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# Role of endoscopic ultrasound in gallbladder and biliary system diseases in patients with normal transabdominal ultrasonography

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## Abstract

**Background** The clinical management of patients experiencing recurrent abdominal pain resembling biliary-type, but with negative findings on conventional transabdominal ultrasound (TUS), poses a challenge. In recent years, endoscopic ultrasound (EUS) has emerged as a valuable tool for diagnosing gallbladder diseases. This study aims to assess the role of EUS in the evaluation of gallbladder and biliary system diseases specifically in patients with normal transabdominal ultrasonography results.

**Methods** This study was a cross-sectional analytic study that enrolled 150 patients with any complaints related to the gallbladder and biliary system necessitating transabdominal ultrasound and endosonography in the period between February 2021 and December 2021.

**Results** The mean age of the studied patients was  $46.1 \pm 10.3$  years; 46.7% were males and 53.3% were females. The main complaint was right abdominal pain in 78.0%; meanwhile, 74.7% had a picture of obstructive jaundice. EUS revealed gallbladder wall thickening in 15 patients (10%), mud and/or small stones inside the gallbladder in 73 patients (48.7%), positive GB mass and/or polyp findings in 30 patients (20%), and biliary lesions such as duct strictures and/or dilatations were detected in 48 patients (32%), while transabdominal ultrasound was normal in all those patients.

**Conclusion** Endoscopic ultrasound (EUS) proves to be a valuable diagnostic modality in patients experiencing biliary-type abdominal pain, despite normal transabdominal ultrasonography results. It not only aids in the accurate diagnosis of underlying conditions but also has the potential to impact the management plan for these patients.

**Keywords** Transabdominal ultrasound (TUS), Endoscopic ultrasound (EUS), Gallbladder diseases, Biliary system diseases

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## Introduction

Gallbladder diseases are quite common, with cholelithiasis being the most frequently observed condition, impacting about 10–15% of adults. Other issues like gallbladder polyps are present in roughly 5% of the global population. The global occurrence of gallbladder cancer is relatively uncommon, with an estimated two cases per 100,000 individuals [1].

Transabdominal ultrasonography (TUS) is often the initial imaging test in cases where choledocholithiasis, cholecystolithiasis, or biliary tree dilation is suspected. TUS is advantageous as it is non-invasive, easily accessible, safe, radiation-free, and cost-effective. However, its effectiveness can vary based on the operator's expertise, and while it visualizes the extrahepatic bile ducts in about 60 to 80% of cases, it may not be entirely effective in all situations [2].

In contrast, endoscopic ultrasound (EUS) is considered superior to transabdominal ultrasonography for biliary system visualization. This superiority arises from EUS's ability to approach the area of interest closely and capture higher-resolution images with higher ultrasound frequencies compared to conventional ultrasonography. The improved image quality from EUS significantly enhances the accuracy and detail of the biliary system evaluation [3].

Endoscopic ultrasound (EUS) significantly aids in diagnosing gallbladder abnormalities, including polypoidal lesions and microlithiasis. It plays a key role in gallbladder carcinoma staging, offering high-resolution images that facilitate a thorough assessment of the gallbladder. When combined with fine needle aspiration, EUS contributes to obtaining histological diagnoses of gallbladder tumors and examining gallbladder thickening, boosting diagnostic accuracy and informing treatment decisions [3].

While EUS shows cases of higher specificity and comparable sensitivity to transabdominal ultrasonography (TUS) in diagnosing neoplastic lesions, using high-frequency transabdominal ultrasound (ranging from 2.5 to 7 MHz) minimizes the sensitivity difference. This approach delivers diagnostic efficacy on par with EUS, computed tomography (CT), or magnetic resonance imaging (MRI) for detecting neoplastic lesions. Employing high-frequency transabdominal ultrasound offers imaging quality and accuracy akin to EUS, CT, or MRI [4].

EUS-guided fine-needle aspiration (FNA) significantly improves the diagnostic yield for evaluating biliary strictures while carrying minimal risk. By allowing direct sampling from the target area, this procedure enhances diagnostic accuracy and safety in assessing biliary strictures. This study aimed to evaluate the role of

endoscopic ultrasound in gallbladder and biliary system diseases in patients with normal transabdominal ultrasonography [5].

