

# Differentiation of Benign from Malignant Induced Ascites by Measuring Gallbladder Wall Thickness

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*I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work.*

## ABSTRACT

**Introduction:** There are multiple causes for ascites and conventional diagnostic method for most of them is paracentesis. This method is invasive and time consuming. The aim of this study is to survey the reliability of measuring gallbladder wall thickness to discriminate between cirrhotic and malignant ascites.

**Materials and Methods:** In our study we measured the gallbladder wall thickness by ultrasonography in 100 consecutive patients with portal hypertension induced ascites and in 100 consecutive patients with peritoneal carcinomatosis induced ascites.

**Results:** The mean Gallbladder wall thickness was  $3.94 \pm 0.69$  mm in cirrhotic patients and  $2.26 \pm 0.62$  mm in patients with peritoneal carcinomatosis. Gallbladder wall thickening in cirrhotic patients was significantly more compared to patients with peritoneal carcinomatosis ( $p$ -value=0.001).

**Conclusion:** This study shows that the thickened gallbladder wall in patients with ascites is highly predictive for diagnosis of portal hypertension induced ascites.

**Keywords:** Gallbladder wall thickness (GBWT), ultrasonography, peritoneal carcinomatosis, portal hypertension

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## INTRODUCTION

**A**scites is an abnormal collection of fluid in the peritoneal cavity (1). It is mostly seen in patients with cirrhosis and other liver diseases. There are some diseases that can either cause exudative or transudative ascites. This includes different neoplasms, tuberculosis peritonitis, purulent peritonitis, congestive heart failure and ascities due to pancreatic diseases (pancreatic pseudocyst) (2,3). Increased gallbladder wall thickness could be due to different etiologies other than gallbladder diseases such as liver diseases, hypoalbuminemia, ascites, hepatitis, congestive heart failure, kidney disease, AIDS, malignancy and sepsis (4,5).

Ultrasonography has an accuracy of 93%, in determination of gallbladder wall thickness, if it is 1mm and 100% for 1.5 mm (6). In most of the previously discussed cause of ascites there is a change in plasma hydrostatic and oncotic pressure, which can explain the gallbladder wall edema. While in peritoneal carcinomatosis there is edema and inflammation of the peritoneum. Thus, this can be used as a diagnostic sign for determining etiology of ascites.

Increase gallbladder wall thickness in cirrhotic patients is due to presence of ascites, decreased peripheral vascular resistance and portal hypertension which shows that gallbladder wall thickness could be multifactorial (7). In our study we aim to determine the diagnostic value of ultrasonographic measurement of GBWT in differentiating of malignant induce from other causes of ascites from those patients with portal hypertension induce ascites. □

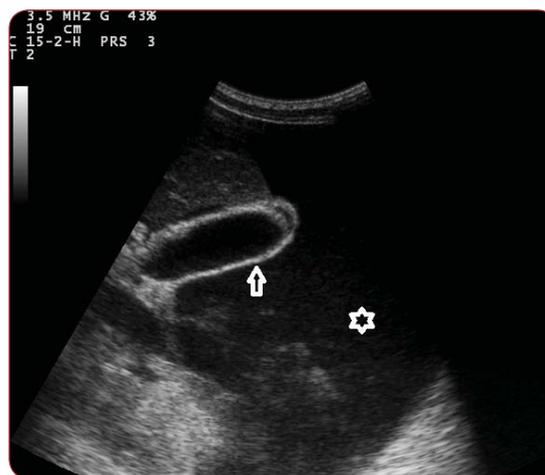
## MATERIAL AND METHODS

In this cross sectional study with descriptive and analytic aims we enrolled all patients diagnosed with ascites using random sampling between February 2005 and March 2008. All the patients referred to a tertiary referral university hospital were consecutively enrolled in the study. All patients underwent total abdominal sonography and gallbladder wall thickness was determined. 100 patients with ascites due to portal hypertension and 100 with known peritoneal carcinomatosis were enrolled in the study and compared with respect to gallbladder wall thickness. The inclusion criteria for diagnosis of cirrhosis were splenomegaly, palmar erythema, spider angioma, and based of labo-

ratory evaluation and liver biopsy. Those of hypoalbuminemia, polyclonal gamopathy, laboratory findings such as plasma bilirubin, prothrombin time, transaminase levels, abdominal sonographic findings of splenomegaly, collateral veins in liver and spleen hilum, ascites, heterogenic liver echo and liver border irregularity were all defined as cirrhosis. Those with biopsy proven cirrhosis were also included. Exclusion criteria included acute and chronic renal failure, heart failure, acute hepatitis, cholecystitis and sepsis. All patients underwent sonography, with Toshiba Nemio 30 Japan, in supine position, with convex transducer of 3.5-5 Mhz frequency in the right upper quadrant below costal margin. The thickness was measured by vertical beam to gallbladder wall and measured from serosa to mucosa (Figure 1).

