ORIGINAL ARTICLE

Diagnostic Accuracy of Emergency Sonographic Signs in Patients with Suspected Acute Cholecystitis Keeping Histopathology as Gold Standard

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ABSTRACT

Background: Acute cholecystitis is the most frequent illnesses that necessitate surgical procedures in an emergency. Research indicates that performing cholecystectomy at an early stage leads to improved results, reduced hospital stays, and lower healthcare expenses. Early diagnosis is crucial during the presentation of a patient in the emergency ward and can be achieved by a precise clinical examination and the use of suitable diagnostic procedures. Ultrasound is regarded as the ideal initial imaging approach for individuals suspected of acute cholecystitis clinically.

Objective: To examine the diagnostic precision of emergency sonographic signs in patients with suspected acute cholecystitis, while considering histopathology as the gold standard.

Methods: A cross-sectional study at the selected hospital of Karachi conducted over one year, on 103 patients who met the diagnostic criteria. Mean and standard deviation for continuous data and frequencies with percentages were calculated for categorical data. Sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy were measured. A p-value of ≤0.05 is significant.

Results: 47 (45.6%) were male and 56 (54.4%) were female. The mean age was 47.47 (8.57) years and the duration of symptoms was 7.19 (2.14) hours. Out of 103 patients, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of emergency sonographic signs for the diagnosis of acute cholecystitis by keeping histopathology as the gold standard was 81.1%, 88.2%, 93.3%, 69.7%, and 83.4% respectively.

Conclusion: Emergency sonographic findings are effective in the identification and diagnosis of acute cholecystitis. The histopathological diagnosis correlated well with the ultrasound diagnosis of acute cholecystitis. This methodology will enhance the quality of medical care and increase patient safety.

Keywords: Acute cholecystitis, emergency sonographic signs, ultrasound, histopathology, right hypochondrial pain.

INTRODUCTION

Acute abdominal pain is a frequent reason for presentation in emergency departments with incidence reaching up to 10% [1-2]. Acute cholecystitis, is the most common cause attributable to acute abdominal pain, with a prevalence of 90% [2]. It is the second most common histopathological diagnosis from all the gall bladder specimens received in Pakistan [3].

Patients with symptomatic gallstones might develop acute cholecystitis, which is a consequence of gallstone disease. The condition known as cholecystitis is an inflammation of the gallbladder that can occur suddenly in people who have gallstones (acute calculous cholecystitis), occur without gallstones (acalculous cholecystitis), or develop gradually and be detected histologically after cholecystectomy [4, 5].

Clinical signs of acute cholecystitis include anorexia, abdominal guarding, fever, positive Murphy's sign, leukocytosis, prolonged and constant severe right upper quadrant or epigastric discomfort, and pain radiating to the right shoulder or back. The first sign of pain is frequently experienced after eating fatty meals an hour or more [6-8].

Ultrasound has emerged as the first line of investigation in the diagnosis of acute cholecystitis. It is rapid, available, accurate, and cost-effective. It also has the advantage of providing real-time imaging and is non-invasive and non-ionizing [8].

The diagnosis cannot be established based solely on the data from history, physical examination, and laboratory tests. Patients exhibiting clinical symptoms indicative of acute cholecystitis should undergo abdominal imaging to verify the diagnosis. To confirm the diagnosis, it is necessary to show evidence of thickening or swelling of the gallbladder wall, the presence of a sonographic Murphy's sign, or the inability of the gallbladder to fill during cholescintigraphy. Nuclear cholescintigraphy is a valuable tool when the diagnosis remains ambiguous even after ultrasonography. Patients suffering from acute cholecystitis often exhibit a positive "Murphy's sign".

Ultrasonography is typically the initial diagnostic test and frequently confirms the diagnosis. The sonographic characteristics consist of gallbladder wall thickening (measuring more than 3 mm) or edema (also known as the double wall sign) [9, 10].

