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## Gallbladder cancer: Progress in the Indian subcontinent

Ashok Kumar, Yajnadatta Sarangi, Annapurna Gupta, Aarti Sharma

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### Abstract

Gallbladder cancer (GBC) is one of the commonest biliary malignancies seen in India, Argentina, and Japan. The disease has dismal outcome as it is detected quite late due to nonspecific symptoms and signs. Early detection is the only way to improve the outcome. There have been several advances in basic as well as clinical research in the hepatobiliary and pancreatic diseases in the West and other developed countries but not enough has been done in GBC. Therefore, it is important and the responsibility of the countries with high burden of GBC to find solutions to the many unanswered questions like etiopathogenesis, early diagnosis, treatment, and prognostication. As India being one of the largest hubs for GBC in the world, it is important to know how the country has progressed on GBC. In this review, we will discuss the outcome of the publications from India highlighting the work and the developments taken place in past several decades both in basic and clinical research.

**Key Words:** Gallbladder cancer; India; basic research; Clinical research; Surgery; Therapeutics

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**Core Tip:** This review is important to know the work done on gallbladder cancer from the country with high incidence of the disease and struggling to do its best. Research outcome may help to compare with the work being done in rest of the world and for the future collaborative research to find way for early diagnosis and to improve the treatment outcome of this aggressive disease.

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## INTRODUCTION

Gallbladder cancer (GBC) is the most common and most aggressive malignancy of the biliary tree. Early diagnosis is crucial for better prognosis of this dreaded disease. However nonspecific clinical presentations often hinder the accurate diagnosis of GBC at an early stage. GBC remains a highly lethal disease, with only 10% of all patients are upfront resectable. People diagnosed with early GBC typically have a 5-year survival rate of 30%-40%, whereas individuals with locally advanced lesions have a one-year survival rate of around 10%[1].

India carries one of the most substantial burdens of this condition, with its peak incidence among women in northern India reaching 21.5 cases per 100000 individuals. The substantial morbidity and mortality from GBC significantly hinder global cancer control efforts, particularly in high-risk populations. Currently, effective strategies to reduce GBC mortality are lacking.

Chile has the highest incidence of GBC globally, with 9.7 new cases per 100000 inhabitants each year. This is followed by Bolivia (8.1 per 100000 inhabitants), South Korea (6.5 per 100000 inhabitants), Laos (4.7 per 100000 inhabitants), and Japan (4.7 per 100000 inhabitants)[2]. In the United Kingdom, GBC accounts for less than 1% of all new cancer cases. In contrast, United States has significantly lower incidence rate compared to global trends, with rates of 1.4 per 100000 among women and 0.8 per 100000 among men.

Despite of large case load of GBC in Indian subcontinent, the extent of advancement in clinical and basic research related to the etiology, pathogenesis, diagnosis, prevention, and treatment of GBC remains unclear. This review seeks to evaluate India's progress in various aspects of GBC research and provide a comprehensive summary of GBC studies conducted across the Indian subcontinent. In this review, we have endeavored to encompass all the significant research conducted in India on GBC.

## METHODOLOGY

We systematically reviewed published literature from India on gall bladder (GB) cancer between year 2000 to 2023 from online search engine PubMed and Medline using the search terms gallbladder, etiopathogenesis, prevention, Indian studies, basic research, epidemiological studies, clinical studies, and bullion operators like AND, OR, NOT. The secondary sources retrieved from these publications were identified through a manual search and assessed for relevance. Publications have been categorized in detail covering the areas of epidemiology, basic and clinical work. The result has been discussed in detail.

## RESULTS

We have categorized the research published from 2000 to 2023 into five distinct areas: Demography and Etiopathogenesis, Clinicopathogenesis, Genetics and Polymorphism, Diagnostics and Imaging, Surgical Approaches and Resection, and Multimodality Therapy.

## STUDIES ON DEMOGRAPHY AND ETIOPATHOGENESIS

### Epidemiology

India has a high incidence of GBC and accounts for approximately 10% of the global burden of this disease. There is a pronounced regional disparity in GBC incidence across India, with considerably higher rates observed in the northern and northeastern regions compared to southern states. For instance, GBC incidence in North India (8.9/100000) is approximately 10 times greater than that in Chennai (0.8/100000). According to data from the National Cancer Registry, Delhi exhibits a similar Age-Standardized Rate (ASR) for GBC comparable to that of Chile. According to a study by Dutta *et al* [3], the ASRs for GBC in northern India and northeastern India are 11.8 per 100000 population and 17.1 per 100000 population, respectively. These rates are comparable to the high incidence areas of Bolivia (14/100000) and Chile (9.3/100000). Phadke *et al*[4] conducted a study to calculate the Annual Percentage Change (APC) in age-adjusted incidence rates of a specific health condition. They found significant APC, in the high-risk regions of Cachar [7.0 ( $P = 0.02$ )], Delhi [4.0 ( $P = 0.04$ )], and Kamrup [4.3 ( $P = 0.02$ )]. Meanwhile, in the low-risk regions of Bengaluru and Pune, the APC was 5.7 ( $P = 0.04$ ) and 3.4 ( $P = 0.04$ ), respectively. S *et al*[5] discovered that GB cancer incidence among women in Kamrup urban (ASR 16.2) was second highest after Chile[5]. Some epidemiological studies have also shown that, the population living in high-risk regions is associated with an elevated risk of developing GBC. Mhatre *et al*[6] from Tata Memorial Hospital

(TMH) in Mumbai conducted a study revealing demographic disparities in GBC. The study revealed 4.82-fold higher odds (95%CI: 3.87-5.99) of developing GBC among individuals born in high-risk regions compared to those born in low-risk regions. Additionally, there was a dose-response relationship observed between GBC risk and length of stay in high-risk regions, showing a lifetime exposure odds ratio (OR) of 5.58 (95%CI: 4.42-7.05) with a significant *P* value ( $\leq 0.001$ ). Notably, the risk of GBC persisted even among individuals who migrated from high-risk to low-risk regions. All these studies indicate a higher disease burden of GBC in India.

### Demographic risk factors

Numerous risk factors contribute to the development of GBC in Indian patients, particularly in high-risk regions, notably in the northern and northeastern states where many studies have been conducted. The Sutlej, Ganges, Yamuna, and Brahmaputra rivers, originating from glaciers in the northern Himalayas, flow east and became contaminated downstream by industrial and human waste. Several studies have explored the hypothesis that increased pollution of these rivers contributes to the risk of GBC in the North Indian population. Gupta *et al*[7] found that exposure to benzene hexachloride, dichlorodiphenyltrichloroethane, and high concentrations of cadmium in the Ganga River contribute to development of GBC. Several studies have shown an increase in *Helicobacter pylori* (*H. pylori*) and coliform counts in drinking water in the rivers mentioned above. Several studies have also shown that *Salmonella typhi* (*S. typhi*) and *H. pylori*, transmitted through fecal contamination, are linked to the development of GBC[8,9]. Evidence suggests that *Helicobacter* species may increase the risk of GBC, with ORs ranging from 2.7 to 12 in different studies from India. Tewari *et al*[10] found that *S. typhi* is significantly associated with GBC compared to gallstone disease (GSD; 33% vs 0%).

Many studies were conducted to find the other demographics risk factors for this dreaded disease. Mhatre *et al*[11] discovered that there is an increased risk of GBC associated with higher parity and a shorter reproductive lifespan. Same authors in another study reported that consumption of mustard oil was associated with increased risk of GBC[12]. In a gallstone-matched study, Mishra *et al*[13] identified several factors associated with GBC, notably age 50 years or older, low literacy, below-poverty-line socioeconomic status, infrequent bowel habits, history of hypertension, use of antihypertensive medications, non-vegetarian diet, cooking with firewood, consumption of hand pump water, and high coffee intake[13]. Gallstones are the most significant risk factor for GBC, present in 60%–90% of GBC patients compared to 20%–25% of an age-matched population[14]. Several studies conducted in the early 2000s explored the relationship between gallstones and GBC. Mhatre *et al*[15] identified that the presence of gallstones is associated with an elevated risk of developing GBC. Dutta *et al*[16] found that the presence of gallstones was an independent determinant associated with a younger age of patients with GBC (OR 4, 95%CI: 1.5-11; *P* = 0.006). Sharma *et al*[17] identified that the duration of symptom for gall stone disease is a significant risk factor for GBC. Conversely, Narang *et al*[18] found that a higher number and larger size of gallstones, along with the presence of cholesterol in gallstones, may also elevate the risk of developing GBC. Singh *et al*[19] reported that as the size of gallstones increases, there is a progression in the gallbladder mucosa response, transitioning from cholecystitis and hyperplasia to metaplasia, ultimately into carcinoma. Studies conducted in India highlighted the composition of bile and its role in gallbladder carcinoma. Sharma *et al*[19] discovered that patients with GBC had a substantial decrease in lipid species and an increase in bacterial taxa in their bile. The summary of other relevant publications on demography and etiopathogenesis is presented in Table 1[20-37].

## STUDIES ON MOLECULAR PATHOGENESIS-GENETICS AND POLYMORPHISM

Our current understanding of the genetic and molecular changes associated with GBC remains limited. GBC, like other tumors, is driven by multiple genetic alterations. Several studies in India have aimed to elucidate the genetic mutations and molecular pathogenesis underlying gallbladder carcinoma. Studies from Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, have identified *KRAS*, *PIK3CA*, and *EGFR* are the some of commonly mutated genes in GBC. A summary of genes related to different stages of pathogenesis is illustrated in Figure 1. Iyer *et al*[38] identified *ERBB2* alterations in early-stage GBC and proposed that anti-EGFR therapy (Afatinib) could be a promising therapeutic option. Kazmi *et al*[39] studied the role of *KRAS* and found that K-ras codon 12 mutations were highly prevalent in GBC and were associated with bad prognoses in resected GBC. Gupta *et al*[40] identified a new protein called Survivin, which was significantly associated with GBC, suggesting its role in the pathogenesis of GBC. Many studies were conducted regarding single gene expression and Global gene expression in GBC.

### Studies on single gene expression

Many studies were conducted in India exploring single gene expression in GBC. Kumari *et al*[41] found that that C-erbB2 positive tumors exhibited a longer median survival compared to C-erbB2 negative tumors. Misra *et al*[42] studies p53 protein overexpression in gallbladder carcinoma. Singh and colleagues reported that MASPIN and THBS1 have an important epigenetic role in GBC[43]. Tekcham *et al*[44] identified downregulation of *PTEN* in GBC. Rai *et al*[45] found that the expression of CCKAR was significantly higher in GBC compared to GSD.

### Studies on global gene expression

Several studies have also investigated global gene expression in GBC. Yadav *et al*[46] conducted a study on targeted gene sequencing of GBC and identified 184 somatic mutations and 60 germline mutations in cancer driver genes such as *SMAD4*, lysine methyltransferase 2C (*KMT2C*), and tumor protein p53. Kumari *et al*[47] used high-throughput methods and detected mutations in *P53*, *STK11*, *RICTOR*, *TSC2*, as well as *FGF3-TACC* fusion and *FGF10* amplification using next-generation sequencing platform.



**Table 1 Studies on etiopathogenesis of gall bladder cancer**

Serial No.	Sample size	Findings	Ref.
1	GBC (214) controls (214)	Biomass burning was recognized as a significant risk factor for GBC	Shridhar <i>et al</i> [20]
2	GBC (200); Gall stone disease (200) controls (200)	Residence in the Gangetic belt, consumption of tea, tobacco, joint family structure, chemical exposure, fried food, and high levels of secondary bile salts are risk factors of GBC	Jain <i>et al</i> [21]
3	GBC (54)	Cholelithiasis is a predisposing factor for GBC	Bhattacharjee and Nanda[22]
4	GBC (1291)	Exposure to high soil arsenic levels and proximity to river ganga are risk factors for GBC	Madhawi <i>et al</i> [23]
5	GBC (333)	Smoking, cholelithiasis, alcohol consumption, typhoid in the past, post-menopausal women are risk factors for GBC	Tyagi <i>et al</i> [24]
6	GBC (63)	Poor hygiene and water supply, malnutrition, cholelithiasis, tobacco and alcohol consumption are modifiable risk factors for GBC	Khan <i>et al</i> [25]
7	GBC (122); controls (122)	Education, intake of vitamin C, parity, and type of fuel used were significant factors for GBC	Panda <i>et al</i> [26]
8	GBC (49)	About 75% of patients diagnosed with GSD showed detectable <i>H. pylori</i> DNA in their gallbladder tissue	Bansal <i>et al</i> [27]
9	GSD (330)	As the stone size increases, gallbladder mucosa changes progress from cholecystitis to carcinoma	Mathur <i>et al</i> [28]
10	GBC ( <i>n</i> = 11), Chronic cholecystitis ( <i>n</i> = 23), Xantho-granulomatous cholecystitis ( <i>n</i> = 11)	The cholesterol content in gallstones of GBC was significantly lower compared to that in benign gallbladder diseases	Srivastava <i>et al</i> [29]
11	GBC (390)	Chronic bacterial infection of bile is considered an etiological factor in the development of gallbladder carcinoma	Sharma <i>et al</i> [30]
12	GSD (101)	<i>H. pylori</i> colonizes regions of gastric metaplasia within the gallbladder	Misra <i>et al</i> [31]
13	GBC (328); controls (328)	Females, consumption of mustard oil, Family history, low socioeconomic status and drinking water from hand pump were the risk factors for GBC	Kumar <i>et al</i> [32]
14	GBC (27), GSD (196)	High prevalence of salmonella typhi in gall bladder carcinoma	Vaishnavi <i>et al</i> [33]
15	GBC (38)	Higher levels of biliary nitrate associated with the gallbladder carcinogenesis	Shukla <i>et al</i> [34]
16	GBC ( <i>n</i> = 30); controls ( <i>n</i> = 30)	Decreased levels of selenium (Se), zinc (Zn), and vitamin E are associated with an increased risk of gallbladder carcinoma	Shukla <i>et al</i> [35]
17	GBC ( <i>n</i> = 30); controls ( <i>n</i> = 30)	Significantly high biliary benzene hexachloride and dichloro diphenyl trichloroethane associated with gallbladder carcinogenesis	Shukla <i>et al</i> [36]
18	150 GBC	Gall stones associated with development of metaplastic, dysplastic and neoplastic mucosal changes of gall bladder mucosa	Gupta <i>et al</i> [37]

GSD: Gallstone disease; GBC: Gallbladder cancer; *H. pylori*: *Helicobacter pylori*.

Loss of heterozygosity (LOH) is frequently observed in GBC. In GBCs this change is commonly seen as the loss of one copy of a gene (heterozygous allelic loss) in multiple chromosomal regions. This phenomenon has been extensively studied and is known as LOH. Priya *et al*[48] observed LOH in *FHIT* gene. Jain *et al*[49] detected LOH at 8 Loci, that is 3p12, 3p14.2, 5q21, 9p21, 9q, 13q, 17p13, and 18q for tumor suppressor genes (*DUTT1*, *FHIT*, *APC*, *p16*, *FCMD*, *RB1*, *p53*, and *DCC* genes). There are few studies that examined the aberrant promoter methylation gene. Pandey *et al*[50] from Lucknow studied candidate genes and identified *GSTT1*, *NAT2*, *APOB*, and *MTHFR* mutations. Numerous other studies on genetics and polymorphisms have been published, and some of them are summarized in Table 2[51-93].

## STUDIES ON CLINICOPATHOLOGICAL ASPECT OF GBC

In this section, we have described clinicopathological parameters including presenting symptoms, screening methods, histopathological findings, prognostic factors, and tumor characteristics.