The patients were examined after 8 hours of fasting and only those patients were included that had a fill gallbladder. Three measurements of gallbladder wall thickness were taken at each site and the average measurement was used.

All sonographies were performed by single abdominal sonographer (A.M) with 6 years experience. The sonographer was blinded to etiology of the ascites in patients. Patients' demographic and current statuses were also extracted from hospital records after consent given by the patients and permission of hospital authorities. Data were analyzed using SPSS version 14. T-test was used for quantitative data, and for comparison between gallbladder thickness and albumin level we used one way ANOVA. The p value of <0.05 was considered significant. □



**FIGURE 1.** Abdominal ultrasonogram revealed (arrow) thin gall bladder wall (2 mm in a patients with malignant ascites (stellate) due to ovarian carcinoma

## RESULTS

200 patients were enrolled in study, 100 of which with known ascites due to portal hypertension and 100 patients with ascites due to known cancer induced peritoneal carcinomatosis.

### Patients with peritoneal carcinomatosis

The minimum and maximum age of patients with peritoneal carcinomatosis was 25 and 80 respectively. The mean age was  $54.9 \pm 11.1$  years. Peritoneal carcinomatosis was mostly in males, 55 patients (55%). The minimum and maximum gallbladder wall thickness was 1.3 mm and 3.71 mm respectively. And mean GBWT was  $2.2 \pm 0.6$  mm. The least common etiologies for peritoneal carcinomatosis were hepatocellular carcinoma, lymphoma, ovarian and prostate cancer, all together being only 2% of the cases. The most common etiology was gastric cancer (21%) followed by colon cancer (15%). Figure 2 shows the distribution of etiologic factors of peritoneal carcinomatosis in 100 patients with malignant ascites.

### Patients with portal hypertension induced ascites (cirrhosis)

The minimum and maximum age of patients with portal hypertension was 30 and 80 years respectively with mean age of 52.18 years. 61% were male and 39% were female. Minimum and maximum gallbladder wall thickness in patients with portal hypertension induced ascites was 2.1 mm and 5.20 mm re-

spectively. The mean thickness was 3.90 mm. The mean serum levels of transamines, albumin, platelet, prothrombin time, bilirubin in cirrhotic patients were: Platelet: ( $\times 10^9/\text{mm}^3$ )  $117.2 \pm 63.1$  (Normal value: 150-450), Albumin (g/dl)  $2.3 \pm 0.7$  (Normal value: 1.5-3.5 g/dl), Bilirubin (mg/dl)  $2.4 \pm 3.7$  (Normal value: 0.5-1.5), Prothrombin time (%)  $70.9 \pm 24.2$ , AST (IU/L)  $72.3 \pm 80.7$  (Normal value  $< 40$ ), ALT (IU/L)  $44.6 \pm 43.6$  (Normal value  $< 40$ ).

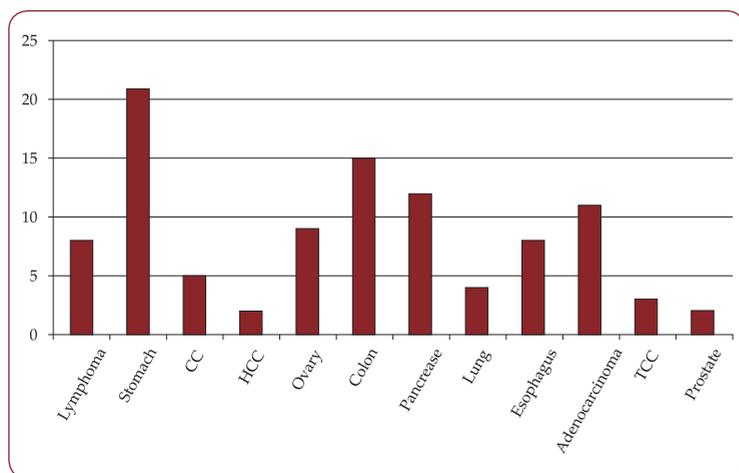
The results showed that there is significant correlation between serum albumin level and gallbladder wall thickness ( $p < 0.001$  and  $r = 0.5$ ). There was no significant correlation between transaminase level and gallbladder wall thickness ( $p = 0.5$  and  $r = 0.07$ ).

In the study population we compared gallbladder wall thickness in patients with portal hypertension and peritoneal carcinomatosis. The thickness was  $3.9 \pm 0.6$  mm in cirrhotic patient and  $2.2 \pm 0.6$  mm patients with peritoneal carcinomatosis, which was significantly higher in patients with ascites due to causes other than peritoneal carcinomatosis. We also determined the cut off value of gallbladder thickness in diagnosis of patients with peritoneal carcinomatosis. The GBWT of less than 3.6 mm, with sensitivity and specificity of 92% and 94% respectively indicated the peritoneal carcinomatosis. □

## DISCUSSION

Abdominal ultrasonography by evaluating irregular liver surface, enlarged spleen, a large portal vein can be a useful imaging tool for the etiological diagnosis of ascites syndrome. Small amorphous echoes within the fluid can be due to exudative ascites (1). However, the differentiation between benign and malignant ascites by means of ultrasound is frequently difficult.