## Materials and methods

This study was a cross-sectional analytic study enrolled 150 patients referred to Kasr Alainy General Surgery, Internal Medicine, and emergency room (ER) units with any complaint related to the gallbladder and biliary system necessitating transabdominal ultrasound and endosonography in the period between February 2021 and December 2021. All included patients were aged 20–67 years old, both sexes were included. Normal gallbladder and biliary system USA in all patients. Those who refused to participate, had a bleeding tendency, or were contraindicated for anesthesia were excluded from the study. The study was approved by our institution's Research Ethical Committee with the reference number: MS-88-2021, and all patients gave their informed written consent before inclusion in the study, according to the ethical guidelines of the 1975 Declaration of Helsinki.

All patients were subjected to thorough history taking and clinical examination including age, gender, body mass index (BMI), comorbid diseases (diabetes, hypertension) family history, serum creatinine, bilirubin, alkaline phosphatase, full blood picture, C-reactive protein (CRP), and international normalized ratio (INR) were measured.

## Procedure steps

- Transabdominal sonography and endoscopic ultrasonography EUS were done on all included patients.
- Before starting
  - All patients were fasting to avoid gallbladder contraction.
  - The patient assumed the left lateral decubitus position as this brings the gallbladder more into the midline for the scan.
- Transabdominal sonography examination was carried out utilizing a Hitachi sonography machine; the technique was performed according to the following steps: position the probe in the epigastric midline with the indicator facing the patient's head then slide laterally (slowly) along the costal margin, toward the patient's right, until clearly see the portal triad with complete evaluation of gallbladder.
- Endoscopic ultrasonography EUS examination was carried out utilizing the oblique viewing linear Pentax (J-10) video machine connected to a Hitachi sonography machine.

The technique was performed according to the following steps; connecting the patient with pulse oximetry, oxygen saturation, and blood pressure measurement devices, the patient lying in the left lateral position, and deep sedation by Propofol 1% IV under anesthesia specialist guidance, and tracing of CBD was done to image the entire course of the duct till its opening in the ampulla of Vater detecting any stones with characteristic posterior shadowing.

### Statistical methods

#### Sample size estimation

To assess the role of EUS in the diagnosis of biliary system disease in patients with normal transabdominal sonography, a prospective cross-sectional study was conducted. Based on previous studies, the expected frequency of biliary diseases detected by EUS was 52.4% in patients with normal transabdominal sonography. For a two-sided 95% confidence interval for a single proportion using the large sample normal approximation which was extended 8% from the expected proportion, a sample size of 150 participants was recruited. Sample size estimation was performed by the Epi Info statistical package.

The collected data were entered on the computer using Microsoft Office Excel Software Program 365. Additionally, pre-coded data were entered into the Statistical Package of Social Science Software program, version 26 (SPSS). Furthermore, quantitative variables were described as mean, standard deviation, median, minimum, and maximum. Qualitative variables were expressed as frequency and percentage and compared using the chi-square test, where the *p* value is significant if less than 0.05.

### Results

This study is a cross-sectional analytical study. It included 150 patients referred to Kasr Alainy General Surgery, Internal Medicine, and ER units with any complaint related to the biliary system necessitating transabdominal ultrasound and endoscopic ultrasound. The mean age of the studied patients was  $46.1 \pm 10.3$  years; 46.7% of them were males and 53.3% were females. The main complaint among studied patients was right abdominal pain in 78.0%; meanwhile, 74.7% had a picture of obstructive jaundice. Laboratory findings of the studied patients were demonstrated in Table 1.

EUS revealed gallbladder wall thickening in 15 patients (10%), mud and/or small stones inside the gallbladder in 73 patients (48.7%), positive GB mass and/or polyp findings in 30 patients (20%), and biliary lesions such as duct strictures and/or dilatations were detected in 48 patients (32%) (Fig. 1), while transabdominal ultrasound was normal in all those patients (Table 2).

**Table 1** Laboratory findings of the studied patients

<i>n</i> = 150	Mean $\pm$ S.D	Range
Total bilirubin	2.25 $\pm$ 2.31	0.80 - 13.00
Direct bilirubin	1.29 $\pm$ 2.97	0.20 - 8.00
TLC	9.22 $\pm$ 2.97	2.50 - 16.00
Hemoglobin	11.88 $\pm$ 1.41	9.00 - 16.20
Platelets	301.26 $\pm$ 79.72	22.00 - 461.00
INR	1.07 $\pm$ 0.15	0.80 - 1.60
CRP	10.22 $\pm$ 10.61	1.00 - 66.00
Creatinine	1.17 $\pm$ 1.50	0.60 - 1.40

TLC total leucocytic count, INR international normalized ratio, CRP C-reactive protein

