Annals of Medicine and Medical Sciences (AMMS)
Volume 05, 2026, *Page No.: 37 to 42*
Available at: *http://ammspub.com*

Original Article

OPEN ACCESS

Xanthogranulomatous Cholecystitis in a GBC Endemic Zone: Diagnostic Uncertainty Drives Unnecessary Extended Resection and Major Surgical Morbidity

Dr. Pushpanjali Behera [1], Dr. Anup Kumar Pramanik [2], Dr. Bagmi Mishra [3], Dr. Sashibhusan Dash [4]

[1]Assistant Professor, Department of Pathology, Institute of Medical Sciences and SUM Hospital, Kalinga Nagar, Bhubaneswar, Odisha, India.
[2]Associate Professor, Department of Radiodiagnosis, Institute of Medical Sciences & SUM Hospital, Kalinga Nagar, Bhubaneswar, Odisha, India.
[3]Assistant Professor, Department of Pathology, Institute of Medical Sciences and SUM Hospital, Kalinga Nagar, Bhubaneswar, Odisha, India.
[4]Scientist C, Multidisciplinary Research Unit, Pandit Raghunath Murmu Medical College and Hospital, Baripada, Odisha, India.

*Corresponding Author: Dr. Sashibhusan Dash; *sashibiotech@gmail.com*

Abstract

Background: Xanthogranulomatous Cholecystitis (XGC) is a benign inflammatory condition whose features often closely mimic Gallbladder Carcinoma (GBC). In GBC-endemic regions like Eastern India, this diagnostic uncertainty is intensified, frequently leading to unnecessary radical surgical intervention. This study aimed to characterize the clinical presentation, diagnostic limitations, and surgical burden of XGC in a high-risk cohort. ***Methods:*** This was a retrospective, single-center study of 48 patients with histopathologically confirmed pure XGC over a two-year period (Jan 2022–Dec 2023). Postoperative outcomes were rigorously assessed using the Clavien-Dindo classification. ***Results:*** The cohort showed a marked female predominance (62.5%) and mean age (53.8 years) consistent with local GBC demographics. Radiological non-specificity was profound: 91.7% of benign XGC cases exhibited mucosal gap/disruption, a feature conventionally associated with malignancy. This severe diagnostic uncertainty resulted in 37.5% of patients undergoing unnecessary extended resections, which translated to a high 20.8% major postoperative complication rate (Clavien-Dindo ≥IIIa). ***Conclusion:*** The high clinical and surgical burden of XGC demands an urgent institutional shift toward a definitive preoperative diagnosis, necessitating immediate review of imaging and frozen section standards. The essential next step is a prospective, multi-center study to develop and validate a Machine Learning (ML)-based predictive nomogram to ensure the diagnostic certainty required for safe, conservative XGC management.

Keywords: ***Xanthogranulomatous cholecystitis, gallbladder neoplasms, diagnostic errors, morbidity, cholecystectomy.***

Introduction

Xanthogranulomatous Cholecystitis (XGC) is a rare, benign, inflammatory condition of the gallbladder, first described in 1976 [1,2]. Pathologically, it is defined by a destructive inflammatory process involving bile extravasation, subsequent foreign body reaction, and the infiltration of lipid-laden macrophages [2-5]. The advanced stage of this inflammation frequently results in dense adhesions to adjacent structures, which makes surgical management challenging [2]. Although XGC incidence globally varies widely (0.7% to 13.2% of cholecystectomy specimens) and typically affects individuals in their 60s and 70s with no established gender bias, its profound clinical significance lies in its mimicry of Gallbladder Carcinoma (GBC) [1-3]. Non-specific symptoms and overlapping radiological features, particularly gallbladder wall thickening, create a critical diagnostic uncertainty that often leads to misinterpretation and potentially unnecessary extended surgical resections [1,3]. Despite GBC representing a significant portion of the global cancer burden in regions like Eastern India, a critical knowledge gap exists concerning the clinical and pathological presentation of XGC within such a high-prevalence, endemic setting [6]. A local study is therefore warranted to provide a nuanced understanding of how regional epidemiological factors–such as local GBC demographics–intensify the clinical dilemma. The primary aim of this study is to provide a comprehensive, single-center description of the histopathological and clinical characteristics of all patients definitively diagnosed with XGC who underwent cholecystectomy at a tertiary care center in Odisha over a two-year period.

