Investigating the Main Complaints, Clinical and Laboratory Findings in Patients with Gallbladder Cancer Referred to Imam Khomeini Hospital during the Years 1990 to 2000

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Abstract:

Introduction & Objective: Gallbladder cancer is one of the gastrointestinal malignancies with a poor prognosis in Iran and other parts of the world. Although various studies have been conducted in Iran on its prevalence and risk factors, a comprehensive study that examines clinical and paraclinical findings in a large sample size has not been conducted. Therefore, this study was conducted to investigate the clinical and laboratory findings of patients with gallbladder cancer in a 10-year period.

Materials & Methods: This retrospective study was conducted on 1856 patients who were referred to Imam Khomeini Hospital in Tehran and underwent open cholecystectomy from 1990 to 2000. First, according to the pathology report, the patients who were given a definitive diagnosis of gallbladder cancer were included in the study. Then clinical, laboratory, and imaging data were recorded using medical files records.

Results: In this study, 32 patients with a definitive diagnosis of gallbladder cancer were enrolled. Most patients were female (18 patients, 56.2%) and the most common age range was 50 to 59 years (57.3±4.1 years). The right upper quadrant pain and loss of appetite were reported as the most (27 patients, 84.4%) and the least (2 patients, 6.2%) main complaints, respectively. Increased alkaline phosphatase and dilation of bile ducts were seen as the most common paraclinical findings in the studied patients.

Conclusions: Gallbladder cancer is one of the invasive malignancies of the gastrointestinal tract in the Iranian population, which is more common among women and in the sixth decade of life. Abdominal pain and increased liver enzymes and alkaline phosphatase were seen as the most common clinical and paraclinical findings along with dilation of the bile ducts in the ultrasound examination among the patients.

Key Words: Gallbladder Cancer, Cholecystectomy, Alkaline Phosphatase, Jaundice, Abdominal Pain, Tumor Marker

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Background and Objective

Gallbladder cancer represents a malignant neoplasm that arises from the epithelial lining of the gallbladder and is recognized as one of the most lethal malignancies within the gastrointestinal tract, frequently associated with a poor prognosis.[1,2] The incidence of gallbladder cancer exhibits significant geographic variability, influenced by both genetic and environmental factors,[3] with notably higher prevalence rates in specific regions. High-incidence areas include South America (particularly Chile and Bolivia), East Asia (notably China and Taiwan), and the Indian subcontinent (especially India and Pakistan).[4-6] These regions demonstrate a marked prevalence of risk factors such as gallstones, chronic gallbladder inflammation, and genetic predispositions.[7,8] Despite being classified as a rare gastrointestinal malignancy overall, gallbladder cancer is acknowledged as one of the most aggressive cancers affecting this system,[9] with particularly elevated incidence rates reported in the northern and northwestern regions of certain countries.[10] Contributing factors to this heightened incidence include a significant prevalence of gallstones, chronic infection with Helicobacter pylori, and specific dietary habits.[11] Furthermore, the observed geographic and ethnic diversity in incidence suggests that genetic factors play a substantial role in the pathogenesis of gallbladder cancer.[12] For example, specific gene polymorphisms associated with lipid metabolism, inflammation, and DNA repair have been correlated with an increased risk of developing this malignancy.[13] Environmental determinants, including exposure to particular chemicals, smoking, obesity, and a high-fat diet, may also contribute to the etiology of the disease.[14] Gallbladder cancer is often diagnosed at advanced stages due to its asymptomatic nature during the initial phases, and the limited availability of effective treatment options exacerbates the poor prognosis associated with this condition.[15] Therefore, early diagnosis and a comprehensive understanding of the clinical features of gallbladder cancer are imperative for improving patient outcomes and survival rates. This study aims to investigate the clinical and laboratory characteristics of patients diagnosed with gallbladder cancer who were referred to Imam Khomeini Hospital in Tehran over a decade-long period.

Materials and Methods

This retrospective study included all patients who underwent open cholecystectomy at Imam Khomeini Hospital in Tehran from 1989 to 1999.