### Discussion

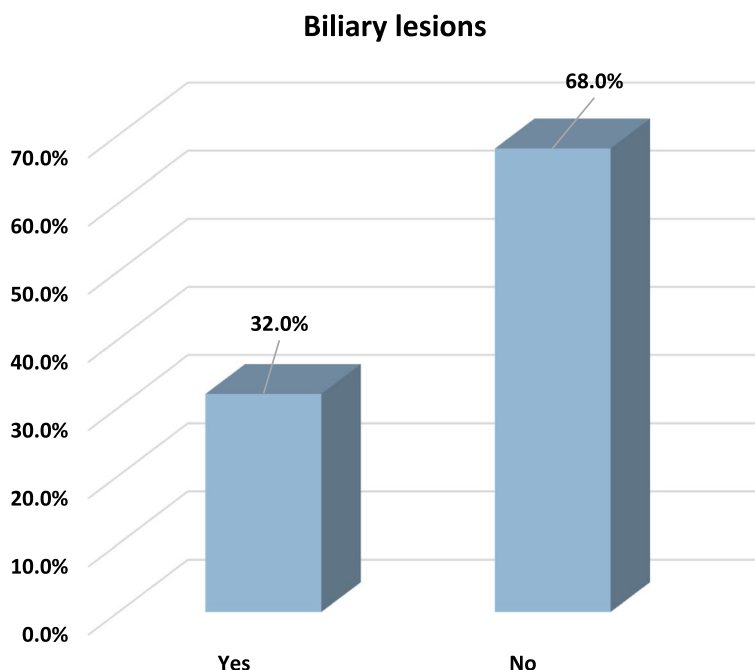
While TUS serves as a widely available and safe initial screening method for hepatobiliary diseases, it shows a sensitivity of 66% in distinguishing between gallbladder polyps and calculi. However, with a specificity of 100%, TUS accurately identifies detected polyps or calculi. Despite its sensitivity limitations, TUS remains valuable for the primary assessment of hepatobiliary conditions [6].

EUS offers exceptional visualization of the extrahepatic biliary tree, effectively detecting bile duct stones as echo-dense structures within the ampulla or common bile duct. These stones may exhibit movement within the duct and are accompanied by acoustic shadowing. Additionally, EUS identifies bile duct wall thickening, offering insights into stone presence or related abnormalities [7].

EUS offers exceptional spatial resolution, surpassing that of abdominal ultrasonography (US). This enhanced resolution allows for a more detailed examination, particularly in assessing tumor characteristics and depth of invasion. By providing higher-resolution images, EUS plays a pivotal role in the diagnostic process and treatment planning for different tumors [8].

EUS consistently outperforms ERCP in detecting small common bile duct (CBD) stones, boasting a high negative predictive value (NPV) of over 95%. It exhibits a specificity of 95% or higher in excluding CBD stones, often overlooked by other imaging techniques. Additionally, EUS effectively identifies bile duct sludge and microlithiasis, underscoring its superior diagnostic capabilities in biliary stone detection and characterization [9].

In the context of cholelithiasis, EUS's role extends beyond detecting small CBD stones. It proves invaluable in cases where patients experience biliary pain despite normal initial imaging results from TUS or CT. Through detailed gallbladder imaging, EUS aids in accurate cholelithiasis diagnosis, guiding appropriate management strategies for such patients [10].



**Fig. 1** Biliary lesions among study patients

**Table 2** EUS findings among studied patients

n = 150	EUS	
	N	%
<b>Gallbladder wall thickness</b>		
Yes	15	10.0
No	135	90.0
<b>Mud and stones</b>		
Yes	73	48.7
No	77	51.3
<b>Pancreatic mass lesions</b>		
Yes	30	20.0
No	120	80.0
<b>Biliary lesions</b>		
Yes	48	32.0
No	102	68.0

In this study, we aimed to evaluate the role of endoscopic ultrasound in gallbladder and biliary system diseases in patients with normal transabdominal ultrasonography. The study included 150 patients; 70 males and 80 females, their ages between 20 and 67 years. The main complaints of the studied patients were right abdominal pain in 117 of 150 patients (78%) and obstructive jaundice in 112 of 150 patients (74.7%).

In our study, EUS revealed gallbladder wall thickening in 15 patients (10%), mud and/or small stones inside the gallbladder in 73 patients (48.7%), positive GB mass, and/or polyp findings in 30 patients (20%), biliary lesions such

as duct strictures and/or dilatations were detected in 48 patients (32%), while transabdominal ultrasound was normal in all those patients.

