

Evaluation of Risk Factors Associated With Carcinoma Gallbladder and Outcome of Treatment in Patients

Attending Tertiary Care Centre Kanpur UP

Anju Yadav¹, Gulab Dhar Yadav², Nikhil Kumar Gupta³

¹Assistant Professor, Department of Paediatrics Rama Medical College Kanpur

²Professor, Department Of General Surgery, Gsvm Medical College Kanpur, India

³Junior Resident, Department Of General Surgery, Gsvm Medical College Kanpur, India

Corresponding Author: Gulab Dhar Yadav , Professor, Department Of General Surgery, Gsvm Medical College Kanpur, India

Type of Publication: Review Paper

Conflicts of Interest: Nil

Abstract

Introduction: Gallbladder carcinoma (GBC) ranks fifth among the gastrointestinal carcinomas and is the most common cancer of the biliary tract. According to the Indian cancer registry data, incidence of GBC is 0.8%–1%. Gallstones are a well-established risk factor associated with the development of GBCs in 75%–90% of cases. Surgery is indicated in only very selected cases. For the majority of patients, non-operative approach to palliation is best. Gall bladder cancer for most patients is a lethal disease with a grim prognosis.

Material & Method: Present study was carried out in the Department of Surgery GSVM Medical College Kanpur from January 2017 to October 2018. 90 Cases with suspected gall bladder cancer were included.

Results: Out of the total 90 subjects in our study, 50 patients (55.55%) were from gangetic plains. 77.77% patients in our study used mustard oil as the cooking medium. Gall stones were present in 73 cases (81.11%). The study shows that all cases of suspected gall bladder cancer presented in later stages (stage III and IV).

Discussion: The incidence of CaGB was found to be significantly high among the people living near the Ganga as compared to the subjects belonging to non-gangetic plain areas. Suspected gall bladder carcinoma cases in our study presented in later stages (stage III and IV) of the disease due to the absence of any early red flag clinical features; leading to non-operability in maximum cases.

Conclusion: Primary prevention of gallbladder cancer is not expected in the near future. However, secondary prevention, primarily oriented to early diagnosis and treatment of symptomatic gallstones must be emphasized in endemic areas where cholelithiasis is highly prevalent. Prophylactic laparoscopic cholecystectomy might be cost effective. It is apparent that interventional programs are urgently needed to decrease the number of gall bladders at risk for gallbladder cancer development in high-risk areas.

Introduction

Gallbladder carcinoma (GBC) ranks fifth among the gastrointestinal carcinomas and is the most common cancer of the biliary tract. According to the Indian cancer registry data, incidence of GBC is 0.8%–1%. While New

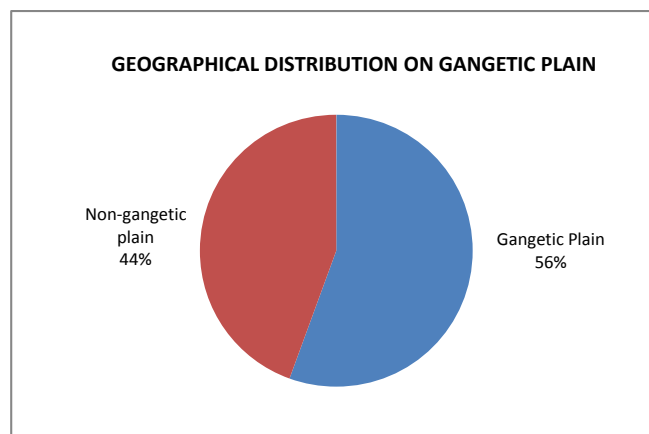
Delhi and Bhopal are the leading states, lowest incidence is seen in Chennai. Risk factors include cholelithiasis, calcified gallbladder wall, adenomatous polyp, obesity, estrogen, choledochal cyst, and chemical carcinogens. Of these, gallstones are a well-established risk factor associated with the development of GBCs in 75%–90% of cases. The highest frequency of the disease is found among females over the age of 65. The majority of patients have advanced disease at presentation and are not candidates for surgical therapy. For the majority of patients, non operative approach to palliation is best. Gall bladder cancer for most patients is a lethal disease with a grim prognosis.

Material And Method

Present study was carried out in the Department of Surgery GSVM Medical College Kanpur from January 2017 to October 2018. 90 Cases with suspected gall bladder cancer were included. They were enrolled from the outpatient Department of Surgery and indoor admissions at the J K Cancer Institute Kanpur. My Inclusion criteria Age at least 18 years and Patients with suspected gall bladder cancer.

