CORRELATION OF GALL BLADDER WALL THICKENING ON ULTRASOUND WITH LIVER FUNCTION TESTS IN PATIENTS OF ACUTE HEPATITIS

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Abstract

Background: Gallbladder wall thickening (GWT) is detected via sonography in various pathological conditions, including acute hepatitis (AH). This study explores the correlation between GWT and liver function test (LFT) parameters in patients of AH. Methods: A cross-sectional study was done from May 2022 to November 2023 involving 67 patients diagnosed with AH. Patients with chronic hepatitis, recurrent hepatitis, or pre-existing gallbladder disease were excluded. GWT was measured using ultrasound, and its correlation with LFT parameters (AST, ALT, total bilirubin, albumin, and ALP) was analyzed using the Karl Pearson coefficient and statistical significance was determined (p<0.05). **Results:**Gallbladder wall thickeningwas noted with a mean thickness of 8 ± 2 mm. Positive correlation was found between anterior GWT and AST (r=0.9) and ALT (r=0.8), both statistically significant (p<0.0001). The anterior-to-posterior GWT ratio also showed a positive correlation with AST (r=0.3, p=0.002) but not with ALT. No significant correlations were found between GWT and direct bilirubin, albumin, or ALP. Discussion and Conclusion: GWT in AH patients is strongly correlated with elevated AST and ALT levels, suggesting that GWT measurement can reflect liver function status in these patients. The ratio of anterior-to-posterior GWT may provide additional insights into liver function. However, the findings are limited by the study's cross-sectional design, sample size, and population specificity. Further research with larger cohorts is recommended to validate these findings and elucidate underlying mechanisms.

INTRODUCTION

Gallbladder wall thickening (GWT) is identified by Sonography in a variety of pathologic circumstances as well as during the Gall Bladder's normal contraction following a meal with highest limit of normal Gall Bladder (GB) thickening being 3 mm by sonography. ⁽¹⁾

Gallbladder wall thickening is a observation that can also be result of secondary inflammatory reaction from other structures including the liver or pancreas, even though it is frequently a defining feature of acute cholecystitis^{[1].} Acute hepatitis (AH) is commonly associated with GWT and GB contraction⁽²⁾.

Various etiologies of acute hepatitis are infectious (hepatotropic viruses, bacteria, fungi), toxins, inflammatory (autoimmune, biliary) and metabolic (non alcoholic liver disease, hemochromatosis)^(3,4).

Reports state that GWT is an inflammatory response to liver parenchymal necrosis and inflammation, which causes hyperemia in the muscle and serosal layers around the liver.⁽²⁾ Few theories have been put up to explain the process underlying the thickening of the gall bladder wall in acute hepatitis patients. Hepatocyte damage may be the source of transient reductions in bile excretion and production.

According to the second theory, the hepatitis virus present in bile fluid directly damages and inflames the GB's muscle and mucosal layers. ^{[5-7].}

In previous reports, ^[11-14] the incidence of gall bladder wall thickeningin acute hepatitis patients was 51–90%. There was a correlation between hepatitis A virus infection, female gender, and an increased total bilirubin level, and the incidence of gall bladder wall thickening in acute hepatitis patients was 63%.^[15] It isfound that patients with raised serum AST or ALT levels are more likely to have gall bladder wall thickening. ^[6,16] On the contrary, other investigators did not find an association between gall bladder wall thickening and the serum AST or ALT level. ^[11,16]

In the absence of any other known etiologic factor, gallbladder wall thickening may be linked to significantly lower serum albumin levels.^[1] There was a correlation between the degree of gall bladder wall thickening and the PT and ALT level laboratory results.. ^[17] A study by Okanobu et al. confirms that anterior wall thickness is a more sensitive and specific indicator of gallbladder wall thickening, which is crucial in the context of various hepatic and systemic conditions, including acute hepatitis ⁽¹⁸⁾In this study, we analyzed the liver function test parameters with GWT in patients of Acute hepatitis.

MATERIALS AND METHODS

From May 2022 to November 2023, we did a cross-sectional evaluation of 67 patients for 18 months who were diagnosed with AH based on biochemical and symptomatic features of acute hepatitis.

Abdominal ultrasonography was performed in the department of Radiology in Sharda hospital. Informed written consent was taken from each patient after getting approval from ethics committee. Patients below age of 18 years, chronic hepatitis, recurrent hepatitis and patients with existing gall bladder disease were excluded. Only those patients of acute hepatitis who had thickened gall bladder wall were included in the study.

All patients underwent grey-scale real time ultrasonography using Philips Epiq 7G and Samsung Ace R 7 Ultrasound machine with curvilinear 2 to 7 MHz probe who were in fasting state of 12 hours. Patients who had their Liver function tests done within 12 hours of scan were included in the study. The gall bladder was visualized in three views (Epigastric, subcostal and coronal).