### Symptomatology

Patients with GBC typically present with pain in the right upper quadrant and epigastrium region of the abdomen, with or without changes in the character of the pain. They may also exhibit symptoms such as jaundice, features of GOO

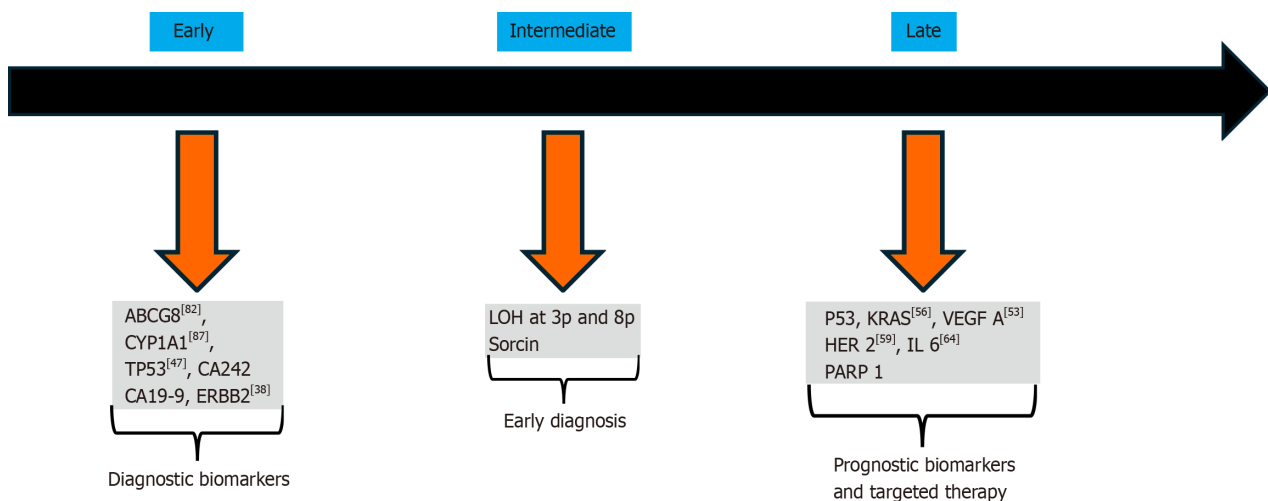


Table 2 Studies on genetics and polymorphism in gall bladder cancer

Serial No.	Sample size	Findings	Ref.
1	-	IGF-MAPK cascade, p38 MAPK pathway, p53 pathway, and FAS signaling pathway as highly enriched among dysregulated miRNAs in GBC	Saxena <i>et al</i> [51]
2	-	<i>PARP1 rs1136410</i> (A/G) associated with early onset of GBC	Anjali <i>et al</i> [52]
3	GBC (29), controls (29)	<i>VEGF-A</i> expression can be used as potential prognostic biomarker in GBC	Singh <i>et al</i> [53]
4	-	Studied the prognostic significance of the oxidative stress marker 8-OH-dG and genes associated with the BER pathway	Singh <i>et al</i> [54]
5	GBC (25)	In gallbladder cancer patients, mutations were identified in both P53 and codon 12 of KRAS	Shukla <i>et al</i> [55]
6	-	Mutations in the sorcin gene associated with poor overall survival in GBC	Shabnam <i>et al</i> [56]
7	GBC (523), controls (274)	Studied the <i>TERT-CLPTM1L</i> and <i>8q24</i> Genetic Variants in GBC	Yadav <i>et al</i> [57]
8	GBC (50)	Individual and repetitive mutations of <i>shh</i> gene in GBC can be used as diagnostic marker	Dixit <i>et al</i> [58]
9	GBC (50)	Overexpression of <i>Her2/neu</i> and <i>Ki67</i> in gallbladder cancer associated with lymph node metastasis	Pujani <i>et al</i> [59]
10	GBC (541), controls (307)	<i>KRAS rs61764370</i> polymorphism is significantly associated with GBC	Kazmi <i>et al</i> [60]
11	-	Studied Epigenetic silencing of <i>APC</i> in advanced GBC.	Tekcham <i>et al</i> [61]
12	GBC (24)	Found 7 hypermethylated or down-regulated ( <i>e.g., FBNI, LPP, and SOD3</i> ) and 61 hypomethylated or up-regulated markers ( <i>e.g., HBE1, SNRPF, TPD52</i> ) for GBC	Sharma <i>et al</i> [62]
13	Cases (50)	The level of <i>EGFR</i> expression correlates with the aggressiveness of the disease	Kumar <i>et al</i> [63]
14	GBC (52)	$\text{T}\gamma\delta 17$ could serve as a potential predictive biomarker in GBC	Patil <i>et al</i> [64]
15	GBC (30)	The <i>MTHFR A1298C</i> polymorphism associated with development of GBC	Dixit <i>et al</i> [65]
16	GBC (37)	Telomere dysfunction and alterations are the earlier events in progression of GBC	Poojary <i>et al</i> [66]
17	GBC (148), controls (256)	<i>CYP-17</i> gene polymorphism is associated with risk of gallbladder cancer	Dwivedi <i>et al</i> [67]
18	-	<i>LXR-<math>\beta</math></i> polymorphisms associated with GBC	Sharma <i>et al</i> [68]
19	GBC (195), controls (300)	Vascular endothelial growth factor single nucleotide polymorphism associated with GBC	Mishra <i>et al</i> [69]
20	GBC (35)	mitochondrial D-loop mutation associated with GBC	Maurya <i>et al</i> [70]
21	GBC (410), controls (210)	Estrogen and progesterone receptor sequence associated with increased risk of GBC	Srivastava <i>et al</i> [71]
22	-	<i>KRAS p.Q25H</i> polymorphism associated with development of GBC	Parmanik <i>et al</i> [72]
23	GBC (230), controls (230)	Caspase-8 polymorphisms associated with GBC	Srivastava <i>et al</i> [73]
24	GBC (51)	p53 mutation are early events in the evolution of GBC	Agrawal <i>et al</i> [74]
25	GBC (185), controls (195)	<i>CYP7A1</i> haplotype associated with GBC	Srivastava <i>et al</i> [75]
26	GBC (230), controls (230)	The role of pre-microRNA variants in GBC uncertain	Srivastava <i>et al</i> [76]
27	GBC (62)	Most common alteration in the p53 was frameshift mutation at codon 271	Nigam <i>et al</i> [77]
28	GBC (40)	High LOH in <i>CDH1</i> associated with pathogenesis of GBC	Priya <i>et al</i> [78]
29	GBC (212), controls (219)	Studied the <i>DNMT3B -579 G &gt; T</i> promoter polymorphism	Srivastava <i>et al</i> [79]
30	GBC (233), controls (260)	Angiotensin I-converting enzyme insertion/deletion polymorphism associated with GBC	Srivastava <i>et al</i> [80]
31	GBC (126), controls (190)	Role of DNA repair pathways GB carcinogenesis	Srivastava <i>et al</i> [81]
32	GBC (171),	Patients with <i>ABCG8</i> variant allele are at a higher risk of GBC	Srivastava <i>et al</i> [82]

	controls (221)		
33	GBC (185), controls (200)	Complement receptor polymorphism associated with pathogenesis of GBC	Srivastava and Mittal[83]
34	GBC (173), controls (204)	Single nucleotide polymorphisms of DNA repair genes <i>OGG1</i> and <i>XRCC1</i> ; associated with low risk for GBC	Srivastava <i>et al</i> [84]
35	GBC (144), controls (210)	Role of <i>CCR5+ / Delta32</i> polymorphism associated with risk of GBC	Srivastava <i>et al</i> [85]
36	GBC (124), controls (166)	<i>IL-1</i> gene polymorphisms associated with GBC	Vishnoi <i>et al</i> [86]
37	GBC (142), controls (217)	<i>CYP1A1</i> C allele frequency associated with GBC	Pandey <i>et al</i> [87]
38	-	<i>CYP7A1</i> polymorphism associated with GBC	Srivastava <i>et al</i> [88]
39	-	The X (+), D haplotype of <i>APOB</i> is associated risk for development of GBC	Pandey <i>et al</i> [89]
40	-	NAT2 slow acetylator phenotype associated with risk of GBC	Pandey <i>et al</i> [90]
41	GBC (129), controls (208)	<i>LRPAP1</i> polymorphism associated with GBC	Pandey <i>et al</i> [91]
42	GBC (39)	Mutation in codon 12 of the K-ras oncogene associated with GBC, which indicate role of chronic inflammation in gallbladder carcinogenesis.	Singh <i>et al</i> [92]
43	GBC (117), controls (137)	The apoB-XbaI gene polymorphism associated with GBC	Singh <i>et al</i> [93]

GBC: Gallbladder cancer; GB: Gallbladder.



**Figure 1** Genes involved in gallbladder cancer pathogenesis at various stages.

(gastric outlet obstruction), and an incidentally detected mass on imaging. In a study conducted by Pandey *et al*[94] the most common symptoms observed were weight loss (reported in 201 patients, 99%) followed by loss of appetite (reported in 197 patients, 97%). Other observed symptoms included pain in the right hypochondrium (reported in 143 patients, 70%), a mass in the right hypochondrium (reported in 107 patients, 53%), jaundice (reported in 79 patients, 39%), and nausea and vomiting (reported in 21 patients, 10%).

### Histopathological types

Many patients in India who undergo cholecystectomy do not routinely have their gallbladder specimens sent for histopathology due to financial burden. However, Agarwal *et al*[95] found that patients whose cholecystectomy specimens were sent for histopathological examination (HPE) experienced earlier management if GBC was found in the specimen, achieved a better R0 resection rate, and had longer overall survival (OS) compared to those in whom specimens were not sent. Histologically most of the GBCs are adenocarcinoma whereas most common architectural pattern observed was sheets and acini, with a predominance of columnar cells[96]. Yadav *et al*[97] classified GBC based on fine needle aspiration cytology (FNAC) into various subtypes, including Adenosquamous, mucinous, signet ring, squamous, small cell, mixed adenoneuroendocrine, undifferentiated carcinomas, as well as spindle and giant cell subtypes.

### Role of FNAC

Chandra *et al*[98] have introduced a classification system based on FNAC, which includes the following categories: Category 1 (inadequate), Category 2 (negative for malignancy), Category 3 (atypical cells), Category 4 (highly atypical cells suggestive of malignancy), and Category 5 (positive for malignancy). Yadav *et al*[99] reported 28 cases of neuroendocrine tumors (NETs) of the gallbladder. They classified these tumors into three categories based on their differentiation: Well-differentiated (grades 1 and 2), small cell carcinoma (grade 3), and mixed adenoneuroendocrine carcinoma. A positive diagnosis of NET was confirmed by the presence of TTF-1 in the nucleus. Kamboj *et al*[100] published 19 cases of NEC of GB and described the aggressive nature of diseases. Krishnani *et al*[101] reported that FNAC demonstrated a high sensitivity of 90.63% and specificity of 94.74% in detecting carcinoma. For locally advanced or metastatic GBC, preoperative histopathological confirmation is mandatory before initiating chemotherapy. Goyal *et al*[102] concluded that FNAC can be a precise and reliable method for diagnosing GBC in these settings. Shukla *et al*[103] found that the diagnostic accuracy of ultrasonography (USG)-guided FNAC was 95%. This is significantly higher compared to a diagnostic accuracy of 60% on blind aspiration.

### Xanthogranulomatous cholecystitis

Xanthogranulomatous cholecystitis (XGC) is malignant masquerade of GBC. Shukla *et al*[104] defined the pathological features of XGC, proposing that they include the presence of foam cells, histiocytes, bile, multinucleate giant cells, and a mixed population of inflammatory cells in varying proportions. These features are observed in a background of pink and granular debris.

### Immunohistochemistry

Some immunohistochemistry (IHC) based study also published to diagnosis and prognosticate the disease. Some studies based on IHC have also been published to aid in the diagnosis and prognosis of the disease. Study conducted by Shukla *et al*[105], revealed that although it is a common occurrence in females, GBC does not express hormone receptor. Yadav *et al*[106] suggest that the overexpression of MMP9 and the loss of membranous beta-catenin may be indicative of poor clinical outcomes and advanced disease. Jain *et al*[107] found significant overexpression of KRT7 and SRI in node positive GBC patients compared to node negative GBC patients. This finding may have important implications for the diagnosis and treatment of GBC.

Analysis of cancer-derived extracellular vesicles (EVs) is an emerging method employed to identify potential biomarkers for disease detection and prognosis. Priya *et al*[108] studies GBC cell line- derived EVs and found 16 proteins including haptoglobin which can be served as circulating biomarkers for early detection of GBC. Akhtar *et al*[109] studied specific proteins (MPO, MMP9, and DEFA1) associated with neutrophil degranulation possess signal sequences. They proposed that these proteins could serve as promising circulating markers for early detection of GBC. Priya *et al*[110] studied plasma-derived biomarker that can help in the early detection of GBC. According to their findings, NT5E and ANPEP biomarkers are associated with advanced-stage GBC, while the MME biomarker is linked with early-stage GBC. These studies could be significant in improving the diagnosis and treatment of GBC, allowing for earlier detection and better patient outcomes.

### Prognostic markers

Numerous studies have been conducted to identify prognostic markers for GBC. Mishra *et al*[111] found that presence of Higher TNM stage, adjacent organ infiltration, nodal involvement, and jaundice predict poor survival. Negi *et al*[112] found that lymph node (LN) ratio is a strong predictor of outcome after curative resection (CR) for GBC. Shah *et al*[113] found that LN micro metastasis did not correlate with survival. Balachandran *et al*[114] found that Adjuvant therapy, R0 resection and extended cholecystectomy associated with improved survival in patient with GBC. Some other pathological studies are described in Table 3[115-126].

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## STUDIES ON DIAGNOSTICS AND IMAGING

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GBC presents significant diagnostic challenges due to its often-asymptomatic nature in the early stages and nonspecific symptoms as it progresses. Early diagnosis of GBC is crucial for improving patient outcomes. Various imaging modalities are critical for detecting and characterizing gallbladder lesions. USG is frequently chosen as the initial imaging modality for its accessibility and capability to visualize gallbladder abnormalities. Computed tomography (CT) and magnetic resonance imaging (MRI) offer detailed information on tumor extent, invasion of adjacent structures, and the presence of distant metastases. Endoscopic ultrasound (EUS) is a valuable tool for staging GBC due to its high sensitivity in detecting small lesions, assessing local tumor invasion, and facilitating biopsy when necessary. Additionally, positron emission tomography (PET) imaging can help evaluate distant metastases and guide treatment decisions.

Ultrasound is an essential diagnostic tool used for investigating medical conditions in patients. It can detect various abnormalities such as masses, ascites, metastasis, liver infiltration, and involvement of surrounding structures. It is considered as the primary investigation method in most cases. Gallbladder adenocarcinomas can appear as one of three morphologies in USG: Intraluminal mass, diffuse mural thickening, or a mass that replaces the gallbladder. Gallstones are commonly present along with mass in 60%–90% cases. Some retrospective studies were conducted to determine the accuracy of USG in diagnosing GBC. In a study conducted by Pandey *et al*[94], a mass lesion in the gallbladder was found in 87% of the 177 patients examined *via* abdominal sonography. The masses were classified as either intraluminal (59%) or

Table 3 Clinico pathological studies

Serial No.	Sample size	Findings	Ref.
1	GBC (50)	Her2 neu, p53, p16, survivin, COX-2, and EZH-2 expression associated with GBC	Gupta <i>et al</i> [115]
2	GBC (200), Dysplasia (32), CC (100)	HER-2/neu overexpression seen in patients with GBC	Jain <i>et al</i> [116]
3	GBC (128)	HER 2 and Ki-67 can be used as a prognostic biomarker for gallbladder carcinoma	Halder <i>et al</i> [117]
4	-	Combination of ALU247 and cfDNA provides good sensitivity, specificity in diagnosis of GBC	Kumari <i>et al</i> [118]
5	-	Proposed a scoring system for XGC	Rajaguru <i>et al</i> [119]
6	GBC (34)	Quantitative analysis of cfDNA may aid in early diagnosis	Kumari <i>et al</i> [120]
7	GBC (39), cholelithiasis (30), and control (25)	Overexpression of survivin is associated with poor prognosis	Nigam <i>et al</i> [121]
8	(GSD, n =30; GBC, n = 39) healthy control (n = 25)	Expression of survivin in peripheral blood could be useful both in the diagnosis and prognosis of GBC	Nigam <i>et al</i> [122]
9	GBC (80)	P53 expression is positively correlated with increasing tumor grade, whereas beta-catenin nuclear expression is associated with tumor grade and depth of invasion	Ghosh <i>et al</i> [123]
10	9 case of Squamous cell carcinoma	Ultrasound-guided fine-needle aspiration is a useful minimally invasive investigation in the preoperative diagnosis of squamous cell carcinoma of the gallbladder	Gupta and Gupta[124]
11	GBC (55), vontrols (8)	Assay of CA242, CA19-9, CA15-3, and CA125 can be used as marker of carcinoma of the gallbladder	Shukla <i>et al</i> [125]
12	GBC (40)	Intraoperative bile cytology can be used for diagnosis of in situ and early invasive GBC	Arora <i>et al</i> [126]

GBC: Gallbladder cancer; CC: Chronic cholecystitis.

infiltrative (41%), with irregular margins and higher echogenicity compared to the liver. Infiltrative lesions were more common at the gallbladder neck and fundus. In study by Batra *et al*[127] mass replacing GB was most common findings (73%) on USG followed by presence of gall stone along with mass (54%). Chhabra *et al*[128] demonstrated a new combined type of GBC when GBC present as both thickening and mass replacing GB. Rana *et al*[129] proposed sonographic “Cervix Sign” for GB neck malignancy. The role of USG for screening of GBC is controversial. In a pilot study conducted by Patel *et al*[130] which included 778 patients from high-risk areas, 4 cases of GBC were detected. Anadure *et al*[131] found 6 GBC among 978 high risk healthy participants. Despite showing positive outcomes, it is challenging to conduct screenings for the Indian population due to practical difficulties in real life.

It's quite challenging to differentiate between malignant and benign Thick-walled GB (TWGB). Many studies were conducted in this regard. Gupta *et al*[132] a recommended scoring system called Gallbladder Reporting and Data System can be used to evaluate gallbladder wall features in ultrasound scans. This system considers various factors such as layered appearance, interface with the liver, symmetry and extent of involvement, intramural features like cysts and echogenic foci. By using this system to risk stratify GB lesions; Surgeon can make more informed decisions about treatment options. Gupta *et al*[133] propose an imaging-based algorithm for gallbladder wall thickening. They suggest that diffuse asymmetrical thickening or focal thickening, discontinuous mucosa or breach in mucosa, loss of layered pattern in the gallbladder, high mean systolic velocity in color Doppler, and high shear velocity in Doppler are more indicative of malignant gallbladder wall thickening. Kapoor *et al*[134] proposed that elastography effectively distinguishes between benign and malignant gallbladder wall thickening. Combining this technique with sonography enables early-stage diagnosis of gallbladder carcinoma, highlighting its value as a diagnostic tool. Kalage *et al*[135] suggested a Multiparametric MRI to distinguish between benign thick walls and malignant thick walls. This approach includes Diffusion-weighted, dynamic contrast-enhanced perfusion, intravoxel incoherent motion, and diffusion tensor sequences. The study found that the Multiparametric MRI technique had a 90% sensitivity and 88% specificity for diagnosing Malignant TWGB, whereas conventional Contrast enhanced MRI had 80% sensitivity and 88% specificity.

Recently some authors studied the utility of EUS fine-needle aspiration (FNA) for evaluation of gallbladder mass. Singla *et al*[136] demonstrated that EUS-FNA is a highly sensitive tool for evaluating gallbladder mass lesions associated with obstructive jaundice. However, due to the low negative predictive value of the test, further evaluation is necessary for cases where FNA results are negative.

### CT scan

CT is the diagnosis modality of choice for staging the disease. Kalra *et al*[137] discovered that MDCT exhibited a sensitivity of 72.7%, a specificity of 100%, and an accuracy of 85% in assessing the resectability of GBC. To diagnose

hepatic and vascular invasion by the tumor, CT showed a 100% correlation with surgical findings. According to the study conducted by Kumaran *et al*[138] CT scan has an overall accuracy of 93.3% in staging of GBC. Therefore Dual-phase helical CT is a comprehensive method that can be used for preoperative staging of GBC to determine if it is resectable. Soundararajan *et al*[139] proposed CT can be routinely used to determine gastro-intestinal tract involvement on GBC.

