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ORIGINAL ARTICLE

A STUDY OF EPIDEMIOLOGY OF GALLBLADDER CARCINOMA AND CHOLELITHIASIS AT A TERTIARY INSTITUTE IN CENTRAL INDIA

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ABSTRACT: BACKGROUND: Gallbladder carcinoma (GBC) is a highly lethal and aggressive disease with a poor prognosis. The etiology of this tumor is complex, but there is a strong association with gallstones. Owing to its nonspecific symptoms, gallbladder carcinoma is generally diagnosed late in the disease course. **METHODS**: Hospital based cross-sectional study was carried out at tertiary care institute either as OPD patients or as admitted patients (with gall bladder disease) in surgery department, from Jan 2010 to Dec 2010. **RESULTS:** carcinoma gall bladder in females was 2.375 times more than males, mean duration of symptoms were 10.36±2.3months in case of females and 9.89± 2.6 months in case of males. Commonest symptoms were pain 92.59% and weight loss 92.59%. Few factors like alcohol were also identified with GBC. **CONCLUSION:** The proportion was more among the elderly females; the average duration of symptoms at the time of presentation was more than one year with commonest symptom being pain.

KEYWORDS: Carcinoma gallbladder, cholelithiasis, risk factors, symptoms

INTRODUCTION: Carcinoma of the gallbladder is a highly fatal disease with poor prognosis. It is the most common malignant lesion of the biliary tract and the fifth most common among malignant neoplasm of the digestive tract. Even with the numerous diagnostic tests available, gallbladder cancer (GBC) is frequently first diagnosed during laparotomy or laparoscopy procedures, which were expected to confirm the presence of benign gallbladder disease.[1, 2] In India, however, the majority of GBC are discovered at an advanced stage during ultrasonography for upper abdominal symptoms. 5-year survival for cancers of the gallbladder lies between 0% and 10% in most reported series.[3]

Poor prognosis of this disease is due to the anatomical position of the gallbladder and the high proportion of tumors that are advanced at the time of presentation. Since the symptoms and signs of gallbladder carcinoma are vague and nonspecific, it is difficult to diagnose clinically. However, with the recent improvements in preoperative imaging, early GBC are now being diagnosed more frequently and the use of radical aggressive surgery promises an improvement in survival. GBC affects women two to six times more commonly than men and its incidence steadily increases with age.[4]

In India, the incidence of gallbladder carcinoma is very high in the north (eg, incidence in Delhi is 4.5 per 100 000 for men and 10·1 per 100 000 for women) compared with the south (eg, in Chennai, Mumbai, Trivandrum, and Bangalore incidence is 1.2 per 100000 for men and 0.9 per 100 000 for women).[5] Gall stones, present in 60%–90% of patients with GBC as compared to 20%–25% of an age-matched population, are the most important risk factor for GBC.[6] A history of symptoms of gall stone disease was a major risk factor (odds ratio 4.4, 95% confidence interval: 2.6–7.5) in a large case–control study.[6] The wide geographical, ethnic, and cultural variations in the incidence of GBC

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suggests that there are major genetic and environmental influences on the development of the disease, which include diet and lifestyle. Identification and elimination of these factors can lead to prevention and control of GBC. In this study we have tried to study the epidemiology of gallbladder carcinoma and cholelithiasis along with various factors that makes gall bladder carcinoma the source of one of the major sufferings in Bhopal region (Central India region).

MATERIAL AND METHODS: After obtaining institutional ethical committee approval this present hospital based cross-sectional study (with follow –up) was carried out on 240 study subject who came to Hamidia hospital and associated Gandhi medical college either as OPD patients or as admitted patients (with gall bladder disease) in surgery department of the hospital from Jan 2010-Dec 2010.

SELECTION OF THE STUDY SUBJECTS: On admission or during examination in the OPDs, a detailed history and clinical examination was carried out, the requisite investigations like hemoglobin, total leucocytic counts, differential leucocytic counts, blood sugar, blood urea, liver function tests (giving main emphasis on serum bilirubin, alkaline phosphatase), serum cholesterol level. Clinical diagnosis was made after this with help of specific investigations like ultrasonography and computerized tomography. If required the patients underwent operative procedures after informed consent. None of the female patients who were pregnant were made part of the study.

METHODOLOGY: The methodology of the study work consists of filling up of the predesigned and pretested proforma after taking informed consent form the participants. The proforma covered all the important risk factors pertaining to GBC and gall bladder disease. With the filling of proforma it was tried to cover the important factors pertaining to the person itself and the factors included in the environment around the person. The person was followed during his clinical and biochemical, pathological, radiological and if present the surgical management of the person. Even when the person went away from the hospital the patient was followed to track the investigations and the management the patient received.

STATISTICAL ANALYSIS: The data collected was entered in to Microsoft office excel 2007. The quantitative variables were summarized as mean and standard deviation while qualitative variables as percentage and proportion. The statistical package used was SPSS 17.