In the present study, the most common age groups with ascites due to portal hypertension are 48-53 years old and the average age is 52.18 years. In a study by Wang et al the mean age group was  $58 \pm 8$  in patients diagnosed with cirrhotic liver disease (8). The lower age group for ascites in our study in comparison to other studies could be due to difference in etiology of hepatic cirrhosis in our country, which is hepatitis B. The most common age for getting hepatitis B in our country is a prenatal period and it is the most common cause of hepatic cirrhosis, the result of which is portal hyperten-



**FIGURE 2.** Distribution of etiologic factors of malignant ascites  
CC: Cholangiocarcinoma TCC: Transitional carcinoma HCC: Hepatocellular carcinoma

sion. While in western countries the most common cause is alcoholic cirrhosis (9).

In patients with ascites due to peritoneal carcinomatosis, the maximum age group is 55-60 years. This is higher when compared with cirrhotic group (54.9), and is expected, due to high the prevalence of cancer in older age groups. The most common cause of peritoneal carcinomatosis was gastric cancer followed by colon cancer. Our results are in agreement with previous studies (10,11).

The ascites due to portal hypertension in our study was 61% in male patients while it was only 39% among the female patients. This again shows the higher risk of hepatitis in male due to involvement in high risk activities (9). In those with ascites due to peritoneal carcinomatosis 55% were male and 45% were female and the difference is minor due to etiology of peritoneal carcinomatosis, which doesn't show gender predilection, then our results is in agreement with previous studies (11). In cirrhotic patients the gallbladder wall thickness was  $3.9 \pm 0.61$  mm and the thickness is evident if we consider a wall thickness of more than 3mm to be thick. But compared to some previous studies, in our study the wall thickness is lesser. Our result is in agreement with the results of Ersozgalip et al (7,12) and is in contrast with the results of other studies (13,14). In a study by Georgiv et al, the gallbladder wall thickness was  $7.07 \pm 3.31$  mm and in a study by Brogna A et al the thickness was  $7.6 \pm 0.21$  mm (13,14). The main cause of this difference is that most of our patients was referred from out-patients clinic and were in stable condition and only 11 patients from 100 patients had decompensated cirrhosis with exacerbated ascites. Previous study (15) showed that ascites is also an indicator of advanced portal hypertension and when ascites develops rapidly it may be the first complication of complicated cirrhosis.

In a study by Galip et al, it showed that those patients with ascites due to cirrhosis, those ones with esophageal varices had a thicker gallbladder wall compared to those without esophageal varices. In those without esophageal varices the thickness was  $3.3 \pm 0.31$  mm, while in those with esophageal varices and hypoalbuminemia the thickness was  $3.8 \pm 0.8$

mm (7). In our study the gallbladder wall thickness in those with known ascites was  $3.9 \pm 0.6$  mm and those with peritoneal carcinomatosis was  $2.2 \pm 0.6$  mm. It was significantly higher in those with portal hypertension compared with those with peritoneal carcinomatosis ( $p=0.001$ ). The previous studies also confirmed with similar results (4,13,14). In the study by Brogna et al, the gallbladder wall thickness in cirrhotic patients ( $6.7 \pm 2.1$  mm) was significantly higher than non-cirrhotic group ( $2.4 \pm 0.9$  mm). In the study by Georgiv, the thickness was higher in cirrhotic group ( $7.07 \pm 3.3$  mm) in comparison with carcinomatosis group ( $2.5 \pm 1.6$  mm). In the study by Dayanada et al, among 60 patients with ascites due to portal hypertension, 53 had a thick gallbladder (more than 3 mm), while in those 34 with ascites due to portal hypertension, 28 had normal gallbladder wall thickness (less than 3 mm) (4). This increase in gallbladder wall thickness in patients with cirrhosis, who have low serum albumin levels due to inability to produce albumin in abnormal liver and consequently decrease in the oncotic pressure and gallbladder wall edema is explainable (4,6,16). In the study by Georgiv et al, it was shown that increase in gallbladder wall in both groups was accompanied by low serum albumin level. The albumin levels were lower in cirrhotic group and consequently the edema and thickness was more in cirrhotic group compare with carcinomatosis one (13). In the study by Wang et al, those with lower albumin had thicker gall bladder wall (8). It is also worth mentioning that in patients with cirrhosis as a result of pathologic changes due to portal hypertension in the liver, there is a stasis of blood in the viscera and gallbladder veins, which leads to congestion and edema of the gallbladder wall, that is more in cirrhotic patients compare to the non-cirrhotics. □

## CONCLUSION

According to our results and those of other studies, it seems reasonable to propose that sonographic study of the gallbladder might be helpful in simple and initial differentiating between ascites due to cirrhosis and peritoneal carcinomatosis.

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