### **Role of PET-CT**

GBC are not pet avid tumors. Standard guidelines do not advocate routine pet scan in GBC. In India Many studies were published exploring the utility of PET-CT in GBC. According to a study conducted by Patkar *et al*[140] found that PET-CT can detect metastatic disease in 46.6% of patients that could not be confidently detected using standard cross-sectional imaging. Goel *et al*[141] found that PET-CT altered the management plan in approximately 25% of resectable GBC cases and 30%-35% of locally advanced cases. Shukla *et al*[142] studied role of PET-CT in incidental GBC and found that MDCT had a sensitivity and positive predictive value (PPV) of 42.8% each for determining residual disease, while PET-CT showed a sensitivity of 28.5% and PPV of 20%. In patients diagnosed incidentally with GBC and no metastatic disease, PET-CT and MDCT appear to offer complementary roles in clinical assessment. Goel *et al*[143] found that, the patients with PET-negative pT1b tumors showed no residual disease, in contrast to PET-positive patients (0% vs 33%,  $P = 0.028$ ). They proposed that PET-negative pT1b patients could be monitored closely due to the low risk of relapse. Kumar *et al* [144] investigated the efficacy of PET-CT in detecting tumor recurrence in GBC. Their study demonstrated that PET/CT exhibited a high sensitivity (97.6%) and specificity (90%) for detecting tumor recurrence. These findings suggest that PET-CT can be a valuable tool in the detection of tumor recurrence, Residual tumor in incidental GBC and in cases with suspicious of distant metastasis.

### **Tumor markers**

In patients with GBC Sinha *et al*[145] discovered a significant association between serum levels of tumor markers (such as CA19-9, CEA, CA125, and CA242) and GBC. Agrawal *et al*[146] suggested that CA19-9, CA125 and CEA may serve as predictors of resectability in GBC. They found that elevated levels of CA19-9 and CA125 associated with poorer prognosis in affected patients. The role of different imaging modalities in the diagnosis of GBC is illustrated in **Figure 2**. Some other studies on diagnostics and imaging modality are described in **Table 4**[147-157].

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## **STUDIES ON SURGICAL APPROACH AND RESECTION**

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In this section, we have described various landmark studies published in the literature from India regarding the surgical approaches for GBC. Staging laparoscopy is highly accurate in identifying peritoneal deposits and sub centimetric metastases over liver surface and should be considered for all patients of GBC undergoing surgery. Agarwal *et al*[158] found, staging laparoscopy prevented laparotomy in 23% of patients with GBC. They suggested performing routine staging laparoscopy for GBC patients undergoing surgery. Another study by Agrawal *et al*[159] reported that staging laparoscopy prevented a nontherapeutic laparotomy in 43% of patients initially deemed resectable based on pre-operative imaging. Both of these studies underscored the importance of staging laparoscopy and advocated for its mandatory use in GBC.

### **TWGB**

Surgeons around the world do not widely accept laparoscopic cholecystectomy for TWGB due to the risk of malignancy. Srikanth *et al*[160] in their study proposed that laparoscopic cholecystectomy can be performed in patients with diffuse TWGB. However, there is an increased risk of to open cholecystectomy. Kapoor *et al*[161] proposed an approach of anticipatory extended cholecystectomy for TWGB (Luckow Approach).

### **Role of 16b1 node**

After staging laparoscopy, the usual first step is the sampling of interaortocaval (IAC) LNs. GBC involving the 16b1 (IAC) LN is considered to be metastatic. Agarwal *et al*[162] studied the role of routine frozen-section HPE of the 16b1 LN in the management of GBC. They recommended the routine sampling of the 16b1 node during surgical procedures to prevent non-therapeutic radical resection. Their study found that routine 16b1 LN biopsy prevented such resections in 18.6% of patients. When 16b1 nodes tested positive, Agarwal *et al*[162] treated them along with systemic disease, and abandoned surgery when these nodes were found to be positive. Ghosh *et al*[163] from SGPGIMS, Lucknow echoed the same finding, they found that the median survival for IAC node positive group and patients with distant metastasis were same. However, Aggarwal *et al*[164] advocated that certain cases of GBC with IAC node metastasis may be eligible for CR followed by adjuvant therapy. However, their study was limited by a small sample size.

### **Extent of resection**

According to previous studies, only 10% of patients with GBC are deemed resectable. For Tis and T1a lesions, a simple cholecystectomy with negative margins at the cystic duct is typically effective and can achieve cure rates ranging from 85% to 100%. However, gallbladder lesions classified as T1b and higher often come with nodal metastases, necessitating radical resection. This typically involves en bloc hepatic bed resection (which may include removing 2-3 cm of liver wedge or performing a formal segment IVb and V resection) along with regional lymphadenectomy. The surgical goal is R0 resection, aiming to achieve negative cystic duct margins (CDMs). In cases of positive margins, revision of the duct



**Table 4 Studies on diagnostic methods and imaging**

Serial No.	Sample size	Findings	Ref.
1	-	PET-CT can be used to rule out metastatic disease and for post-therapy surveillance for recurrence in patients of GBC	Bisht <i>et al</i> [147]
2	GBC (38)	Potential utility of CT texture-based radiomics analysis in patients with GBC.	Gupta <i>et al</i> [148]
3	GBC (141)	Raised levels of serum CA19-9 beyond 20 units/mL should be used for prognostication purposes after EC	Agrawal <i>et al</i> [149]
4	GBC (141)	NMR-based methods can be used as a diagnostic modality for GBC	Sharma <i>et al</i> [150]
5	GBC (41)	CEA expression may help in diagnosis of GBC	Mondal <i>et al</i> [151]
6	GBC (203)	Discontinuous mucosal lining, diffuse wall thickening, intramural nodules, and cholelithiasis may indicate XGC rather than gallbladder carcinoma	Sureka <i>et al</i> [152]
7	GBC (74)	Duodenal involvement significantly decreases resectability but does not preclude resection	Kalayarasan <i>et al</i> [153]
8	XGC (31)	Mass-forming XGC mimics GBC	Agarwal <i>et al</i> [154]
9	GBC (117)	CA 242 is a promising tumor marker for GBC and performs better than CEA and CA19-9.	Rana <i>et al</i> [155]
10	GBC (15)	Dynamic MRI with MRCP is a reliable method of showing gall bladder carcinoma.	Kaza <i>et al</i> [156]
11	GBC (60)	Color Doppler USG together can improve pickup rate of GBC	Pradhan <i>et al</i> [157]

PET: Positron emission tomography; CT: Computed tomography; GBC: Gallbladder cancer; MRI: Magnetic resonance imaging; MRCP: Magnetic resonance cholangiopancreatography.

USG	CECT	PET
<ul style="list-style-type: none"> <li>• Intraluminal mass<sup>[94]</sup></li> <li>• Diffuse mural thickening<sup>[12]</sup></li> <li>• Irregular wall thickening<sup>[132]</sup></li> <li>• Layered appearance</li> <li>• Cervix sign<sup>[129]</sup></li> <li>• Liver infiltration</li> </ul>	<ul style="list-style-type: none"> <li>• Vascular invasion<sup>[137]</sup></li> <li>• Liver infiltration</li> <li>• Metastasis</li> <li>• GIT involvement<sup>[139]</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Distant metastasis<sup>[140]</sup></li> <li>• Equivocal findings on CT<sup>[141]</sup></li> </ul>

**Figure 2 Role of diagnostic modalities in gallbladder cancer.** USG: Ultrasonography; CECT: Contrast-enhanced computed tomography; PET: Positron emission tomography.

margin or extrahepatic bile duct (EHBD) excision may be necessary. Studies published in India exploring the ideal surgical approach for GBC have not yet provided concrete recommendations.

Singh *et al*[165] found that CR is the only chance of cure, aggressive surgical approach and improve OS. Wagholikar *et al*[166] advocated that simple cholecystectomy is effective only for GBC limited to the mucosa. However, patients diagnosed with pT1b tumors should undergo extended cholecystectomy. The study proposes that for cases where incidental GBC extends to the muscularis layer, early reoperation to complete an extended cholecystectomy is recommended.

There has been considerable debate regarding the optimal approach to liver resection in GBC, specifically whether anatomical segment IVb and V resection is superior to non-anatomical wedge excision of the liver. There are some studies regarding the same with conflicting results. Pottakkat *et al*[167] demonstrated that the extended criteria for radical resection (Segment 4b and 5) are highly effective, achieving R0 status in over 80% of GBC patients and yielding acceptable long-term outcomes. Nag *et al*[168] from GB Pant Hospital, New Delhi, discovered that there was no significant difference in mean recurrence-free survival (RFS) between segment 4b and 5 resections compared to wedge resection, with 58.2 months *vs* 42.3 months, respectively ( $P = 0.264$ ). The OS was also similar between both of these groups. Therefore, they concluded that segment 4b and 5 resections were not superior to wedge resection. Tewari *et al*[169] from Banaras Hindu University (BHU) found that wedge resection of the gallbladder achieves adequate oncological clearance in early GBC.



### Margin status

Studies have shown that the surgical margin status is the most important factor in determining the overall outcome of liver resection surgeries, rather than the type of resection performed. Behari *et al*[170] found similar results, with patients who underwent R0 resections having significantly better survival rates than those who underwent R1 resections (median 25.8 months *vs* 17.0 months;  $P = 0.03$ ). Hence, the primary objective should be to achieve complete removal of the disease with clear histologic margins.

### Frozen section of CDM

Routine use of CDM frozen section analysis is controversial. Some study from India refuted this practice. Jajal *et al*[171] suggest that routine CDM frozen analysis may not be necessary in patients with resectable GBC who do not have jaundice. They found that a positive CDM has comparable survival outcomes to a negative CDM, with similar R0 resection rates and tumor stages. Some authors suggest that routine resection of the common bile duct during surgery may aid in lymphadenectomy and increase LN yield. However, a study by Behari *et al*[170] from India found that EHBD resection does not offer significant survival benefits.

### Standard lymphadenectomy

The standard lymphadenectomy for GBC involves removing LNs located along the hepatoduodenal ligament, common hepatic artery, and peri-pancreatic region (stations 8, 12, and 13). Pandey *et al*[172] from BHU proposed this systemic regional lymphadenectomy in GBC gives a good lymph nodal yield and better outcome. Negi *et al*[112] suggested that the retrieval and examination of at least 6 nodes can have a positive impact on the quality of staging and disease-free survival (DFS) in node-negative patients. Goel *et al*[173] from TMH found that for individuals diagnosed with T1b GB cancer, the likelihood of nodal positivity is approximately 21%. Therefore, they recommended that radical surgery, including comprehensive periportal lymphadenectomy, should be considered the standard of care.

### Excision of extra-hepatic bile duct

Some authors believe that the presence of obstructive jaundice is a sign of inoperability. Agarwal *et al*[174] conducted a study on 51 patients with GB cancer and obstructive jaundice. Of these 51 patients, 14 underwent resection with curative intent, resulting in a resectability rate of 27.45%. Despite being jaundiced, these patients were able to undergo successful resection. They found a mortality rate of 7.14% and a morbidity rate of 50%. The mean DFS was 23.46 months, with a median of 26 months and a range spanning from 2 to 62 months. Among patients who underwent resection, 50% survived beyond two years. They concluded that Biliary obstruction in GB cancer is not signs of inoperability and resection results in prolongation of survival[174]. Pandey *et al*[172] found that EHBD resection to achieve R0 resection is safe, associated with acceptable postoperative morbidity, and may increase survival. A positive CDM, direct infiltration of the hepatoduodenal ligament, and densely adherent peri-choledochal LNs were the indicators of EHBD resection. K *et al*[175] studied 59 GBC patients who had jaundice. Total of 61.7% and 84%, respectively, of patients underwent CR and non-CR had common bile duct involvement ( $P = 0.062$ ). They found that Patients with GBC and jaundice have better significant survival after CR.

### Extended resection in GBC

There are some reserves among surgeons for extended resection in carcinoma GB. As operative techniques improve and new technology develops, there is an increasing trend in extended resection. Commonly performed extended procedures are segmentectomy 4B + 5, extended right hepatectomy, median sectorectomy and hepatopancreaticoduodenectomy. Pottakkat *et al*[167] studied the outcomes of extended resection in GBC and identified postoperative complications in 60% of patients. They achieved acceptable R0 resection (83%) and survival rates. But Behari *et al*[170] could find that only 43% of GBC undergoing extended resection could achieved R0 resection. Singh *et al*[176] from Rajiv Gandhi Cancer institute first to explore PVE followed by extended hepatectomy in GBC. In their study on 14 patients following Neo adjuvant chemo therapy (NACT) and portal vein embolization. Seven (50%) underwent CR (extended hepatectomy). The median OS was 27 months for resectable patients and 15 months for unresectable patients.

Agarwal *et al*'s[177] study, which examined the duodenum's involvement in GBC, revealed that, of the 43 patients with duodenal involvement, 26 had R0 resection (61.9%). Of these, 16 had duodenal sleeve resection (61.54%), 9 had distal gastrectomy with resection of the first part of the duodenum (34.62%), and 1 patient had hepato-pancreatoduodenectomy (HPD; 3.85%). They concluded that duodenal infiltration does not serve as a sign of unresectability or a reason to undergo HPD. For the majority of these patients, a distal gastrectomy combined with resection of the first segment of the duodenum, or a duodenal sleeve resection can accomplish an oncologically appropriate R0 resection[178].

With surgeons now willing for extended resection, further some studies published for resection in presence of metastasis. Patkar *et al*[179] from TMH propose a potential role for aggressive treatment of advanced GBC with limited metastatic burden, such as microscopic disease in the station 16b1 node, low-burden peritoneal disease with deposits smaller than 1 cm in adjacent omentum or diaphragm, isolated N2 disease, or a solitary discontinuous liver metastasis in adjacent liver parenchyma.

### Minimally invasive surgery in GBC

With advance laparoscopic and robotic surgery now getting prominence, Agarwal *et al*[180] found that laparoscopic radical cholecystectomy is safe and feasible for selected patients with GBC, and the outcomes are comparable to those of open radical cholecystectomy. Nag *et al*[181] found laparoscopic hepatic bisegmentectomy is safe and feasible. Palanisamy *et al*[182] from GEM hospital published their study and suggested that laparoscopic radical cholecystectomy

may serve as a viable and feasible option for managing GBC, providing effective oncological clearance. Additionally, it offers the typical benefits associated with minimal access procedures. Goel *et al*[183] from TMH suggested robotic radical cholecystectomy is safe and feasible and the short-term results are compared with Open radical cholecystectomy.

### **Incidentally detected GBC**

Incidentally detected carcinoma GB is another debatable topic. Some studies have been published on incidentally detected gallbladder carcinoma from India. Shukla *et al*[184] studied the factors influencing operability in incidentally detected GBC and found that stage is the most important factor in determining resectability. They found that as the T-stage of the disease progressed, the probability of finding residual disease increased, while operability decreased. They also found that incidence of lymph nodal disease is higher for pT1b cancers. Wagholikar *et al*[166] suggested that, incidental GBC extending up to the muscularis requires completion extended cholecystectomy. Although there are no prospective clinical trials, it is widely believed that complete resection of residual disease leads to improved survival. Multiple studies have shown a survival advantage with CR, thereby supporting re-resection in incidental GBC beyond pT1b. Patkar *et al*[185] from TMH, found contrasting results in their study on 425 patients of PT2 of GBC out of which 118 (27.7%) and 307 (72.23%) patients were in the upfront operated GBC and incidental GBC groups, respectively. They found that incidentally detected pT2 GBCs have significantly worse outcomes compared to similarly staged patients undergoing an upfront radical cholecystectomy. Some other studies on surgical management are described in Table 5[186-189].

## **STUDIES ON MULTIMODALITY THERAPY.**

Despite improvement in surgical techniques, survival and resection rate of GBC remained the same. Gradually multimodality therapy evolved with the aim of improving survival. Patkar *et al*[190] published the experience of TMH, Mumbai with largest cohort of 1307 patients with GBC. They advocated peri-operative chemotherapy both in adjuvant and neo adjuvant settings in properly selected patients. We will first discuss adjuvant therapy followed by neoadjuvant therapy and advances made in these fields.

### **Studies on adjuvant therapy in GBC**

The role of adjuvant therapy on increasing survival in GBC is controversial. To date, there have been only a few randomized studies conducted in India exploring the role of adjuvant radiotherapy (RT) or chemo RT (CRT) in resected GBC.

Ostwal *et al*[191] from TMH, Mumbai in their study of 242 resectable stage II and III GBC patients found that patients undergoing R0 resections receiving adjuvant Gemcitabine and cisplatin bases chemotherapy have high completion rates and good tolerance. Kattapur *et al*[192] found that adjuvant chemotherapy reduces distant failure rates but did not improve OS in completely resected GBC patients. They found that lymphovascular invasion important predictor of RFS in T2N0 patients. Some centers tried RT in adjuvant setting. Mahantshetty *et al*[193] from TMH suggested adjuvant RT along with CT improve survival in GBC after resection. Authors used 5 FU bases regimen in their cohort of patients. Choudhary and Asthana[194] studied the effect of adjuvant treatment, including RT, CT, or CRT, following CR and found improved survival compared to surgery alone but the difference was not statistically significant. Agrawal *et al*[195] found that Adjuvant CRT followed by adjuvant chemotherapy improves outcomes in patients with R1 and node-positive disease. There is only one Randomized control trial available that examines the function of CT and RT in adjuvant situations.

The GB-GECCOR trial, a phase II multicenter study, investigated two treatment arms: CAPE-RT (consisting of 2-4 cycles of capecitabine followed by RT: 45 Gy over 25 fractions concurrent with capecitabine: 825 mg/m<sup>2</sup> twice daily, followed by 2-4 additional cycles of capecitabine) *vs* GC (gemcitabine at 1000 mg/m<sup>2</sup> and cisplatin at 25 mg/m<sup>2</sup> administered on days 1 and 8, every 3 wk) following resection. The DFS rate for the GC group was 88.9% *vs* 77.8% for CAPE-RT group. These outcomes support the application of both regimens as appropriate care[196].

