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Original Research Article

Clinicopathological study of gall bladder carcinoma with special reference to its management in a tertiary care hospital

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ABSTRACT

Background: Incidence of gallbladder carcinoma is increasing progressively among Indians and is regarded as a major cause of mortality and morbidity. In spite of this, limited studies have been conducted so far. Objective of the study was to know the prevalence, clinicopathological aspects, and prevalent treatment protocol of gall bladder cancer in a tertiary care hospital in Eastern India.
Methods: 64 cases of histologically proven gallbladder cancer patients were studied. Patient characteristics were recorded using pretested proforma along with relevant investigations, and histopathology and treatment provided were recorded.
Results: Our study reveals that gallbladder cancer has a prominent peak in the 7th decade of life with male: female ratio of 1:2.2. Most of the patients were having body mass index between 20.0 and 24.99, which is in sharp contrast to the available literatures. Pain is the most common symptom followed by constitutional symptoms. Majority of cases presented at advanced stage (64.1%) with significantly elevated CA19.9 level, and were managed with palliative chemotherapy.35.9% of our cases were respectable at the time of diagnosis, and extended cholecystectomy could be performed in 31.3%. Log rank test showed pattern of survival of the patients who were resected was significantly better than those of who were not resected.
Conclusions: We know gallbladder cancer is a disease with very few patients amenable to surgery at the time of presentation. Thus, instead of retrospectively analyzing individual institutional data, high volume institutions with the necessary expertise for treating gallbladder cancer should collaborate with a view of generating strong evidence-based surgical guidelines.

Keywords: Cancer, Carcinoma, Gallbladder, Stage

INTRODUCTION

Carcinoma of the gallbladder (GBC) is the most common cancer of the biliary tract and one of the most extremely aggressive malignant tumors with poor prognosis.[1] It is the fifth most common GI malignancy following colon, pancreas, stomach, and esophagus.[2] There is a prominent geographic variation in incidence of gallbladder carcinoma on a global basis. High incidence of gallbladder cancer is found in South American countries, specially Chile, Bolivia, and Ecuador, and few areas of India, Pakistan, Japan, and Korea. Mortality rates from GBC are the

highest in the world in Chile, where it is the most common cancer affecting women and is the leading cause of cancer-related mortality among women.[2,3] Its incidence varies over a wide range from 27/ 100,000 in Chile to 1/100,000 in US. In India, the incidence of GBC is in the range of 1.01/100000 for males and 10.1/100000 for females, but the real number may be more in the endemic zones of Eastern Uttar Pradesh and Western Bihar where it is the third most common malignancy of the GI tract.[4,5] Gallbladder carcinoma is two to six times commoner in women than men. The incidence of GBC is directly proportional with age with highest incidence seen in the seventh and eighth decades of life. The incidence is increasing in younger individuals as per evidence.[3] The incidence of GBC is parallel with the prevalence of gallstone disease; longstanding large gallstones is associated with a higher risk of GBC and the risk of GBC has been reported to have increased four to seven-folds.[6] The association between an anomalous pancreaticobiliary duct junction (APBDJ), a porcelain gallbladder, and other biliary conditions such as choledochal cyst, Mirizzi's syndrome, primary sclerosing cholangitis (PSC), and GBC has been recognized.[7] About 1% of all elective cholecystectomies done for gallstone diseases harbor an occult gallbladder carcinoma.[8]

Surgery is the only curative option for gallbladder carcinoma. However, palliative interventions for unresectable disease, jaundice and/or duodenal obstruction are the most commonly performed surgery for gallbladder cancers. At present, patients with obstructive jaundice can be managed with either endoscopic or percutaneously placed biliary stents. There are no proven effective options for adjuvant chemotherapy or radiotherapy for patients with gallbladder cancer. The pathologic stage of gallbladder cancer determines the operative treatment for patients with localized gallbladder cancer. Patients with no evidence of distant metastasis should undergo exploration for tissue diagnosis, pathologic staging, and possible curative resection.

In this study, the clinicopathological aspects of gallbladder cancer as well as the prevalent treatment protocols and their outcomes was reviewed.