Received: November 12, 2025; **Revised:** December 24, 2025; **Accepted:** January 04, 2026

Materials and Methods

Study Design and Setting

This was a descriptive observational study with a retrospective design, suitable for examining a rare condition like XGC, where a prospective or experimental study would not have been feasible. The research was conducted in a hospital-based setting at a single tertiary care teaching hospital located in Odisha, India, specifically utilizing records from the Departments of General Surgery and Pathology. Patient data were reviewed over a two-year period, spanning from January 2022 to December 2023.

Study Population and Sampling

The study population consisted of all patients who underwent a cholecystectomy at the study center during the specified period and received a definitive final diagnosis of XGC following histopathological examination of the resected gallbladder specimen. A consecutive, non-randomized sampling procedure was employed, wherein all cases meeting the inclusion criteria were identified from the hospital's electronic medical records and pathology database and included in the final cohort.

Inclusion Criteria

- All patients, irrespective of age or gender, who underwent cholecystectomy at the study center during the two-year study period.
- Patients with a definitive histopathological diagnosis of XGC.
- Availability of complete clinical, radiological, and surgical records for review.

Exclusion Criteria

- Patients with an incomplete or missing histopathological report.
- Patients with incomplete or unavailable medical records.
- Patients with a co-existing confirmed diagnosis of gallbladder carcinoma on the final histopathological report.

Data Collection and Measures

Data were extracted directly from the hospital's electronic medical records and the Department of Pathology's database. The following variables were collected for each included patient:

1. *Patient Demographics:* Age and gender.
2. *Preoperative Clinical Data:* Clinical symptoms and preoperative laboratory values, including Complete Blood Count (CBC) and Liver Function Tests (LFTs).
3. *Radiological Findings:* Preoperative findings from ultrasounds (US) and CT scans.
4. *Surgical Data:* Intraoperative findings, the use of frozen section analysis, the type of surgical management performed, and the final pathological diagnosis confirmation.
5. *Surgical Outcomes:* Intraoperative complications, length of hospital stay, and short-term postoperative complications.

To ensure data security and patient confidentiality, all collected data were anonymized (patient identifiers removed) and stored on a password-protected system.

Statistical Analysis

Descriptive statistics were used to summarize the characteristics of the patient cohort. Continuous variables were reported as mean ±standard deviation (SD) for normally distributed data, or as median with an interquartile range (IQR) for non-normally distributed data. Categorical variables were presented using frequencies and percentages.

All statistical analyses were performed using a standard statistical software package.

Ethical Considerations

Given the retrospective nature of the study involving only review of existing medical records, the need for individual patient consent was waived by the Institutional Ethics Committee (IEC). The study design adhered to the principles of the Declaration of Helsinki. Patient confidentiality was strictly maintained through the anonymization and password-protected storage of all collected data.

Results

A total of 48 patients with histopathologically confirmed XGC were included in this study. The mean age of the cohort was 53.79 ±13.16 years, with a female predominance (n=30, 62.5%) over males (n=18, 37.5%). Clinically, all patients presented with abdominal pain (n=48), followed by fever/chills (n=42, 87.5%), while 12 patients (25%) exhibited jaundice. Laboratory analysis showed a mean Total Leucocyte Count (TLC) of 11690 ±871.25 (cells/mm3), and median levels of Total Bilirubin and Alkaline Phosphatase were 1.2 mg/dL and 215 IU/L, respectively (**Table 1**).

Table 1: Demographic and Clinical Profile of Patients with Xanthogranulomatous Cholecystitis (N=48).

Characteristic	Category	Total n (%)
Demographics	Age (years), Mean ±SD	53.79 ± 13.16
	Male	18 (37.5)
	Female	30 (62.5)
Clinical Presentation	Duration of symptoms (days), Median	34
	Abdominal Pain (Right Upper Quadrant)	48(100)
	Jaundice	12 (25)
	Fever/Chills	42 (87.5)
	Palpable Mass on examination	4 (8.3)
Preoperative Labs	Total Leucocyte Count, Mean ±SD	11690±871.25
	Total Bilirubin (mg/dL), Median	1.2
	Alkaline Phosphatase (IU/L), Median	215

Preoperative radiological evaluation (US/CT) consistently revealed gallbladder wall thickening (n=44) and mucosal gap/disruption (n=44). Despite these non-specific findings, the preoperative clinical suspicion of GBC was high or moderate in 18 patients (37.5%) (**Table 2**).

