Research Article

Serial Ultrasonographic Evaluation of Gallbladder Morphology in Critically Ill Patients for Early Detection of Acute Acalculous Cholecystitis

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Abstract

Acute acalculous cholecystitis is an inflammatory condition of the gallbladder that occurs in the absence of gallstones. Critically ill patients admitted to the Intensive Care Unit (ICU) are at high risk of developing acute acalculous cholecystitis due to several predisposing factors, including epithelial ischemia, mechanical ventilation, parenteral nutrition, and opioid use. The purpose of this study was to assess temporal changes in gallbladder sonomorphology through serial ultrasonographic examinations on the first and third days of ICU admission in critically ill patients. This prospective longitudinal observational study included patients admitted to the ICU of Dr. Zainoel Abidin General Hospital between June and August 2025 who met the inclusion and exclusion criteria. Gallbladder morphology was evaluated sonographically on the first and third days of ICU admission. Bivariate analysis was performed using the McNemar test. A total of 41 patients were included with a mean age of 52 years. Twenty-four patients (58.5%) demonstrated changes in gallbladder sonomorphology on the third day compared to the first day. Significant changes were observed in gallbladder wall thickening (p=0.031) and gallbladder sludge (p<0.001). Gallbladder hydrops increased in frequency from day 1 to day 3, although the difference was not statistically significant (p=0.063). No cases of intramural gas or mucosal sloughing were identified. Serial ultrasonographic evaluation demonstrated changes in gallbladder morphology between the first and third days of ICU admission, particularly an increase in the occurrence of gallbladder wall thickening and biliary sludge.
Keywords: *acute acalculous cholecystitis, critically ill, intensive care unit, ultrasonography.*

Evaluasi Serial Sonomorfologi Kandung Empedu pada Pasien Critically Ill sebagai Upaya Deteksi Dini Kolesistitis Akalkulus Akut

Abstrak

Kolesistitis akalkulus akut merupakan suatu kondisi peradangan pada kandung empedu yang terjadi tanpa adanya batu kandung empedu. Pasien critically ill yang dirawat di Intensive Care Unit (ICU) memiliki risiko tinggi mengalami kolesistitis akalkulus akut karena berbagai faktor predisposisi, seperti iskemia epitel kandung empedu, penggunaan ventilasi tekanan positif, nutrisi parenteral serta penggunaan obat-obatan opioid. Tujuan penelitian ini adalah untuk menilai perubahan morfologi kandung empedu melalui pemeriksaan ultrasonografi serial pada hari pertama dan ketiga perawatan ICU pada pasien kritis. Penelitian ini merupakan studi observasional dengan desain longitudinal prospektif. Subjek penelitian adalah pasien yang dirawat di Intensive Care Unit (ICU) RSUD dr. Zainoel Abidin Banda Aceh pada periode Juni-Agustus 2025 yang memenuhi kriteria inklusi. Pemeriksaan sonomorfologi kandung empedu dilakukan pada hari pertama dan ketiga perawatan. Analisis bivariat dilakukan menggunakan uji McNemar. Sebanyak 41 subjek diikutsertakan dalam penelitian ini dengan rata-rata usia 52 tahun. Sebanyak 24 pasien (58,5%) menunjukkan perubahan sonomorfologi kandung empedu pada hari ketiga perawatan dibandingkan hari pertama. Aspek sonomorfologi yang menunjukkan perubahan bermakna secara statistik pada hari ketiga adalah penebalan dinding kandung empedu (p=0,031) dan sludge empedu (p<0,001). Sementara itu, frekuensi hydrops kandung empedu menunjukkan peningkatan dari hari pertama ke hari ketiga meskipun perbedaan tersebut tidak bermakna secara statistik (p=0,063). Evaluasi ultrasonografi serial menunjukkan adanya perubahan morfologi kandung empedu antara hari pertama dan ketiga perawatan ICU, terutama berupa peningkatan frekuensi penebalan dinding kandung empedu dan terbentuknya sludge bilier.
Kata kunci: *kolesistitis akalkulus akut, critically ill, intensive care unit, ultrasonografi.*

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Introduction

Acute cholecystitis is a condition characterized by inflammation of the gallbladder. Gallstones are the primary precipitating factor in 90% of cases of acute cholecystitis. However, in 2-15% of cases, it may occur in the absence of gallstones, referred as acute acalculous cholecystitis (AAC).[1,2] Acute acalculous cholecystitis generally develops following severe illness or trauma, including extensive burns, multiple trauma, major surgery, chronic kidney disease, leukemia, and severe infections.[2] In such conditions, cholecystitis may serve as a predictor of subsequent multiple organ failure.[1]