METHODS

Descriptive observational study with a cross-sectional design was done at Department of Surgery, R.G. Kar Medical College and Hospital, Kolkata for 1.5 year between January 2015 and June 2016. 64 patients diagnosed with primary gallbladder carcinoma being treated in all units of General Surgery department were included in the study. The diagnosed cases of secondary carcinoma of gallbladder, patients with history of any co-existent malignancy were excluded from the study.

Patient characteristics were recorded using pretested proforma along with relevant investigations like routine blood investigations, specific blood parameters, imaging investigations like ultrasound (USG), CECT, MRCP, histopathology and treatment provided were recorded.

Statistical analysis

Statistical analysis was conducted with help of Epi Info (TM) (version 3.5.3) which is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive data were analyzed to calculate the means with related standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviation (Z) for comparison of the difference proportions and chi-square (χ^2) test was performed to find the associations. Corrected chi-square test was performed where the cell frequencies was in negative i.e. less than zero, t-test was used to compare the means.

Kaplan-Meier survival analysis followed by Log-Rank test was used to compare the survival pattern of the patients. $p<0.05$ was taken to be statistically significant.

RESULTS

Table 1: Age and gender distribution of the patients.

Age and gender	Number	%
Age group (in years)		
40-49	2	3.10
50-59	10	15.60
60-69	44	68.80
70-79	8	12.50
Total	64	100.00
Mean±S.D.	63.31±6.24	
Median	64	
Range	40 - 75	
Gender		
Male	20	31.30
Female	44	68.80
Total	64	100.00
Female: Male	2.2:1.0	

The mean age (mean ± s.d.) of the patients was 63.31±6.24 years with range 40 - 75 years and the median age was 64 years. Test of proportion showed that the patients in the age group 60-69 years (68.8%) were significantly higher than other age group ($Z=7.61$; $p<0.0001$).

Table 2: Distribution of blood group of the patients.

Blood group	Number	%
A+ve	26	40.70
A-ve	1	1.60
B+ve	11	17.20
B-ve	3	4.70
AB+ve	6	9.40
O+ve	15	23.40
O-ve	2	3.10
Total	64	100.00

Test of proportion showed that females (68.8%) were significantly higher than that of males (31.3%) (Z=5.30; p<0.0001). The ratio of female and male was 2.2:1.0. Test of proportion showed that proportion of Hindu (51.6%) was higher than Muslim (48.4%) but it was not significant (Z=0.45; p=0.65). Test of proportion showed that patients with A+ve blood group (40.7%) was higher than other blood group (Z=2.62; p=0.0088). Test of proportion showed that proportion of patients from rural area (71.9%) was significantly higher than other place of residence (Z=7.54; p<0.0001).

Table 3: Distribution of socio-economic status of the patients.

Socio-economic status	Number	%
Lower class	18	28.10
Lower middle class	35	54.70
Upper middle class	11	17.20
Total	64	100.00

Test of proportion showed that proportion of patients from lower middle class (54.7%) was significantly higher than other place of residence (Z=3.81; p<0.0001) followed by from lower class (28.1%). Most of the patients were housewife (59.4%) followed by labour (17.2%) (Z=6.31; p<0.001). Most of the patients had habit of use of tobacco (chewing or smoking) (34.4%). Majority of them had no addiction (51.6%).

Table 4: Distribution of presentation by the patients.

Presentation	Number	%
RUQ mass	2	3.1
Anorexia	20	31.3
Nausea	21	32.8
Vomiting	3	4.7
RUQ pain	35	54.7
Ascites	17	26.6
Hepatomegaly	14	21.9
Anemia	14	21.9
Weight loss	28	43.8
Acute cholecystitis	4	6.3
Obstructive Jaundice	10	15.6

Table 5: Distribution of CA-19.9.

CA-19.9	Number	%
0-37	1	1.60
38-100	16	25.00
100-1000	12	18.80
>1000	35	54.70
Total	64	100.00

Non-vegetarian patients (84.4%) were significantly higher than that of vegetarian (45.6%) (Z=9.72; p<0.001). Only 2(3.1%) patient had history of typhoid. 18(28.1%) patients had gallstone. 14 (31.8%) of them were exposed to hormone. Proportion of patients with overweight (60.9%) was significantly higher than other BMI (Z=7.61; p<0.0001). Only 1 (1.6%) patient had obesity. 24(37.5%) were underweight. Pain (54.7%) is the most common symptom followed by constitutional symptoms. Most of the patients had level of CA-19.9>1000 which was significantly higher (Z=4.33; p<0.001)

Table 6: Distribution of TNM and stage.

