

Spectrum of Carcinoma Gall Bladder At Tertiary Health Care Centre(IGMC Shimla H.P.)

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Abstract-

Introduction-Gall bladder carcinoma was first described in 1777, even after two centuries of its first description; the tumor remains characterized by an unfavorable prognosis due to silent progression of the clinical course and limited knowledge of its etiology and poor scientific capability for epidemiological forecasting. The incidence of GBC varies in different parts of the world. Overall incidence ranges from 0.11/100000 to 10.6/100000 in different cancer registries worldwide.¹

Methods-This study was a prospective cohort study and was carried out among newly diagnosed, intraoperative and referred cases of carcinoma gall bladder at IGMC Shimla. All newly diagnosed, intraoperative and referred cases of carcinoma gallbladder were recruited in the study. The total duration of study was of one year.

Result-Mean age of presentation is 61 year with female sex ore commonly involved. Most of the patients are from normal BMI group. Gall stones are associated with 56% of the patients. Most common chief complaint is pain abdomen followed by jaundice, Dyspepsia, anorexia and weight loss. In usg most common finding is asymmetrical gall bladder wall thickening. In CECT abdomen most common finding is of metastatic disease. Adenocarcinoma is most common HPE finding.

Conclusion-Gall bladder carcinoma has a highly variable prevalence becoming a common gastro intestinal malignancy in certain population most notably north India and Himachal Pradesh. Chronic inflammation and cholelithiasis are major risk factors. Carcinoma is more common in females with variable age of presentation but mainly in middle age. Surgery represents the only possible cure provided patient is diagnosed early. Improved outcome greatly depend upon the recognition of major risk factors, accurate tumor staging and meticulous surgical intervention. Primary prevention will arrive once high risk environmental toxins and genetic abnormalities are clearly identified.

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I. Introduction

Gall bladder carcinoma was first described in 1777, even after two centuries of its first description; the tumor remains characterized by an unfavorable prognosis due to silent progression of the clinical course and limited knowledge of its etiology and poor scientific capability for epidemiological forecasting. The incidence of GBC varies in different parts of the world. Overall incidence ranges from 0.11/100000 to 10.6/100000 in different cancer registries worldwide.¹ The prognosis is poor, only about a 32 percent 5 year survival rate for lesions confined to the gallbladder mucosa and a 10 percent one-year survival rate for more advanced stages.² The incidence in northern Indian cities is much higher than the southern Indian cities. In Delhi and Bhopal the incidence is 7 and 1.6 per 100,000 for male and 10.6 and 4 per 100,000 for females.¹ The residents of Indo-Gangetic belt particularly females of northern India (21.5/100000) and South Karachi Pakistan (13.8/100000) have been reported as one of the highest affected regions.³ Although Gallbladder cancer is more common in females, still in some countries like Korea, Iceland and Costa Rica, higher mortality rate has been reported for males as compare to females.⁴ The development of gallbladder cancer has been linked to various genetic and environmental factors. Chronic infection of gallbladder or/and environmental exposure to specific chemicals, heavy metals, and even many dietary factors, have been found to be associated with GBC formation. The dramatic association of GBC with female gender and certain geographical regions (mostly developing countries) has been proposed to be influenced by various female hormones, cholesterol cycling and salmonella infections in existing literature.^{5,6} Incidence of cancer gall bladder in Himachal Pradesh is high. In Himachal

Pradesh (HBCR)Hospital based cancer registry data indicates it is the seventh most common malignancy among the females, eighth common malignancy among males.

II. Methods

Our study is intended –

1. To study the epidemiology of disease in tertiary health care centre.
2. To measure strength of association between selected risk factors and gall bladder cancer.
3. To study various treatment modalities done according to stage of the disease including palliative procedures.