TUS faces challenges in accurately detecting small gallbladder lesions and microlithiasis. EUS, superior to TUS for imaging the biliary system, offers higher-resolution images using ultrasound frequencies ranging from 5 to 12 MHz. In diagnosing small polypoid lesions (<2 cm), EUS exhibits notably higher diagnostic sensitivity (up to 91.7%) and specificity (up to 87.7%) compared to TUS (sensitivity of 54.2% and specificity of 53.8%). This highlights EUS's diagnostic superiority over TUS for detecting and characterizing small gallbladder lesions [3].

EUS has shown superior performance to the conventional US in identifying choledocholithiasis. EUS demonstrated a sensitivity, specificity, and accuracy of 91%, 100%, and 97%, respectively, while the US showed a lower sensitivity (50%) but similar specificity (100%) and accuracy (83%). Factors such as body habitus and bowel gas interference contribute to the US's reduced sensitivity. Furthermore, EUS displayed a higher positive predictive value (100%) and negative predictive value (95%) compared to the US, which had a positive predictive value of 100% but a lower negative predictive value of 74%. These results underscore EUS's accuracy in detecting common bile duct stones over conventional US [10].

When using endoscopic ultrasonography (EUS), a substantial portion of cases (ranging from 52.4 to 94.2%) with previous negative transabdominal ultrasonography

(TUS) results can reveal gallbladder sludge or microlithiasis. EUS demonstrates high sensitivity (92.6 to 100%) and specificity (55.6 to 91%) in diagnosing gallbladder microlithiasis. These results underline the advanced diagnostic capabilities of EUS in detecting gallbladder sludge and microlithiasis, especially in cases where TUS did not show abnormalities. Notably, EUS's high sensitivity in detecting these conditions highlights its diagnostic value in such scenarios [11].

In a prospective study spanning 2001 to 2003 at a Tehran hospital, 35 patients with biliary-type abdominal pain and normal TUS results were examined. EUS, utilizing a GF UM-20 echoendoscope, was performed for all patients. The study revealed that out of the 35 patients, 33 (approximately 94%) had gallbladder sludge or small stones, indicating a prevalence rate of 34%. Additionally, 21 patients (approximately 60%) were found to have common bile duct (CBD) sludge or microlithiasis. This study underscores the diagnostic importance of EUS in identifying gallbladder and CBD sludge, as well as microlithiasis, in patients with biliary-type abdominal pain despite initially normal TUS findings [12].

In a study by Sugiyama et al., the diagnostic precision of endoscopic ultrasonography (EUS) was compared to that of transabdominal ultrasonography (TAUS) for polypoid gallbladder lesions in a surgical series. The results indicated a higher level of accuracy with EUS, achieving a diagnostic precision of 97%. In contrast, TAUS exhibited a lower accuracy of 76%. This study emphasizes the superior diagnostic ability of EUS over TAUS in characterizing and diagnosing polypoid gallbladder lesions [13].

EUS is an essential imaging tool for assessing gallbladder lesions, especially in distinguishing benign gallbladder wall thickening from gallbladder carcinoma. A distinctive feature is the preservation of gallbladder wall layers in benign thickening, whereas gallbladder carcinoma often involves thickening and the loss of the multi-layer pattern. Fourteen EUS has demonstrated superior capabilities compared to transabdominal ultrasonography (TUS), computed tomography (CT), and magnetic resonance imaging (MRI) in visualizing gallbladder wall layers. Its higher resolution and proximity provide a detailed view of the gallbladder wall, allowing for the identification of subtle layering changes that may indicate malignant transformation. These results underscore the superior diagnostic capacity of EUS in evaluating gallbladder lesions, particularly in distinguishing gallbladder carcinoma from benign gallbladder wall thickening by observing the preservation or loss of gallbladder wall layers [14].

In a prospective multicenter study in the USA involving 36 patients, the efficacy of endoscopic ultrasonography (EUS) in identifying choledocholithiasis was assessed,

comparing it to transabdominal ultrasonography (US). The study showed that EUS had a sensitivity of 91%, a specificity of 100%, and an overall accuracy of 97% in detecting choledocholithiasis. In comparison, the US demonstrated a lower sensitivity of 50% but maintained a specificity of 100% and an accuracy of 83%. The positive predictive value (PPV) and negative predictive value (NPV) for EUS were both reported as 100%, indicating high confidence in their results. For the US, the PPV was 100%, but the NPV was 74%, suggesting a higher likelihood of false-negative results. These findings underscore EUS's superiority over the US in sensitivity, accuracy, and predictive values for detecting choledocholithiasis. EUS serves as a reliable diagnostic tool, providing more accurate and conclusive results compared to transabdominal ultrasonography [15].