### **Unresectable and metastatic diseases**

The appropriate regimen for unresectable and metastatic disease has not yet been defined. Many studies have been published studying different therapies in these settings. Many studies shown that Gemcitabine/cisplatin combination well tolerated and in advanced unresectable GBC[197-199]. Chatni *et al*[200] studied infusion chemotherapy with cisplatin and fluorouracil. Sharma *et al*[201] studied the gemcitabine and oxaliplatin regimen in unresectable GB cancer and found a survival benefit. Same authors studied the efficacy of chemotherapy compared to best supportive care and reported that chemotherapy improved OS and progression free survival (PFS) in unresectable GBC. Ali *et al*[202] in their comparative study between Cisplatin-5-Fluorouracil and Gemcitabine-Cisplatin and found overall more benefit in Gemcitabine-Cisplatin arm. Singh *et al*[203] advocated use of Gemcitabine based regimen in metastatic and advanced GBC which improved PFS.

Currently there is no “standard” second-line therapy after failure of first-line gemcitabine and cisplatin in patients with GBC. Ramaswamy *et al*[204] found that CAP-IRI is a well-tolerated second-line chemotherapeutic regimen in advanced GBC. In GB-SELECT trial they found that single agent irinotecan can be used as second line treatment in palliative setting. Some other important study on Adjuvant therapy in metastatic disease are described in Table 6[205-214].

**Table 5 Studies on surgical approaches and resection**

Serial No.	Sample size	Findings	Ref.
1	GBC (521)	Surgical resection improves survival in GBC with jaundice	Goel <i>et al</i> [186]
2	GBC (97)	Radical cholecystectomy with wedge resection of the liver oncological equivalence compared to formal segment IVb/V excision	Patkar <i>et al</i> [187]
3	GBC (20)	The technique of LHBRL is safe and feasible for patients with GBC	Nag <i>et al</i> [188]
4	07 incidental GBC	Re-exploration and aggressive resection followed by adjuvant chemotherapy for incidental gallbladder carcinoma are safe and provide hope for long-term survival	Kaman <i>et al</i> [189]

GBC: Gallbladder cancer; LHBRL: Laparoscopic hepatic bisegmentectomy with regional lymphadenectomy.

**Table 6 Studies on adjuvant therapy on gall bladder carcinoma**

Serial No.	Sample size	Findings	Ref.
1	GBC (176)	CT followed by CRT improves outcomes in patients with limited volume disease	Alam <i>et al</i> [205]
2	GBC (550)	CT followed by cCRT appears to improve survival in responders with good PS	Alam <i>et al</i> [206]
3	GBC (38)	Her2neu directed therapy significantly improved survival	Das <i>et al</i> [207]
4	GBC (66)	FOLFOX-4 is an effective and well-tolerated regimen as a second-line treatment	Dodagoudar <i>et al</i> [208]
5	GBC (87)	CAP-IRI is a well-tolerated second-line chemotherapeutic regimen in advanced GBC	Ramaswamy <i>et al</i> [209]
6	GBC (121)	Reduced dose intensity of chemotherapy in GBC	Gangopadhyay <i>et al</i> [210]
7	GBC (210)	Use of gem-platinum in Indian patients associated with slightly worse outcomes	Sirohi <i>et al</i> [211]
8	-	Autologous immune enhancement therapy associated with, an improvement of the quality of life	Bhamare <i>et al</i> [212]
9	GBC (104)	Adjuvant chemoradiation improve survival	Mallick <i>et al</i> [213]
10	-	Chemoradiation improve survival in locally advanced GBC	Engineer <i>et al</i> [214]

GBC: Gallbladder cancer; CRT: Chemo-radiotherapy; cCRT: Consolidation chemoradiation.

## STUDIES ON NEOADJUVANT TREATMENT

Surgical resection is the only potential cure for GBC. However, many patients are present with locally advanced state, making it difficult to perform curative surgery. Neoadjuvant therapy can effectively downstage tumors in these patients and help assess disease biology to identify the most suitable candidates for surgery. TMH has taken a step ahead and started using NACT as an option in locally advanced GBC. Chaudhari *et al*[215] introduced the TMH criteria for neoadjuvant chemotherapy in locally advanced or borderline resectable GBC, leading to curative surgical resection in a significant percentage of patients. Agrawal *et al*[216] demonstrated the benefit of neoadjuvant chemo-RT in locally advanced GBC. In their study they have reported Radiologic downstaging of liver involvement is 40.5% and lymphadenopathy is 67.5%[216].

A group of investigators is presently carrying out a prospective clinical experiment called POLCA-GB at TMH in Mumbai. This experiment aims to assess the efficacy of chemotherapy administered alone (four cycles of gemcitabine-cisplatin or gemcitabine-oxaliplatin) *vs* chemotherapy administered in combination with radiation treatment (RT) contemporaneous with gemcitabine, followed by two rounds of gemcitabine-cisplatin or gemcitabine-oxaliplatin chemotherapy. This trial aims to enable potentially CR by downstaging locally advanced GBC. The trial is now in the recruiting stage[217]. Few other series from India have demonstrated a benefit of gemcitabine-platinum based neoadjuvant therapy in GBC described in Table 7[218-221].

## CONCLUSION

This review has found significant work and efforts made by India in addressing GBC over the past two decades. India has produced a substantial number of quality research publications on GBC-epidemiology, etiopathogenesis, pathology, surgery, and multimodal treatment approaches. Country has progressed well on surgical management and multimodal

**Table 7 Studies on neo-adjuvant therapy on gall bladder carcinoma**

Serial No.	Sample size	Findings	Ref.
1	GBC (510)	Surgery and peri-operative systemic therapy associated with improved survival	Patkar <i>et al</i> [218]
2	GBC (28)	Locally advanced GBC may benefit from neoadjuvant chemoradiation	Engineer <i>et al</i> [219]
3	GBC (37)	Neoadjuvant chemotherapy in patients with locally advanced gallbladder cancer	Sirohi <i>et al</i> [220]
4	GBC (21)	Resection after neoadjuvant chemotherapy improve survival	Selvakumar <i>et al</i> [221]

GBC: Gallbladder cancer.

treatment strategies. However, there remains a lack of specific research on etiopathogenesis, early diagnosis, preventive measures, and emerging treatments such as immunotherapy. The coming decades should prioritize efforts towards screening strategy in high-risk zone, early detection, and the development of well-defined treatment protocol/ policy. Collaborative international research would be useful to achieve and overcome the deficient areas.

## FOOTNOTES

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## REFERENCES

- Zhu AX, Hong TS, Hezel AF, Kooby DA. Current management of gallbladder carcinoma. *Oncologist* 2010; **15**: 168-181 [PMID: [20147507](https://pubmed.ncbi.nlm.nih.gov/20147507/) DOI: [10.1634/theoncologist.2009-0302](https://doi.org/10.1634/theoncologist.2009-0302)]
- Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; **74**: 229-263 [PMID: [38572751](https://pubmed.ncbi.nlm.nih.gov/38572751/) DOI: [10.3322/caac.21834](https://doi.org/10.3322/caac.21834)]
- Dutta U, Bush N, Kalsi D, Popli P, Kapoor VK. Epidemiology of gallbladder cancer in India. *Chin Clin Oncol* 2019; **8**: 33 [PMID: [31484488](https://pubmed.ncbi.nlm.nih.gov/31484488/) DOI: [10.21037/cco.2019.08.03](https://doi.org/10.21037/cco.2019.08.03)]
- Phadke PR, Mhatre SS, Budukh AM, Dikshit RP. Trends in gallbladder cancer incidence in the high- and low-risk regions of India. *Indian J Med Paediatr Oncol* 2019; **40**: 90-93 [DOI: [10.4103/ijmpo.ijmpo\\_164\\_18](https://doi.org/10.4103/ijmpo.ijmpo_164_18)]
- S ST, Krishnan SK, Das P, Sudarshan KL, Kotian CM, Santhappan S, Vishwakarma MB, N S, Mathur P. Descriptive Epidemiology of Gastrointestinal Cancers: Results from National Cancer Registry Programme, India. *Asian Pac J Cancer Prev* 2022; **23**: 409-418 [PMID: [35225451](https://pubmed.ncbi.nlm.nih.gov/35225451/) DOI: [10.31557/APJCP.2022.23.2.409](https://doi.org/10.31557/APJCP.2022.23.2.409)]
- Mhatre SS, Nagrani RT, Budukh A, Chiplunkar S, Badwe R, Patil P, Laversanne M, Rajaraman P, Bray F, Dikshit R. Place of birth and risk of gallbladder cancer in India. *Indian J Cancer* 2016; **53**: 304-308 [PMID: [28071634](https://pubmed.ncbi.nlm.nih.gov/28071634/) DOI: [10.4103/0019-509X.197723](https://doi.org/10.4103/0019-509X.197723)]
- Gupta SK, Ansari MA, Shukla VK. What makes the Gangetic belt a fertile ground for gallbladder cancers? *J Surg Oncol* 2005; **91**: 143-144 [PMID: [16028289](https://pubmed.ncbi.nlm.nih.gov/16028289/) DOI: [10.1002/jso.20292](https://doi.org/10.1002/jso.20292)]
- Mishra RR, Tewari M, Shukla HS. Helicobacter pylori and pathogenesis of gallbladder cancer. *J Gastroenterol Hepatol* 2011; **26**: 260-266 [PMID: [21261714](https://pubmed.ncbi.nlm.nih.gov/21261714/) DOI: [10.1111/j.1440-1746.2010.06435.x](https://doi.org/10.1111/j.1440-1746.2010.06435.x)]
- Nath G, Singh YK, Kumar K, Gulati AK, Shukla VK, Khanna AK, Tripathi SK, Jain AK, Kumar M, Singh TB. Association of carcinoma of the gallbladder with typhoid carriage in a typhoid endemic area using nested PCR. *J Infect Dev Ctries* 2008; **2**: 302-307 [PMID: [19741293](https://pubmed.ncbi.nlm.nih.gov/19741293/) DOI: [10.3855/jidc.226](https://doi.org/10.3855/jidc.226)]
- Tewari M, Mishra RR, Shukla HS. Salmonella typhi and gallbladder cancer: report from an endemic region. *Hepatobiliary Pancreat Dis Int*



- 2010; **9**: 524-530 [PMID: [20943463](#)]
- 11 **Mhatre S**, Lacey B, Sherliker P, Chatterjee N, Rajaraman P, Goel M, Patkar S, Ostwal V, Patil P, Shrikhande SV, Chitkara G, Badwe R, Lewington S, Dikshit R. Reproductive factors and gall-bladder cancer, and the effect of common genetic variants on these associations: a case-control study in India. *Int J Epidemiol* 2022; **51**: 789-798 [PMID: [34550362](#) DOI: [10.1093/ije/dyab197](#)]
  - 12 **Mhatre S**, Rajaraman P, Chatterjee N, Bray F, Goel M, Patkar S, Ostwal V, Patil P, Manjrekar A, Shrikhande SV, Badwe R, Dikshit R. Mustard oil consumption, cooking method, diet and gallbladder cancer risk in high- and low-risk regions of India. *Int J Cancer* 2020; **147**: 1621-1628 [PMID: [32142159](#) DOI: [10.1002/ijc.32952](#)]
  - 13 **Mishra K**, Behari A, Shukla P, Tsuchiya Y, Endoh K, Asai T, Ikoma T, Nakamura K, Kapoor VK. Risk factors for gallbladder cancer development in northern India: A gallstones-matched, case-control study. *Indian J Med Res* 2021; **154**: 699-706 [PMID: [35532588](#) DOI: [10.4103/ijmr.IJMR\\_201\\_19](#)]
  - 14 **Zatonski WA**, Lowenfels AB, Boyle P, Maisonneuve P, Bueno de Mesquita HB, Ghadirian P, Jain M, Przewozniak K, Baghurst P, Moerman CJ, Simard A, Howe GR, McMichael AJ, Hsieh CC, Walker AM. Epidemiologic aspects of gallbladder cancer: a case-control study of the SEARCH Program of the International Agency for Research on Cancer. *J Natl Cancer Inst* 1997; **89**: 1132-1138 [PMID: [9262251](#) DOI: [10.1093/jnci/89.15.1132](#)]
  - 15 **Mhatre S**, Richmond RC, Chatterjee N, Rajaraman P, Wang Z, Zhang H, Badwe R, Goel M, Patkar S, Shrikhande SV, Patil PS, Davey Smith G, Relton CL, Dikshit RP. The Role of Gallstones in Gallbladder Cancer in India: A Mendelian Randomization Study. *Cancer Epidemiol Biomarkers Prev* 2021; **30**: 396-403 [PMID: [33187967](#) DOI: [10.1158/1055-9965.EPI-20-0919](#)]
  - 16 **Dutta U**, Nagi B, Garg PK, Sinha SK, Singh K, Tandon RK. Patients with gallstones develop gallbladder cancer at an earlier age. *Eur J Cancer Prev* 2005; **14**: 381-385 [PMID: [16030429](#) DOI: [10.1097/00008469-200508000-00011](#)]
  - 17 **Narang S**, Goyal P, Bal M, Bandlish U, Goyal S. Gall stones size, number, biochemical analysis and lipidogram- an association with gall bladder cancer: a study of 200 cases. *Int J Cancer Ther Oncol* 2014; **2**: 020310 [DOI: [10.14319/ijeto.0203.10](#)]
  - 18 **Singh A**, Singh G, Kaur K, Goyal G, Saini G, Sharma D. Histopathological Changes in Gallbladder Mucosa Associated with Cholelithiasis: A Prospective Study. *Niger J Surg* 2019; **25**: 21-25 [PMID: [31007507](#) DOI: [10.4103/njs.NJS\\_15\\_18](#)]
  - 19 **Sharma N**, Yadav M, Tripathi G, Mathew B, Bindal V, Falari S, Pamecha V, Maras JS. Bile multi-omics analysis classifies lipid species and microbial peptides predictive of carcinoma of gallbladder. *Hepatology* 2022; **76**: 920-935 [PMID: [35357716](#) DOI: [10.1002/hep.32496](#)]
  - 20 **Shridhar K**, Krishnatreya M, Kumar R, Kondal D, Bhattacharyya M, Kalita B, Snehil P, Singh AK, Kataki AC, Ghosh A, D Prabhakaran, Prabhakaran P, Dhillion PK. Household cooking fuel and gallbladder cancer risk: a multi-centre case-control study in India. *Cancer Causes Control* 2024; **35**: 281-292 [PMID: [37733135](#) DOI: [10.1007/s10552-023-01787-8](#)]
  - 21 **Jain K**, Sreenivas V, Velpandian T, Kapil U, Garg PK. Risk factors for gallbladder cancer: a case-control study. *Int J Cancer* 2013; **132**: 1660-1666 [PMID: [22890893](#) DOI: [10.1002/ijc.27777](#)]
  - 22 **Bhattacharjee PK**, Nanda D. Prospective observational study on cholelithiasis in patients with carcinoma gall bladder in a tertiary referral hospital of Eastern India. *J Cancer Res Ther* 2019; **15**: 153-156 [PMID: [30880772](#) DOI: [10.4103/jcrt.JCRT\\_939\\_17](#)]
  - 23 **Madhawi R**, Pandey A, Raj S, Mandal M, Devi S, Sinha PK, Singh RK. 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; **7**: 167-170 [PMID: [30112331](#) DOI: [10.4103/sajc.sajc\\_37\\_18](#)]
  - 24 **Tyagi BB**, Manoharan N, Raina V. Risk factors for gallbladder cancer : A population based case-control study in Delhi. *Indian J Med Paediatr Oncol* 2008; **29**: 16-26 [DOI: [10.4103/0971-5851.51442](#)]
  - 25 **Khan I**, Panda N, Banerjee M, Das R. Epidemiological factors in gall bladder cancer in eastern India-a single centre study. *Indian J Surg Oncol* 2013; **4**: 67-72 [PMID: [24426702](#) DOI: [10.1007/s13193-012-0203-x](#)]
  - 26 **Panda D**, Sharma A, Shukla NK, Jaiswal R, Dwivedi S, Raina V, Mohanti BK, Deo SV, Patra S. Gall bladder cancer and the role of dietary and lifestyle factors: a case-control study in a North Indian population. *Eur J Cancer Prev* 2013; **22**: 431-437 [PMID: [23462456](#) DOI: [10.1097/CEJ.0b013e32835f3b45](#)]
  - 27 **Bansal VK**, Misra MC, Chaubal G, Datta Gupta S, Das B, Ahuja V, Sagar S. Helicobacter pylori in gallbladder mucosa in patients with gallbladder disease. *Indian J Gastroenterol* 2012; **31**: 57-60 [PMID: [22350820](#) DOI: [10.1007/s12664-012-0162-8](#)]
  - 28 **Mathur SK**, Duhan A, Singh S, Aggarwal M, Aggarwal G, Sen R, Garg S. Correlation of gallstone characteristics with mucosal changes in gall bladder. *Trop Gastroenterol* 2012; **33**: 39-44 [PMID: [22803294](#) DOI: [10.7869/tg.2012.6](#)]
  - 29 **Srivastava M**, Sharma A, Kapoor VK, Nagana Gowda GA. Stones from cancerous and benign gallbladders are different: A proton nuclear magnetic resonance spectroscopy study. *Hepatol Res* 2008; **38**: 997-1005 [PMID: [18507688](#) DOI: [10.1111/j.1872-034X.2008.00356.x](#)]
  - 30 **Sharma V**, Chauhan VS, Nath G, Kumar A, Shukla VK. Role of bile bacteria in gallbladder carcinoma. *Hepatogastroenterology* 2007; **54**: 1622-1625 [PMID: [18019679](#)]
  - 31 **Misra V**, Misra SP, Dwivedi M, Shouche Y, Dharne M, Singh PA. Helicobacter pylori in areas of gastric metaplasia in the gallbladder and isolation of H. pylori DNA from gallstones. *Pathology* 2007; **39**: 419-424 [PMID: [17676484](#) DOI: [10.1080/00313020701444473](#)]
  - 32 **Kumar JR**, Tewari M, Rai A, Sinha R, Mohapatra SC, Shukla HS. An objective assessment of demography of gallbladder cancer. *J Surg Oncol* 2006; **93**: 610-614 [PMID: [16724352](#) DOI: [10.1002/jso.20526](#)]
  - 33 **Vaishnavi C**, Kochhar R, Singh G, Kumar S, Singh S, Singh K. Epidemiology of typhoid carriers among blood donors and patients with biliary, gastrointestinal and other related diseases. *Microbiol Immunol* 2005; **49**: 107-112 [PMID: [15722595](#) DOI: [10.1111/j.1348-0421.2005.tb03709.x](#)]
  - 34 **Shukla VK**, Prakash A, Chauhan VS, Singh S, Puneet. Biliary nitrate and risk of carcinoma of the gallbladder. *Eur J Cancer Prev* 2004; **13**: 355-356 [PMID: [15554566](#) DOI: [10.1097/01.cej.0000137514.48974.89](#)]
  - 35 **Shukla VK**, Adukia TK, Singh SP, Mishra CP, Mishra RN. Micronutrients, antioxidants, and carcinoma of the gallbladder. *J Surg Oncol* 2003; **84**: 31-35 [PMID: [12949988](#) DOI: [10.1002/jso.10283](#)]
  - 36 **Shukla VK**, Rastogi AN, Adukia TK, Raizada RB, Reddy DC, Singh S. Organochlorine pesticides in carcinoma of the gallbladder: a case-control study. *Eur J Cancer Prev* 2001; **10**: 153-156 [PMID: [11330456](#) DOI: [10.1097/00008469-200104000-00006](#)]
  - 37 **Gupta SC**, Misra V, Singh PA, Roy A, Misra SP, Gupta AK. Gall stones and carcinoma gall bladder. *Indian J Pathol Microbiol* 2000; **43**: 147-154 [PMID: [11217272](#)]
  - 38 **Iyer P**, Shrikhande SV, Ranjan M, Joshi A, Gardi N, Prasad R, Dharavath B, Thorat R, Salunkhe S, Sahoo B, Chandrani P, Kore H, Mohanty B, Chaudhari V, Choughule A, Kawle D, Chaudhari P, Ingle A, Banavali S, Gera P, Ramadwar MR, Prabhaskar K, Barreto SG, Dutt S, Dutt A. ERBB2 and KRAS alterations mediate response to EGFR inhibitors in early stage gallbladder cancer. *Int J Cancer* 2019; **144**: 2008-2019