The inclusion criteria for the study encompassed patients of all ages and genders who received a diagnosis of gallbladder cancer within this ten-year timeframe. Conversely, patients with incomplete medical records, those diagnosed with other malignancies, and individuals who underwent gallbladder surgery for non-cancerous conditions were excluded from the analysis.

To gather clinical and laboratory data, all patients who underwent open cholecystectomy during the specified period were initially selected. Subsequently, those with a definitive diagnosis of gallbladder cancer, as confirmed by pathology reports, were included in the study. Data collection involved a comprehensive review of medical records, laboratory results, imaging studies, and pathology reports, focusing on age, gender, chief complaints, clinical symptoms and signs, ultrasound findings, the presence or absence of gallstones, and the histological type of gallbladder cancer. For improved data classification, laboratory findings were categorized as binary variables indicating either elevated or normal levels, as delineated in Table 1.

Table 1 - Classification of symptoms and laboratory findings

Variable		Normal values	Abnormal values
Anemia (hemoglobin level)	male	≥ 13.5	< 13.5
	female	≥ 11.5	< 11.5
Total bilirubin (mg/dl)		≤ 1	> 1
Direct bilirubin (mg/dl)		≤ 0.2	> 0.2
ALT (U/lit)		≤ 20	> 20
AST (U/lit)		≤ 30	> 30
Alkp (U/lit)	male	≤ 128	> 128
	femal	≤ 98	> 98

Throughout the study, ethical guidelines were strictly adhered to in order to protect patient privacy and confidentiality. The research received review and approval from the Ethics Committee of Tehran University of Medical Sciences. Informed consent was not deemed necessary, as the study utilized retrospective data that had been anonymized to ensure patient confidentiality. Access to patient records was limited to authorized research personnel, and data handling practices were in compliance with relevant data protection regulations. Finally, the findings were presented in terms of frequency and percentage to provide a clear statistical overview.

Findings

Characteristics of Participants

This study evaluated a cohort of 1,856 patients who underwent cholecystectomy between 1989 and 1999, resulting in the identification of gallbladder cancer in 32 individuals, which corresponds to a prevalence rate of 1.72%. All diagnosed cases were classified as adenocarcinoma. Among the 32 patients, 18 (56.2%) were female and 14 (43.8%) were male.

The mean age of the cohort was 57.3 years (± 4.1), with ages ranging from 31 to 76 years.

Table 2 presents the distribution of participants by age range and gender. Notably, there were no patients aged 40-49 years within either gender group. The predominant age range for male patients was 50-59 years, encompassing 6 individuals (42.9%), while for female patients, this age range included 7 individuals (38.9%).

Table 2- Frequency of patients with gallbladder cancer by gender in different age ranges

Age range (years)	Gender			
	male		female	
	Frequency	Percentage	Frequency	Percentage
30-39	1	7.1	1	5.5
40-49	0	0	0	0
50-59	6	42.9	7	38.9
60-69	5	35.7	6	33.3
70-79	2	14.3	4	22.3

Chief Complaints and Clinical Symptoms

The most frequently reported chief complaint was generalized abdominal pain, experienced by 20 patients (62.5%). The most commonly observed clinical finding was right upper quadrant abdominal pain, noted in 27 patients (84.4%). Other prevalent complaints included jaundice and weakness or fatigue, which were reported by 20 patients (31.25%) and 10 patients (31.25%), respectively. Anorexia constituted the least common chief complaint, occurring in only 2 patients (6.2%). Additional clinical findings are summarized in Table 3.

Table 3 - Frequency of chief complaints and clinical symptoms in patients with gallbladder cancer

Clinical signs	Frequency	Percentage
Pain in the right upper quadrant of the abdomen	27	84.4
Jaundice	24	75
Generalized abdominal pain	20	62.5
Weight loss	10	31.2
Palpable mass	8	25
Nausea and vomiting	6	18.7
Pruritus	3	9.3
Anorexia	2	6.2

Imaging Findings

Among the 32 patients diagnosed with gallbladder cancer, ultrasound examinations revealed the presence of gallstones in only 10 patients (31.25%). The most common imaging finding was the dilation of biliary ducts, observed in 18 patients (56.25%). Additionally, gallbladder wall thickening was identified in 4 patients (12.5%).