The gall bladder wall thickness was measured along the perpendicular to the long axis of gall bladder at the place of maximum anterior wall thickness. Posterior gall bladder wall was also measured along this line. Gall bladder wall thickness was compared in tabular format with different liver function test parameters.

STATISTICAL ANALYSIS

All the data obtained has been analyzed statistically using Microsoft excel, Statistical Package for Social Sciences (SPSS) software ver. 21.0. Categorical variables are expressed in number and percentages (%). Receiver operating characteristic curve (ROC) analysis is performed to find out cut off points. Karl Pearson coefficient of correlation is used for analysis of this study.Statistical Analysis is used to describe the findings of study.

RESULTS

The mean gall bladder wall thickening was 8 ± 2.6 mm. This study included 67 participants, of those, we found that there was a male preponderance(51%). Anterior gall bladder wall showed positive correlation with AST (Karlpearson coefficient 0.9) (Fig 1, table 1), and ALT (Karl pearson coefficient 0.8) (fig 2, table 1). They showed statistical significant p values less than 0.05 (0.0001).

There was negative correlation of anterior gall bladder wall with direct bilirubin, albumin and ALP, however none of them were stastistically significant. The ratio of anterior and posterior gall bladder shows positive correlation (Karlpearson coefficient 0.3) with AST and with ALT (Karl pearson coefficient 0.2). AST showed statistical significant p value less than 0.05 (0.002), however p value was not significant for ALT.

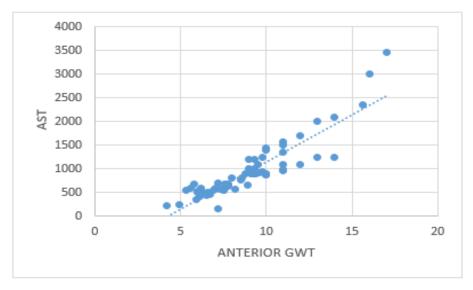


Figure 1: Scatter diagram showing linear positive correlation between anterior								
gall bladder wall and AST								

Table 1: karl Pearson coefficient and p values between gall bladder wall and								
various liver function test parameters								

		ANTERIOR GB WALL THICKNESS	POST GB WALL THICKNESS	A/P	AST	ALT	direct Bilirubin	total Bilirubin	Albumin	ALP
ANTERIOR GB WALL THICKNESS	Karl Pearson Correlation	1	0.598**	.368**	0.900**	.841**	-0.142	-0.158	-0.101	-0.039
	Sig. (2-tailed)		0.000	0.002	0.000	0.000	0.250	.202	0.416	0.752
	Ν	67	67	67	67	67	67	67	67	67
POST GB WALL	Karl Pearson Correlation	.598**	1	-0.475**	0.480**	0.541**	-0.096	-0.092	-0.009	-0.108
	Sig. (2-tailed)	0.000		0.000	0.000	0.000	0.439	0.459	0.940	0.385
THICKNESS	Ν	67	67	67	67	67	67	67	67	67
	Karl Pearson Correlation	0.368**	-0.475**	1	0.365**	0.279*	-0.091	-0.098	-0.138	0.086
A/P	Sig. (2-tailed)	0.002	0.000		0.002	0.022	0.465	0.432	0.266	0.491
	Ν	67	67	67	67	67	67	67	67	67

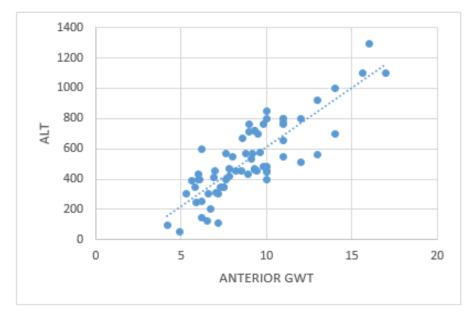


Figure 2: Scatter diagram showing linear positive correlation between anterior gall bladder wall and ALT



Figure 3: The ultrasound image of a patient with acute hepatitis(AST- 890 , ALT - 567) showing thickenedwall of gall bladder (the anterior gall bladder measures9.1 mm and Posterior wall measures 6.8mm)



Figure 4: The ultrasound image of another patient with acute hepatitis (AST -697 and AST - 390) showing thickenedwall of gall bladder (the anterior gall bladder measures7.4 mm and Posterior wall measures 6.1mm)