Patients receiving intensive care are at increased risk of developing AAC due to several predisposing factors, including gallbladder epithelial ischemia, positive pressure mechanical ventilation, parenteral nutrition, and opioid use.[3] The gallbladder mucosa is highly susceptible to injury when alterations in bile composition occur as a result of biliary stasis. Increased bile viscosity leads to elevated intraluminal pressure and ischemia, which are further exacerbated by hypotension and atherosclerosis. Hypovolemia and sepsis are also associated with the release of cytokine-mediated systemic inflammatory responses affecting the gallbladder.[4]

Gallbladder inflammation and biliary stasis may develop through several interrelated mechanisms. Bacterial pathogens in the biliary tract can hydrolyze bile salts into bile acids, resulting in alterations in serum lipid profiles and the production of hydrophobic substances that may impair gallbladder smooth muscle function, ultimately promoting biliary stasis. In addition, biliary infection may increase histamine levels, leading to increased cystic duct resistance and further impairment of bile flow. Alternatively, systemic inflammation and ischemic injury have been proposed as the primary mechanisms of underlying acute acalculous cholecystitis.[5-7]

Acute acalculous cholecystitis is associated with increased morbidity and mortality, reaching up to 50%, and carries a worse prognosis compared to calculous cholecystitis.[1] Other studies have reported complications such as gallbladder gangrene in up to 50% of cases and gallbladder perforation in up to 10% of cases based on histopathological findings.[8] Lee et al[9] in their study demonstrated that gallbladder perforation was observed more frequently in the acalculous cholecystitis than in the calculous cholecystitis group (5.6% vs 1.0%, $p<0.001$).

Given the high morbidity and mortality associated with gangrene and perforation, which may develop rapidly, prompt and accurate diagnosis is essential.[10] Ultrasonography is the first-line imaging modality used in critically ill patients. Ultrasonographic findings in patients with AAC include gallbladder distension, gallbladder wall thickening, and pericholecystic fluid. Potential complications include gallbladder perforation, gangrene, empyema, and sepsis.[1] A previous study by Molenat et al[11] in 1996 reported that 61% of patients who underwent ultrasonographic evaluation during the first 24–48 hours after ICU admission demonstrated gallbladder abnormalities. Another study from Kim et al[12] concluded that the interval between ICU admission and diagnosis of AAC was approximately 11 days and associated with a mortality rate of 42.1% in the reported patient population. These findings highlight the clinical importance of recognizing temporal gallbladder morphology changes as early as possible in critically ill patients.[12] However, no studies to date have compared gallbladder conditions at the time of ICU admission and after shorter intervals during the early phase of ICU admission (after 48 hours or on day 3 of ICU admission), which could help prevent disease progression and its associated adverse outcomes. Based on this background, the present study aims to compare gallbladder sonomorphology findings between the first and third days of ICU admission in critically ill patients using serial ultrasonographic examinations.

Methods

This study was an observational study with a prospective longitudinal design. The subjects were patients admitted to the Intensive Care Unit (ICU) of Dr. Zainoel Abidin General Hospital, Banda Aceh, between June and August 2025 who met inclusion and exclusion criteria. Sonographic evaluation of gallbladder morphology was performed on the first and third day of ICU

admission. Bivariate analysis was conducted using the McNemar test.

The inclusion criteria comprised patients who had been admitted to the ICU for at least one day with informed consent provided either directly from the patient or through family consent. The exclusion criteria included patients with a history of gallbladder disease or congenital gallbladder abnormalities, as well as patients who were discharged from the ICU before the second ultrasonographic evaluation on the third day of admission. A total of 53 patients initially underwent ultrasonographic examination. However, 8 patients died and 4 patients were transferred out of the ICU before the scheduled third-day examination. Consequently, complete paired ultrasonographic data were available for 41 patients, who were included in the final analysis.

The primary outcome was to compare gallbladder sonomorphological findings between the first and third days of ICU admission on critically ill patients and the secondary outcome was to analyze changes in the number of sonomorphological abnormalities observed in each patient between the two examination time points.