Multiple studies have assessed the precision of ultrasonography in diagnosing acute cholecystitis. A review briefed the findings of 30 trials on the use of ultrasonography in detecting gallstones and acute cholecystitis. The sensitivity and specificity for diagnosing acute cholecystitis were adjusted to 88% (95% CI 0.74 to 1.00) and 80% (95% CI 0.62 to 0.98), respectively [6, 11].

The ultrasonography has a sensitivity of approximately 84% (95% CI 0.76 to 0.92) and a specificity of 99% (95% CI 0.97 to 1.00) for detecting gallstones. Ultrasonography is the primary imaging technique used to diagnose and evaluate the biliary system. It is generally accessible, safe, harmless, and cost-effective. This technique enables a thorough and immediate examination of the gallbladder, as well as the assessment of additional observations that aid in reaching a definitive diagnosis. As a result, it helps prevent unnecessary cholecystectomies and the associated difficulties [12, 13].

Radiological investigations are employed for diagnosing acute cholecystitis and also assist in decision-making for appropriate management. Ultrasonography is among the common ones with different diagnostic accuracies [13].

Despite the wide availability and use of ultrasound in cases of suspected acute cholecystitis, the accuracy of different ultrasound findings remains questionable. Therefore, it is essential to examine the diagnostic accuracy of the common sonographic findings in patients who present to the ultrasound department with suspected acute cholecystitis [14].

The utilization of hepatobiliary iminodiacetic acid (HIDA) was limited, but it provided an exact diagnosis in the only patient who experienced this procedure. Considering the evidence in the literature, HIDA should be used more frequently in cases where there is uncertainty in diagnosis. It has been suggested that HIDA has a higher sensitivity than ultrasonography equally for calculus cholecystitis and acalculous cholecystitis [15].

Adverse results were associated with increased gallbladder wall thickness and postponed surgical intervention. The study revealed that a wall thickness of 5 mm or greater was linked to acute cholecystitis, necrosis, and prolonged surgical duration. However, the rates of conversions, complications, and extent of hospital visits were comparable. Individuals aged 70 years or older exhibited a notable rise in both complications and hospitalization duration. Ultrasonography is the preferred approach for examining the gallbladder, as it has a high

sensitivity for detecting thickening of the gallbladder wall but does not indicate acute cholecystitis. It is crucial to establish a link between sonographic, clinical, laboratory, and epidemiological findings to prevent unnecessary cholecystectomies [16, 17].

Babak Schekarchi *et al.* described sensitivity, specificity, PPV, and NPV as cholelithiasis to be 92.7%, 97.1%, 88.8% and 98.1%, PCFF to be 68.2%, 97.8%, 98.1% and 97.8%, GBWT to be 75.0%, 97.3%, 80.5%, and 96.3% and wall edema to be 40.0%, 97.5%, 33.3%, and 98.2% respectively [13].

After a thorough literature search, no local data about the diagnostic accuracy of emergency sonographic signs was found to be available. Moreover, international data does not apply to our local population because of delayed presentation, due to cost issues and lack of diagnostic facilities. The objective was to investigate the diagnostic accuracy of emergency sonographic signs in suspected patients with acute cholecystitis considering histopathology as the gold standard.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Radiology department at PNS Shifa Naval Hospital, Karachi, over six months from 08-01-19 till 08-07-19. The sample size was calculated by taking, a sensitivity of 84%, and specificity of 49% [18]. The margin of error d=7.5% for sensitivity and 7.5% for specificity, confidence interval 95% and Prevalence 90% [2]. The estimated sample size was 103 patients.