RESULTS: A total of 240 cases of gall bladder disease were studied. Out of which 27(11.25%) cases were of GBC, 198(82.5%) cases had cholelithiasis and 15(6.25%) were other cases of gall bladder diseases. Table 1 provides the break- up of males and females and we can already see the bias of gall bladder diseases in the favor of females. Mean age of GBC patients were 61±4.3 years in case of females and 54± 5.2 in case of males varying from 35 to 72 in case of females and 44 to 70 in case of males.

The average duration of symptoms at the time of presentation was 10.36±2.3 months for cholelithiasis for females and 9.89±2.6 months for males. The GBC patients presented late with average duration of symptom for females being 16.5±3.4 months varying from 3-35 months and for males it was 15.4±4.1 months varying from 1-31 months. Table no. 2 and 3 shows the list of

symptoms at the time of presentation and past illness. In case of male cases, one interesting thing that was found out was the fact that 40 out of 56 cholelithiasis cases were regular alcoholics and in case of GBC 3 out of 8 patients were regular alcoholics. Average level of total bilirubin in cases with GBC was 4.5 mg/dl while in cholelithiasis mean level was 1.5 mg/dl. The mean cholesterol in GBC cases was 256.5 mg/dl ± 28 while in cholelithiasis mean level was 175.7 mg/dl ± 27.

Discussion: Although the precise etiology is unknown, the presence of gallstones is considered to be an important risk factor for GBC and the epidemiological characteristics of these two diseases are closely linked.[6] However, it is not clear whether the association represents a causal link or the presence of common risk factors.

Elderly females are main victims of GBC. The peak incidence occurs in 6th or 7th decade of life with a mean age of 65 years.[7, 8] In present study mean age for GBC has come out to be 61±4.3 years for females and 54±5.3 years for males which corresponds to the usual way this malignancy behaves at large. GBC shows a female preponderance of 2.13 to 3:1[9, 10] in our study it was 2.375:1 in favor of females, which again is corresponding to the benchmarks. Chao et al (1996)[11] reported the mean duration of symptoms prior to admission to be from 1 day to 10 years (mean 210.1+84.2 days). Our study observed a mean symptom period of 15.4±3.4 months for males and 16.5±4.1 months for females with a variance of 10-11 months. It only tells that most of the people in our study were from Lower income strata and were ignorant about their symptoms till the increasing pain and jaundice and loss of weight forced them to take medical advice.

Commonest symptoms in our study for GBC was pain 92.59% and weight loss 92.59% followed by anorexia and loss of appetite along with a palpable lump at the time of presentation standing a 88.88% malaise 77.77% nausea, vomiting 62.96% and jaundice at 29.62% followed in frequency distension was present in only 7% of cases. In another series pain was present in 75%; jaundice was present in 38%, nausea vomiting in 32% and weight loss in 30%. [7, 11, 12] The mean bilirubin level of gall bladder patients at presentation was 4.5mg/dl and varied from 0.7 to 20.1 mg/dl. Statistical significance from general population could not be found out, because no controls were taken from general population.

The reason that association between GBC and cholesterol level, past illness, alcohol, non-vegetarian diet etc. could not be shown was that GBC is an entity where multiple factors have an interplay to produce the disease so if the association of a particular factor has to be found out then a case control study has to done .our study just points out that the specific factors were the main contributory factors in the mentioned proportion of the patients and not the absolute association in the patients admitted in our study. Abdominal distention, flatulence, dyspepsia was found in 63.63% patients which again corresponds to the fact that most of the patients of gall stones have non-specific distension flatulence, dyspepsia as said by text book of gastrointestinal and liver disease.[13]

Pain, right hypochondriac or on other sites was presents in 60.6% patients which corresponds nearly to the 75% figure given by Sleisinger's text book of gastrointestinal and liver disease.[13] Early GBC does not have any specific symptoms, but the general warning signs. These nonspecific symptoms have been grouped into five clinical syndromes.[14] The first is acute cholecystitis—about 1% of patients operated on for acute cholecystitis have GBC. Patients with this syndrome generally have an earlier stage of carcinoma than those who don't, and they have improved survival. Patients with chronic cholecystitis fall into the second category. The third syndrome is

biliary-tract disease which includes symptoms of jaundice, weight loss, general weakness, and pain in the right upper quadrant. Patients with this clinical syndrome have extensive disease.

In the fourth category are the clinical features of malignant tumors outside the biliary tract, which include: anorexia, weight loss, general weakness, and local complications of the tumor such as a fistula or invasion of adjacent organs.

These patients usually have extensive disease. The final syndrome includes benign manifestations outside the biliary tract; the small group of patients with this syndrome present with gastrointestinal bleeding and upper gastrointestinal obstruction. Jaundice is common and is an indicator of poor prognosis—it was associated with un-resectable disease in about 44% of our patients.[1, 15] Patients with advanced disease may also present with a palpable gallbladder mass, hard nodular liver, and malignant ascites from carcinomatosis.

This study has tried to enumerate various factors for the GBC but further studies like case control studies are required to establish the association. This study also has tried to build the back ground for the further studies and for hypothesis generation.