- [PMID: 30304546 DOI: 10.1002/jjc.31916]
- 39 **Kazmi HR**, Chandra A, Nigam J, Noushif M, Parmar D, Gupta V. Prognostic significance of K-ras codon 12 mutation in patients with resected gallbladder cancer. *Dig Surg* 2013; **30**: 233-239 [PMID: 23838952 DOI: 10.1159/000353133]
- 40 **Gupta V**, Goel MM, Chandra A, Gupta P, Kumar S, Nigam J. Expression and clinicopathological significance of antiapoptosis protein survivin in gallbladder cancer. *Indian J Pathol Microbiol* 2016; **59**: 143-147 [PMID: 27166029 DOI: 10.4103/0377-4929.182035]
- 41 **Kumari N**, Kapoor VK, Krishnani N, Kumar K, Baitha DK. Role of C-erbB2 expression in gallbladder cancer. *Indian J Pathol Microbiol* 2012; **55**: 75-79 [PMID: 22499306 DOI: 10.4103/0377-4929.94862]
- 42 **Misra S**, Chaturvedi A, Goel MM, Mehrotra R, Sharma ID, Srivastava AN, Misra NC. Overexpression of p53 protein in gallbladder carcinoma in North India. *Eur J Surg Oncol* 2000; **26**: 164-167 [PMID: 10744937 DOI: 10.1053/ejso.1999.0763]
- 43 **Singh TD**, Gupta S, Shrivastav BR, Tiwari PK. Epigenetic profiling of gallbladder cancer and gall stone diseases: Evaluation of role of tumour associated genes. *Gene* 2016; **576**: 743-752 [PMID: 26456195 DOI: 10.1016/j.gene.2015.10.004]
- 44 **Tekcham DS**, Gupta S, Shrivastav BR, Tiwari PK. Epigenetic Downregulation of PTEN in Gallbladder Cancer. *J Gastrointest Cancer* 2017; **48**: 110-116 [PMID: 28124240 DOI: 10.1007/s12029-017-9919-8]
- 45 **Rai R**, Tewari M, Kumar M, Singh TB, Shukla HS. Expression profile of cholecystokinin type-A receptor in gallbladder cancer and gallstone disease. *Hepatobiliary Pancreat Dis Int* 2011; **10**: 408-414 [PMID: 21813391 DOI: 10.1016/S1499-3872(11)60069-6]
- 46 **Yadav S**, DE Sarkar N, Kumari N, Krishnani N, Kumar A, Mittal B. Targeted Gene Sequencing of Gallbladder Carcinoma Identifies High-impact Somatic and Rare Germline Mutations. *Cancer Genomics Proteomics* 2017; **14**: 495-506 [PMID: 29109099 DOI: 10.21873/cgp.20059]
- 47 **Kumari N**, Corless CL, Warrick A, Beadling C, Nelson D, Neff T, Krishnani N, Kapoor VK. Mutation profiling in gallbladder cancer in Indian population. *Indian J Pathol Microbiol* 2014; **57**: 9-12 [PMID: 24739824 DOI: 10.4103/0377-4929.130849]
- 48 **Priya TP**, Kapoor VK, Krishnani N, Agrawal V, Agarwal S. Fragile histidine triad (FHIT) gene and its association with p53 protein expression in the progression of gall bladder cancer. *Cancer Invest* 2009; **27**: 764-773 [PMID: 19452299 DOI: 10.1080/07357900802711304]
- 49 **Jain K**, Mohapatra T, Das P, Misra MC, Gupta SD, Ghosh M, Kabra M, Bansal VK, Kumar S, Sreenivas V, Garg PK. Sequential occurrence of preneoplastic lesions and accumulation of loss of heterozygosity in patients with gallbladder stones suggest causal association with gallbladder cancer. *Ann Surg* 2014; **260**: 1073-1080 [PMID: 24827397 DOI: 10.1097/SLA.0000000000000495]
- 50 **Pandey SN**, Jain M, Nigam P, Choudhuri G, Mittal B. Genetic polymorphisms in GSTM1, GSTT1, GSTP1, GSTM3 and the susceptibility to gallbladder cancer in North India. *Biomarkers* 2006; **11**: 250-261 [PMID: 16760134 DOI: 10.1080/13547500600648697]
- 51 **Saxena R**, Chakrapani B, Sarath Krishnan MP, Gupta A, Gupta S, Das J, Gupta SC, Mirza AA, Rao S, Goyal B. Next generation sequencing uncovers multiple miRNAs associated molecular targets in gallbladder cancer patients. *Sci Rep* 2023; **13**: 19101 [PMID: 37925508 DOI: 10.1038/s41598-023-44767-3]
- 52 **Anjali K**, Singh D, Kumar P, Kumar T, Narayan G, Singh S. PARP1 rs1136410 (A/G) polymorphism is associated with early age of onset of gallbladder cancer. *Eur J Cancer Prev* 2022; **31**: 311-317 [PMID: 34406176 DOI: 10.1097/CEJ.0000000000000708]
- 53 **Singh P**, Jain SL, Sakhuja P, Agarwal A. Expression of VEGF-A, HER2/neu, and KRAS in gall bladder carcinoma and their correlation with clinico-pathological parameters. *Indian J Pathol Microbiol* 2021; **64**: 687-692 [PMID: 34673587 DOI: 10.4103/IJPM.IJPM\_248\_20]
- 54 **Singh N**, Kazim SN, Sultana R, Tiwari D, Borkotoky R, Kakati S, Nath Das N, Kumar Saikia A, Bose S. Oxidative stress and deregulations in base excision repair pathway as contributors to gallbladder anomalies and carcinoma - a study involving North-East Indian population. *Free Radic Res* 2019; **53**: 473-485 [PMID: 31117842 DOI: 10.1080/10715762.2019.1606423]
- 55 **Shukla SK**, Singh G, Shahi KS, Bhuvan, Pant P. Genetic Changes of P(53) and Kras in Gallbladder Carcinoma in Kumaon Region of Uttarakhand. *J Gastrointest Cancer* 2020; **51**: 552-559 [PMID: 31396884 DOI: 10.1007/s12029-019-00283-0]
- 56 **Shabnam B**, Padmavathi G, Banik K, Girisa S, Monisha J, Sethi G, Fan L, Wang L, Mao X, Kunnumakkara AB. Sorcin a Potential Molecular Target for Cancer Therapy. *Transl Oncol* 2018; **11**: 1379-1389 [PMID: 30216763 DOI: 10.1016/j.tranon.2018.08.015]
- 57 **Yadav S**, Chandra A, Kumar A, Mittal B. Association of TERT-CLPTMIL and 8q24 Common Genetic Variants with Gallbladder Cancer Susceptibility and Prognosis in North Indian Population. *Biochem Genet* 2018; **56**: 267-282 [PMID: 29450669 DOI: 10.1007/s10528-018-9843-z]
- 58 **Dixit R**, Pandey M, Tripathi SK, Dwivedi AN, Shukla VK. Comparative Analysis of Mutational Profile of Sonic hedgehog Gene in Gallbladder Cancer. *Dig Dis Sci* 2017; **62**: 708-714 [PMID: 28058596 DOI: 10.1007/s10620-016-4438-1]
- 59 **Pujani M**, Makker I, Makker A, Jetley S, Goel MM. Expression of Human Epidermal Growth Factor Receptor (Her 2/neu) and Proliferative Marker Ki-67: Association with Clinicopathological Parameters in Gallbladder Carcinoma. *Asian Pac J Cancer Prev* 2016; **17**: 3903-3909 [PMID: 27644637]
- 60 **Kazmi HR**, Chandra A, Kumar S, Satyam LK, Gupta A, Nigam J, Srivastava M, Mittal B. A let-7 microRNA binding site polymorphism in the KRAS 3'UTR is associated with increased risk and reduced survival for gallbladder cancer in North Indian population. *J Cancer Res Clin Oncol* 2016; **142**: 2577-2583 [PMID: 27620744 DOI: 10.1007/s00432-016-2254-9]
- 61 **Tekcham DS**, Poojary SS, Bhunia S, Barbhuiya MA, Gupta S, Shrivastav BR, Tiwari PK. Epigenetic regulation of APC in the molecular pathogenesis of gallbladder cancer. *Indian J Med Res* 2016; **143**: S82-S90 [PMID: 27748282 DOI: 10.4103/0971-5916.191792]
- 62 **Sharma P**, Bhunia S, Poojary SS, Tekcham DS, Barbhuiya MA, Gupta S, Shrivastav BR, Tiwari PK. Global methylation profiling to identify epigenetic signature of gallbladder cancer and gallstone disease. *Tumour Biol* 2016; **37**: 14687-14699 [PMID: 27623942 DOI: 10.1007/s13277-016-5355-9]
- 63 **Kumar N**, Khan MA, Kumar N; Rigvardhan, Ranjan R, Hazra N. Epidermal growth factor receptor expression in carcinoma gallbladder: A prospective study in Indian scenario. *J Cancer Res Ther* 2016; **12**: 959-962 [PMID: 27461681 DOI: 10.4103/0973-1482.179063]
- 64 **Patil RS**, Shah SU, Shrikhande SV, Goel M, Dikshit RP, Chiplunkar SV. IL17 producing  $\gamma\delta$ T cells induce angiogenesis and are associated with poor survival in gallbladder cancer patients. *Int J Cancer* 2016; **139**: 869-881 [PMID: 27062572 DOI: 10.1002/ijc.30134]
- 65 **Dixit R**, Singh G, Pandey M, Basu S, Bhartiya SK, Singh KK, Shukla VK. Association of Methylenetetrahydrofolate Reductase Gene Polymorphism (MTHFR) in Patients with Gallbladder Cancer. *J Gastrointest Cancer* 2016; **47**: 55-60 [PMID: 26687138 DOI: 10.1007/s12029-015-9794-0]
- 66 **Poojary SS**, Mishra G, Gupta S, Shrivastav BR, Tiwari PK. Dysfunction of subtelomeric methylation and telomere length in gallstone disease and gallbladder cancer patients of North Central India. *J Hepatobiliary Pancreat Sci* 2016; **23**: 276-282 [PMID: 26856965 DOI: 10.1002/jhbp.332]
- 67 **Dwivedi S**, Agrawal S, Singh S, Madeshiya AK, Singh D, Mahdi AA, Chandra A. Association of Cytochrome-17 (MspA1) Gene Polymorphism with Risk of Gall Bladder Stones and Cancer in North India. *Asian Pac J Cancer Prev* 2015; **16**: 5557-5563 [PMID: 26225710]



DOI: [10.7314/APJCP.2015.16.13.5557](https://doi.org/10.7314/APJCP.2015.16.13.5557)]

