

## DIAGNOSTIC ACCURACY OF TISSUE HARMONIC IMAGING IN OBSTRUCTIVE JAUNDICE

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**ABSTRACT: INTRODUCTION:** Tissue harmonic imaging (THI) is a new ultrasound imaging technique providing the images which are much superior in quality compare to conventional ultrasound images by improving lateral resolution, signal to noise ratio and reducing side-lobe artifacts. **AIM:** Our aim is to estimate diagnostic accuracy of THI in diagnosing the cause of obstructive jaundice and to compare it with previous studies. **MATERIAL AND METHODS:** 125 cases of obstructive jaundice were evaluated with THI for the cause of obstructive jaundice by three radiologists separately during period of two year interval on Phillips HD 11 XE ultrasound scanner. Follow up done with ERCP, surgery and histopathology. CT and MRCP done wherever needed. Sensitivity, specificity, PPV, NPV, accuracy, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and Youden's index were calculated and compared with previous studies. **RESULT:** In our study we found choledocholithiasis as most common cause for obstructive jaundice. Sensitivity of 80%, 57.49%, 70.97% and specificity of 90%, 90.59%, 89.36% was noted for choledocholithiasis, neoplasm and benign stricture respectively. Accuracy of 86.4%, 80%, 84.8% was found for choledocholithiasis, neoplasm and benign stricture respectively. PPV of 81.81%, 74.19%, 68.75% and NPV of 88.88%, 81.91%, 90.32% was observed for choledocholithiasis, neoplasm and benign stricture respectively. Positive likelihood ratio of 8, 6.10, 6.67 and negative likelihood ratio of 0.22, 0.46, 0.32 was noted for choledocholithiasis, neoplasm and benign stricture respectively. Diagnostic odds ratio and Youden's index of 36 and 0.7, 13.02 and 0.48, 20.53 and 0.60 was seen for choledocholithiasis, neoplasm and benign stricture respectively. **CONCLUSION:** Introduction of THI in the modern ultrasound equipment had made improvement in the diagnosis of cause for biliary tract obstruction. Till today even with THI ultrasound doesn't have higher diagnostic value.

**KEYWORDS:** Tissue harmonic imaging, Obstructive jaundice, Choledocholithiasis, neoplasm, Benign stricture.

**INTRODUCTION:** Jaundice is a symptom characterized by yellowish discoloration of tissues and body fluids due to an increase in the bile pigments.<sup>1</sup> It is of two types: obstructive (surgical) or non-obstructive (Medical). Obstructive jaundice may be attributable to multiple causes including stones, intrinsic tumor, stricture or compression by extrinsic masses.<sup>2,3,4</sup> It can present with jaundice with or without pain, dark urine, pruritus, pale stools, weight loss and anorexia.<sup>5</sup>

There are various investigations which could be carried out for the diagnosis of obstructive jaundice like ultrasonography, CT, MRCP, ERCP. After Laboratory investigations ultrasonography of abdomen is considered first preliminary investigation of choice for evaluation of obstructive jaundice due to its accessibility, speed, ease of performance and low cost.<sup>6</sup>

## ORIGINAL ARTICLE

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Modern ultrasound equipment's with inbuilt THI facility has contributed to significant improvement in sonographic performance for the assessment of biliary tract.<sup>7</sup>

Tissue harmonic imaging was first utilized as a technique for the detection of nonlinear vibrations of microbubble contrast agent.<sup>8</sup> It is based on the phenomenon known as nonlinear propagation.<sup>9</sup> Now THI is also used to image body tissue. Conventional ultrasound waves are generated at the surface of the transducer and its intensity decrease progressively as they traverse the body. In comparison harmonic waves are generated within the tissue and build up to a point of maximum intensity before they decrease due to attenuation. Harmonic wave frequencies are multiples of the transmitted frequency and present technology uses only second harmonic for imaging.<sup>10</sup>

Relatively small amplitude of the harmonic waves reduces the detection of echoes from multiple scattering events and side lobe artifacts are less likely to occur in THI. Shorter wavelength and improve focusing with higher frequencies had improved the axial and lateral resolution respectively.<sup>10</sup>

New ultrasound equipment's with THI has made it necessary to re-defined the diagnostic value of ultrasound with tissue harmonic imaging in detection of cause for obstructive jaundice. It is important preoperatively to determine the cause of obstruction because ill-chosen procedure can lead to high morbidity and mortality. We describe our experience regarding the diagnostic accuracy of sonography in detection of the cause of obstructive jaundice using modern equipment with tissue harmonic imaging.