This study was a prospective cohort study and was carried out among newly diagnosed, intraoperative and referred cases of carcinoma gall bladder at IGMC Shimla. All newly diagnosed, intraoperative and referred cases of carcinoma gallbladder were recruited in the study. The total duration of study was of one year. Patients included were having

- (1) Thickening of gall bladder wall on U.S.G abdomen.
- (2) Incidental carcinoma gall bladder.
- (3) Intraoperative diagnosed carcinoma gall bladder.
- (4) Consented to participate in study

All previously treated patients, all those who did not give written consents and patients who were mentally not sound enough to give consent or interview were excluded from the study. All those patients coming to IGMC Shimla general surgery department fulfilling the inclusion criteria for first 9 months were included in the study. Detailed history was taken and clinical examination of patients was done. Blood investigations namely complete haemogram, renal function tests, liver function tests, serum electrolyte levels, blood glucose level, PT/INR, serum total protein and albumin levels, and relevant tumour markers was done. Radiological evaluation namely chest X-ray, ultrasound abdomen and contrast enhanced CT scan and MRCP as per requirement was done. Patients were treated according to cancer stage, TNM classification and staging was used to classify the disease and treatment modality.

III. Results

The mean age of participants was 61.0 ± 12.8 . 56% of patients are in age group of 60-80. In present study out of 45 patient 36(80%) were females and 9(20%) were males.

AGE GROUPS	FREQUENCY	PERCENT
20-40	4	8.90%
41-60	16	35.55%
61-80	25	55.55%
TOTAL	45	100%

37.78 % patients belong to district Shimla.

Out of 45 patients of carcinoma gall bladder 27(60%) were average weight 11(24.44%) were underweight, 5(11.11%) were overweight and 2(4.44%) were obese.

Out of 45 patients 25(55.56 %) patients had ultrasonographically proven cholelithiasis.

Out of 45 patients 16(35.56%) patients had history of excessive consumption of fats in their diet.

Out of 45 patients none of them had any relevant family history of carcinoma gall bladder. Out of 45 patients of carcinoma gall bladder 37(82.22%) were presented with pain Right upper quadrant of abdomen as chief complaint abdomen followed by jaundice(55.56%) , Dyspepsia(53.33%), anorexia(62.22%) and weight loss(53.33 %).

21 patients (46.67 %) had normal serum CEA levels, 20(44.44 %) patients had moderately raised CEA levels and 4(8.89 %) had extensively raised CEA levels.

CEA	FREQUENCY	PERCENT
NORMAL (<2.5ng/ml)	21	46.67%
MODERATELY RAISED (2.5 to 500ng/ml)	20	44.44%
EXENTENSIVELY RAISED (>550ng/ml)	4	8.89%
TOTAL	45	100.00%

25 patients (55.56 %) patients had normal serum CA 19-9 levels, 12(26.67 %) patients had moderately raised CA 19-9 levels and 8(17.78 %) had extensively raised CA 19-9 levels.

CA 19 -9	FREQUENCY	PERCENT
NORMAL (<37U/ml)	25	55.56%
MODERATELY RAISED (>90U/ml)	12	26.67%
EXTENSIVELY RAISED (>450U/ml)	8	17.78%
TOTAL	45	100.00%

31patients(68.89 %) patients had asymmetrical thickening of gall bladder wall , 12(26.67%) had no asymmetrical thickening and 2(4.44 %) had GB focal mass.

9patients(20%) patients had non metastatic disease in which fat plains were well maintained,13(28.88%) patients had non metastatic disease in which disease was locally advanced and in 23(51.12%) patients disease was metastatic.

28 patients (62.22 %) patients had adenocarcinoma on HPE and in 17(37.78 %) tissue diagnosis was not present. 23 patients (51.11 %) were inoperable, 13(28.89 %) patients had resectable growth and 9(20.00 %) patients had unresectable growth.

TREATMENT PROFILE	FREQUENCY	PERCENT
IN OPERABLE	23	51.11%
RESECTABLE	13	28.89%
UNRESECTABLE	9	20.00%
TOTAL	45	100.00%

7 patients (15.56 %) received neoadjuvant chemotherapy, 4(8.89 %) received adjuvant chemotherapy, 2(4.44 %) received both NACT and adjuvant chemotherapy and 32(71.11 %) received no chemotherapy.