CONCLUSION: The proportion was more among the elderly females; the average duration of symptoms at the time of presentation was more than one year with commonest symptom being pain. The GBC and cholelithiasis had elevated level of bilirubin and cholesterol. Few factors like alcohol was identified but a case control study is required to establish the association

REFERENCES:

1. Misra NC, Misra S, Chaturvedi A. Carcinoma gallbladder. In: Johnson CD, Taylor I (Eds). Recent advances in surgery, volume 20. London: Churchill Livingstone, 1997: 69–87.
2. Nagorney DM, McPherson GA. Carcinoma of the gallbladder and extrahepatic bile ducts. Semin Oncol 1988; 15: 106–15.
3. Piehler JM, Crichlow RW. Primary carcinoma of the gallbladder. Surg Gynaecol Obstet 1978; 146: 929–42.
4. Lazcano-Ponce EC, Miquel JF, Munoz N, et al. Epidemiology and molecular pathology of gallbladder cancer. CA Cancer J Clin 2001; 51: 349–64.
5. Indian Council of Medical Research (ICMR). Annual report of population based cancer registries of the National Cancer Registry Programme (1993). New Delhi: ICMR Publication, 1996: 18.
6. Zatonski WA, Lowenfelds AB, Boyle P, Maisonneuve P, Bueno de Mesquita HB, Ghadirian P, et al. Epidemiologic aspects of gall bladder cancer: A case–control study of the SEARCH programme of the International Agency for Research on Cancer. J Natl Cancer Inst 1997; 89: 1132–8.
7. Piehler JM, Crichlow RW. Primary carcinoma of the gall bladder. Surg Gynaecol Obst 1978, 147:927-42.
8. Chao TC, Greager JA primary carcinoma of the gall bladder. J Durg Onco l991; 46: 215-221.
9. Arminski TC. Primary carcinoma of the gall bladder: A Collective review with addition of 25 cases from Grace Hospital, Detroi, Michigan, cancer 1949:2:379-98,
10. Piehler JM, Crichlow RW. Primary carcinoma of the gall bladder. Surg Gynaecol Obst 1978, 147:927-42.
11. Chao TC, Wang Cs, JENG LB et al. primary carcinoma of the gall bladder. Taiwan J Surg Oncol 61:1996, 49-55.

12. Kelly TR. Chamberlain Tr. Carcinoma of the gall bladder. The American J Surg 1982; 143:737-741
13. Fledman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 8th edition. Saunders. 2011
14. Piehler JM, Crichlow RW. Primary carcinoma of the gallbladder. Surg Gynaecol Obstet 1978; 146: 929–42.
15. Misra NC, Misra S, Chaturvedi A. Epidemiology, etiology and new perspective in carcinoma gallbladder. Indian J Surg 1998; 60: 167–75.

	cholelithiasis	**Ca gallbladder**	**others**
Female	142(71.9%)	19 (70.3%)	11 (73.4%)
Male	56(28.1%)	8 (29.7%)	4 (26.7)
total	198 (100%)	27 (100%)	15 (100%)

Table 1: Gender wise distribution of cases

Groups	**Cholelithiasis**		**Ca Gall bladder**		**Others**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Pain	120	60.6	25	92.6	4	26.7
Jaundice	10	5.1	8	29.6	2	13.3
Abdominal distension	126	63.6	2	7.4	4	26.7
Lump Right Hypochondrium	3	1.5	24	88.9	0	0.0
Lump other sites	8	4.0	2	7.4	0	0.0
Nausea	78	39.4	17	63.0	6	40.0
Vomiting	78	39.4	17	63.0	6	40.0
Anorexia	10	5.1	24	88.9	0	0.0
Decreased appetite	10	5.1	24	88.9	0	0.0
Weight loss	7	3.5	25	92.6	0	0.0
Malaise	34	17.2	21	77.8	4	26.7
Salty sweat	76	38.4	10	37.0	2	13.3

Table 2: Symptom wise distribution

Groups	**Cholelithiasis**		**Ca Gall bladder**		**Others**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Hypertension	27	13.6	3	11.1	3	20.0
Diabetes	30	15.2	6	22.2	2	13.3
Previous jaundice episode	10	5.1	9	33.3	2	13.3
Typhoid	21	10.6	2	7.4	1	6.7
Liver disease	2	1.0	8	29.6	2	13.3
Past history of ascites	0	0.0	0	0.0	0	0.0
Total parenteral nutrition	0	0.0	0	0.0	0	0.0

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Prolonged immobilization	0	0.0	0	0.0	0	0.0
Any medical/surgical intervention	7	3.5	1	3.7	0	0.0
Pregnancy history*	136	68.7	19	70.4	2	13.3
h/o OCP intake	2	1.0	0	0.0	0	0.0
Any chronic drug intake	0	0.0	0	0.0	0	0.0
Altered bowel activity	0	0.0	8	29.6	0	0.0
h/o radiologically proven liver anomaly	7	3.5	0	0.0	0	0.0
History of any endocrinopathy	32	16.2	6	22.2	2	13.3
* applicable to female cases						

Table 3: Distribution of cases based on past illnesses

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