Variables	Number	%
TNM		
T2N0M0	10	15.60
T2N1M0	4	6.30
T3N0M0	9	14.10
T3N1M0	12	18.80
T3N1M1	28	43.80
T4N1M1	1	1.60
Total	64	100.00
Stage		
II	10	15.60
IIIA	9	14.10
IIIB	16	25.00
IVA	1	1.60
IVB	28	43.80
Total	64	100.00

Most of the patients (43.8%) were having tumor stage as T3N1M1 which indicated that most of the patients of this region reported to hospital at semi-advanced to advanced stages of their disease. Thus, there was limited scope of resection for the curative treatment of the treatment. Only 15.6% of them were with TNM staging as T2N0M0. 43.8% of the patients were with their disease at Stage-IVB. In overall 45.4 % of the patients were with Stage-IV and 15.6% were with Stage-II. 35.9% of the patients were at respectable stage at the time of diagnosis.

Table 7: Distribution of stage at diagnosis.

Stage at diagnosis	Number	%
Resectable	23	35.9
Unresectable	41	64.1
Total	64	100.0

Table 8: Distribution of treatment received.

Treatment received	Number	%
Extended cholecystectomy	20	31.30
Open biopsy	6	9.40
Palliative chemotherapy	35	54.70
Simple cholecystectomy	3	4.70
Total	64	100.00

Most of them (54.7%) were treated with palliative chemotherapy due to advanced stage of their diseases. 81.3% of the of the histopathological findings was Adenocarcinoma which was significantly higher in

incidence than Adeno-squamous Carcinoma (18.8%) (Z=8.83; p<0.0001).

Most of the patients (60.9%) were alive by the end of the study which was significant (Z=3.75; p=0.0002). 4.7% were lost to follow-up after the completion of their treatment.

Table 9: Distribution of status at last follow-up.

Chemotherapy	Number	%
Alive	39	60.90
Dead	22	34.40
Lost to Follow-up	3	4.70
Total	64	100.00

Table 10: Distribution of duration of follow-up and status at last contact.

Duration of follow-up (in months)	Alive	Dead	Total
<1	0	1	1
Row %	0	100	100
Col %	0	4.5	1.6
6-January	1	14	15
Row %	6.7	93.3	100
Col %	2.6	63.6	24.6
12-July	30	7	37
Row %	81.1	18.9	100
Col %	76.9	31.8	60.7
>12	8	0	8
Row %	100	0	100
Col %	20.5	0	13.1
Total	39	22	61*
Row %	63.9	36.1	100
Col %	100	100	100
Duration of follow-up (in months)	**Alive**	**Dead**	**Lost to Follow-up**	**Total**
Resectable	22	1	0	23
Row %	95.7	4.3	0	100
Col %	56.4	4.5	0	35.9
Unresectable	17	21	3	41
Row %	41.5	51.2	7.3	100
Col %	43.6	95.5	100	64.1
Total	39	22	3	64
Row %	60.9	34.4	4.7	100
Col %	100	100	100	100

*3 patients were lost to follow-up

15 (24.6%) patients died within 06 months and 7 (11.5%) patients died after 06 months. Only 1 (4.3%) who was resected died and 22(95.7%) of them were alive by the end of study which was significantly higher (Z=12.92; p<0.0001). 21 (51.2%) who were not resected died and 17 (41.5%) of them were alive by the end of study, but there was no significant difference between the two proportions (Z=1.37; p=0.17). Log Rank test showed pattern of survival of the patients who were resected was significantly better than that of who were not resected. (Log Rank Test-20.13; p<0.00001)

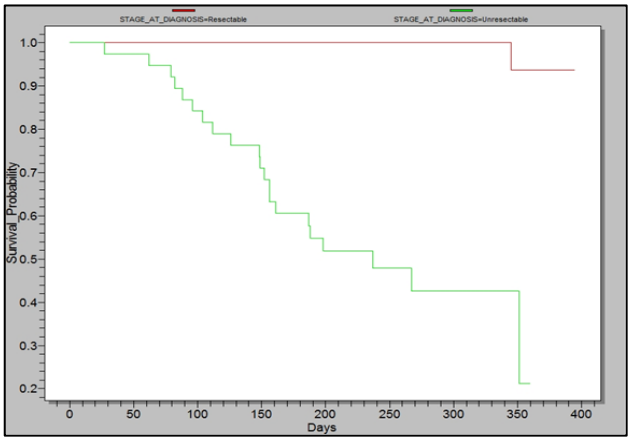

Figure 1: Graph for Kaplan-Meier Survival Analysis for comparison of pattern of survival of the resected and unresected patients.