- 68 **Sharma KL**, Misra S, Kumar A, Mittal B. Association of liver X receptors (LXRs) genetic variants to gallbladder cancer susceptibility. *Tumour Biol* 2013; **34**: 3959-3966 [PMID: [23838803](https://pubmed.ncbi.nlm.nih.gov/23838803/) DOI: [10.1007/s13277-013-0984-8](https://doi.org/10.1007/s13277-013-0984-8)]
- 69 **Mishra K**, Behari A, Kapoor VK, Khan MS, Prakash S, Agrawal S. Vascular endothelial growth factor single-nucleotide polymorphism in gallbladder cancer. *J Gastroenterol Hepatol* 2013; **28**: 1678-1685 [PMID: [23962084](https://pubmed.ncbi.nlm.nih.gov/23962084/) DOI: [10.1111/jgh.12343](https://doi.org/10.1111/jgh.12343)]
- 70 **Maurya SK**, Tewari M, Shukla HS. Gallbladder carcinoma: high rate of mitochondrial D-loop mutations. *Diagn Mol Pathol* 2013; **22**: 119-122 [PMID: [23628824](https://pubmed.ncbi.nlm.nih.gov/23628824/) DOI: [10.1097/PDM.0b013e31827a0d5a](https://doi.org/10.1097/PDM.0b013e31827a0d5a)]
- 71 **Srivastava A**, Sharma KL, Srivastava N, Misra S, Mittal B. Significant role of estrogen and progesterone receptor sequence variants in gallbladder cancer predisposition: a multi-analytical strategy. *PLoS One* 2012; **7**: e40162 [PMID: [22808109](https://pubmed.ncbi.nlm.nih.gov/22808109/) DOI: [10.1371/journal.pone.0040162](https://doi.org/10.1371/journal.pone.0040162)]
- 72 **Pramanik V**, Sarkar BN, Kar M, Das G, Malay BK, Sufia KK, Lakkakula BV, Vadlamudi RR. A novel polymorphism in codon 25 of the KRAS gene associated with gallbladder carcinoma patients of the eastern part of India. *Genet Test Mol Biomarkers* 2011; **15**: 431-434 [PMID: [21375404](https://pubmed.ncbi.nlm.nih.gov/21375404/) DOI: [10.1089/gtmb.2010.0194](https://doi.org/10.1089/gtmb.2010.0194)]
- 73 **Srivastava K**, Srivastava A, Mittal B. Caspase-8 polymorphisms and risk of gallbladder cancer in a northern Indian population. *Mol Carcinog* 2010; **49**: 684-692 [PMID: [20564345](https://pubmed.ncbi.nlm.nih.gov/20564345/) DOI: [10.1002/mc.20641](https://doi.org/10.1002/mc.20641)]
- 74 **Agrawal V**, Goel A, Krishnani N, Pandey R, Agrawal S, Kapoor VK. p53, carcinoembryonic antigen and carbohydrate antigen 19.9 expression in gall bladder cancer, precursor epithelial lesions and xanthogranulomatous cholecystitis. *J Postgrad Med* 2010; **56**: 262-266 [PMID: [20935395](https://pubmed.ncbi.nlm.nih.gov/20935395/) DOI: [10.4103/0022-3859.70933](https://doi.org/10.4103/0022-3859.70933)]
- 75 **Srivastava A**, Choudhuri G, Mittal B. CYP7A1 (-204 A>C; rs3808607 and -469 T>C; rs3824260) promoter polymorphisms and risk of gallbladder cancer in North Indian population. *Metabolism* 2010; **59**: 767-773 [PMID: [20005541](https://pubmed.ncbi.nlm.nih.gov/20005541/) DOI: [10.1016/j.metabol.2009.09.021](https://doi.org/10.1016/j.metabol.2009.09.021)]
- 76 **Srivastava K**, Srivastava A, Mittal B. Common genetic variants in pre-microRNAs and risk of gallbladder cancer in North Indian population. *J Hum Genet* 2010; **55**: 495-499 [PMID: [20520619](https://pubmed.ncbi.nlm.nih.gov/20520619/) DOI: [10.1038/jhg.2010.54](https://doi.org/10.1038/jhg.2010.54)]
- 77 **Nigam P**, Misra U, Negi TS, Mittal B, Choudhuri G. Alterations of p53 gene in gallbladder cancer patients of North India. *Trop Gastroenterol* 2010; **31**: 96-100 [PMID: [20862982](https://pubmed.ncbi.nlm.nih.gov/20862982/)]
- 78 **Priya TP**, Kapoor VK, Krishnani N, Agrawal V, Agrawal S. Role of E-cadherin gene in gall bladder cancer and its precursor lesions. *Virchows Arch* 2010; **456**: 507-514 [PMID: [20376482](https://pubmed.ncbi.nlm.nih.gov/20376482/) DOI: [10.1007/s00428-010-0908-6](https://doi.org/10.1007/s00428-010-0908-6)]
- 79 **Srivastava K**, Srivastava A, Mittal B. DNMT3B -579 G>T promoter polymorphism and risk of gallbladder carcinoma in North Indian population. *J Gastrointest Cancer* 2010; **41**: 248-253 [PMID: [20480259](https://pubmed.ncbi.nlm.nih.gov/20480259/) DOI: [10.1007/s12029-010-9156-x](https://doi.org/10.1007/s12029-010-9156-x)]
- 80 **Srivastava K**, Srivastava A, Mittal B. Angiotensin I-converting enzyme insertion/deletion polymorphism and increased risk of gall bladder cancer in women. *DNA Cell Biol* 2010; **29**: 417-422 [PMID: [20438364](https://pubmed.ncbi.nlm.nih.gov/20438364/) DOI: [10.1089/dna.2010.1033](https://doi.org/10.1089/dna.2010.1033)]
- 81 **Srivastava K**, Srivastava A, Mittal B. Polymorphisms in ERCC2, MSH2, and OGG1 DNA repair genes and gallbladder cancer risk in a population of Northern India. *Cancer* 2010; **116**: 3160-3169 [PMID: [20564624](https://pubmed.ncbi.nlm.nih.gov/20564624/) DOI: [10.1002/cncr.25063](https://doi.org/10.1002/cncr.25063)]
- 82 **Srivastava A**, Tulsyan S, Pandey SN, Choudhuri G, Mittal B. Single nucleotide polymorphism in the ABCG8 transporter gene is associated with gallbladder cancer susceptibility. *Liver Int* 2009; **29**: 831-837 [PMID: [19018975](https://pubmed.ncbi.nlm.nih.gov/19018975/) DOI: [10.1111/j.1478-3231.2008.01907.x](https://doi.org/10.1111/j.1478-3231.2008.01907.x)]
- 83 **Srivastava A**, Mittal B. Complement receptor 1 (A3650G RsaI and intron 27 HindIII) polymorphisms and risk of gallbladder cancer in north Indian population. *Scand J Immunol* 2009; **70**: 614-620 [PMID: [19906204](https://pubmed.ncbi.nlm.nih.gov/19906204/) DOI: [10.1111/j.1365-3083.2009.02329.x](https://doi.org/10.1111/j.1365-3083.2009.02329.x)]
- 84 **Srivastava A**, Srivastava K, Pandey SN, Choudhuri G, Mittal B. Single-nucleotide polymorphisms of DNA repair genes OGG1 and XRCC1: association with gallbladder cancer in North Indian population. *Ann Surg Oncol* 2009; **16**: 1695-1703 [PMID: [19266243](https://pubmed.ncbi.nlm.nih.gov/19266243/) DOI: [10.1245/s10434-009-0354-3](https://doi.org/10.1245/s10434-009-0354-3)]
- 85 **Srivastava A**, Pandey SN, Choudhuri G, Mittal B. CCR5 Delta32 polymorphism: associated with gallbladder cancer susceptibility. *Scand J Immunol* 2008; **67**: 516-522 [PMID: [18405329](https://pubmed.ncbi.nlm.nih.gov/18405329/) DOI: [10.1111/j.1365-3083.2008.02097.x](https://doi.org/10.1111/j.1365-3083.2008.02097.x)]
- 86 **Vishnoi M**, Pandey SN, Choudhuri G, Mittal B. IL-1 gene polymorphisms and genetic susceptibility of gallbladder cancer in a north Indian population. *Cancer Genet Cytogenet* 2008; **186**: 63-68 [PMID: [18940468](https://pubmed.ncbi.nlm.nih.gov/18940468/) DOI: [10.1016/j.cancergencyto.2008.05.004](https://doi.org/10.1016/j.cancergencyto.2008.05.004)]
- 87 **Pandey SN**, Choudhuri G, Mittal B. Association of CYP1A1 MspI polymorphism with tobacco-related risk of gallbladder cancer in a north Indian population. *Eur J Cancer Prev* 2008; **17**: 77-81 [PMID: [18287863](https://pubmed.ncbi.nlm.nih.gov/18287863/) DOI: [10.1097/CEJ.0b013e318282b6fdd2](https://doi.org/10.1097/CEJ.0b013e318282b6fdd2)]
- 88 **Srivastava A**, Pandey SN, Choudhuri G, Mittal B. Role of genetic variant A-204C of cholesterol 7alpha-hydroxylase (CYP7A1) in susceptibility to gallbladder cancer. *Mol Genet Metab* 2008; **94**: 83-89 [PMID: [18178499](https://pubmed.ncbi.nlm.nih.gov/18178499/) DOI: [10.1016/j.ymgme.2007.11.014](https://doi.org/10.1016/j.ymgme.2007.11.014)]
- 89 **Pandey SN**, Srivastava A, Dixit M, Choudhuri G, Mittal B. Haplotype analysis of signal peptide (insertion/deletion) and XbaI polymorphisms of the APOB gene in gallbladder cancer. *Liver Int* 2007; **27**: 1008-1015 [PMID: [17696941](https://pubmed.ncbi.nlm.nih.gov/17696941/) DOI: [10.1111/j.1478-3231.2007.01516.x](https://doi.org/10.1111/j.1478-3231.2007.01516.x)]
- 90 **Pandey SN**, Modi DR, Choudhuri G, Mittal B. Slow acetylator genotype of N-acetyl transferase2 (NAT2) is associated with increased susceptibility to gallbladder cancer: the cancer risk not modulated by gallstone disease. *Cancer Biol Ther* 2007; **6**: 91-96 [PMID: [17224641](https://pubmed.ncbi.nlm.nih.gov/17224641/) DOI: [10.4161/cbt.6.1.3554](https://doi.org/10.4161/cbt.6.1.3554)]
- 91 **Pandey SN**, Dixit M, Choudhuri G, Mittal B. Lipoprotein receptor associated protein (LRPAP1) insertion/deletion polymorphism: association with gallbladder cancer susceptibility. *Int J Gastrointest Cancer* 2006; **37**: 124-128 [PMID: [17987404](https://pubmed.ncbi.nlm.nih.gov/17987404/) DOI: [10.1007/s12029-007-9002-y](https://doi.org/10.1007/s12029-007-9002-y)]
- 92 **Singh MK**, Chetri K, Pandey UB, Kapoor VK, Mittal B, Choudhuri G. Mutational spectrum of K-ras oncogene among Indian patients with gallbladder cancer. *J Gastroenterol Hepatol* 2004; **19**: 916-921 [PMID: [15242496](https://pubmed.ncbi.nlm.nih.gov/15242496/) DOI: [10.1111/j.1440-1746.2004.03355.x](https://doi.org/10.1111/j.1440-1746.2004.03355.x)]
- 93 **Singh MK**, Pandey UB, Ghoshal UC, Srivenu I, Kapoor VK, Choudhuri G, Mittal B. Apolipoprotein B-100 XbaI gene polymorphism in gallbladder cancer. *Hum Genet* 2004; **114**: 280-283 [PMID: [14618390](https://pubmed.ncbi.nlm.nih.gov/14618390/) DOI: [10.1007/s00439-003-1056-8](https://doi.org/10.1007/s00439-003-1056-8)]
- 94 **Pandey M**, Sood BP, Shukla RC, Aryya NC, Singh S, Shukla VK. Carcinoma of the gallbladder: role of sonography in diagnosis and staging. *J Clin Ultrasound* 2000; **28**: 227-232 [PMID: [10800001](https://pubmed.ncbi.nlm.nih.gov/10800001/) DOI: [10.1002/\(sici\)1097-0096\(200006\)28:5<227::aid-jcu4>3.0.co;2-4](https://doi.org/10.1002/(sici)1097-0096(200006)28:5<227::aid-jcu4>3.0.co;2-4)]
- 95 **Agarwal AK**, Kalayarsan R, Singh S, Javed A, Sakhuja P. All cholecystectomy specimens must be sent for histopathology to detect inapparent gallbladder cancer. *HPB (Oxford)* 2012; **14**: 269-273 [PMID: [22404266](https://pubmed.ncbi.nlm.nih.gov/22404266/) DOI: [10.1111/j.1477-2574.2012.00443.x](https://doi.org/10.1111/j.1477-2574.2012.00443.x)]
- 96 **Rana C**, Krishnani N, Kumari N. Ultrasound-guided fine needle aspiration cytology of gallbladder lesions: a study of 596 cases. *Cytopathology* 2016; **27**: 398-406 [PMID: [26990137](https://pubmed.ncbi.nlm.nih.gov/26990137/) DOI: [10.1111/cyt.12296](https://doi.org/10.1111/cyt.12296)]
- 97 **Yadav R**, Jain D, Mathur SR, Sharma A, Iyer VK. Gallbladder carcinoma: An attempt of WHO histological classification on fine needle aspiration material. *Cytojournal* 2013; **10**: 12 [PMID: [23858322](https://pubmed.ncbi.nlm.nih.gov/23858322/) DOI: [10.4103/1742-6413.113627](https://doi.org/10.4103/1742-6413.113627)]
- 98 **Chandra S**, Chandra H, Shukla SK, Sahu S. Fine-needle aspiration cytology of gallbladder with an attempt of cytomorphological classification. *Cytojournal* 2019; **16**: 1 [PMID: [30820231](https://pubmed.ncbi.nlm.nih.gov/30820231/) DOI: [10.4103/cytojournal.cytojournal\\_5\\_18](https://doi.org/10.4103/cytojournal.cytojournal_5_18)]

- 99 **Yadav R**, Jain D, Mathur SR, Iyer VK. Cytomorphology of neuroendocrine tumours of the gallbladder. *Cytopathology* 2016; **27**: 97-102 [PMID: 25689921 DOI: 10.1111/cyt.12239]
- 100 **Kamboj M**, Gandhi JS, Gupta G, Sharma A, Pasricha S, Mehta A, Chandragouda D, Sinha R. Neuroendocrine Carcinoma of Gall Bladder: A Series of 19 Cases with Review of Literature. *J Gastrointest Cancer* 2015; **46**: 356-364 [PMID: 26208508 DOI: 10.1007/s12029-015-9745-9]
- 101 **Krishnani N**, Shukla S, Jain M, Pandey R, Gupta RK. Fine needle aspiration cytology in xanthogranulomatous cholecystitis, gallbladder adenocarcinoma and coexistent lesions. *Acta Cytol* 2000; **44**: 508-514 [PMID: 10934941 DOI: 10.1159/000328522]
- 102 **Goyal S**, Prasad G, Chaudhary D, Sakhuja P, Srivastava S, Aggarwal AK. Role of Guided FNA in Gallbladder Cancer: A Retrospective 3-Year Study. *J Cytol* 2023; **40**: 12-18 [PMID: 37179960 DOI: 10.4103/joc.joc\_224\_21]
- 103 **Shukla VK**, Pandey M, Kumar M, Sood BP, Gupta A, Aryya NC, Shukla RC, Verma DN. Ultrasound-guided fine needle aspiration cytology of malignant gallbladder masses. *Acta Cytol* 1997; **41**: 1654-1658 [PMID: 9390120 DOI: 10.1159/000333156]
- 104 **Shukla S**, Krishnani N, Jain M, Pandey R, Gupta RK. Xanthogranulomatous cholecystitis. Fine needle aspiration cytology in 17 cases. *Acta Cytol* 1997; **41**: 413-418 [PMID: 9100775 DOI: 10.1159/000332533]
- 105 **Shukla PJ**, Barreto SG, Gupta P, Neve R, Ramadwar M, Deodhar K, Mehta S, Shrikhande SV, Mohandas KM. Is there a role for estrogen and progesterone receptors in gall bladder cancer? *HPB (Oxford)* 2007; **9**: 285-288 [PMID: 18345306 DOI: 10.1080/13651820701481489]
- 106 **Yadav K**, Agarwal P, Kumar M, Gupta S, Mishra M, Maurya MK, Qayoom S, Goel MM. Immunohistochemical appraisal of epithelial mesenchymal transition type III in gall bladder cancer. *Indian J Pathol Microbiol* 2023; **66**: 44-53 [PMID: 36656209 DOI: 10.4103/ijpm.ijpm\_876\_21]
- 107 **Jain V**, Akhtar J, Priya R, Sakhuja P, Goyal S, Agarwal AK, Ghose V, Polisetty RV, Sirdeshmukh R, Siraj F, Gautam P. Tissue proteome analysis for profiling proteins associated with lymph node metastasis in gallbladder cancer. *BMC Cancer* 2023; **23**: 402 [PMID: 37142981 DOI: 10.1186/s12885-023-10840-3]
- 108 **Priya R**, Jain V, Akhtar J, Saklani N, Sakhuja P, Agarwal AK, Polisetty RV, Sirdeshmukh R, Kar S, Gautam P. Proteomic profiling of cell line-derived extracellular vesicles to identify candidate circulatory markers for detection of gallbladder cancer. *Front Oncol* 2022; **12**: 1027914 [PMID: 36505879 DOI: 10.3389/fonc.2022.1027914]
- 109 **Akhtar J**, Jain V, Kansal R, Priya R, Sakhuja P, Goyal S, Agarwal AK, Ghose V, Polisetty RV, Sirdeshmukh R, Kar S, Gautam P. Quantitative tissue proteome profile reveals neutrophil degranulation and remodeling of extracellular matrix proteins in early stage gallbladder cancer. *Front Oncol* 2022; **12**: 1046974 [PMID: 36686780 DOI: 10.3389/fonc.2022.1046974]
- 110 **Priya R**, Jain V, Akhtar J, Chauhan G, Sakhuja P, Goyal S, Agarwal AK, Javed A, Jain AP, Polisetty RV, Sirdeshmukh R, Kar S, Gautam P. Plasma-derived candidate biomarkers for detection of gallbladder carcinoma. *Sci Rep* 2021; **11**: 23554 [PMID: 34876625 DOI: 10.1038/s41598-021-02923-7]
- 111 **Mishra PK**, Saluja SS, Prithiviraj N, Varshney V, Goel N, Patil N. Predictors of curative resection and long term survival of gallbladder cancer - A retrospective analysis. *Am J Surg* 2017; **214**: 278-286 [PMID: 28233537 DOI: 10.1016/j.amjsurg.2017.02.006]
- 112 **Negi SS**, Singh A, Chaudhary A. Lymph nodal involvement as prognostic factor in gallbladder cancer: location, count or ratio? *J Gastrointest Surg* 2011; **15**: 1017-1025 [PMID: 21487831 DOI: 10.1007/s11605-011-1528-4]
- 113 **Shah SH**, Gupta N, Gupta G, Mehta A, Singh S. Lymph node micrometastasis in gallbladder cancer. *Indian J Gastroenterol* 2017; **36**: 268-274 [PMID: 28782079 DOI: 10.1007/s12664-017-0775-z]
- 114 **Balachandran P**, Agarwal S, Krishnani N, Pandey CM, Kumar A, Sikora SS, Saxena R, Kapoor VK. Predictors of long-term survival in patients with gallbladder cancer. *J Gastrointest Surg* 2006; **10**: 848-854 [PMID: 16769541 DOI: 10.1016/j.gassur.2005.12.002]
- 115 **Gupta A**, Gupta S, Mani R, Durgapal P, Goyal B, Rajput D, Rao S, Dhar P, Gupta M, Kishore S, Kant R. Expression of Human epidermal growth factor receptor 2, Survivin, Enhancer of zeste homolog -2, Cyclooxygenase-2, p53 and p16 molecular markers in Gall bladder carcinoma. *J Carcinog* 2021; **20**: 7 [PMID: 34321957 DOI: 10.4103/jcar.JCar\_4\_21]
- 116 **Jain P**, Goyal S, Chauhan G, Majumdar K, Ali S, Sakhuja P, Agarwal AK. HER-2/neu over expression in gall bladder adenocarcinoma: A quest for potential therapeutic target. *Indian J Pathol Microbiol* 2020; **63**: 214-220 [PMID: 32317518 DOI: 10.4103/IJPM.IJPM\_664\_19]
- 117 **Halder S**, Kundu S, Chakraborty J, Chakrabarti S. Significance of HER2 and Ki-67 in Preneoplastic Lesions and Carcinoma of Gallbladder. *J Gastrointest Cancer* 2019; **50**: 848-854 [PMID: 30155833 DOI: 10.1007/s12029-018-0162-8]
- 118 **Kumari S**, Husain N, Agarwal A, Neyaz A, Gupta S, Chaturvedi A, Lohani M, Sonkar AA. Diagnostic Value of Circulating Free DNA Integrity and Global Methylation Status in Gall Bladder Carcinoma. *Pathol Oncol Res* 2019; **25**: 925-936 [PMID: 29376201 DOI: 10.1007/s12253-017-0380-6]
- 119 **Rajaguru K**, Mehrotra S, Lalwani S, Mangla V, Mehta N, Nundy S. New scoring system for differentiating xanthogranulomatous cholecystitis from gall bladder carcinoma: a tertiary care centre experience. *ANZ J Surg* 2018; **88**: E34-E39 [PMID: 27599003 DOI: 10.1111/ans.13733]
- 120 **Kumari S**, Tewari S, Husain N, Agarwal A, Pandey A, Singhal A, Lohani M. Quantification of Circulating Free DNA as a Diagnostic Marker in Gall Bladder Cancer. *Pathol Oncol Res* 2017; **23**: 91-97 [PMID: 27475647 DOI: 10.1007/s12253-016-0087-0]
- 121 **Nigam J**, Chandra A, Kazmi HR, Parmar D, Singh D, Gupta V. Prognostic significance of survivin in resected gallbladder cancer. *J Surg Res* 2015; **194**: 57-62 [PMID: 25472573 DOI: 10.1016/j.jss.2014.07.054]
- 122 **Nigam J**, Chandra A, Kazmi HR, Parmar D, Singh D, Gupta V, M N. Expression of survivin mRNA in gallbladder cancer: a diagnostic and prognostic marker? *Tumour Biol* 2014; **35**: 9241-9246 [PMID: 24935470 DOI: 10.1007/s13277-014-2200-x]
- 123 **Ghosh M**, Sakhuja P, Singh S, Agarwal AK. p53 and beta-catenin expression in gallbladder tissues and correlation with tumor progression in gallbladder cancer. *Saudi J Gastroenterol* 2013; **19**: 34-39 [PMID: 23319036 DOI: 10.4103/1319-3767.105922]
- 124 **Gupta P**, Gupta RK. Preoperative diagnosis of squamous cell carcinoma of the gallbladder by ultrasound-guided aspiration cytology: clinical and cytological findings of nine cases. *J Gastrointest Cancer* 2012; **43**: 638-641 [PMID: 22791136 DOI: 10.1007/s12029-012-9413-2]
- 125 **Shukla VK**, Gurubachan, Sharma D, Dixit VK, Usha. Diagnostic value of serum CA242, CA 19-9, CA 15-3 and CA 125 in patients with carcinoma of the gallbladder. *Trop Gastroenterol* 2006; **27**: 160-165 [PMID: 17542293]
- 126 **Arora VK**, Kumar S, Singh N, Bhatia A. Intraoperative bile cytology of the dysplasia-carcinoma in situ sequence of gallbladder carcinoma. *Cancer* 2005; **105**: 277-281 [PMID: 16047358 DOI: 10.1002/encr.21320]
- 127 **Batra Y**, Pal S, Dutta U, Desai P, Garg PK, Makharia G, Ahuja V, Pande GK, Sahni P, Chattopadhyay TK, Tandon RK. Gallbladder cancer in India: a dismal picture. *J Gastroenterol Hepatol* 2005; **20**: 309-314 [PMID: 15683437 DOI: 10.1111/j.1440-1746.2005.03576.x]
- 128 **Chhabra M**, Kalage D, Gupta P, Siddiqui R, Singh S, Yadav TD, Gupta V, Kaman L, Singh H, Irrinki S, Das C, Prakash G, Saikia UN, Nada R, Dutta U, Sandhu MS. Proposal for a new morphological "combined type" of gallbladder cancer: description of radiopathological characteristics and comparison with other morphological types. *Abdom Radiol (NY)* 2024; **49**: 703-709 [PMID: 37973653 DOI: 10.1007/s00067-023-05840-3]