**MATERIAL & METHODS:** Our study population included 125 patients referred from gastroenterology department of our institute for abdominal ultrasound examination over a period of past two years intervals having confirmed diagnostic cause of obstructive jaundice on follow up. All patients were above 18 year of age. Patients having previous history of pancreatico-biliary surgery, patients with inconclusive ultrasound finding, patient who lost follow up were excluded from the study.

All the scans were obtained on sonographic equipment with tissue harmonic imaging capability, Phillips HD11XE Scanner. Sonographic probe used was C5-2 MHz. Harmonic mode setting done by means of a toggle switch on scanner control panel. All patients underwent abdominal ultrasound examination in which cause of obstruction was observed by three expert radiologists separately. These radiologists were had designation assistant professor and above. Bile duct was measured from inner border to inner border. CBD greater than 8mm was labeled as abnormal. For USG of pancreatico-biliary tree, fasting for six hours was ensured. Scanning was done in supine and left lateral position. Pressure was applied wherever needed to displace the bowel gases. In some cases oral water was administered for better demonstration of pancreas. When anterior epigastric approach fail to demonstrate distal CBD, right lateral or anterolateral approach with patient in left posterior oblique position was helpful. Out of three radiologists the cause confirmed by two or more was labeled as a cause on ultrasound.

Any intraluminal, hyperechoic structure with or without posterior acoustic shadowing was labeled as calculus. Intraluminal or intra-extraluminal hypoechoic or isoechoic mass causing abrupt interruption of dilated bile duct was labeled as neoplasm. Smooth tapering of dilated bile duct without any mass lesion was labeled as benign stricture.

## ORIGINAL ARTICLE

All the patients were followed for ERCP, surgery and histopathology. CT and MRCP were done wherever needed for diagnosis. Data was analyzed on statistical software SPSS.

**RESULT:** Out of 125 patients youngest was 20 year old and oldest was 83 year old. Maximum numbers of patients were in the age group 50-59 year. Out of 125 patient studied 68 were male and 57 were female. Major presenting complaints were jaundice (100%), abdominal pain (60%), nausea & vomiting (58.7%), dark colored urine (52.5%), pruritus (43.7%). In our study, we had found choledocholithiasis in 45, pancreatico-biliary neoplasm in 40, benign strictures in 31 and miscellaneous causes in 9 as a cause for obstruction.

Out of total 45 cases of choledocholithiasis (Figure 1), 36 were detected on THI (Figure 4). Nine patients were false negative and eight patients were false positive on THI. We found sensitivity, specificity, PPV, NPV, accuracy of 80%, 90%, 81.81% 88.88% and 86.4% respectively in case of choledocholithiasis. Positive and negative likelihood ratios were 8 and 0.22 respectively. Diagnostic odds ratio of 36 and Youden's index of 0.70 was observed for choledocholithiasis (Table 1).

**Figure 1:** Ultrasound image (A) showing hyperechoic structure in common hepatic duct giving posterior acoustic shadowing which on ERCP (B) seen as oval filling defect representing a calculus which was removed during ERCP.