Laboratory Findings

As delineated in the methodology section, laboratory data were recorded as binary variables, indicating either elevated or normal levels. According to Table 4, a significant majority of patients (93.7%) exhibited elevated levels of alkaline phosphatase (ALP) and alanine transaminase (ALT). Anemia was documented in 15 patients (46.8%).

Table 4- Frequency of laboratory findings in patients with gallbladder cancer

Paraclinical findings	Frequency	Percentage
Increased Alkp	30	93.7
Increased ALT	30	93.7
Increased AST	25	78.1
Increased total bilirubin	23	71.9
Increased direct bilirubin	23	71.9
Anemia	15	46.8

Discussion and Conclusion

This study aimed to evaluate the clinical and laboratory characteristics of patients diagnosed with gallbladder cancer, including 32 individuals who underwent cholecystectomy over a decade-long period. The findings reveal a higher incidence of gallbladder cancer among females, predominantly affecting individuals in the 50 to 59-year age group.

Similarly, a study conducted by Ahadi et al.[9] reported a majority of female patients, thus reinforcing the consistency of these findings with prior research.[16,17] The average age of patients in this study was 57 years, with the most common age range being 50 to 59 years.[18-20] This finding contrasts with other studies,[18,19] such as that conducted by Ahadi et al.[9], where patients were primarily in the 31-40 age range.

Additionally, research by Teyvardi et al.[20] indicated that patients were typically diagnosed at older ages (41 to 50 years), which does not align with the present findings, potentially suggesting racial or demographic differences. While this study did not specifically examine the type of gallstones, it is noteworthy that the presence of gallstones

was documented as the second most common ultrasound finding among patients.

In contrast, previous studies involving Iranian patients, including those by Samanani et al.[21] and Ahadi et al.[9], reported differing findings in relation to gallstones, thereby highlighting the necessity for further research in this area.

According to the current body of evidence, gallstones have been recognized as a potential contributing factor in approximately 85% of cancer cases, despite the incidence of gallbladder cancer among patients with gallstones being notably less than 0.5%.[9] In the present study, increased gallbladder wall thickness was observed in only 12.5% of the patients, rendering it the least common finding. This observation is inconsistent with previous studies[9,16-21]; for instance, Ahadi et al.[9] reported that increased gallbladder wall thickness (exceeding 3 mm) was noted in approximately 82% of patients, whereas Avasti et al.[22] indicated an incidence of about 27%, a finding that is more congruent with the results of the current investigation. Such discrepancies may be attributed to variations in patient symptoms and the timing of presentations. Specifically, the study conducted by Ahadi et al.[9] primarily involved patients with acute cholecystitis resulting from obstruction due to gallstones.

In our investigation, although right upper quadrant pain was the most prevalent clinical symptom, observed in 87% of patients—consistent with findings from other studies[17-21]—it appears that the causative factors for pain following acute cholecystitis attributed to gallstones, as reported in the literature[9,18], do not align with the results of our study.

Furthermore, laboratory assessments revealed elevated alkaline phosphatase levels among the majority of patients, consistent with earlier research.[16-22]

While the current study represents one of the few long-term (10-year) investigations conducted in Iran, it is not without its limitations. A primary limitation of this study is its retrospective design, which may account for discrepancies in findings when compared to more recent studies. Additionally, the lack of examination regarding the specific pathology of gallbladder cancer and its correlation with other clinical and paraclinical findings constitutes a significant limitation. Moreover, the study exclusively focused on individuals with confirmed pathology, thus resulting in the absence of data on supplementary tests—such as tumor marker assessments or advanced imaging—conducted in patients suspected of having gallbladder cancer.

The findings of the current study corroborate previous reports indicating that age over 50 years and female gender are prevalent among patients diagnosed with gallbladder cancer. Additionally, abdominal pain, elevated liver enzymes, alkaline phosphatase levels, and bile duct dilation were identified as the most common clinical and paraclinical findings. Nonetheless, further research involving larger sample sizes and a comprehensive examination of histopathological findings is warranted to enhance our understanding of this condition.

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