Results

The total number of registries of all types of cancer in Dept. of surgery L.L.R.H and J.K cancer institute from January 2017 to October 2018 are 25797, out of which 90 cases are of carcinoma gall bladder. So the hospital based incidence showing magnitude of Ca GB is $(90/25797 \times 1000)$ 3.49 per 1000 cancer cases.



Out of the total 90 subjects in our study, 57 patients (63.33%) were from urban areas; while only 33 patients (36.67%) belonged to rural areas. The peak incidence is in 51-60 years age group. 32 patients (35.55 %) were in this age group. Male to female ratio in this study is 1: 2.1, higher for females. 77.77% patients in our study used mustard oil as the cooking medium which was significantly higher than the proportion of CaGB patients using refined oil. 12 patients (13.33%) had past history of typhoid. 17 patients (18.88%) had family history of Ca gall bladder.

Sign/Symptom	No. of patients	Percentage
Abdominal Pain	71	78.88%
Jaundice	40	44.44%
Abdominal Lump	68	75.55%
TLC raised	12	13.33%
Bilirubin raised	36	40.00%
SGOT / SGPT raised	42	46.66%
ALP raised	36	40.00%

Fundus was involved in 62.2% cases, body of gall bladder was involved in 31.1% patients while the neck was found to be involved in 11.1% of cases. Among the cases involving fundus, jaundice was clinically present in 12.5% cases. 82% cases with body involvement and all the cases

with neck involvement clinically developed jaundice. Gall stones were present in 73 cases (81.11%) as per ultrasonography and per operative findings; out of which multiple gall stones were seen in 54 cases (60.00%) while single gall stone of size more than 10mm in 11 cases (12.22%).

Structure involved	No. of cases	Percentage
Lymph node	61	61.9%
Liver	55	61.1%
Others (eg. Omentum/colon)	18	30%

The study shows that all cases of suspected gall bladder cancer presented in later stages (stage III and IV). most cases of gall bladder cancer were non-operable (97.77%), clearly correlating to late presentation. most carcinoma gall bladder cases on USG guided FNAC were adenocarcinomas (93.18%). In our study of 90 subjects, conducted from Jan 2017 to March 2018, 23 patients (34.85%) had a survival time of less than 3 months, 26 patients (39.40%) had a survival time of 3-6 months, while 17 patients (25.75%) survived for more than 6 months out of 66 cases evaluated completely. Overall, out of 66 patients evaluated within the study time period, around 75% cases expired within 6 months despite treatment. So, in our study comprising of 90 suspected gall bladder cases, 69 patients (76.67%) expired during follow up despite treatment.

Discussion

Out of the total 90 subjects in our study, 50 patients (55.55%) were from gangetic plains (Kanpur Nagar, Kannauj, Hardoi, Unnao); while only 40 patients (44.44%) belonged to non-gangetic plains (Kanpur Dehat, Sitapur, Jalaun, Etawah, Auraiya). The incidence of CaGB was found to be significantly high among the people

living near the Ganga as compared to the subjects belonging to non-gangetic plain areas. Similar results were obtained in a study conducted over a period of six years by a team of doctors under the guidance of **Dr. P. Jagannath**¹ from Tata Memorial Hospital in Parel Mumbai along with the International Institute of Population Studies and the results were attributed to the high concentrations of DDT and heavy metals like nickel, cadmium, chromium in Ganga water and soil. our study male to female ratio of 1 : 2.1. These results are consistent with the results of other studies (**Beltz et al., 1974**²; **Shukla et al., 1985**³; **Pandey et al., 2001**⁴) where it was reported to be 1:3, 1:3 and 1:2.5 respectively. The present study revealed the mean age of the patients to be 56 years, with a range of 31-80 years and sixth decade as the peak age of presentation. Similar results were observed in other studies from India (**Shukla et al., 1985**³; **Pandey et al., 2001**⁴; **Kapoor et al., 2003**⁵). In contrast, studies from west reported the mean age of 67 years (**Beltz et al., 1974**)² and the peak age of incidence in 7th decade of life (**Perpetuo et al., 1978**)⁶. Our result showed that non-vegetarians were more prone to gallbladder cancer rather than vegetarians and the fact was supported by **Pandey et al. (2002)**⁴. The study of **Mishra S., et al, (2003)**⁷ was consistent with our finding that the consumption of carcinogenic impurities in mustard oil may contribute to elevated incidence of gall bladder cancer in North India. The study of **Dubey A. P. et al, 2018**⁸ also recognized non-vegetarian diet, especially the consumption of red meat and carcinogenic impurities in mustard oil as independent risk factors in the pathogenesis of carcinoma gall bladder. Suspected gall bladder carcinoma cases in our study presented in later stages (stage III and IV) of the disease due to the absence of any early red flag clinical features; leading to non-operability in maximum cases.