- 10.1007/s00261-023-04090-x]
- 129 **Rana P**, Pruthi H, Gupta P, Chhabra M, Soundararajan R, Singh S, Gulati A, Das CK, Yadav TD, Gupta V, Saikia UN, Dutta U, Sandhu M. Sonographic "Cervix Sign": A New Ancillary Sign of Gallbladder Neck Malignancy. *J Clin Exp Hepatol* 2023; **13**: 972-976 [PMID: 37975041 DOI: 10.1016/j.jceh.2023.05.013]
- 130 **Patel A**, Singh H, Nair R, Buva D. 50P Ultrasound guided screening of gallbladder cancer in healthy volunteers: A prospective study from Northern India. *Annals of Oncology* 2020; **31**: S260 [DOI: 10.1016/j.annonc.2020.08.028]
- 131 **Anadure R**, Sreen A, Singh H, Sharma A, Sharma R, Mohimen A, Gupta S. The utility of screening ultrasound in early diagnosis of gall bladder cancer among high-risk population. *Oncol J India* 2021; **5**: 8 [DOI: 10.4103/oji.oji\_51\_20]
- 132 **Gupta P**, Dutta U, Rana P, Singhal M, Gulati A, Kalra N, Soundararajan R, Kalage D, Chhabra M, Sharma V, Gupta V, Yadav TD, Kaman L, Irrinki S, Singh H, Sakaray Y, Das CK, Saikia U, Nada R, Srinivasan R, Sandhu MS, Sharma R, Shetty N, Eapen A, Kaur H, Kambadakone A, de Haas R, Kapoor VK, Barreto SG, Sharma AK, Patel A, Garg P, Pal SK, Goel M, Patkar S, Behari A, Agarwal AK, Sirohi B, Javle M, Garcea G, Nervi F, Adsay V, Roa JC, Han HS. Gallbladder reporting and data system (GB-RADS) for risk stratification of gallbladder wall thickening on ultrasonography: an international expert consensus. *Abdom Radiol (NY)* 2022; **47**: 554-565 [PMID: 34851429 DOI: 10.1007/s00261-021-03360-w]
- 133 **Gupta P**, Marodia Y, Bansal A, Kalra N, Kumar-M P, Sharma V, Dutta U, Sandhu MS. Imaging-based algorithmic approach to gallbladder wall thickening. *World J Gastroenterol* 2020; **26**: 6163-6181 [PMID: 33177791 DOI: 10.3748/wjg.v26.i40.6163]
- 134 **Kapoor A**, Kapoor A, Mahajan G. Differentiating malignant from benign thickening of the gallbladder wall by the use of acoustic radiation force impulse elastography. *J Ultrasound Med* 2011; **30**: 1499-1507 [PMID: 22039022 DOI: 10.7863/jum.2011.30.11.1499]
- 135 **Kalage D**, Gupta P, Gulati A, Yadav TD, Gupta V, Kaman L, Nada R, Singh H, Irrinki S, Das C, Dutta U, Sandhu M. Multiparametric MR imaging with diffusion-weighted, intravoxel incoherent motion, diffusion tensor, and dynamic contrast-enhanced perfusion sequences to assess gallbladder wall thickening: a prospective study based on surgical histopathology. *Eur Radiol* 2023; **33**: 4981-4993 [PMID: 36826499 DOI: 10.1007/s00330-023-09455-w]
- 136 **Singla V**, Agarwal R, Anikhindi SA, Puri P, Kumar M, Ranjan P, Kumar A, Sharma P, Bansal N, Bakshi P, Verma K, Arora A. Role of EUS-FNA for gallbladder mass lesions with biliary obstruction: a large single-center experience. *Endosc Int Open* 2019; **7**: E1403-E1409 [PMID: 31673611 DOI: 10.1055/a-0982-2862]
- 137 **Kalra N**, Suri S, Gupta R, Natarajan SK, Khandelwal N, Wig JD, Joshi K. MDCT in the staging of gallbladder carcinoma. *AJR Am J Roentgenol* 2006; **186**: 758-762 [PMID: 16498103 DOI: 10.2214/AJR.04.1342]
- 138 **Kumaran V**, Gulati S, Paul B, Pande K, Sahni P, Chattopadhyay K. The role of dual-phase helical CT in assessing resectability of carcinoma of the gallbladder. *Eur Radiol* 2002; **12**: 1993-1999 [PMID: 12136317 DOI: 10.1007/s00330-002-1440-0]
- 139 **Soundararajan R**, Vanka S, Gupta P, Chhabra M, Rana P, Gulati A, Das CK, Saikia UN, Yadav TD, Gupta V, Kaman L, Singh H, Irrinki S, Dutta U, Sandhu MS. Gastrointestinal involvement in gallbladder cancer: Computed tomography findings and proposal of a classification system. *Indian J Gastroenterol* 2023; **42**: 708-712 [PMID: 37318744 DOI: 10.1007/s12664-023-01388-y]
- 140 **Patkar S**, Chaturvedi A, Goel M, Rangarajan V, Sharma A, Engineer R. Role of positron emission tomography-contrast enhanced computed tomography in locally advanced gallbladder cancer. *J Hepatobiliary Pancreat Sci* 2020; **27**: 164-170 [PMID: 31945262 DOI: 10.1002/jhbp.712]
- 141 **Goel S**, Aggarwal A, Iqbal A, Gupta M, Rao A, Singh S. 18-FDG PET-CT should be included in preoperative staging of gall bladder cancer. *Eur J Surg Oncol* 2020; **46**: 1711-1716 [PMID: 32331985 DOI: 10.1016/j.ejso.2020.04.015]
- 142 **Shukla PJ**, Barreto SG, Arya S, Shrikhande SV, Hawaldar R, Purandare N, Rangarajan V. Does PET-CT scan have a role prior to radical resection for incidental gallbladder cancer? *HPB (Oxford)* 2008; **10**: 439-445 [PMID: 19088931 DOI: 10.1080/13651820802286910]
- 143 **Goel M**, Tamhankar A, Rangarajan V, Patkar S, Ramadwar M, Shrikhande SV. Role of PET CT scan in redefining treatment of incidental gall bladder carcinoma. *J Surg Oncol* 2016; **113**: 652-658 [PMID: 26847023 DOI: 10.1002/jso.24198]
- 144 **Kumar R**, Sharma P, Kumari A, Halanaik D, Malhotra A. Role of 18F-FDG PET/CT in detecting recurrent gallbladder carcinoma. *Clin Nucl Med* 2012; **37**: 431-435 [PMID: 22475890 DOI: 10.1097/RLU.0b013e31824d24e4]
- 145 **Sinha SR**, Prakash P, Singh RK, Sinha DK. Assessment of tumor markers CA 19-9, CEA, CA 125, and CA 242 for the early diagnosis and prognosis prediction of gallbladder cancer. *World J Gastrointest Surg* 2022; **14**: 1272-1284 [PMID: 36504513 DOI: 10.4240/wjgs.v14.i11.1272]
- 146 **Agrawal S**, Gupta A, Gupta S, Goyal B, Siddeek RAT, Rajput D, Chauhan U, Kishore S, Gupta M, Kant R. Role of carbohydrate antigen 19-9, carcinoembryonic antigen, and carbohydrate antigen 125 as the predictors of resectability and survival in the patients of Carcinoma Gall Bladder. *J Carcinog* 2020; **19**: 4 [PMID: 33033460 DOI: 10.4103/jcar.JCar\_10\_20]
- 147 **Bisht N**, Lohia N, Singh S, Sarin A, Mahato A, Paliwal D, Sinha I, Bhatnagar S. Utility of 18-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography ((18) FDG PET-CT) in Gallbladder Cancer: Experience from a Tertiary Care Hospital. *World J Nucl Med* 2023; **22**: 276-283 [PMID: 38152099 DOI: 10.1055/s-0043-1777699]
- 148 **Gupta P**, Rana P, Ganeshan B, Kalage D, Irrinki S, Gupta V, Yadav TD, Kumar R, Das CK, Gupta P, Endozo R, Nada R, Srinivasan R, Kalra N, Dutta U, Sandhu M. Computed tomography texture-based radiomics analysis in gallbladder cancer: initial experience. *Clin Exp Hepatol* 2021; **7**: 406-414 [PMID: 35402717 DOI: 10.5114/ceh.2021.111173]
- 149 **Agrawal S**, Lawrence A, Saxena R. Does CA 19-9 Have Prognostic Relevance in Gallbladder Carcinoma (GBC)? *J Gastrointest Cancer* 2018; **49**: 144-149 [PMID: 28105553 DOI: 10.1007/s12029-016-9914-5]
- 150 **Sharma RK**, Mishra K, Farooqui A, Behari A, Kapoor VK, Sinha N. (1)H nuclear magnetic resonance (NMR)-based serum metabolomics of human gallbladder inflammation. *Inflamm Res* 2017; **66**: 97-105 [PMID: 27770143 DOI: 10.1007/s00011-016-0998-y]
- 151 **Mondal SK**, Bhattacharjee D, Mandal PK, Biswas S. Histopathological study of gallbladder carcinoma and its mimics with role of carcinoembryonic antigen immunomarker in resolving diagnostic difficulties. *Indian J Med Paediatr Oncol* 2017; **38**: 411-415 [PMID: 29333003 DOI: 10.4103/ijmpo.ijmpo\_230\_15]
- 152 **Sureka B**, Singh VP, Rajesh SR, Laroia S, Bansal K, Rastogi A, Bihari C, Bhadoria AS, Agrawal N, Arora A. Computed Tomography (CT) and Magnetic Resonance (MR) Findings in Xanthogranulomatous Cholecystitis: Retrospective Analysis of Pathologically Proven 30 Cases - Tertiary Care Experience. *Pol J Radiol* 2017; **82**: 327-332 [PMID: 28685006 DOI: 10.12659/PJR.901728]
- 153 **Kalayarasan R**, Javed A, Puri AS, Puri SK, Sakhuja P, Agarwal AK. A prospective analysis of the preoperative assessment of duodenal involvement in gallbladder cancer. *HPB (Oxford)* 2013; **15**: 203-209 [PMID: 23036027 DOI: 10.1111/j.1477-2574.2012.00539.x]
- 154 **Agarwal AK**, Kalayarasan R, Javed A, Sakhuja P. Mass-forming xanthogranulomatous cholecystitis masquerading as gallbladder cancer. *J Gastrointest Surg* 2013; **17**: 1257-1264 [PMID: 23615807 DOI: 10.1007/s11605-013-2209-2]



- 155 **Rana S**, Dutta U, Kochhar R, Rana SV, Gupta R, Pal R, Jain K, Srinivasan R, Nagi B, Nain CK, Singh K. Evaluation of CA 242 as a tumor marker in gallbladder cancer. *J Gastrointest Cancer* 2012; **43**: 267-271 [PMID: 21573879 DOI: 10.1007/s12029-011-9288-7]
- 156 **Kaza RK**, Gulati M, Wig JD, Chawla YK. Evaluation of gall bladder carcinoma with dynamic magnetic resonance imaging and magnetic resonance cholangiopancreatography. *Australas Radiol* 2006; **50**: 212-217 [PMID: 16732816 DOI: 10.1111/j.1440-1673.2006.01564.x]
- 157 **Pradhan S**, Shukla VK, Agrawal S, Dixit VK, Sharma OP. Sonographic and colour doppler morphology in carcinoma gallbladder. *Indian J Cancer* 2002; **39**: 143-148 [PMID: 12928573]
- 158 **Agarwal AK**, Kalayarsan R, Javed A, Gupta N, Nag HH. The role of staging laparoscopy in primary gall bladder cancer--an analysis of 409 patients: a prospective study to evaluate the role of staging laparoscopy in the management of gallbladder cancer. *Ann Surg* 2013; **258**: 318-323 [PMID: 23059504 DOI: 10.1097/SLA.0b013e318271497e]
- 159 **Agrawal S**, Sonawane RN, Behari A, Kumar A, Sikora SS, Saxena R, Kapoor VK. Laparoscopic staging in gallbladder cancer. *Dig Surg* 2005; **22**: 440-445 [PMID: 16479113 DOI: 10.1159/000091447]
- 160 **Srikanth G**, Kumar A, Khare R, Siddappa L, Gupta A, Sikora SS, Saxena R, Kapoor VK. Should laparoscopic cholecystectomy be performed in patients with thick-walled gallbladder? *J Hepatobiliary Pancreat Surg* 2004; **11**: 40-44 [PMID: 15754045 DOI: 10.1007/s00534-003-0866-3]
- 161 **Kapoor VK**, Singh R, Behari A, Sharma S, Kumar A, Prakash A, Singh RK, Saxena R. Anticipatory extended cholecystectomy: the 'Lucknow' approach for thick walled gall bladder with low suspicion of cancer. *Chin Clin Oncol* 2016; **5**: 8 [PMID: 26932432 DOI: 10.3978/j.issn.2304-3865.2016.02.07]
- 162 **Agarwal AK**, Kalayarsan R, Javed A, Sakhuja P. Role of routine 16b1 lymph node biopsy in the management of gallbladder cancer: an analysis. *HPB (Oxford)* 2014; **16**: 229-234 [PMID: 23869478 DOI: 10.1111/hpb.12127]
- 163 **Ghosh NK**, Rahul R, Singh A, Sharma S, Kumar A, Singh RK, Behari A, Kapoor VK, Saxena R. Retroperitoneal Lymph Node Metastasis in Gallbladder Cancer: As Bad as Distant Metastasis. *South Asian J Cancer* 2022; **11**: 195-200 [PMID: 36588607 DOI: 10.1055/s-0042-1742595]
- 164 **Aggarwal A**, Goel S, Sayed AI, Goel V, Talwar V, Singh S. Interaortocaval Lymph Node Metastasis in Gall Bladder Cancer: Is It Regional Node or Metastatic Disease? *J Gastrointest Cancer* 2023; **54**: 1252-1260 [PMID: 36729244 DOI: 10.1007/s12029-023-00914-7]
- 165 **Singh SK**, Talwar R, Kannan N, Tyagi AK, Jaiswal P, Kumar A. Aggressive Surgical Approach for Gallbladder Cancer: a Single-Center Experience from Northern India. *J Gastrointest Cancer* 2015; **46**: 399-407 [PMID: 26410686 DOI: 10.1007/s12029-015-9766-4]
- 166 **Waghlikar GD**, Behari A, Krishnani N, Kumar A, Sikora SS, Saxena R, Kapoor VK. Early gallbladder cancer. *J Am Coll Surg* 2002; **194**: 137-141 [PMID: 11848630 DOI: 10.1016/S1072-7515(01)01136-X]
- 167 **Pottakkat B**, Kapoor A, Prakash A, Singh RK, Behari A, Kumar A, Kapoor VK, Saxena R. Evaluation of a prospective surgical strategy of extended resection to achieve R0 status in gall bladder cancer. *J Gastrointest Cancer* 2013; **44**: 33-40 [PMID: 22987147 DOI: 10.1007/s12029-012-9432-z]
- 168 **Nag HH**, Nekarakanti PK, Sachan A, Nabi P, Tyagi S. Bi-segmentectomy versus wedge hepatic resection in extended cholecystectomy for T2 and T3 gallbladder cancer: A matched case-control study. *Ann Hepatobiliary Pancreat Surg* 2021; **25**: 485-491 [PMID: 34845120 DOI: 10.14701/ahbps.2021.25.4.485]
- 169 **Tewari M**, Kumar S, Shukla S, Shukla HS. Analysis of wedge resection of gallbladder bed and lymphadenectomy on adequate oncologic clearance for gallbladder cancer. *Indian J Cancer* 2016; **53**: 552-557 [PMID: 28485349 DOI: 10.4103/ijc.IJC\_88\_17]
- 170 **Behari A**, Sikora SS, Waghlikar GD, Kumar A, Saxena R, Kapoor VK. Longterm survival after extended resections in patients with gallbladder cancer. *J Am Coll Surg* 2003; **196**: 82-88 [PMID: 12517555 DOI: 10.1016/S1072-7515(02)01611-3]
- 171 **Jajal V**, Nekarakanti PK, K S, Nag H. Effects of Cystic Duct Margin Involvement on the Survival Rates of Patients With Gallbladder Cancer: A Propensity Score-Matched Case-Control Study. *Cureus* 2023; **15**: e50585 [PMID: 38226074 DOI: 10.7759/cureus.50585]
- 172 **Pandey D**, Garg PK, Jakhetiya A, Jain N, Rai S. Surgico-pathological Outcomes of 148 Radical Cholecystectomies Using Systematic Regional Lymphadenectomy Protocol: a Retrospective Study. *J Gastrointest Cancer* 2018; **49**: 221-224 [PMID: 29691709 DOI: 10.1007/s12029-018-0106-3]
- 173 **Goel M**, Pandrowala S, Patel P, Patkar S. Node positivity in T1b gallbladder cancer: A high volume centre experience. *Eur J Surg Oncol* 2022; **48**: 1585-1589 [PMID: 35341609 DOI: 10.1016/j.ejso.2022.03.013]
- 174 **Agarwal AK**, Mandal S, Singh S, Bhojwani R, Sakhuja P, Uppal R. Biliary obstruction in gall bladder cancer is not sine qua non of inoperability. *Ann Surg Oncol* 2007; **14**: 2831-2837 [PMID: 17632759 DOI: 10.1245/s10434-007-9456-y]
- 175 **K S**, Jajal VM, Nekarakanti PK, Choudhary D, Nag HH. Gallbladder Cancer With Jaundice: Surgery Versus No Surgery. *Cureus* 2022; **14**: e30594 [PMID: 36420237 DOI: 10.7759/cureus.30594]
- 176 **Singh S**, Goel S, Aggarwal A, Iqbal A, Hazarika D, Talwar V. Combination of portal vein embolization and neoadjuvant chemotherapy for locally advanced gallbladder cancer requiring extended hepatectomy - A novel approach. *Indian J Gastroenterol* 2021; **40**: 580-589 [PMID: 34966973 DOI: 10.1007/s12664-021-01182-8]
- 177 **Agarwal AK**, Mandal S, Singh S, Sakhuja P, Puri S. Gallbladder cancer with duodenal infiltration: is it still resectable? *J Gastrointest Surg* 2007; **11**: 1722-1727 [PMID: 17906907 DOI: 10.1007/s11605-007-0320-y]
- 178 **Sharma A**, Nagar A, Varshney P, Tomar M, Sarin S, Choubey RP, Kapoor VK. Pancreas-preserving limited duodenal resection: Minimizing morbidity without compromising oncological adequacy. *Ann Hepatobiliary Pancreat Surg* 2022; **26**: 149-158 [PMID: 35168204 DOI: 10.14701/ahbps.21-124]
- 179 **Patkar S**, Patel S, Kazi M, Goel M. Radical surgery for stage IV gallbladder cancers: Treatment strategies in patients with limited metastatic burden. *Ann Hepatobiliary Pancreat Surg* 2023; **27**: 180-188 [PMID: 36882899 DOI: 10.14701/ahbps.22-111]
- 180 **Agarwal AK**, Javed A, Kalayarsan R, Sakhuja P. Minimally invasive versus the conventional open surgical approach of a radical cholecystectomy for gallbladder cancer: a retrospective comparative study. *HPB (Oxford)* 2015; **17**: 536-541 [PMID: 25727091 DOI: 10.1111/hpb.12406]
- 181 **Nag HH**, Sachan A, Nekarakanti PK. Laparoscopic versus open extended cholecystectomy with bi-segmentectomy (s4b and s5) in patients with gallbladder cancer. *J Minim Access Surg* 2021; **17**: 21-27 [PMID: 31603079 DOI: 10.4103/jmas.JMAS\_98\_19]
- 182 **Palanisamy S**, Patel N, Sabnis S, Palanisamy N, Vijay A, Palanivelu P, Parthasarathi R, Chinnusamy P. Laparoscopic radical cholecystectomy for suspected early gall bladder carcinoma: thinking beyond convention. *Surg Endosc* 2016; **30**: 2442-2448 [PMID: 26416372 DOI: 10.1007/s00464-015-4495-0]
- 183 **Goel M**, Khobragade K, Patkar S, Kanetkar A, Kurunkar S. Robotic surgery for gallbladder cancer: Operative technique and early outcomes. *J Surg Oncol* 2019; **119**: 958-963 [PMID: 30802316 DOI: 10.1002/jso.25422]
- 184 **Shukla PJ**, Barreto G, Kakade A, Shrikhande SV. Revision surgery for incidental gallbladder cancer: factors influencing operability and

