gastroenterology and Hepatology. 2005 Feb; 20(2):309–14.

21.Madhawi R, Pandey A, Raj S, Mandal M, Devi S, Sinha PK, et al. Geographical pattern of carcinoma gallbladder in Bihar and its association with river Ganges and arsenic levels: Retrospective individual consecutive patient data from Regional Cancer Centre. South Asian J Cancer. 2018 Jul-Sep; 7(3): 167–170.

22.Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: Geographical distribution and risk factors. International Journal of Cancer. 2006 Apr 1; 118(7):1591–602.

23.Zatonski WA, Przewozniak K, Lowenfels AB, Boyle P, Maisonneuve P, Bueno de Mesquita HB, et al. Epidemiologic Aspects of Gallbladder Cancer: A Case-Control Study of the SEARCH Program of the International Agency for Research on Cancer. JNCI Journal of the National Cancer Institute. 1997 Aug 6; 89(15):1132–8.

24.Nandakumar A, Gupta PC, Gangadharan P, Visweswara RN, Parkin DM. Geographic pathology revisited: Development of an atlas of cancer in India. International Journal of Cancer. 2005; 116(5):740–54.

25.Dhir V, Mohandas KM. Epidemiology of digestive tract cancers in India IV. Gall bladder and pancreas. Indian J Gastroenterol. 1999; 18:24–8.

26.Bala S, Prasad Ks, Ravichandran A, Sadashivudu G. Secondary osteosarcoma of pelvic bone: Long- term complication of bladder cancer radiotherapy. Indian Journal of Medical and Paediatric Oncology. 2019; 40(4):579.

27.Shaffer E, Hundal R. Gallbladder cancer: epidemiology and outcome. Clinical Epidemiology. 2014 Mar; 99.

28.Joo I, Lee JY, Kim JH, Kim SJ, Kim MA, Han JK, et al. Differentiation of adenomyomatosis of the gallbladder from early-stage, wall-thickening-type gallbladder cancer using high-resolution ultrasound. European Radiology. 2012 Dec 18; 23(3):730–8.