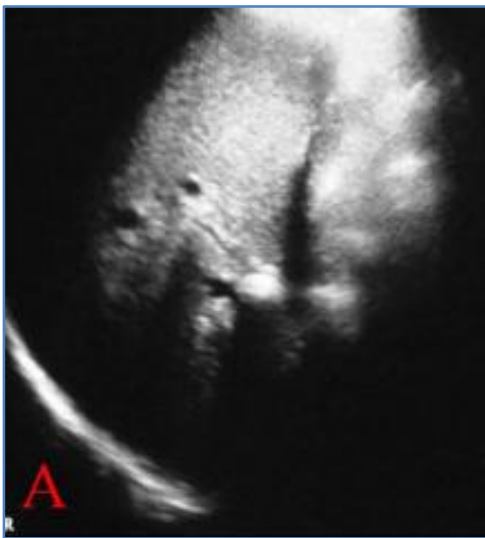


Fig. 1A

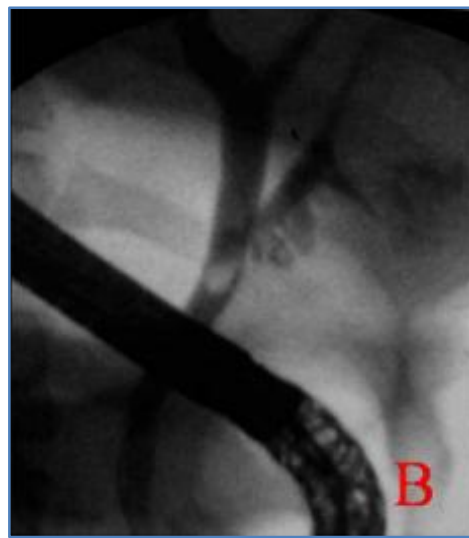


Fig. 1B

THI had detected 23 cases of pancreatico-biliary neoplasm (Figure 2) out of total 40 cases (Figure 4). Eight cases were false positive and seventeen cases were false negative on THI. For pancreatico-biliary neoplasms we had found sensitivity, specificity, PPV, NPV, accuracy of 57.49%, 90.59%, 74.19%, 81.91% and 80% respectively. Positive likelihood ratio of 6.10 and negative likelihood ratio of 0.46 was observed. Diagnostic odds ratio of 13.02 and Youden's index of 0.48 was found for pancreatico-biliary neoplasm (Table 1).

## ORIGINAL ARTICLE

**Figure 2:** Ultrasound image (A) showing hypoechoic mass lesion in the distal CBD which is causing abrupt cut off of dilated biliary system on ERCP (B). Biopsy of the lesion revealed cholangiocarcinoma.

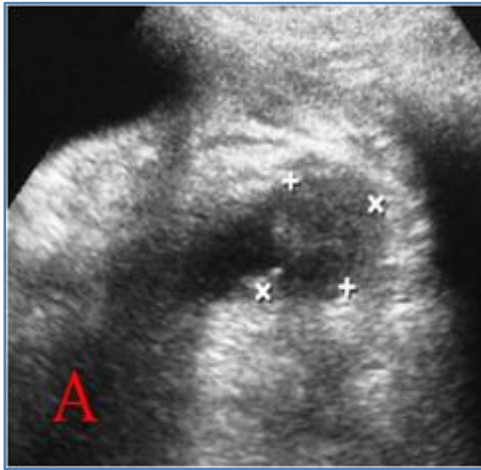


Fig. 2A

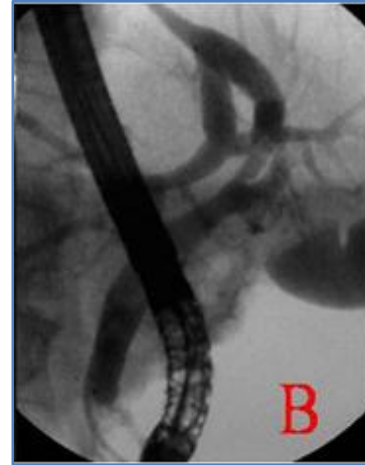


Fig. 2B

Out of total 31 cases of benign stricture (Figure 3A), 22 were true positive on THI (Figure 4). False positive diagnosis was made in ten cases whereas false negative diagnosis was made in nine cases. We had got sensitivity, specificity, PPV, NPV, accuracy of 70.97%, 89.36%, 68.75%, 90.32% and 84.8% respectively in case of benign stricture. Positive likelihood ratio and negative likelihood ratio of 6.67, 0.32 was found respectively. Diagnostic odds ratio of 20.53 and Youden's index of 0.60 was noted for benign stricture (Table 1).

**Figure 3:** Ultrasound image (A) showing smooth tapering of distal CBD which on ERCP (B) giving similar appearance without any mass lesion representing benign stricture.