Table 2: Preoperative Radiological Features and Clinical Suspicion of Malignancy

Radiological Feature (US/CT)	Findings n (%)
Gallbladder Wall Thickening (>4mm)	44 (91.7)
Diffuse Wall Thickening	26 (54.2)
Focal/Asymmetric Wall Thickening	18 (37.5)
Gallstones/Calculi Present	34 (70.8)
Mucosal Gap/Disruption (CT specific)	44 (91.7)
Hypodense Nodules/Striae in Wall (CT specific)	4 (8.3)
Lymphadenopathy Present (Regional)	4 (8.3)
Adhesions to Adjacent Organs evident on imaging	32 (66.7)
Preoperative Clinical Suspicion of GBC (High/Moderate Suspicion)	18 (37.5)
Preoperative Clinical Suspicion of GBC (Low Suspicion/Benign Cholecystitis)	30 (62.5)

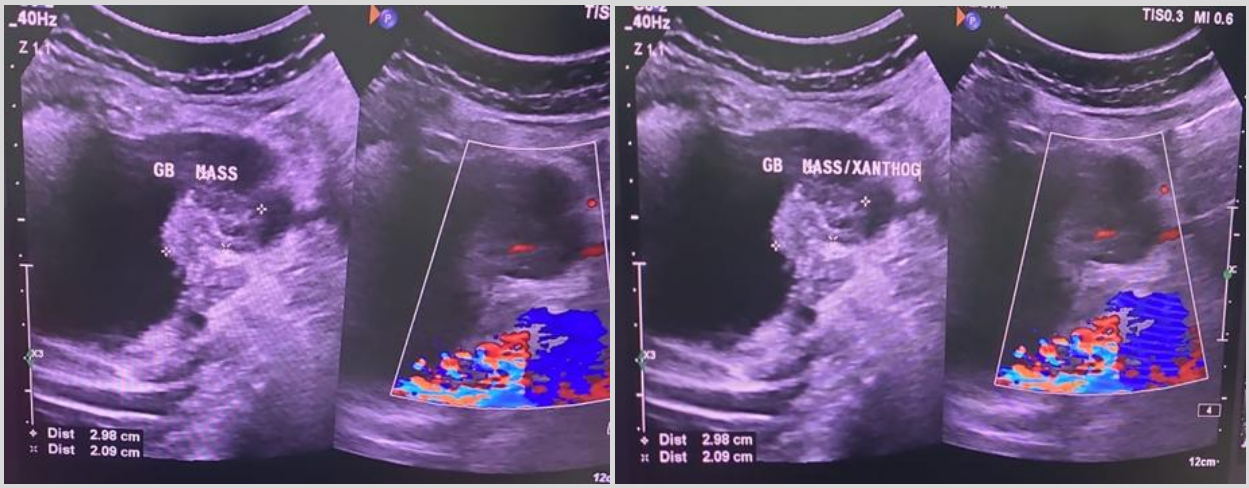

Figure 1 (a&b): Complex, Infiltrative Gallbladder Mass: Dual-panel ultrasound (B-mode and Color Doppler) demonstrates a solid, hypervascular gallbladder mass measuring 2.98cmx 2.09cm. The infiltrative morphology and internal vascularity are non-specific features, creating a critical diagnostic dilemma between aggressive inflammatory disease (Xanthogranulomatous Cholecystitis) and Gallbladder Carcinoma, requiring definitive histopathological confirmation.