Moreover, EUS-FNA (endoscopic ultrasonography-guided fine-needle aspiration) demonstrates high accuracy in diagnosing malignancy in distal biliary strictures, especially for masses in the pancreatic head. A meta-analysis involving 20 studies and 957 patients found EUS-FNA had a sensitivity of 80% and a specificity of 97% for diagnosing malignant biliary strictures. These results indicate that EUS-FNA is valuable in differentiating between benign and malignant biliary strictures. It shows high sensitivity in identifying malignancy and high specificity in ruling it out when absent. EUS-FNA assists in guiding appropriate management decisions, especially for patients with distal biliary strictures and masses in the pancreatic head [5].

While endoscopic ultrasonography (EUS) is highly beneficial in the management of choledocholithiasis, it does have some limitations to consider. One of these is the challenge of visualizing the gallbladder in cases of atypical anatomical positions or patients with altered gastroduodenal anatomy. This difficulty can make it hard to assess the presence of gallstones or sludge based on positional mobility since repositioning the patient during an EUS procedure can be quite complex. Additionally, EUS's limited depth of penetration might hinder a comprehensive assessment of the hilum and right hepatic duct. This can impact the thorough examination of these structures [16].

Furthermore, retropancreatic bile duct imaging becomes more challenging in cases where there are parenchymal alterations like necrosis, fluid collections, fat infiltration, or calcifications. These factors can impede clear visualization of the bile ducts during the procedure. Also, previous endoscopic sphincterotomy can cause air artifacts in the distal bile duct, making it challenging to obtain a clear and adequate view. These limitations should be considered when utilizing EUS for managing choledocholithiasis, and healthcare providers may need

to explore alternative imaging modalities in certain cases to address these challenges [10].

Similarly, the effectiveness of EUS imaging in diagnosing choledocholithiasis can be limited when the EUS transducer cannot pass into the duodenal bulb. This might happen due to conditions such as pyloric stenosis or after a Billroth II anastomosis procedure. In such situations, obstructions or altered anatomical structures could prevent the accurate imaging of the biliary system. Healthcare providers should remain mindful of these limitations and adapt their diagnostic and therapeutic approaches accordingly, exploring alternative options for imaging and intervention when EUS is not feasible or effective [10, 17, 18].

## Conclusion

Our research offers robust evidence supporting the significant role of endoscopic ultrasonography (EUS) in detecting cholelithiasis, choledocholithiasis, and pancreato-biliary lesions in patients with negative transabdominal ultrasonography (TUS) results. We assert that EUS stands as the superior diagnostic method for individuals experiencing biliary-type pain, having normal TUS results, and suspected microlithiasis. The findings suggest that EUS holds promise as a diagnostic tool for patients exhibiting clinical suspicion of cholelithiasis and choledocholithiasis, even in cases where TUS results are normal. EUS exhibits outstanding diagnostic performance in managing gallbladder and biliary system diseases.

However, it is crucial to emphasize the necessity for extensive, long-term, controlled prospective studies to gain a deeper understanding of EUS's role in identifying the pathogenesis, clinical significance, and best treatment strategies for patients with microlithiasis. Our study results overall advocate for EUS's use as a valuable instrument in diagnosing and managing biliary diseases, especially in situations where TUS outcomes are inconclusive or negative. Further exploration will enrich our understanding of the potential benefits and applications of EUS in this particular context.

## Abbreviations

TUS	Transabdominal ultrasound
EUS	Endoscopic ultrasound
CT	Computed tomography
MRI	Magnetic resonance imaging
FNA	Fine-needle aspiration
ER	Emergency room
CRP	C-reactive protein
BMI	Body mass index
INR	International normalized ratio
CBD	Common bile duct
US	Ultrasonography
ERCP	Endoscopic retrograde cholangiopancreatography
NPV	Negative predictive value
EUS-FNA	Endoscopic ultrasonography-guided fine-needle aspiration

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## Authors' contributions

AM was the main endoscopist and did the final review and editing. AN helped in investigations, YM collected the data, AA wrote the manuscript, and YA designed the methodology and helped in writing. All authors read and approved the final manuscript.

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## Availability of data and materials

Not applicable.

## Declarations

### Ethics approval and consent to participate

The study was approved by the institution's ethical committee and review board of Kasr Al Ainy Hospital with the reference number: MS-88-2021. Oral and written informed consents were obtained from the patient or from his eligible relatives.

### Consent for publication

Oral and written informed consents were obtained from the patients or from their eligible relatives.

### Competing interests

The authors declare that they have no competing interests.

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