(Lal M., Raheja S., Bhowmik K.T. et al, 2018)⁹The prognosis of patients with carcinoma gall bladder is dismally poor. In our study, out of 66 patients evaluated completely within the study time period, around 75% cases expired within 6 months despite treatment, because a majority of the patients present with advanced disease. The presentation at an advanced stage can be attributed to multiple factors including lack of knowledge and education in patients, predominantly belonging to lower class, inability to differentiate symptoms of early gall bladder cancer from those of gall stone disease and poor response to available chemotherapy options (Batra et al, 2005)¹⁰.

Conclusion

Based on the findings of our study the elderly females with age group of 51-60 years were found to be more prone for gall bladder cancer. The consumption of non-vegetarian diet, mustard oil and lack of knowledge regarding the health may also be a risk factor.

- Primary prevention of gallbladder cancer is not expected in the near future. However, secondary prevention, primarily oriented to early diagnosis and treatment of symptomatic gallstones must be emphasized in endemic areas where cholelithiasis is highly prevalent. Prophylactic laparoscopic cholecystectomy in asymptomatic gall stone might be cost effective. It is apparent that interventional programs are urgently needed to decrease the number of gall bladders at risk for gallbladder cancer development in high-risk areas.
- Most gallbladder cancers, unfortunately, are discovered incidentally at routine cholecystectomy or present as advanced stage disease. The role of radiological imaging, therefore, is limited to the use of ultrasound, CT scans, MRCP and endoscopic/FNAC

procedures for diagnostic and staging purposes. Adenocarcinoma accounts for the majority of gallbladder cancers. Surgery is the only curative therapy for gallbladder cancer. However, at diagnosis, less than 10% of patients are candidates for curative surgery.

- The role of adjuvant therapy in CaGB is not well defined. Nevertheless, in T2 or node-positive disease, due to the high risk of recurrence, six months of gemcitabine or fluoropyrimidine-based chemotherapy can be considered. Such systemic chemotherapy has shown modest survival benefit in the management of advanced gallbladder cancer and is recommended in patients with good performance status along with best supportive care.
- Despite rapid developments in targeted therapies, the result of established molecules in the management of gall bladder cancer have been disappointing. There is a need for the development of newer targeted agents keeping gall bladder cancer in mind.

References

1. Jagnanath P, Dhir V, Mohandas KM (2000). Geographic patterns in incidence of gallbladder cancer in india and the possible etiopathological factors HPBm 2, 168-936
2. BeltzWr, Condon RE (1974) Primary carcinoma of the gallbladder. Ann Surg 180:180-184.
3. Shukia VK, Khandelwal C, Roy SK, Vaidya MP. Primary carcinoma of the gallbladder. J SurgOncol 1985; 28: 32-35.
4. Pandey M, Shukia VK. Diet and gallbladder cancer: a case control study. Eur J Cancer Prey 2002; 11(4): 365-68.
5. Kapoor VK, Mc Michael AJ (2003) Gallbladder cancer : an Indian disease. Natl Med J Ind, 16, 209-13

6. Perpetuo MM, Valdivieso M, Heilbrun LK, et al. Natural history study of gallbladder cancer. *Cancer* 1978;42:330-5.
7. Misra S, Chaturvedi AMisra NC Sharma ID Carcinoma of the gallbladder. *LacetOncol* 2003; 4:167-76.
8. Dubey AP : Carcinoma of gallbladder : Demographic and clinicopathological profile in Indian patients. *Oncology Journal of India* (2018)
9. Lal M., Raheja S., Bhowmik K.T. et al, Safdarjung Hospital and VMMC, New Delhi; *Arch. Surg. Oncol* 4: 131, Jul 06, 2018.
10. Batra Y : Gallbladder cancer in india : A dismal picture ; *Journal of gastroentrology and hepatology* 20 (2), 309-314, 2005.