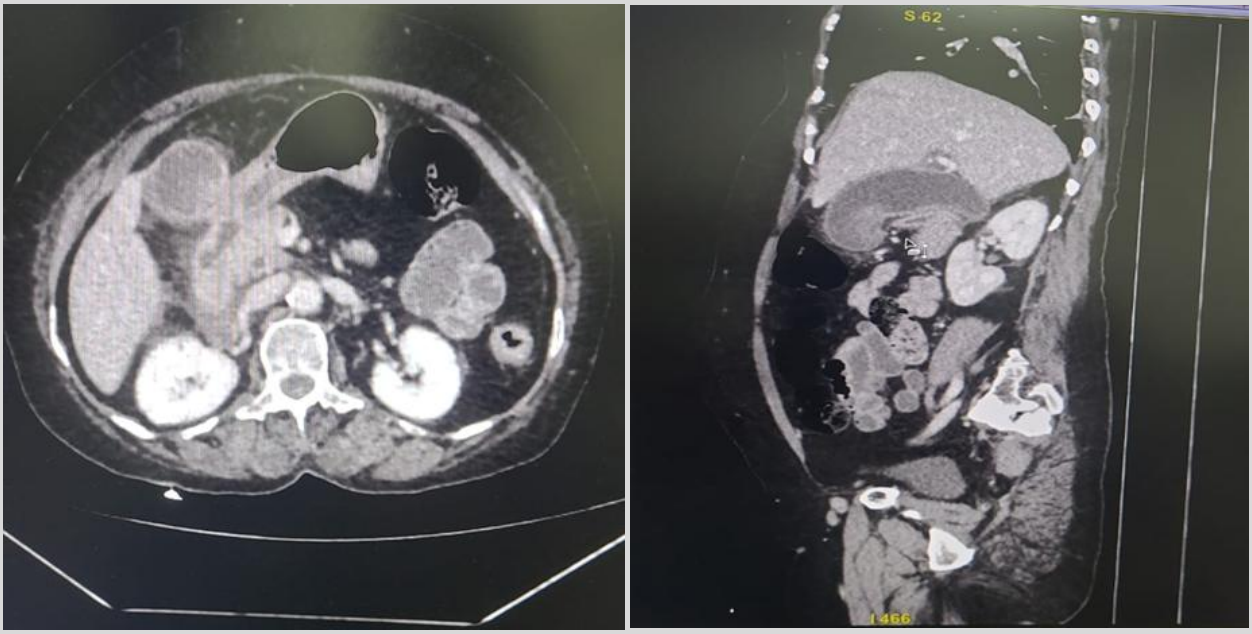

Figure 2 (a&b): CT Impression: Axial CT shows pronounced, irregular gallbladder wall thickening with aggressive infiltration into the liver bed. This finding mandates surgical management as it represents a critical diagnostic challenge, highly suspicious Gallbladder Carcinoma (GBC).

The surgical approach was primary open cholecystectomy in 18 cases, with the remainder initiated laparoscopically. Intraoperatively, extensive pericholecystic adhesions were noted in 28 patients, and infiltration to the liver bed was documented in 42 patients, further compounding the suspicion of malignancy (n=18). Consequently, 18 patients underwent extended resection due to intraoperative suspicion of GBC, while 30 patients were managed with simple cholecystectomy (**Table 3**) (**Figure 2**).

Table 3: Surgical Management, Intraoperative Findings, and Extent of Resection

Surgical Characteristic		Findings n (%)
Surgical Approach	Laparoscopic Cholecystectomy (LC)	30 (62.5)
	Conversion from LC to Open Cholecystectomy	0
	Primary Open Cholecystectomy	18 (37.5)
Intraoperative Findings	Dense Pericholecystic Adhesions	28 (58.3)
	Adhesion/Infiltration to Liver Bed	42 (87.5)
	Adhesion/Infiltration to Adjacent Organ (Colon/Duodenum)	16 (33.3)
	Suspicion of GBC Intraoperatively	18 (37.5)
Diagnostic Use & Extent of Resection	Simple Cholecystectomy	30 (62.5)
	Extended Resection/Liver Bed Excision (Due to suspicion)	18 (37.5)