The gallbladder sonomorphological parameters measured and compared between the first and third day included gallbladder wall thickening (≥3.5 mm), pericholecystic fluid in the absence of ascites, intramural gas, mucosal sloughing, biliary sludge, and gallbladder hydrops (longitudinal diameter >8 cm, or transverse diameter >4 cm). The clinical variables described in this study included sex, age, type of nutrition administered (parenteral, enteral, combined), opioid use, mechanical ventilation, presence of leukocytosis, hypoalbuminemia, and a history of diabetes mellitus.

Gallbladder ultrasonography was performed at the patients' bedside using a high resolution ultrasound system equipped with curvilinear abdominal transducer. All examinations and interpretations were performed by a fourth-year radiology resident under the supervision of a board-certified abdominal consultant radiologist. Each patient was examined in the supine position, and the gallbladders were evaluated in the longitudinal and transverse planes.

This study was conducted after obtaining ethical approval from the Ethics Committee of Dr. Zainoel Abidin General Hospital (127/ETIK-RSUDZA/2025).

Results

This study included 41 subjects who met the inclusion and exclusion criteria, consisting of 24 females (58.5%) and 17 males (41.5%), with a mean age of 52 years.

The most common primary diagnosis among the study subjects was postoperative respiratory failure (48.8%), followed by acute respiratory failure (29.3%) and other diagnoses (21.9%). A total of 29.3% of subjects received total parenteral nutrition (TPN). All subjects received opioid therapy. Mechanical ventilation was used in 97.6% of subjects. Leukocytosis was observed in 53.7% of subjects, hypoalbuminemia in 46.3%, and a history of diabetes mellitus in 17.1% of cases (Table 1).

The McNemar test demonstrated that five patients (12.2%) who did not exhibit gallbladder wall thickening on the first day developed wall thickening on the third day, while 36 patients (87.8%) remained normal, with a statistically significant p-value of 0.031. Pericholecystic fluid on the third day was observed in four patients (9.8%), comprising three newly developed cases (7.3%) and one patient (2.4%) who consistently demonstrated pericholecystic fluid from the first day (p=0.125). Biliary sludge on the third day was identified in 20 patients (48.8%), consisting of 15 newly developed cases (36.6%) and five patients (12.2%) who had already shown biliary sludge since the first day ($p < 0.001$). Gallbladder hydrops on the third day was observed in seven patients (17.1%), comprising six newly developed cases (14.6%) and one patient (2.4%) who consistently demonstrated hydrops from the first day of ICU admission, while one patient (2.4%) had demonstrated hydrops on the first day thatresolved on the third day (p=0.063). No cases of intramural gas or mucosal sloughing were identified (Table 2).

Table 1. Characteristic of Study Subjects

Variable	Frequency (n=41)	Percentage (%)
Sex		
Male	17	41.5
Female	24	58.5
Primary diagnosis		
Acute respiratory failure	12	29.3
Postoperative respiratory failure	20	48.8
Others	9	21.9
Type of nutrition		
Parenteral	12	29.3
Enteral and parenteral	29	70.7
Opioid use		
Yes	41	100
No	0	0
Mechanical ventilator		
Yes	40	97.6
No	1	2.4
Leukocytosis		
Yes	22	53.7
No	19	46.3
Hypoalbuminemia		
Yes	19	46.3
No	22	53.7
History of diabetes mellitus		
Yes	7	17.1
No	34	82.9

Table 2. Analysis of Changes in Gallbladder Sonomorphology in Critically Ill Patients on the First and Third Days of ICU Admission

Sonographic Findings	Day 1, n (%)	Day 3, n (%)	Persistent (Day 1+/Day 3+), n (%)	Newly Developed (Day 1−/Day 3+), n (%)	Resolved (Day 1+/Day 3−), n (%)	Net Change, n (Percentage Points)	p-value*
Wall thickening	0 (0%)	5 (12.2%)	0 (0%)	5 (12.2%)	0 (0%)	+5 (+12.2)	0.031
Pericholecystic fluid	1 (2.4%)	4 (9.8%)	1 (2.4%)	3 (7.3%)	0 (0%)	+3 (+7.3)	0.125
Biliary sludge	5 (12.2%)	20 (48.8%)	5 (12.2%)	15 (36.6%)	0 (0%)	+15 (+36.6)	<0.001
Gallbladder hydrops	2 (4.9%)	7 (17.1%)	1 (2.4%)	6 (14.6%)	1 (2.4%)	+5 (+12.2)	0.063
Intramural gas	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-
Mucosal sloughing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-