Fig. 3A

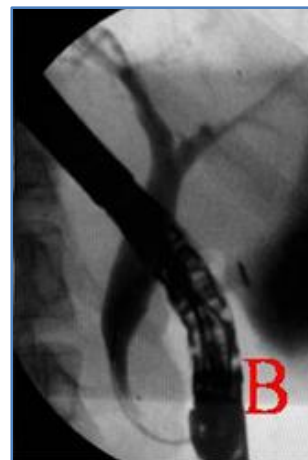
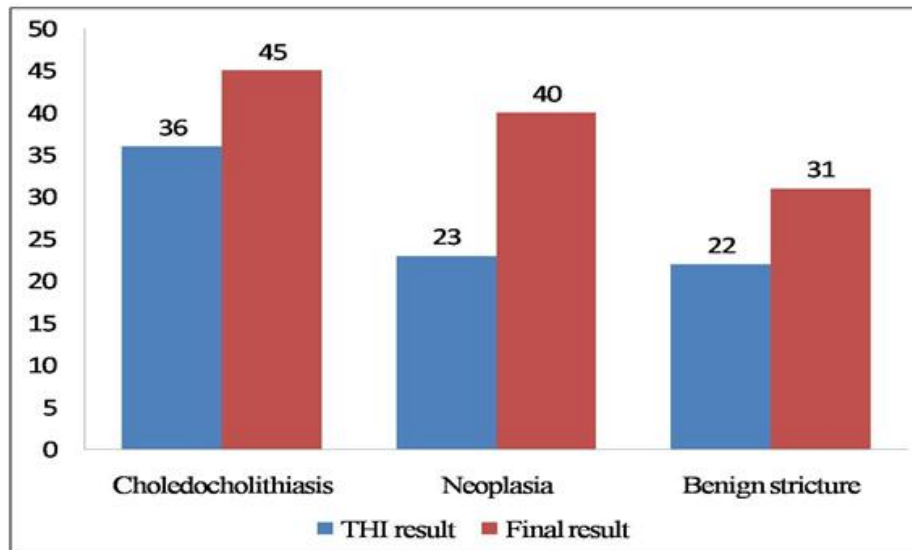


Fig. 3B



**Figure 4: Comparative chart of THI and final result regarding the cause of obstructive jaundice**

Sl. No.	Measures of Diagnostic Accuracy	Cause of Obstructive Jaundice		
		Cholelithiasis	Neoplasm	Benign Stricture
1.	Sensitivity	80	57.49	70.97
2.	Specificity	90	90.59	89.36
3.	Accuracy	81.81	74.19	68.75
4.	Positive predictive value	88.88	81.91	90.32
5.	Negative predictive value	86.4	80	84.8
6.	Positive likelihood ratio	8	5.31	7.8
7.	Negative likelihood ratio	0.22	0.47	0.27
8.	Diagnostic odds ratio	36	13.02	20.53
9.	Youden's index	0.7	0.48	0.6

**Table 1: Our test results regarding diagnostic accuracy of THI in diagnosing cause of obstructive jaundice**

**DISCUSSION:** Diagnosing successfully the specific cause of obstructive jaundice has continued to improve with advanced imaging technique and equipment's. Availability of ultrasound, CT, MRCP, ERCP, PTC has combined increased the diagnostic accuracy rate to approximately 98%.<sup>11</sup> Despite of all the new imaging modalities ultrasound is still continued as a first line investigation in cases of obstructive jaundice<sup>12</sup>

Tissue harmonic imaging is a new sonographic technique that provides image which is much superior in quality compare to conventional ultrasound image. It improve lateral resolution, reduce side-lobe artifacts and improve signal to noise ratio. Because the harmonic waves are formed within

## ORIGINAL ARTICLE

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the body, they suffer less from the reverberation artifacts generated in the overlying fat and muscle. Identification of these artifacts is possible in a large viscous like GB or urinary bladder, but in small cystic structure like bile duct, this artifact may be a source of misinterpretation.

Suppression of artifacts with increased contrast resolution in THI was reported to improve the visualization of fluid filled or cystic structure in the form of wall and lumen visualization, length assessment, intraluminal mass or stone assessment.<sup>7</sup> In our study we had tried to reduce the operator related error of ultrasound imaging technique by using three expert radiologists.