DISCUSSION

The primary aim of this particular study was to investigate the correlation between gallbladder wall thickening on ultrasound and liver function test parameters like AST, ALT, ALP, Total Bilirubin and Albumin focusing on patients diagnosed with acute hepatitis. The primary objective was to assess the correlation of anterior gallbladder wall thickness and the ratio of anterior gallbladder to posterior gallbladder wall thickness with liver function test parameters in this patient population. In previous reports, ⁽¹¹⁻¹⁴⁾ gall bladder wall thickening had the incidence of 51–90% in patients with acute hepatitis. The analysis of anterior gallbladder wall thickness revealed strong positive correlations with liver function test parameters like AST and ALT as seen in the study by Kim et al ⁽¹⁰⁾, where the correlations were statistically significant with the liver function test parameters. However, few researchers could not find a connection between GWT and the levels of AST, ALP, total bilirubin or ALT in the serum⁽²⁷⁾. Patients with an ALT and AST levels showing significantly higher values (normal AST values: 8-48 U/L, normal ALT values: 7-55 U/L) (28) had a substantially greater GWT than other patients in our study. In the Karl Pearson coefficient analysis, these relationships showed statistically significant results (p< 0.05). Similar results were also seen in the study conducted by Juttner et al.⁽⁶⁾ The study by Fiske et al ⁽¹⁾ found that patients with hypoalbuminemia frequently exhibited thickened gallbladder walls. However, our study did not find any statistically significant correlation.

Reports state that GWT is an inflammatory response to liver parenchymal necrosis and inflammation, which causes hyperemia in the muscle and serosal layers around the liver.⁽²⁾ Few theories have been put up to explain the process underlying the thickening of the gall bladder wall in acute hepatitis patients. Hepatocyte damage may be the source of transient reductions in bile excretion and production. According to the second theory, the hepatitis virus present in bile fluid directly damages and inflames the GB's muscle and mucosal layers. ^[5-7] The proposed mechanism suggests that

hypoalbuminemia leads to increased capillary permeability and subsequent interstitial edema, resulting in gallbladder wall thickening. Serum albumin plays a crucial role in maintaining oncotic pressure, and its deficiency can lead to fluid shifts and edema. ⁽¹⁾

The analysis of ratio of anterior and posterior gallbladder wall thickness revealed strong positive correlations with liver function test parameters like AST and ALT. Although, there is no prior information regarding comparison of ratio of anterior and posterior gall bladder wall thickness with LFT parameters in acute hepatitis patients. Our study implies that the ratio of anterior to posterior gallbladder wall thickness may also provide substantial additional information regarding liver function in patients with acute hepatitis. The strong correlations observed between gallbladder wall thickness and liver function test parameters (AST and ALT) have implications for clinical practice. While gallbladder wall thickening on ultrasound is often considered indicative of gallbladder pathology, its association with liver function abnormalities in the context of acute hepatitis appears limited. Clinicians should interpret gallbladder wall thickness measurements cautiously and consider additional diagnostic modalities to evaluate liver function comprehensively in patients of acute hepatitis. Several limitations of the study needs to be acknowledged. The cross-sectional nature of the study and the reliance on correlational data preclude establishing causality or elucidating underlying mechanisms. Additionally, the study population consisted solely of patients with acute hepatitis, limiting the generalizability of the findings to other patient populations or liver conditions. There was limited sample size which could have affected the results of the study. Future research could include prospective studies with larger, more diverse patient cohorts to validate the findings of this study and explore potential mechanisms underlying the observed correlations.

CONCLUSION

Gallbladder wall thickening in AH patients is strongly correlated with elevated AST and ALT levels(p<0.05), suggesting that GWT measurement can reflect liver function status in these patients. The ratio of anterior-to-posterior GWT may provide additional insights into liver function.

Bibliography

- 1) Fiske CE, Laing FC, Brown TW. Ultrasonographic evidence of gallbladder wall thickening in association with hypoalbuminemia. Radiology. 1980;135(3):713-716. PMID: 7384460. DOI: 10.1148/radiology.135.3.7384460.
- Engel JM, Deitch EA, Sikkema W. Gallbladder wall thickness: sonographic accuracy and relation to disease. AJR Am J Roentgenol. 1980;134(5):907-909. PMID: 6768264. DOI: 10.2214/ajr.134.5.907.
- Kwong S, Meyerson C, Zheng W, Kassardjian A, Stanzione N, Zhang K, Wang HL. Acute hepatitis and acute liver failure: Pathologic diagnosis and differential diagnosis. Semin DiagnPathol. 2019 Nov;36(6):404-414. PubMed.
- 4) Stravitz RT, Lee WM. Acute liver failure. Lancet. 2019 Sep 07;394(10201):869-881. PubMed.
- 5) Montrief T, Koyfman A, Long B. Acute liver failure: A review for emergency physicians. Am J Emerg Med. 2019 Feb;37(2):329-337. PubMed.
- 6) Rails PW, Quinn MF, Juttner HU, Halls JM, Boswell WD. Gallbladder Wall Thickening: Patients without Intrinsic Gallbladder Disease. AJR. 1981 Jul;137:65-68.
- 7) Kim MY, Baik SK, Choi YJ, et al. Endoscopic sonographic evaluation of the thickened gallbladder wall in patients with acute hepatitis. J Clin Ultrasound. 2003;31:245.