*McNemar test

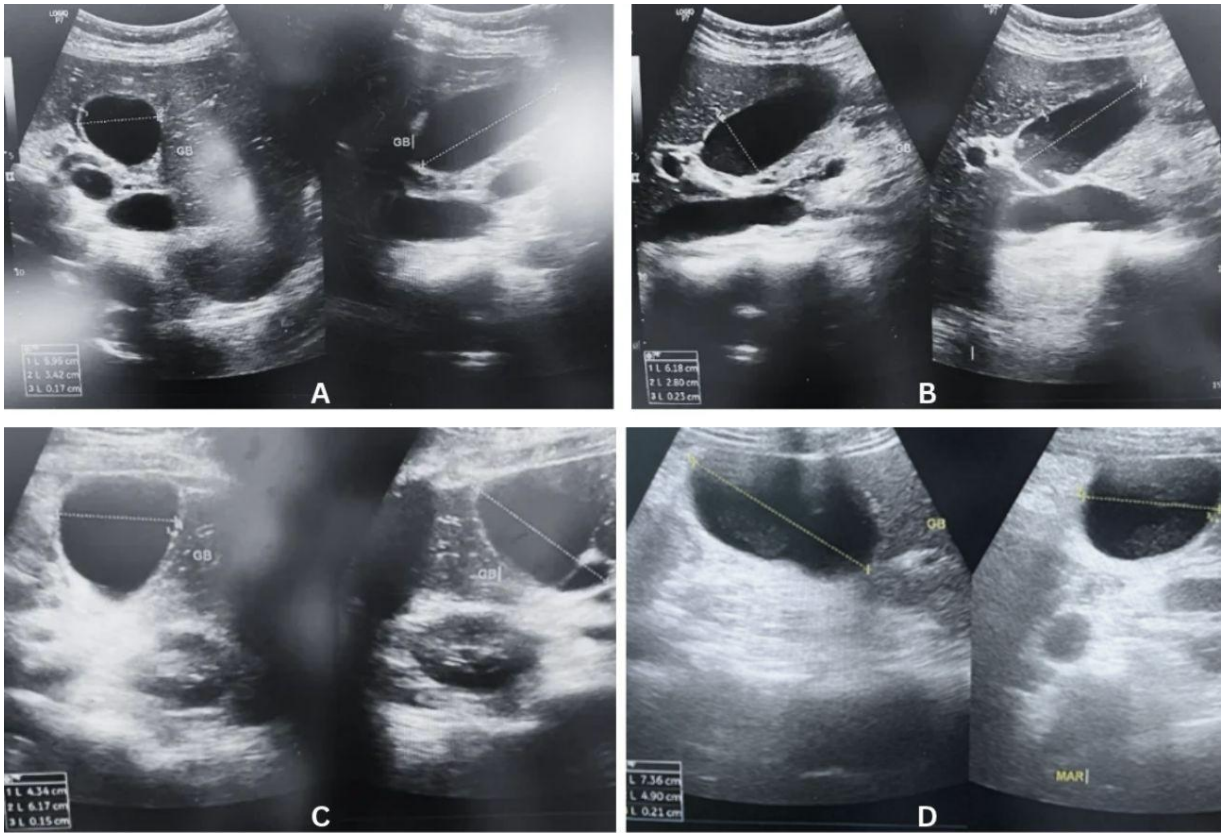


Figure 1. Comparison of Serial Ultrasonographic Findings in Two Different Patients.
Images A and B were Obtained on Day 1 and Day 3 of ICU Admission, Respectively, Showing Biliary Sludge on Day 3 (B). Images C and D Represent the Second Patient Examined on Day 1 and Day 3, Respectively, Demonstrating Gallbladder Hydrops on Both Occasions and Sludge on Day 3 (D)