DISCUSSION

From this study GBC has a peak incidence in the 7th decade of life both in males and females. Nearly 68.8% cases (44 out of 64 cases), were clustered in the age group of 60-69 years. The youngest case in our study was 40 years old lady. The mean age of presentation in our case group was 63.31years. Indian perspective is different from that of Western data. There are increasing number of patients presenting at younger age group. The lower age of presentation in the Indian population has also been observed in previous registers. Shukla et al. reported mean age of the patient to be 50 years (range 40- 60 years) in Indian scenario. The mean age of the patients with carcinoma of the gallbladder was 50±1.39 years.[1] According to presently available world literatures, carcinoma of the gallbladder is predominantly a disease of elderly population, with the peak incidence being in the seventh decade.

In our study disease shows a majority in females, the male: female ratio being 1:2.2 and in every age group female almost invariably out represents male. In almost all countries, age-standardized incidence rates are less for men than women. In India, the incidence of gall bladder carcinoma is in the range between 1.01/100000 for males and 10.1/100000 for females (ICMR 1996).[7]

In respect to blood groups, 40.7% of patients are from blood group A+ve and 23.4% of patients having blood group O+ve; which may be opened the doors for further studies in this category. Pandey et al have shown increased frequency of carcinoma gallbladder in patients with A+ and AB+ blood group.[9] Majority of patients belong to lower or lower-middle socio-economic status. Most of

them are housewife followed by labour and farmer. This stratification is done according to modified Prasad's scale for socio-economic status. This finding may also be part of the fact that this institution mainly serves the population belonging to middle or poor socio-economic condition. So, data from other institutions of this region should also be taken into consideration before concluding. The national level data reflects that incidence of gall bladder cancer is predominant of in rural population with lower income and education, who are either unaware of the extreme consequences or are too poor to afford the cost of diagnosis and treatment and hence, continue to suffer.[10]

In the existing literature higher incidence of this carcinoma is reported in relation to lifestyle factors like smoking, tobacco chewing and alcohol consumption.[1] The risk of cancer was more than twice in patients who used to chew tobacco. In our study, most of the patients had habit of use of tobacco (chewing or smoking) (34.4%). Majority of them had no addiction (51.6%).

Gall stone, which is a risk factor for gall bladder carcinoma, is present in 28.1% of cases in our study population.3.1% of patients were presented with documented *S. typhi* infection. No positive family history of Gallbladder malignancies are present in our study. 47.7% of carcinoma gallbladder patients are having increased hormonal exposure of estrogen and progesterone in body in the form of OCP intake, early age at menarche, late age of first pregnancy, late menopause etc. Existing literatures support our findings. Cholelithiasis is frequently associated with carcinoma gallbladder in up to 40%-100% patients and is the most common associated factor independent of age or sex (Hart et al). Singh et al reported a high risk of carcinoma gallbladder in women having early menarche, late marriage, late pregnancy, and prolonged reproductive phase.[11]

From our study the mean BMI of the patients was 20.95±2.10 kg/m^2 with range 17 - 29.3 kg/m^2 and the median was 20.7 kg/m^2. Proportion of patients with overweight (60.9%) was significantly higher than other BMI. Only 1 (1.6%) patient had obesity and 24 (37.5%) cases were underweight. Current literatures support that increased BMI and obesity is a causative factor for development of carcinoma gallbladder. Due to the late presentation of the disease and advanced stage at presentation the actual causal relationship between obesity and carcinoma gall bladder is exceedingly difficult.[11]

Now coming to clinical presentation most common symptom to be presented with is pain (54.7%). Pain is due to acute (6.3%) or chronic cholecystitis, due to stretching of capsule of the gallbladder or due to malignant infiltration of surrounding visceral structures. Constitutional symptoms like nausea and vomiting are present in 32.8% and 4.7% of patients, respectively. In Indian scenario Shukla et al reviewed 315 patients treated at their centre and reported pain (85%) to be the commonest symptoms followed by icterus (60.3%), Lump and loss of appetite (40%) each. They noted hepatomegaly in 85.7% and jaundice in 72.3% patients.[1] Western studies also reflect remarkably similar results. Symptoms are typically indolent. Chronic abdominal pain, anorexia, or weight loss are common initial complaints (Levy et al).