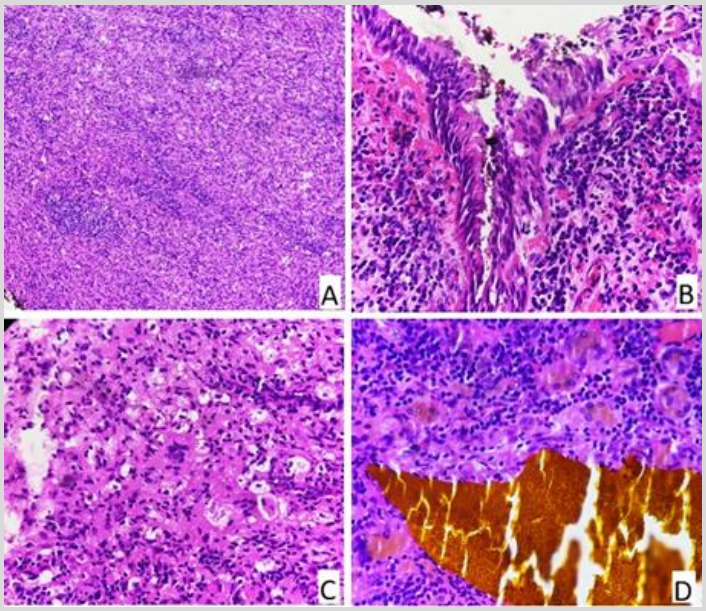

Figure 2: Sheets of foamy histiocytes admixed with chronic inflammatory cells (scanner view, A). Ulcerated mucosa (40x, B). Touton giant cells (10x, C). Calculi with foreign body type of giant cells and dense chronic inflammatory infiltrate (40x, D)

Postoperative outcomes included a prolonged median length of hospital stay of six days. Overall, 10 patients (20.8%) developed major complications (Clavien-Dindo Grade IIIa), primarily due to bile leak (n=6) and Surgical Site Infection (SSI) (n=8), with no observed mortality (Grade V) (**Table 4**).

Table 4: Postoperative Outcomes and Short-Term Complications

Outcome Parameter		Findings n (%)
Length of Hospital Stay	(days), Median	6
Postoperative Complications (Clavien-Dindo)	Grade I/II (Minor)	26 (54.2)
	Grade IIIa/IIIb (Surgical/Endoscopic Intervention)	10 (20.8)
	Grade IV/V (ICU Care/Mortality)	0
Specific Complications	Bile Leak/Biliary Injury	6 (12.5)
	Surgical Site Infection (SSI)	8 (16.7)
	Postoperative Pancreatitis	0

Discussion

The Confusion in Diagnosis Caused by Local High Cancer Rates

The results of this single-center study on 48 histopathologically confirmed cases of XGC in Odisha, India, illuminate a critical intersection of regional epidemiology and diagnostic challenges in a region highly endemic for GBC. The findings confirm that XGC here is not merely a diagnostic mimic but a condition whose local presentation, compounded by contextual bias, fundamentally drives a costly strategy of defensive oncology.

The study's demographic profile reinforces the local diagnostic challenge. The mean patient age of 53.79 ±13.16 years is consistent with the pooled global average (approx. 53.1 years) [7], yet this demographic critically overlaps with the peak incidence age of GBC locally reported in Eastern India (the 41–50 year group) [8]. This age congruence, coupled with a distinct 62.5% female predominance a ratio that perfectly mirrors the established gender epidemiology of GBC in the Gangetic belt [8] creates a potent, inherent epidemiological bias. A female patient in her early 50s presenting with an inflammatory gallbladder mass in this endemic zone is automatically placed into a high-risk category, thereby intensifying the clinical suspicion of malignancy. This contextual pressure is the foundational driver for the 37.5% high preoperative GBC suspicion rate observed in this cohort. Furthermore, the observation that XGC incidence may be higher in Indian cohorts (up

to 8.8%) [7] compared to Western counterparts (1.3%–1.9%) only magnifies the importance of accurate local differentiation.

The Failure of Preoperative Radiological Specificity

The high preoperative suspicion directly results from the fundamental radiological non-specificity of routine imaging (Ultrasound and CT). The dominant findings, such as gallbladder wall thickening (44 patients) and dense adjacent organ infiltration (32 patients), are non-differentiating features shared by both advanced XGC and infiltrative GBC [9]. This pathological mimicry forces a malignant interpretation.

A critical finding is the reported frequency of "Mucosal Gap/Disruption" in 91.7% of this benign XGC cohort. This result fundamentally contradicts established differentiating criteria, which consider a continuous, intact mucosal line as a key feature highly suggestive of benign XGC [10]. The widespread reporting of mucosal disruption suggests either an exceptionally destructive local inflammatory phenotype or, more likely, a significant interpretation imprecision on standard imaging, leading to the mistaking of severe inflammatory ulceration or artifact for malignant breach. This ambiguity severely undermines the confidence in a benign diagnosis.