Modalities of treatment-

MODALITIES OF TREATMENT	FREQUENCY	PERCENT
EXTENDED CHOLECYSTECTOMY	10	22.22%
PTBD	9	20.00%
METASTATIC (PALLIATION)	23	51.11%
COMPLETION EXTENDED CHOLECYSTECTOMY	3	6.67%
TOTAL	45	100.00%

IV. Discussion

Primary carcinoma gall bladder is an uncommon malignancy with a distinctive demographic and geographical distribution. In United States it is the sixth common gastrointestinal malignancy.⁹In our analysis of 45 patients, females outnumbered males and constituted 80% of total cases with a male to female ratio of 1:4.This finding was consistent with other studies where male to female ratio was in favor of females, however it was more than other studies with most series reporting a ratio of 1:3,1:2.5.^{7,8,10,11}However Liang¹² reported a male to female ratio of 1:1.Although women are two to six times more commonly affected by gall bladder cancer than men, the incidence steadily rises with age.¹³ In the present study it was observed that most of the patients were from age group 61-80years followed by 41-60years this was in sharp contrast to the concept given by Kapoor S et al¹⁴ as maximum number of patients were in the age group 30-40years. And in the present study age at diagnosis ranged from 33 to 80years which is consistent with the study done by Gulwani HV et al.¹⁵The most common presenting symptom in our study was abdominal pain (82.22%) followed by anorexia (62.22%), dyspepsia (53.33%), weight loss (53.33%). This is consistent with results from other studies which have reported abdominal pain to be the most common presenting symptom.In our study, gall stones were seen in 25 cases (55.56% of all the cases). Cholelithiasis is a well established risk factor for the development of gall bladder carcinoma¹⁶ and gall stones were present in 74%-92% of affected patients.However in our study, gall stones were seen only in 55.56% of cases with carcinoma gall bladder .This is a significant finding in an area where gall stones have a high prevalence.¹⁷

CT is better than ultrasound in detecting the gall bladder lesion and helpful to know the status of liver involvement but of little value in knowing the nodal status. Consistent with our study.Elevated Retinol binding protein 4 has been shown to increase the incidence rate of gallstone disease . Wang et al. ¹⁸ reported that bile Retinol binding protein 4 was correlated with body mass index positively. But it is in contrast to our study as in our study maximum number of patients fall in normal BMI category.In the study conducted by Shukla et al. ¹⁹ 335 GBC patients were analysed, They reported that when the serum CA19-9 level is >90 U/mL,94% of the patients were unresectable, and when the level rose to >450 U/mL, 100% of those patients were unresectable. The scoring system, inspired by child standards, was widely used to assess patients with liver disease under

consideration for surgical resection ,but in our study it is not statistically significant . It may be due to small size of our study.A study by Singh et al. reported that median overall survival(OS) for unresectable GBC patients was 11.3 months.²⁰ Median OS for unresectable GBC patients who were treated with best supportive care, fluorouracil and folinic acid, and modified gemcitabine and oxaliplatin were 4.5, 4.6, and 9.5 months, respectively.In conclusion, this study identified a combination of an elevated CEA and CA19-9 was independent predictor of a poor prognosis in GBC patients undergoing resection.

V. Conclusion

Gall bladder carcinoma has a highly variable prevalence becoming a common gastro intestinal malignancy in certain population most notably north India and Himachal Pradesh. Unfortunately the usual presentation at an advanced stage because of non specific symptoms is associated with high mortality. Chronic inflammation and cholelithiasis are major risk factors. Carcinoma is more common in females with variable age of presentation but mainly in middle age. Surgery represents the only possible cure provided patient is diagnosed early.Improved imaging modalities as well as accurate diagnostic tumor markers will probably help outcome. Improved outcome greatly depend upon the recognition of major risk factors, accurate tumor staging and meticulous surgical intervention. Primary prevention will arrive once high risk environmental toxins and genetic abnormalities are clearly identified.

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