Among clinical findings ascites is most commonly present. It occurs due to dissemination process and due to hypoproteinemia. Existing literature supports our findings as Piehlar and Crichlow state that a small percentage of patients present with benign appearing symptoms appear to arise from some other adjacent organs. These symptoms too represent a locally advanced disease and curative resection is seldom possible. Survival is poor in this group of patients.[12]

In our series only 3 cases were incidentally detected gallbladder carcinoma. All these three patients had undergone laparoscopic cholecystectomy outside for chronic calculous cholecystitis and later presented to us with histopathological diagnosis of carcinoma gallbladder. No patient had port site metastasis.

Most of the patients (54.7%) had level of CA-19.9 >1000U/ml which was significantly higher. This could be attributed to the presentation of the patients in their later stage. CA-19.9 has a prognostic importance and elevated preoperative serum CA-19.9 level is associated with poor prognosis in gallbladder cancer.[13]

CT has better accuracy for detecting lesions than US, but CT has low sensitivity for picking up lymph node metastasis, though its positive predictive value > 90%. Both Ultrasound and CT scan may not show locoregional GI and omental infiltration as well as peritoneal deposits (Shiwani et al). In our study, preoperative imaging of the abdomen (both US and CT) showed the presence of gallstones in 18 (28.1%) cases and a mass in the gallbladder was evident in 61 patients (95.3%) (3 cases were incidentally diagnosed GBC). Hepatic involvement was picked up accurately in almost all the patients; however, the pickup rate for lymph nodes was rather low; peritoneal deposits were not picked up in any case.

Regarding stage at presentation we have found that majority of the patients (45.3%) presented with advanced disease i.e. stage IV disease that means tumor invasion to main portal vein or hepatic artery or two or more extrahepatic organs or structures or metastases to periaortic, pericaval, superior mesenteric artery, and/or celiac artery lymph nodes or distant metastasis. Only 15.6% of patients presented early at stage I and II i.e. tumor limited within serosa.

In our study most of the cases presented at advanced stage (64.1%), they were referred to Department of Radiotherapy of our Institute for palliative therapy. They were managed with palliative chemotherapy with 2-weekly regime with Gemcitabine and Oxaliplatin for 6 to 8 cycles as they could tolerated.35.9% of our cases were

resectable at the time of diagnosis and extended cholecystectomy could be performed in 31.3% cases. In 9.4% cases only open biopsy was taken and further procedure with curative intent was abandoned as there was M1 disease (per operative findings). Based on literature, simple cholecystectomy is the treatment for patients with T1a GBC limited to mucosa, laparoscopic approach is an accepted and appropriate modality in this regard.[14,15] The five-year survival is 95%-100% after simple cholecystectomy. An extended cholecystectomy is not recommended unless there are tumor invasions cystic duct margin.[16] As per T1a GB cancer literature, the recurrence rate is about 1.1%. The most frequent site of recurrence was the common bile duct (more than 50% of the total cases).[14] Therefore, histopathologic examination is recommended to rule out tumor invasions in cystic duct margin. If this is the case, extrahepatic bile duct (EHBD) resection should be considered.[14] Lymph node metastasis has been reported in less than 2.5% of total cases; therefore, lymph node dissection is not recommended for patients with T1a GB cancer.[14] An extended cholecystectomy is generally recommended for patients with GB cancer at stage T2 or above.[17] Lymph node metastasis is an established prognostic factor, and its occurrence varies based upon the depth of tumor invasion: pT1a=0%-2.5%; pT1b=5%-16%; pT2=9%-30%; T3=39%-72%; and T4=67%- 80%.[14,18] There is no evidence-based guideline regarding the extent of lymph node dissection in extended cholecystectomy. There is no effective treatment modality other than surgery for GBC. Surgical treatments are recommended for GB cancer patients if complete tumor removal (R0 resection) can be achieved through a combined resection of the hepatic artery and portal vein. Combined resection is recommended for advanced cases with invasion to adjacent organs (colon and duodenum), but favorable prognoses are not guaranteed despite R0 resection. The selection of appropriate patients is essential.[19] The median and one-year survival rates in patients with unresectable GB cancer are reported to be approximately 2-4 months and less than 5%, respectively. It is also known that cytoreductive surgery is not useful in patients with GB cancer.[20] Palliative surgery is usually done to improve the quality of life and prolong the short-term survival period in patients with unresectable advanced GBC. Palliative options are simple cholecystectomy in a nonradical way. In presence of concurrent biliary obstruction or gastric outlet obstruction, bypass surgery would improve the quality of life. The fundamental principles for the treatment of incidental GB cancer found on postoperative histopathology are similar to those described earlier, i.e. no additional intervention is required for histologically proven T1a GBC if the GB was completely resected during previous surgery.[14] However, in cases of histologically proven T1b GB cancer, there is still controversy regarding whether extended cholecystectomy or follow-up without additional surgeries should be performed.[14,21] In GB cancer of T2 or above, the additional extended cholecystectomy is recommended. There are no established reports regarding the timing of additional surgeries; however, some studies have been performed immediately after GB cancer diagnosis.[22,23]