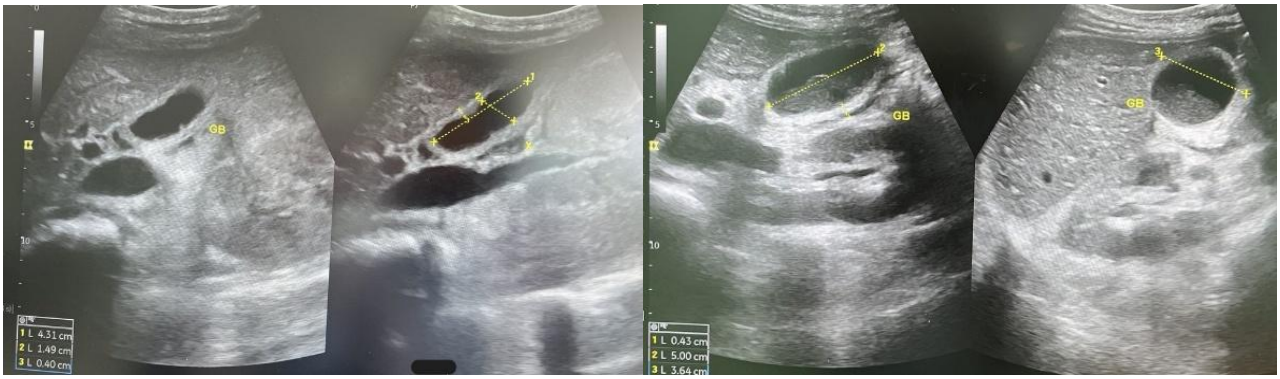


Figure 2. Sonographic Images From Two Different Patients Demonstrating Gallbladder Wall Thickening, Biliary Sludge, and Pericholecystic Fluid On The First Day Of ICU Care. These Patients Died Due to Systemic Illness Before the Scheduled Ultrasonography on the Third Day of ICU Admission

Based on the results of this study, 24 patients (58.5%) admitted to the ICU demonstrated changes in gallbladder sonomorphology on the third day compared to the first day of ICU care. These findings indicate that morphological changes of the gallbladder are relatively common among critically ill patients during ICU hospitalization. This study identified 16 patients (39.0%) who exhibited at least one gallbladder abnormality, five patients (12.2%) demonstrated two abnormalities, two patients (4.9%) demonstrated three abnormalities, and one patient (2.4%) demonstrated four gallbladder abnormalities (Table 3).

Table 3. Distribution of Gallbladder Abnormalities on the Third Day of ICU Admission

Number of Gallbladder Abnormalities	Number of Patients (n)	Percentage (%)
No abnormalities	17	41.5
1 abnormality	16	39.0
2 abnormalities	5	12.2
3 abnormalities	2	4.9
4 abnormalities	1	2.4
Total	41	100

Discussion

In this study, changes in gallbladder sonomorphology were observed between the first and third days of ICU admission among critically ill patients. The most prominent increase in gallbladder morphology was biliary sludge in 20 patients (48.8%), followed by the appearance of wall thickening in 5 patients (12.2%). Descriptively we also found that 16 patients (39.0%) presented with at least with one abnormality, five with two abnormalities, two with three abnormalities and one with four abnormalities.

These changes are presumed to be associated with unstable hemodynamic conditions, biliary stasis resulting from immobilization and reduced gallbladder contractility, as well as the effects of total parenteral nutrition and certain medications that may reduce bile flow.[13-14] These findings emphasize the importance of serial sonographic monitoring in patients with clinical risk factors to detect early gallbladder morphological changes that may progress to acute acalculous cholecystitis, particularly since clinical manifestations in critically ill patients may be maskes by other systemic conditions.[8,15]

Gallbladder wall thickening on the third day of ICU care was observed in five patients (12.2%), whereas no patients exhibited wall thickening on the first day. This finding suggests a tendency toward increased gallbladder wall thickening with longer ICU stays (p=0.031). A previous study by Laurila et al[16] involving 39 ICU patients who underwent cholecystectomy for acute acalculous cholecystitis reported operative findings of gallbladder necrosis and gangrene in 17 patients (44%), as well as gallbladder distension and wall thickening in 22 patients (56%). Gallbladder wall thickening is the most reliable criterion, with reported specificity of 90% at 3 mm and 98.5% at 3.5 mm wall thickness and sensitivity of 100% at 3 mm and 80% at 3.5 mm.[15]

According to this study, one patient (2.4%) demonstrated pericholecystic fluid from the first day of ICU admission, while three additional patients developed pericholecystic fluid on the third day (p = 0.125). Another study by Boland et al[17] involving 44 ICU patients reported pericholecystic fluid in eight patients (18%), four of whom also had ascites not adjacent to the gallbladder fossa. Similarly, a study by Myrianthefs et al[15] reported pericholecystic fluid in five of 25 patients (20%) with gallbladder abnormalities identified on ICU ultrasonography. Although the present study did not demonstrate a statistically significant association, the increased number of patients with pericholecystic fluid on the third day remains clinically relevant, as it may reflect an ongoing inflammatory process.