The study was conducted after approval by the hospital ethical review board ERB. The subjects were recruited by a non-probability consecutive sampling technique after giving informed consent and presenting in the emergency department. Participants were enrolled based on the inclusion criteria: patients referred from the emergency department for an ultrasound abdomen with suspected acute cholecystitis, patients with ultrasound findings of wall thickening or stone in the gall bladder, and an age range between 18-60 years. Patients were excluded who were diagnosed with carcinoma of the gall bladder or a history of cholecystectomy. Each patient presenting with suspected acute cholecystitis underwent a sonographic scan of the abdomen on Toshiba Xario 100 Platinum machine by a trained sonographer having undergone at least 6 months of supervised training. The right hypochondriac region was specifically assessed for the presence of emergency sonographic signs of acute cholecystitis. The patients were then diagnosed sonographically with acute cholecystitis and subsequently underwent cholecystectomy and were followed for histopathological confirmation. The data sets were used to calculate the diagnostic accuracy of emergency sonographic signs for acute cholecystitis. Demographic data such as age and gender of patients were recorded on proforma.

Table 1: Descriptive statistics.

Variables	Mean (Standard Deviation)
Age (Years)	47.47 (8.57)
Duration of Symptoms (Hours)	7.19 (2.14)
Variables	Frequency (%)
Age groups	
18-40years	31 (30.1)
41-60 years	72 (69.9)
Gender	
Male	47(45.63)
Female	56(54.37)
Duration of Symptoms	
≤ 1 hour	24(23.3)
>1 hour	79(76.7)
Acute Cholecystitis Confirmed by Histopathology	
Had acute cholecystitis	69 (67)
Did not have acute cholecystitis	34 (33)
Acute Cholecystitis Confirmed by Emergency Sonographic Signs	
Had acute cholecystitis	60 (58.3)
Did not have acute cholecystitis	43 (41.7)

*Mean (± Standard Deviation).

The data was analyzed using the statistical software SPSS version 22. Descriptive statistics were computed for variables of both qualitative and quantitative nature. Qualitative variables include gender, duration of symptoms, sonographic signs, and histopathological findings.

The presentation included the mean and standard deviation for quantitative factors such as age. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. Stratification was used to account for effect modifiers such as age and gender. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using a post-stratification 2 x 2 table.

RESULTS

The ages of the 103 patients ranged from a minimum of 25 years to a maximum of 60 years. The average age in our sample was 47.47 years, with a standard deviation of 8.57. The mean duration of symptoms was 7.19 (2.14) hours, as seen in Table **1**.

The frequency distribution of age, gender, symptom duration, and acute cholecystitis confirmed by histopathology & by emergency sonographic signs are present in Table **1**.

Out of 103 patients, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of emergency sonographic signs for the diagnosis of acute cholecystitis by keeping histopathology as the gold standard was found to be 81.1%, 88.2%, 93.3%, 69.7%, and 83.4% respectively as shown in Table **2**.

Table 2: Diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of emergency sonographic signs for the diagnosis of acute cholecystitis by keeping histopathology as the gold standard.

Diagnostic Accuracy Parameters	Formula	Percentage (%)
Sensitivity	TP/TP+FN x 100	81.1
Specificity	TN/TN+FP x 100	88.2
Positive Predictive Value	TP/TP+FP x 100	93.3
Negative Predictive Value	TN/FN+TN x 100	69.7

The stratification of age in the 18-40-year age group revealed the following percentages for sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of emergency sonographic signs in diagnosing acute cholecystitis using histopathology as the gold standard: 78.5%, 88.2%, 84.6%, 83.3%, and 83.8% respectively. Furthermore, the percentages for the age range 41-60 years were determined to be 81.8%, 88.2%, 95.7%, 60%, and 83.3% accordingly, as stated in Table **3**.

The gender-based analysis of emergency sonographic signs for diagnosing acute cholecystitis, using histopathology as the gold standard, showed the following results in the male group: sensitivity - 81.8%, specificity - 85.7%, positive predictive value - 93.1%, negative

Table 3: Diagnostic accuracy of emergency sonographic signs for the diagnosis of acute cholecystitis by taking histopathology as the gold standard stratified by age, gender, and duration of symptoms.