Concurrently, the failure to identify the most reliable positive differentiating sign for XGC—the presence of intramural hypoattenuated nodules/striae (lipid-laden foam cells)—in only 8.3% of patients further exacerbated the dilemma [10]. This low detection rate, substantially below that of some global series (e.g., 73% on sonography) [11], leaves clinicians without a definitive non-invasive benign marker. The combination of high-risk epidemiological profile, non-specific aggressive findings, and the absence of a reliable benign marker structurally compels the surgical team to operate with the mindset of GBC until proven otherwise [12].

The Clinical Cost of Diagnostic Uncertainty

In this study, the n=0 conversion rate is not due to a high success rate of LC in complex cases, but rather reflects the strategic triaging of patients to the primary open cholecystectomy OC group. Given the high preoperative suspicion of GBC 37.5% and the aggressive radiological signs (liver bed infiltration), any case presenting with high-risk features was initially prioritized for OC (n=18) to enable adequate exposure and potential extended resection, aligning with defensive oncological principles. The 30 cases initiated via LC were thus inherently the lower-suspicion or less complex cases of XGC, thereby leading to the observed zero conversion rate.

This profound diagnostic uncertainty translated directly into substantial surgical burden and patient morbidity. 18 patients (37.5%) underwent an extended resection, typically involving liver bed excision. While unnecessary for a benign condition, this high rate represents a necessary strategic trade-off or form of defensive oncology. Operating in a high-endemic zone necessitates prioritizing the prevention of incomplete GBC resection, even at the cost of maximizing morbidity for a benign disease [13,14].

The clinical cost is evident: a prolonged median Length of Hospital Stay (LoS) of six days, which, while within the range for complex open cholecystectomy, constitutes a significant consumption of institutional resources compared to standard surgery. Most critically, 20.8% of patients experienced major postoperative complications (Clavien-Dindo Grade III), primarily bile leaks and Surgical Site Infections. This morbidity profile is a direct and inevitable consequence of the aggressive surgical approach mandated by the diagnostic failure. The high rate of unnecessary extended resections strongly implies a systemic failure in definitive intraoperative diagnostics, namely the inability or unreliability of Frozen Section Analysis (FSA) to guide conservative management in these complex inflammatory cases [13,2].

Study Limitation

The study's primary constraints stem from its single-center, retrospective design, limiting generalizability and preventing a critical, direct comparison with a local Gallbladder Carcinoma GBC cohort. Diagnostic accuracy was constrained by reliance on routine US/CT, with internal validity impacted by information bias and radiological interpretation imprecision; notably, the contradictory 91.7% report of mucosal disruption in benign cases. Furthermore, precise intraoperative data on FSA results were not consistently retrievable.

Conclusion and Future Research Directions

The study demonstrates the severe clinical burden of XGC in GBC-endemic regions, where inadequate diagnostic pathways result in a 37.5% rate of unnecessary extended resection and subsequent 20.8% major surgical morbidity. A critical shift is required from reactive intraoperative decisions to definitive preoperative diagnosis. This necessitates an immediate institutional review of imaging standards, focusing on the interpretation of mucosal integrity and intramural nodules and frozen section analysis. We hypothesize that a regionally optimized, integrated model combining quantitative CT features and local epidemiological risk factors will significantly reduce misdiagnosis. The essential next step is a prospective, multi-center study to develop and validate a Machine Learning (ML)-based predictive nomogram to achieve the diagnostic certainty needed for safe, conservative management of XGC.

Declaration

Acknowledgment

The authors gratefully acknowledge the support of the Multi-Disciplinary Research Unit (MRU), Pandit Raghunath Murmu Medical College and Hospital (PRMMCH), Baripada, funded by the Department of Health Research, Govt. of India, for providing technical assistance in preparing this manuscript

Funding

No funding was obtained for this study.

Ethics declarations

IEC Approval: The study was performed according to ethical parameters, after receiving the IEC approval letter.

Consent for publication: Not applicable

All research involving human participants, human data, or human material was conducted in full compliance with the ethical principles of the World Medical Association Declaration of Helsinki.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed substantially to the preparation of the research concepts, study design, and data acquisition, as well as

defining the intellectual content, conducting the literature search, and completing the drafting, editing, and final review of the manuscript.