81.3% of the histopathological findings was Adenocarcinoma in our study. Adenocarcinoma is the most common histological subtype of gallbladder malignancy, contributing 90-95% of all cases.

All patients were followed-up at 1-month, 3-month, 6-month and at 1- year.60.9% cases were alive after 1 year. 4.7% were lost to follow-up after the completion of their treatment. 15 (24.6%) patients died within 06 months and 7 (11.5%) patients died after 06 months. Log Rank test showed pattern of survival of the patients who were resected was significantly better than that of who were not resected.

Surgical resection with R0 margin is the only radical treatment modality for GBC at present, but the resection rate is unfortunately about 25%-30% only. Nearly 50% of patients are at risk of recurrence even after undergoing R0 resection.[24,25] Recurrent GBC cases are managed with local treatment modalities like postoperative adjuvant chemotherapy or concurrent chemoradiation therapy (CCRT).

CONCLUSION

GBC is not a rare clinical entity among Indians, unlike western countries. Gallbladder cancer incidence was found mostly at seventh decades in the study population with a predominance among rural population. Gallbladder cancer in the eastern Indian population differs in a few epidemiological parameters from this cancer elsewhere, and further study is needed to identify unknown environmental factors if any, as the underlying cause. It is predominantly a disease of females. Smoking, tobacco use, betel nut and alcohol addiction have a contributory effect. Some association with gallstone and increased hormonal exposure is found in carcinoma of gallbladder in our study.

As the volume of patients studied was low for full-fledged epidemiologic study, further research is needed for identification of factors responsible for occurrence of gallbladder carcinoma. There are only a few systematic reviews of the GB cancer surgical literature. There are many retrospective studies in this series, but when taken as a whole, these have the following limitations: 1) small numbers of enrolled patients; 2) heterogeneity of patient populations across studies, and 3) inconsistent surgical procedures across studies. Therefore, we have experienced significant difficulty in coming to conclusion and generating recommendations based on the existing clinical evidence.

We must accept the fact that very few numbers of patients with gallbladder cancer are amenable to surgery at the time of presentation. Thus, instead of analyzing individual institutional data retrospectively, high volume centres with optimum expertise for treating gallbladder cancer should

collaborate for generating strong evidence-based surgical guidelines to face this dreadful disease.