- further evidence for T1b tumours. *HPB (Oxford)* 2008; **10**: 43-47 [PMID: 18695758 DOI: 10.1080/13651820701867794]
- 185 **Patkar S**, Kunte A, Chaudhari V, Goel M. Outcomes of incidental versus non-incidental T2 gallbladder cancer: A single-institute experience of 425 cases. *J Surg Oncol* 2024; **129**: 754-764 [PMID: 38088226 DOI: 10.1002/jso.27562]
- 186 **Goel M**, Gupta AM, Patkar S, Parray AM, Shetty N, Ramaswamy A, Patil P, Chopra S, Ostwal V, Kulkarni S, Engineer R, Mehta S. Towards standardization of management of gallbladder carcinoma with obstructive jaundice: Analysis of 113 cases over 10 years at a single institution. *J Surg Oncol* 2021; **124**: 572-580 [PMID: 34106475 DOI: 10.1002/jso.26564]
- 187 **Patkar S**, Patil V, Acharya MR, Kurunkar S, Goel M. Achieving margin negative resection-doing less is justified: oncological outcomes of wedge excision of liver in gallbladder cancer (GBC) surgery. *Chin Clin Oncol* 2019; **8**: 38 [PMID: 31431034 DOI: 10.21037/cco.2019.07.07]
- 188 **Nag HH**, Raj P, Sisodia K. The technique of laparoscopic hepatic bisegmentectomy with regional lymphadenectomy for gallbladder cancer. *J Minim Access Surg* 2018; **14**: 124-129 [PMID: 28928327 DOI: 10.4103/jmas.JMAS\_181\_16]
- 189 **Kaman L**, Behera A, Singh G, Nedounsejane M. Radical surgery for incidental cancer gallbladder after laparoscopic cholecystectomy. *Trop Gastroenterol* 2009; **30**: 233-236 [PMID: 20426289]
- 190 **Patkar S**, Patel S, Gupta A, Ostwal V, Ramaswamy A, Shetty N, Goel M. Lessons learnt from 1300 consecutive gallbladder cancer surgeries: Evolving role of peri-operative chemotherapy in the treatment paradigm. *Eur J Surg Oncol* 2023; **49**: 107035 [PMID: 37604098 DOI: 10.1016/j.ejso.2023.107035]
- 191 **Ostwal V**, Swami R, Patkar S, Majumdar S, Goel M, Mehta S, Engineer R, Mandavkar S, Kumar S, Ramaswamy A. Gemcitabine-cisplatin (GC) as adjuvant chemotherapy in resected stage II and stage III gallbladder cancers (GBC): a potential way forward. *Med Oncol* 2018; **35**: 57 [PMID: 29564657 DOI: 10.1007/s12032-018-1115-6]
- 192 **Kattepur AK**, Patkar S, Goel M, Ramaswamy A, Ostwal V. Role of Adjuvant Chemotherapy in Resected T2N0 Gall Bladder Cancer. *J Gastrointest Surg* 2019; **23**: 2232-2238 [PMID: 30706378 DOI: 10.1007/s11605-019-04104-4]
- 193 **Mahantshetty UM**, Palled SR, Engineer R, Homkar G, Shrivastava SK, Shukla PJ. Adjuvant radiation therapy in gall bladder cancers: 10 years experience at Tata Memorial Hospital. *J Cancer Res Ther* 2006; **2**: 52-56 [PMID: 17998675 DOI: 10.4103/0973-1482.25850]
- 194 **Choudhary S**, Asthana AK. Impact of Adjuvant Therapy on Survival in Curatively Resected Gallbladder Carcinoma. *J Clin Diagn Res* 2015; **9**: XC01-XC04 [PMID: 26500994 DOI: 10.7860/JCDR/2015/15113.6436]
- 195 **Agrawal S**, Gupta PK, Rastogi N, Lawrence A, Kumari N, Das KJ, Saxena R. Outcomes of adjuvant chemoradiation and predictors of survival after extended cholecystectomy in gall bladder carcinoma: a single institution experience from an endemic region. *J Gastrointest Cancer* 2015; **46**: 48-53 [PMID: 25511013 DOI: 10.1007/s12029-014-9676-x]
- 196 **Ramaswamy A**, Ostwal VS, Engineer R, Parulekar M, Mandavkar S, Aier N, Bhargava PG, Srinivas S, Patkar S, Krishnatry R, Gudi S, Kapoor A, Pandey D, Patel S, Shinghal A, Goel A, Dora TK, Chaudhary D, Ankathi SK, Goel M. A multicenter, open-label, randomized phase II study evaluating adjuvant gemcitabine plus cisplatin (GC) and capecitabine with concurrent capecitabine radiotherapy (CAPE-RT) in patients with operated gallbladder adenocarcinoma (GBC): The GECCOR-GB trial. *JCO* 2023; **41**: 4017-4017 [DOI: 10.1200/JCO.2023.41.16\_suppl.4017]
- 197 **Doval DC**, Sekhon JS, Gupta SK, Fuloria J, Shukla VK, Gupta S, Awasthy BS. A phase II study of gemcitabine and cisplatin in chemotherapy-naive, unresectable gall bladder cancer. *Br J Cancer* 2004; **90**: 1516-1520 [PMID: 15083178 DOI: 10.1038/sj.bjc.6601736]
- 198 **Julka PK**, Puri T, Rath GK. A phase II study of gemcitabine and carboplatin combination chemotherapy in gallbladder carcinoma. *Hepatobiliary Pancreat Dis Int* 2006; **5**: 110-114 [PMID: 16481295]
- 199 **Ramaswamy A**, Ostwal V, Pinninti R, Kannan S, Bhargava P, Nashikkar C, Mirani J, Banavali S. Gemcitabine-cisplatin versus gemcitabine-oxaliplatin doublet chemotherapy in advanced gallbladder cancers: a match pair analysis. *J Hepatobiliary Pancreat Sci* 2017; **24**: 262-267 [PMID: 28196310 DOI: 10.1002/jhbp.439]
- 200 **Chatni SS**, Sainani RS, Mehta SA, Mohandas KM. Infusion chemotherapy with cisplatin and fluorouracil in the treatment of locally-advanced and metastatic gallbladder cancer. *J Cancer Res Ther* 2008; **4**: 151-155 [PMID: 19052386 DOI: 10.4103/0973-1482.43341]
- 201 **Sharma A**, Dwary AD, Mohanti BK, Deo SV, Pal S, Sreenivas V, Raina V, Shukla NK, Thulkar S, Garg P, Chaudhary SP. Best supportive care compared with chemotherapy for unresectable gall bladder cancer: a randomized controlled study. *J Clin Oncol* 2010; **28**: 4581-4586 [PMID: 20855823 DOI: 10.1200/JCO.2010.29.3605]
- 202 **Ali D**, Alam N, Yasmin F, Ali S, Anwer T, Alam S, Ahmad S. Comparative Study Between Two Treatment Regimens of Cisplatin-5-Fluorouracil and Gemcitabine-Cisplatin in Gallbladder Cancer Patients. *Iran J Pharm Res* 2017; **16**: 798-804 [PMID: 28979334]
- 203 **Singh SK**, Talwar R, Kannan N, Tyagi AK, Jaiswal P, Kumar A. Chemotherapy Compared with Best Supportive Care for Metastatic/Unresectable Gallbladder Cancer: a Non-randomized Prospective Cohort Study. *Indian J Surg Oncol* 2016; **7**: 25-31 [PMID: 27065678 DOI: 10.1007/s13193-015-0443-7]
- 204 **Ramaswamy A**, Ostwal V, Sharma A, Bhargava P, Srinivas S, Goel M, Patkar S, Mandavkar S, Jadhav P, Parulekar M, Choudhari A, Gupta S. Efficacy of Capecitabine Plus Irinotecan vs Irinotecan Monotherapy as Second-line Treatment in Patients With Advanced Gallbladder Cancer: A Multicenter Phase 2 Randomized Clinical Trial (GB-SELECT). *JAMA Oncol* 2021; **7**: 436-439 [PMID: 33270098 DOI: 10.1001/jamaoncol.2020.6166]
- 205 **Alam MN**, Agrawal S, Rastogi N, Saxena R. Chemotherapy or chemotherapy followed by consolidation chemoradiation in postoperative (simple cholecystectomy) gall bladder cancer with residual disease, unsuitable for revision surgery? Risk stratification and outcomes. *J Cancer Res Ther* 2023; **19**: 259-264 [PMID: 37313904 DOI: 10.4103/jert.jert\_1161\_21]
- 206 **Alam MN**, Agrawal S, Rastogi N, Maria Das KJ. Consolidation chemoradiation (cCIRT) improves survival in responders to first-line chemotherapy (CT) in locally advanced gallbladder cancer (LA-GBC): A new standard of care? *Indian J Cancer* 2022; **59**: 577-583 [PMID: 36861528 DOI: 10.4103/ije.IJC\_1145\_20]
- 207 **Das CK**, Patel A, Raj A, Gupta VG, Mehta P, Bhethanabhotla S, Reddy R, Yadav A. Anti-Her2neu directed therapy in advanced gall bladder cancer: A prospective, multicenter experience from India. *JCO* 2020; **38**: e16682-e16682 [DOI: 10.1200/JCO.2020.38.15\_suppl.e16682]
- 208 **Dodagoudar C**, Doval DC, Mahanta A, Goel V, Upadhyay A, Goyal P, Talwar V, Singh S, John MC, Tiwari S, Patnaik N. FOLFOX-4 as second-line therapy after failure of gemcitabine and platinum combination in advanced gall bladder cancer patients. *Jpn J Clin Oncol* 2016; **46**: 57-62 [PMID: 26603355 DOI: 10.1093/jco/hyv148]
- 209 **Ramaswamy A**, Ostwal V, Pande N, Sahu A, Jandyal S, Ramadwar M, Shetty N, Patkar S, Goel M, Gupta S. Second-Line Palliative Chemotherapy in Advanced Gall Bladder Cancer, CAP-IRI: Safe and Effective Option. *J Gastrointest Cancer* 2016; **47**: 305-312 [PMID: 27211249 DOI: 10.1007/s12029-016-9828-2]
- 210 **Gangopadhyay A**, Nath P, Biswas J. Reduced Dose Intensity of Chemotherapy may not Lead to Inferior Palliation in Locally Advanced Carcinoma of the Gall Bladder: An Experience from a Regional Cancer Centre in Eastern India. *J Gastrointest Cancer* 2015; **46**: 297-300

- [PMID: 26116258 DOI: 10.1007/s12029-015-9742-z]
- 211 **Sirohi B**, Rastogi S, Singh A, Sheth V, Dawood S, Talole S, Ramadwar M, Kulkarni S, Shrikhande SV. Use of gemcitabine-platinum in Indian patients with advanced gall bladder cancer. *Future Oncol* 2015; **11**: 1191-1200 [PMID: 25832876 DOI: 10.2217/fon.14.295]
- 212 **Bhamare S**, Prabhakar P, Dharmadhikari A, Dedeepiya VD, Terunuma H, Senthilkumar R, Srinivasan T, Reena HC, Preethy S, Abraham SJ. Autologous immune enhancement therapy in a case of gall bladder cancer stage IV after surgical resection and chemotherapy yielding a stable non-progressive disease. *J Cancer Res Ther* 2014; **10**: 752-754 [PMID: 25313776 DOI: 10.4103/0973-1482.136048]
- 213 **Mallick S**, Benson R, Julka PK, Rath GK. Adjuvant chemoradiotherapy for squamous cell carcinoma of gallbladder. *J Gastrointest Cancer* 2014; **45** Suppl 1: 237-240 [PMID: 25119385 DOI: 10.1007/s12029-014-9641-8]
- 214 **Engineer R**, Wadasadawala T, Mehta S, Mahantshetty U, Purandare N, Rangarajan V, Kishore Shrivastava S. Chemoradiation for unresectable gall bladder cancer: time to review historic nihilism? *J Gastrointest Cancer* 2011; **42**: 222-227 [PMID: 20803101 DOI: 10.1007/s12029-010-9179-3]
- 215 **Chaudhari VA**, Ostwal V, Patkar S, Sahu A, Toshniwal A, Ramaswamy A, Shetty NS, Shrikhande SV, Goel M. Outcome of neoadjuvant chemotherapy in "locally advanced/borderline resectable" gallbladder cancer: the need to define indications. *HPB (Oxford)* 2018; **20**: 841-847 [PMID: 29706425 DOI: 10.1016/j.hpb.2018.03.008]
- 216 **Agrawal S**, Mohan L, Mourya C, Neyaz Z, Saxena R. Radiological Downstaging with Neoadjuvant Therapy in Unresectable Gall Bladder Cancer Cases. *Asian Pac J Cancer Prev* 2016; **17**: 2137-2140 [PMID: 27221908 DOI: 10.7314/APJCP.2016.17.4.2137]
- 217 **Engineer R**, Patkar S, Lewis SC, Sharma AD, Shetty N, Ostwal V, Ramaswamy A, Chopra S, Agrawal A, Patil P, Mehta S, Goel M. A phase III randomised clinical trial of perioperative therapy (neoadjuvant chemotherapy versus chemoradiotherapy) in locally advanced gallbladder cancers (POLCAGB): study protocol. *BMJ Open* 2019; **9**: e028147 [PMID: 31253621 DOI: 10.1136/bmjopen-2018-028147]
- 218 **Patkar S**, Ostwal V, Ramaswamy A, Engineer R, Chopra S, Shetty N, Dusane R, Shrikhande SV, Goel M. Emerging role of multimodality treatment in gall bladder cancer: Outcomes following 510 consecutive resections in a tertiary referral center. *J Surg Oncol* 2018; **117**: 372-379 [PMID: 28940502 DOI: 10.1002/jso.24837]
- 219 **Engineer R**, Goel M, Chopra S, Patil P, Purandare N, Rangarajan V, Ph R, Bal M, Shrikhande S, Shrivastava SK, Mehta S. Neoadjuvant Chemoradiation Followed by Surgery for Locally Advanced Gallbladder Cancers: A New Paradigm. *Ann Surg Oncol* 2016; **23**: 3009-3015 [PMID: 27075323 DOI: 10.1245/s10434-016-5197-0]
- 220 **Sirohi B**, Mitra A, Jagannath P, Singh A, Ramadwar M, Kulkarni S, Goel M, Shrikhande SV. Neoadjuvant chemotherapy in patients with locally advanced gallbladder cancer. *Future Oncol* 2015; **11**: 1501-1509 [PMID: 25963427 DOI: 10.2217/fon.14.308]
- 221 **Selvakumar VP**, Zaidi S, Pande P, Goel A, Kumar K. Resection after neoadjuvant chemotherapy in advanced carcinoma of the gallbladder: a retrospective study. *Indian J Surg Oncol* 2015; **6**: 16-19 [PMID: 25937758 DOI: 10.1007/s13193-015-0377-0]





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