Biliary sludge was identified in five patients (12.2%) on the first day and increased to 20 patients (48.8%) on the third day of ICU care. This finding indicates that 15 patients (36.6%) who initially showed no sludge on the first day developed biliary sludge by the third day (p<0.001). Statistical analysis demonstrated a highly significant difference, suggesting that biliary sludge tends to increase substantially with prolonged ICU stay. These findings are consistent with a previous study by Laurila et al[16] which reported that biliary sludge was the most frequently observed sonomorphological abnormality (55%) among ICU patients. Therefore, biliary sludge may serve as an early indicator of biliary stasis and has the potential to progress to inflammation if not promptly detected. Early identification of sludge may enable early interventions, such as optimization of enteral nutrition, reduction of opioid use when feasible, and improved hemodynamic management.[4] Shao

et al[18] in their study which evaluated the relationship between bowel disuse duration and acute acalculous cholecystitis suggest early introduction of minimal enteral nutrition, periodic cycling of parenteral nutrition and vigilant management of dehydration and anemia. Similarly, a previous study by Chang et al[19] involving critically ill trauma patients reported significant reduction in the incidence of AAC-related complications following the implementation of a nutritional protocol.

According to the present study, six patients (14.6%) who did not initially exhibit gallbladder hydrops on the first day developed hydrops by the third day of ICU care, one patient consistently showed hydrops from the first day, and one patient showed hydrops on the first day that resolved on the third day (p=0.063). Although this finding did not reach conventional statistical significance, descriptively there was increased number of patients with gallbladder hydrops on day 3 of ICU admission. This tendency toward an increased incidence of gallbladder hydrops remains clinically meaningful, suggesting that gallbladder physiological alterations may occur in critically ill patients even in the absence of mechanical obstruction such as gallstones.

No cases of intramural gas or mucosal sloughing were identified on either the first or third days of ICU care. These findings suggest that intramural gas and mucosal sloughing are rare and typically reflect advanced inflammatory processes of the gallbladder wall, often associated with severe mucosal ischemia, necrosis, and gangrene in acute acalculous cholecystitis.

According to Huang et al[20] no significant associations were observed between gallbladder abnormalities and age, sex, ICU admission diagnosis, or the use of mechanical ventilation. In contrast, patients with gallbladder abnormalities had significantly lower serum albumin levels than those without abnormalities. Additionally, longer fasting duration was significantly associated with the presence of gallbladder abnormalities.[20]

A strenght of this study is its prospective longitudinal design, which allowed serial evaluation of gallbladder sonomorphology within the same critically ill patients at two different time points during ICU admission. However, several limitations should be acknowledged, such as relatively small sample size and single-center setting may limit the generalizability of the findings and reduce the statistical power to detect associations between clinical risk factors and gallbladder abnormalities. Finally, this study focused on sonographic morphological changes rather than establishing a definitive diagnosis of AAC. We recommend further multicenter studies with larger sample sizes and longer follow-up periods to clarify the clinical significance of these sonographic changes and their potential role in the early detection for AAC.

Conclusion

Descriptively, gallbladder sonomorphological changes were observed in 24 patients (58.5%) on the third day compared with the first day of ICU care. The most significant sonomorphological changes identified on the third day were biliary sludge formation and gallbladder wall thickening. These findings indicate that gallbladder abnormalities may develop within the first three days of ICU hospitalization. The authors recommend risk stratification and close clinical monitoring of patients admitted to the Intensive Care Unit (ICU), with gallbladder sonography evaluation when indicated to detect early sonomorphological changes as part of early detection strategies for acute acalculous cholecystitis.

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Authors' contributions

The first author contributed in research idea, data collection, data analysis and manuscript drafting. The second author contributed in interpretation of results from the ultrasonography, and the third author contributed in study design and critical revision. All authors have read and approved the final manuscript.

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Data and Materials Availability

The full data from this research cannot be shared due to legal restrictions.

Consent to Participate

Informed consent to participate in this research was all obtained from the family/legal guardian of participants on the first day of ICU care.

Ethic Statement

This research was conducted after obtaining ethical approval from the Ethics Committee of Dr. Zainoel Abidin General Hospital (127/ETIK-RSUDZA/2025) in accordance with the Declaration of Helsinki and International ethical guidelines.

Consent for Publication

Not applicable.

Competing Interest

No competing interest.

AI usage Declaration

Artificial intelligence tools were used solely for limited English-language editing during manuscript preparation. All content has been reviewed and approved by the authors.

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