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REFERENCES

1. Shukla VK, Khandelwal C, Roy SK, Vaidya MP. Primary carcinoma of the gallbladder: a review of a 16-year period at the University hospital. J Surg Oncol. 1985;28:32-5.
2. Orth K, Berger HG. Gallbladder carcinoma and surgical treatment. Langenbecks Arch Surg. 2000;382:501-8.
3. Carriaga MT, Henson DE. Liver, gallbladder, extrahepatic bile ducts, and pancreas. Cancer. 1995;75:171.
4. Kiran RP, Pokala N, Dudrick SJ. Incidence pattern and survival for gallbladder cancer over three decades--an analysis of 10301 patients. Ann Surg Oncol. 2007;14:827.
5. Yang JD, Kim B, Sanderson SO. Biliary tract cancers in Olmsted County, Minnesota, 1976-2008. Am J Gastroenterol. 2012;107:1256.
6. Diehl AK. Epidemiology of gallbladder cancer: a synthesis of recent data. J Natl Cancer Inst. 1980;65:1209.
7. Indian Council of Medical Research (ICMR) Annual report of population-based cancer registries of the National Cancer Registry Program (1993), (1996). New Delhi: ICMR publication.
8. Randi G, Franceschi S, Vecchia C. Gall bladder Cancer worldwide: Geographical distribution and Risk Factors. Int J Cancer. 2006;118:1591-602.
9. Pandey M, Gautam A, Shukla VK. ABO and Rh blood groups in patients with cholelithiasis and carcinoma of the gallbladder. BMJ. 1995;310:1639
10. Shukla VK, Singh H, Pandey M, Upadhyay SK, Nath G. Carcinoma of the gallbladder: is it a sequel of typhoid. Dig Dis Sci. 2000;45:900-3.
11. Singh S, Sah S, Shukla VK. Cytochrome P-450: its association with lipid peroxidation and gallbladder carcinogenesis. Cancer J. 1998;11:315-7.
12. Piehler JM, Crechlow RW. Primary carcinoma of the gallbladder. Surg Gynecol Obstet. 1978;146:929-42.
13. Ritts RE, Nagomey DM, Jacobson DJ. Comparison of preoperative CA 19-9 levels with result of diagnostic imaging modalities in patients undergoing laparotomy for suspected pancreatic or gall bladder disease. Pancreas. 1994;9:707-16.
14. Lee SE, Jang JY, Lim CS, Kang MJ, Kim SW. Systematic review on the surgical treatment for T1 gallbladder cancer. World J Gastroenterol. 2011;17:174-80.
15. Choi SB, Han HJ, Kim CY, Kim WB, Song TJ, Suh SO, et al. Incidental gallbladder cancer diagnosed following laparoscopic cholecystectomy. World J Surg. 2009;33:2657-63.
16. Isambert M, Leux C, Métairie S, Paineau J. Incidentally discovered gallbladder cancer: When, why and which reoperation? J Visc Surg. 2011;148:77-84.
17. Kohya N, Miyazaki K. Hepatectomy of segment 4a and 5 combined with extra-hepatic bile duct resection for T2 and T3 gallbladder carcinoma. J Surg Oncol. 2008;97:498-502.
18. Miyakawa S, Ishihara S, Horiguchi A, Takada T, Miyazaki M, Nagakawa T. Biliary tract cancer treatment: 5,584 results from the biliary tract cancer statistics registry from 1998 to 2004 in Japan. J Hepatobiliary Pancreatic Surg. 2009;16:1-7.
19. Lim CS, Jang JY, Lee SE, Kang MJ, Kim SW. Reappraisal of hepatopancreatoduodenectomy as a treatment modality for bile duct and gallbladder cancer. J Gastrointestinal Surg. 2012;16:1012-8.
20. Batra Y, Pal S, Dutta U, Desai P, Garg PK, Makharia G, et al. Gallbladder cancer in India: a dismal picture. J Gastroenterol Hepatol. 2005;20:309-14.
21. Choi ST, Hwang S, Lee SG, Lee YJ, Park KM, Kim KH, et al. Prognosis of patients with the gallbladder carcinoma undergone laparoscopic cholecystectomy as an initial operation. J Korean Surg Soc. 2003;65:140-4.
22. Goetze TO, Paolucci V. Immediate re-resection of T1 incidental gallbladder carcinomas: a survival analysis of the German Registry. Surg Endosc. 2008;22:2462-5.
23. Goetze TO, Paolucci V. Adequate extent in radical re-resection of incidental gallbladder carcinoma: analysis of the German Registry. Surg Endosc. 2010;24:2156-64.
24. Macdonald OK, Crane CH. Palliative and postoperative radiotherapy in biliary tract cancer. Surg Oncol Clin N Am. 2002;11:941-54.
25. Kim WS, Choi DW, You DD, Ho CY, Heo JS, Choi SH. Risk factors influencing recurrence, patterns of recurrence, and the efficacy of adjuvant therapy after radical resection for gallbladder carcinoma. J Gastrointest Surg. 2010;14:679-87.

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