Variables	Emergency Sonographic Sign	Histopathology Positive	Histopathology Negative	Total	Diagnostic accuracy	
Age (Years)						
18-40	POSITIVE	11(TP)	02(FP)	13	SEN	78.5%
	NEGATIVE	03(FN)	15(TN)	18	SPE	88.2%
	Total	14	17	31	PPV	84.6%
					NPV	83.3%
					DA	83.8%
41-60	POSITIVE	45(TP)	02(FP)	47	SEN	81.8%
	NEGATIVE	10(FN)	15(TN)	25	SPE	88.2%
	Total	55	17	72	PPV	95.7%
					NPV	60%
					DA	83.3%
Gender						
MALE	POSITIVE	27(TP)	02(FP)	29	SEN	81.8%
	NEGATIVE	06(FN)	12(TN)	18	SPE	85.7%
	Total	33	14	47	PPV	93.1%
					NPV	66.6%
					DA	82.9%
FEMALE	POSITIVE	29(TP)	02(FP)	31	SEN	80.5%
	NEGATIVE	07(FN)	18(TN)	25	SPE	90.0%
	Total	36	20	56	PPV	93.5%
					NPV	72.0%
					DA	83.9%
DURATION OF SYMPTOMS (HOUR)						
≤ 1 hour	POSITIVE	04(TP)	02(FP)	06	SEN	57.1%
	NEGATIVE	03(FN)	15(TN)	18	SPE	88.2%
	Total	07	17	24	PPV	66.6%
					NPV	83.3%
					DA	79.1%
> 1 hour	POSITIVE	52(TP)	02(FP)	54	SEN	83.8%
	NEGATIVE	10(FN)	15(TN)	25	SPE	88.2%
	Total	62	17	79	PPV	96.2%
					NPV	60.1%
					DA	84.8%

predictive value - 66.6%, and diagnostic accuracy - 82.9%. Furthermore, the percentage of females in the group was determined to be 80.5%, 90%, 93.5%, 72%, and 83.9% accordingly as shown in Table **3**.

The stratification analysis of symptom duration in the ≤ 1-hour group revealed the values for sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of emergency sonographic signs for diagnosing acute cholecystitis using histopathology as the gold standard: 57.1%, 88.2%, 66.6%, 83.3%, and 70.1% respectively. Furthermore, the percentages for the > 1-hour group were determined to be 83.8%, 88.2%, 96.2%, 60.1%, and 84.8% correspondingly (**Table 3**).

DISCUSSION

Approximately 9% of admissions to the hospital for acute abdominal pain are attributed to acute cholecystitis [17, 18]. Acute cholecystitis is a disorder characterized by inflammation of the gallbladder [19-22]. In 95% of cases, this inflammation is caused by a blockage in the gallbladder neck or cystic duct, usually due to a gallstone [23]. Sonographic data, including the detection of stones, gallbladder distention, wall thickness, and, are often utilized to diagnose cholecystitis due to the inconsistent nature of its clinical presentation [22-24].

Our study showed that the mean age and duration of symptoms in our study were 47.47(8.57) years and 7.19 (2.14) hours. Males were 47 (45.6%) and females were 56 (54.4%). Out of 103 patients, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of emergency sonographic signs for the diagnosis of acute cholecystitis by keeping histopathology as the gold standard was found to be 81.1%, 88.2%, 93.3%, 69.7%, and 83.4% respectively.

Shekarchi *et al.* study examined ED patients with RUQ pain for acute cholecystitis. The study included 342 patients (63.2% female) with a mean age of 53.92 (20-83 years). Based on ED and radiology reports, 53 (15.50%) and 48 (14.00%) patients had acute cholecystitis sonograms (Kappa = 0.826). Bedside sonography had sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of 89.58 (95%CI: 76.55-96.10), 96.59 (95%CI: 93.63-98.29), 81.13, 98.26, 4.30, and 0.017 [17].