References

[1] Makimoto S, Takami T, Hatano K, Kataoka N, Yamaguchi T, Tomita M, Shono Y. Xanthogranulomatous cholecystitis: a review of 31 patients. Surg Endosc. 2021 Jul;35(7):3874-3880. doi: 10.1007/s00464-020-07828-6.

[2] Feng L, You Z, Gou J, Liao E, Chen L. Xanthogranulomatous cholecystitis: experience in 100 cases. Ann Transl Med. 2020 Sep;8(17):1089. doi: 10.21037/atm-20-5836.

[3] Akkurt G, Birben B, Çoban S, Akgül Ö, Kulaçoğlu S, Doğanay M. Xanthogranulomatous Cholecystitis and Gallbladder Cancer: Two Diseases with Difficult Differential Diagnoses. Turk J Gastroenterol. 2021 Aug;32(8):694-701. doi: 10.5152/tjg.2021.201006.

[4] Yang T, Zhang BH, Zhang J, Zhang YJ, Jiang XQ, Wu MC. Surgical treatment of xanthogranulomatous cholecystitis: experience in 33 cases. Hepatobiliary Pancreat Dis Int. 2007 Oct;6(5):504-8.

[5] Suzuki H, Wada S, Araki K, Kubo N, Watanabe A, Tsukagoshi M, Kuwano H. Xanthogranulomatous cholecystitis: Difficulty in differentiating from gallbladder cancer. World J Gastroenterol. 2015 Sep 21;21(35):10166-73. doi: 10.3748/wjg.v21.i35.10166.

[6] Dutta U, Bush N, Kalsi D, Popli P, Kapoor VK. Epidemiology of gallbladder cancer in India. Chin Clin Oncol. 2019 Aug;8(4):33. doi: 10.21037/cco.2019.08.03.

[7] Hale MD, Roberts KJ, Hodson J, Scott N, Sheridan M, Toogood GJ. Xanthogranulomatous cholecystitis: a European and global perspective. HPB (Oxford). 2014 May;16(5):448-58. doi: 10.1111/hpb.12152.

[8] 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 Mar;4(1):67-72. doi: 10.1007/s13193-012-0203-x.

[9] Deng YL, Cheng NS, Zhang SJ, Ma WJ, Shrestha A, Li FY, Xu FL, Zhao LS. Xanthogranulomatous cholecystitis mimicking gallbladder carcinoma: An analysis of 42 cases. World J Gastroenterol 2015; 21(44): 12653-12659.doi: 10.3748/wjg.v21.i44.12653]

[10] Chang BJ, Kim SH, Park HY, Lim SW, Kim J, Lee KH, Lee KT, Rhee JC, Lim JH, Lee JK. Distinguishing xanthogranulomatous cholecystitis from the wall-thickening type of early-stage gallbladder cancer. Gut Liver. 2010 Dec;4(4):518-23. doi: 10.5009/gnl.2010.4.4.518.

[11] Suzuki H. Specific radiological findings, if present, can offer high accuracy for the differentiation of Xanthogranulomatous cholecystitis and gallbladder cancer. Ann Transl Med. 2020 Jun;8(11):662. doi: 10.21037/atm.2020.03.193.

[12] Pandey A, Kumar D, Masood S, Chauhan S, Kumar S. Is Final Histopathological Examination the Only Diagnostic Criteria for Xanthogranulomatous Cholecystitis? Niger J Surg. 2019 Jul-Dec;25(2):177-182. doi: 10.4103/njs.NJS_1_19.

[13] Yüksel E, Dinçer B, Ömeroğlu S. Factors affecting the risk of conversion from laparoscopy to open surgery in xanthogranulomatous cholecystitis: a retrospective cohort study. BMC Surg. 2025 Sep 29;25(1):416. doi: 10.1186/s12893-025-03097-z.

[14] Noji T, Takeuchi S, Wada M, Tanaka K, Matsui A, Nakanishi Y, Asano T, Nakamura T, Kawamoto Y, Hirano S. Short- and Long-term Surgical Results of Extended Surgery for Widespread Gallbladder Carcinoma. In Vivo. 2025 Mar-Apr;39(2):1022-1032. doi: 10.21873/invivo.13907.