- 8) Maudgal DP, Wansbrough-Jones MH, Joseph AE. Gallbladder abnormalities in acute infectious hepatitis. A prospective study. Dig Dis Sci. 1984;29:257.
- 9) Han KS, Choi GB, Chang IJ, et al. Thickening of the gallbladder wall in acute viral hepatitis; ultrasound consideration. Korean J Med. 1985;28:823.
- 10) Kim MY, Baik SK, Choi YJ, Park DH, Kim HS, Lee DK, Kwon SO. Endoscopic sonographic evaluation of the thickened gallbladder wall in patients with acute hepatitis. J Clin Ultrasound. 2003;31(5):245–249. DOI: 10.1002/jcu.10167.
- 11) Wegener M, Borsch G, Schneider J, et al. Gallbladder wall thickening: a frequent finding in various nonbiliary disorders–a prospective ultrasonographic study. J Clin Ultrasound. 1987;15:307.
- 12) Park YW, Choi JS, Ahn JH, et al. Ultrasonographic measurement of the thickness of gallbladder wall in patients with acute hepatitis. Korean J Gastroenterol. 1988;20:608.
- 13) Giorgio A, Francica G, Amoroso P, et al. Morphologic and motility changes of the gallbladder in response to acute liver injury. A prospective real-time sonographic study in 255 patients with acute viral hepatitis. J Ultrasound Med. 1989;8:499.
- 14) Zimmerman HJ. Intrahepatic cholestasis. Arch Intern Med. 1979;139:1038-1045.
- 15) Siegers CP, Schutt A. Dose-dependent biliary and renal excretion of paracetamol in the rat. Pharmacology. 1979;18:175-179.
- 16) Ferin P, Lerner RM. Contracted gallbladder: a finding in hepatic dysfunction. Radiology. 1985;154:769-770.
- Ahn JH, Chung JJ, Yu JS, Kim JH, Cho ES, Kim DJ. Prognostic value of gallbladder wall thickening in patients with acute hepatitis A. Ultrasonography. 2015;34(2):139–143. DOI: 10.14366/usg.14052.
- Okanobu H, Matsuo Y, Okamura S, Hirakata H, Konishi J. Measurement of Anterior Gallbladder Wall Thickness: Its Role in Assessing Gallbladder Wall Thickening in Hepatic Diseases. J Ultrasound Med. 2008;27(4):543-550.
- 19) Lichtenstein D, Mezière G, Biderman P, Gepner A, Barré O. The Comet-tail Artifact: An Ultrasound Sign of Alveolar-interstitial Syndrome. Am J Respir Crit Care Med. 2009;180(5):417-423.
- Gupta P, Marodia Y, Bansal A, Kalra N, Kumar-M P, Sharma V, Dutta U, Sandhu MS. Imagingbased algorithmic approach to gallbladder wall thickening. World J Gastroenterol. 2020;26(40):6163. DOI: 10.3748/wjg.v26.i40.6163.
- Wheeler MH, Powell EA, Osman M. Rapid resolution of extreme gallbladder wall thickening in a patient with acute hepatitis C. Radiol Case Rep. 2018;13(2):324–327. DOI: 10.1016/j.radcr.2017.11.013.
- 22) Suk KT, Kim CH. Gallbladder Wall Thickening in Patients with Acute Hepatitis. J Clin Ultrasound. 2009;37:144–148. DOI: 10.1002/jcu.20542.
- 23) Shin JH, Lee JH, Kim CJ, et al. Ultrasonographic Findings and Their Clinical Implications in Patients with Acute Hepatitis. BMC Gastroenterol. 2007.
- 24) Portincasa P, Moschetta A, Di Ciaula A, et al. Changes of gallbladder and gastric dynamics in patients with acute hepatitis A. Eur J Clin Invest. 2001;31(7):617-622.
- 25) Dogra R, Singh J, Sharma MP. Enterically transmitted non-A, non-B hepatitis mimicking acute cholecystitis. Am J Gastroenterol. 1995;90(5):764–766.
- 26) Maudgal DP, Wansbrough-Jones MH, Joseph AE. Gallbladder abnormalities in acute infectious hepatitis. A prospective study. 1984;29(3):257–60.
- 27) Han KS, Choi GB, Chang IJ, et al. Thickening of the gallbladder wall in acute viral hepatitis; ultrasound consideration. Korean J Med 1985;28:823.
- 28) McPherson, R. A., & Pincus, M. R. (2017). Henry's Clinical Diagnosis and Management by Laboratory Methods (23rd ed.). Elsevier.