Another study included a total of 291 cases. 120 individuals had a nonbiliary diagnosis, 114 had cholelithiasis only (39%), and 57 patients total had AC (20%). Of the 57 patients who were diagnosed with AC, 46 had post-cholecystectomy confirmatory pathology, five had post-cholecystectomy bile cultures, three had post-endoscopic retrograde cholangiopancreatography confirmatory cultures, and three had confirmation by hepatobiliary iminodiacetic acid scan. Within a month of being released from the ED, no patients had an AC diagnosis. The study sensitivity, specificity, PPV, and NPV for cholelithiasis to be 84%, 49%, 29%, and 93%, sludge to be 23%, 91%, 38% and 83%, pericholecystic fluid (PCCF) to be 23%, 98%, 72% and 84% and gall bladder wall thickening (GBWT)> 3 mm to be 54%, 92%, 63% and 89% respectively [18].

Hwang *et al.* included 107 patients who needed an urgent cholecystectomy; 83 of them received ultrasonography. For ultrasonography, there was 92% inter-radiologist agreement. Ultrasonography exhibited 100% sensitivity, 18% specificity, 81% positive predictive value (PPV), and 100% negative predictive value (NPV) for the diagnosis of cholelithiasis. On histology, all patients showed chronic cholecystitis, and 67% of them had acute cholecystitis. An ultrasound indicating cholelithiasis or acute cholecystitis produced a sensitivity of 74%, specificity of 62%, PPV of 80%, and NPV of 53% for the diagnosis of acute cholecystitis when paired with a positive Murphy sign and an increased neutrophil count [19].

189 participants who received bedside ultrasonography were part of a different prospective evaluation. The test's sensitivity was 87% (95% confidence interval [CI] 66% to 97%), specificity was 82% (95% CI 74% to 88%), positive likelihood ratio was 4.7 (95% CI 3.2 to 6.9), negative likelihood ratio was 0.16 (95% CI 0.06 to 0.46), positive predictive value was 44% (95% CI 29% to 59%), and negative predictive value was 97% (95% CI 93% to 99%). Radiology ultrasonography test characteristics included sensitivity of 83% (95% CI 61% to 95%), specificity of 86% (95% CI 77% to 92%), positive likelihood ratio of 5.7 (95% CI 3.3 to 9.8), negative likelihood ratio of 0.20 (95% CI 0.08 to 0.50), positive predictive value of 59% (95% CI 41% to 76%), and negative predictive value of 95% (95% CI 88% to 99%) [20].

The study evaluated emergency department referrals and only a small section of patients that attended ER were analyzed, representing a selection bias, limited to a group of patients, potentially impacting the generalizability of the results.

CONCLUSION

Emergency sonographic findings are effective due to high specificity in the identification and diagnosis of acute cholecystitis. The histopathological diagnosis of the present study correlated well with the ultrasound diagnosis of acute cholecystitis. This approach will contribute to improvement in patient care and enhance patient safety.

FUTURE RECOMMENDATIONS

This study would develop better insight into the topic on a local and regional level and would also provide necessary data that could be used in the future as a reference to better understand and utilize emergency sonographic signs in the context of suspected acute cholecystitis.

LIST OF ABBREVIATIONS

AC   Acute Cholecystitis
GBCA Gall Bladder Carcinoma
ERCP Endoscopic Retrograde Cholangiopancreatography
MRCP Magnetic Resonance Cholangiopancreatography
CT   Computed Tomography
MRI   Magnetic Resonance Imaging
US   Ultrasonography
SPSS   Statistical Package for the Social Sciences
PPV   Positive Predictive Value
NPV   Negative Predictive Value

ETHICAL APPROVAL

Ethical approval of the study has been granted by the hospital's ethical review board ERB. All procedures performed in studies involving human participants were following the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

An informed consent form was signed by the patients presenting in the emergency department.

AVAILABILITY OF DATA

The data set will be available from the corresponding authors upon a reasonable request.

FUNDING

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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AUTHORS' CONTRIBUTION

MSN guarantor of integrity of the entire study. MSN and MA generate study concepts and design. NS did literature research, and ST collected data. NS and MA analyze the data. MSN and NS prepared a manuscript. The manuscript was critically reviewed and revised by MA, NS & ST. All authors have read and approved the manuscript.

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