We found choledocholithiasis as the most common cause of obstructive jaundice in our study. Calculus location in distal CBD was most commonly seen in our study. According to the study which was done by Mitchell et al (1984) the sensitivity of ultrasound in diagnosis of choledocholithiasis was 18%.<sup>13</sup> Another study done by Cronan et al (1986) had reported sensitivity of 55%.<sup>14</sup> Continuous improvement in sensitivity was reported in subsequent studies with highest sensitivity of 90% reported in the studies done by Kiani et al (2012), Admassie et al (2005).<sup>6,15</sup> Our study showed sensitivity of 80% for choledocholithiasis and our result was consistent with the sensitivity of 79.42% which was found in a study done by Bader A et al (2011).<sup>5</sup> The study done by Kiani et al (2012) revealed specificity of 90% for choledocholithiasis which was consistent with our study.<sup>6</sup> Accuracy of 71%, 55%, and 85% was reported in the studies done by Rigants et al (1992), Dixit et al (1993) and Haung et al (1993) respectively.<sup>16,17,18</sup> In another study done by Tomus et al (2009) showed the accuracy of 86% for choledocholithiasis which was consistent with our study.<sup>19</sup> In our study we found PPV of 81.81% which was ranging between the study done by Mandelia A et al (2013) and Kiani et al (2012) but NPV was more than both the studies in case of choledocholithiasis.<sup>6,20</sup>

Pancreatic head malignancy was the most common neoplastic lesion found in our study. Specificity of 90% in a study done by Admassie et al (2005) was consistent with our study result for pancreatobiliary neoplasm.<sup>15</sup> Sensitivity, Accuracy and NPV in our study were consistent with the study done by Kiani et al (2012) for neoplasm. PPV in our study for pancreatobiliary neoplasm was less compare to previous study done by Kiani et al (2012).<sup>6</sup>

Benign strictures can be postoperative or postinflammatory. Postoperative strictures are the result of injury to bile duct at the time of biliary tract surgery and postinflammatory strictures are caused by cholangitis, chronic pancreatitis, gallstones, penetrating or perforating duodenal ulcer.<sup>1</sup> We are reporting here our statistical observations such as sensitivity 70.97%, specificity 89.36%, PPV 68.75%, NPV 90.32%, and accuracy 84.8% for benign strictures. We could not found any data regarding this in literature.

Nine miscellaneous cases including ruptured liver hydatid into biliary tree, biliary ascariasis, choledochal cyst, Mirrizi's syndrome etc. were found in our study.

Several studies had shown high sensitivity of ultrasonography (upto 97%) in differentiating obstructive from nonobstructive jaundice.<sup>6</sup> In literature older studies showed less sensitivity, accuracy in comparison to recent studies.<sup>5,6,13-30</sup> Our study also showed higher sensitivity and accuracy compare to older studies for choledocholithiasis. Introduction of newer ultrasound equipments with tissue harmonic imaging has attributed significantly for this difference.<sup>31</sup>

Positive likelihood ratio of greater than one in the detection of causes like choledocholithiasis, pancreatobiliary neoplasm and benign stricture by tissue harmonic imaging implies significant association between positive test on THI and having same cause. Negative likelihood ratio of less than one in our study for choledocholithiasis, pancreatobiliary neoplasia and benign stricture implies significant association between negative test on THI and not having same cause. As in our study

## ORIGINAL ARTICLE

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positive likelihood ratio is less than 10 and negative likelihood ratio of greater than 0.1 implies tissue harmonic imaging is not having higher diagnostic value in detection of the cause.

Diagnostic odds ratio and Youden's index in our study was highest for choledocholithiasis and lowest for pancreatobiliary neoplasm. These observations are ranging between poor diagnostic test and perfect diagnostic test.

**CONCLUSION:** Recent foreign studies are consistent with our local study with respect to choledocholithiasis and pancreatobiliary neoplasm. We added our statistical observations in case of benign stricture which would be helpful for future studies. We conclude that advances in the ultrasound equipment with introduction of new imaging technology of tissue harmonic imaging have improved the diagnostic performance of ultrasound in diagnosing the cause of obstructive jaundice. But still it is not having the higher diagnostic value to replace the further diagnostic investigations. As ultrasound technique is easily available and cheap, we recommend further research to improve the technology for better diagnosis so that we can diagnose the cause at the earliest with this noninvasive, non-radiative modality.

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