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A COMPARATIVE ANALYSIS OF ULTRASOUND'S ACCURACY IN DIAGNOSING HEPATOCELLULAR CARCINOMA USING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Objective: *To assess the diagnostic performance of ultrasound (US) for detection of hepatocellular carcinoma (HCC) compared to histopathology as the gold standard.*

Methodology*: It was a cross-sectional study carried out at Medcare International Hospital, Gujranwala, from July to December 2023. One hundred patients diagnosed with HCC were included; 90 patients were clinically suspected of having HCC and aged ≥ 18 years. Patients with previous treatment for liver cancer or incomplete diagnostic data were excluded. US was performed in all participants, followed by histopathological confirmation. The results are analyzed for the calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy.*

Results: *US correctly detected 62 cases of true positive (TP) and 18 cases of true negative (TN) HCC among the 90 patients. Five cases were FP and five were FN. The sensitivity, specificity, PPV, NPV, and total diagnostic accuracy were 92.5%, 78.2%, 92.1%, 78.3%, and 88.9%, respectively ($p < 0.05$).*

In conclusion, the study shows that US is a low-cost, highly sensitive, and diagnostic imaging modality with noninvasive characteristics for the diagnosis of HCC. This reinforces its importance as a screening tool, especially in resource-poor areas.

Keywords: *Diagnostic accuracy, Hepatocellular carcinoma, Ultrasonography, Sensitivity, Specificity.*

INTRODUCTION

Hepatocellular carcinoma (HCC) is a significant global health challenge owing to its aggressive behavior and high mortality rate. HCC accounts for 85–90% of primary liver cancers, and its incidence shows a strong inclination in areas burdened with high prevalence of chronic hepatitis B and C infection (e.g., Southeast Asia and sub-Saharan Africa) (1). Other major risk factors include cirrhosis, non-alcoholic fatty liver disease (NAFLD), and exposure to environmental toxins such as aflatoxins (2). In Pakistan, HCC accounts for 3.5–16% of all malignancies, with hepatitis-induced cirrhosis being the leading cause (3).

Hepatocellular carcinoma (HCC) is the most common type of liver cancer, but its clinical features are often nonspecific and the disease is often diagnosed at advanced stages when curative treatments are not possible (4). Therefore, early diagnosis is crucial in enhancing patient outcomes and survival rates. Imaging modalities are crucial to this effort, and there has been a push for ultrasound (US)-based imaging to serve as

the primary screening and surveillance method for atrisk populations (5). It is non-invasive, cost-effective, and widely available. In addition, US provides fast real-time imaging, which is useful for identifying liver lesions and assisting in biopsy (6).

The diagnostic performance of US in differentiating HCC from benign liver lesions is still muddy although it is very useful. A variety of factors, including tumor size, operator expertise, and underlying liver pathology, have a major impact on its sensitivity and specificity (7, 8). Liver biopsy specimens is the gold standard for the diagnosis of HCC. However, this invasive approach is not always possible because of the characteristics of the patient or the location of lesions (9).

This study is to assess the accuracy of the diagnosis of HCC by US, in comparison to the findings of US to the histopathological results to determine the sensitivity, specificity, PPV, and NPV of US for the diagnosis of HCC. This study was conducted to assess the diagnostic efficacy of US in a clinical setting and collected data from Medcare International Hospital, Gujranwala, over a period of six months, until October 2023.

Methodology

This cross-sectional validation study, including 90 patients clinically suspected of hepatocellular carcinoma (HCC), was performed. Participants were aged 18 years or older, of both sexes, and referred for ultrasound between July and December 2023 at Medcare International Hospital, Gujranwala. The hospital's ethical committee approved the study. Patients with incomplete diagnostic information, previous treatment of liver cancer, or lesions in which biopsy was potentially fraught with complications were excluded.

Ultrasonography was conducted using a high-resolution curvilinear probe (3.5 MHz) after taking informed consent and relevant clinical history. Both supine and left lateral scans were performed on patients, and images were obtained in radial and anti-radial projections. Liver lesions were defined using segmental anatomy and evaluated sonographically according to size, shape, margins, echotexture, posterior acoustic features, and surrounding tissue changes.

An ultrasound-guided aspiration was done under aseptic conditions with the help of an 18G needle, and the aspirated samples were fixed in slides that were sent for a histopathological examination. Ultrasonographic findings were compared with histopathology (gold standard). Second, all ultrasound findings were validated by an independent radiologist to minimize observer bias.

Data were analyzed using SPSS version 20.0. Age was described by mean and standard deviation, and gender by frequency and percentage. Ultrasonography sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy for diagnosing HCC were calculated using a 2×2 contingency table.

Results

Ninety cases were included in the study, with a mean age of 56.3 years (30–70 years). In total, there were 62.2% male and 37.8% female participants, reflecting a higher prevalence of HCC in males than females worldwide. Ultrasound diagnosed 62 cases as positive true HCC, and 18 negative true HCCs, while noting 5 false positive and 5 false negative cases. US had a sensitivity of 92.5%, which demonstrates its strong ability to detect real cases of HCC. The specificity was

78.2%, indicating moderate ability to rule out the non-HCC cases. The positive predictive value (PPV) and negative predictive value (NPV) were 92.1% and 78.3%, respectively, indicating the usefulness of US as an effective diagnostic modality for initial HCC screening.

Lesion size also turned out to be a major influence on diagnostic accuracy. Sensitivity increased in larger lesions, achieving around 95% with lesions >3 cm. However, smaller lesions (≤3 cm) proved difficult, and false negative rates increased. This highlights the variation in performance metrics of US for HCC diagnosis according to lesion size.

A detailed analysis revealed:

- **Lesions ≤3 cm:** 18 cases with benign lesions were reported, without a confirmed case of HCC.
- **Lesions >3 cm:** 72 cases, 54 (75%) identified as HCC and 18 benign.

US was able to identify 62 out of 90 cases as true positive and 18 as true negative. However, 5 cases were wrongly diagnosed as positive, and another 5 cases as negative. US demonstrated the highest sensitivity of 92.5% for detecting HCC in practice. A specificity of 78.2% indicated its ability to correctly identify non-HCC cases. The PPV was 92.1%, and the NPV was 78.3%. **Patient Distribution by Age**

Age (years)	No. of Patients	Percentage (%)
18-40	29	32.22
41-60	41	45.56
>60	20	22.22
Total	**90**	**100.0**

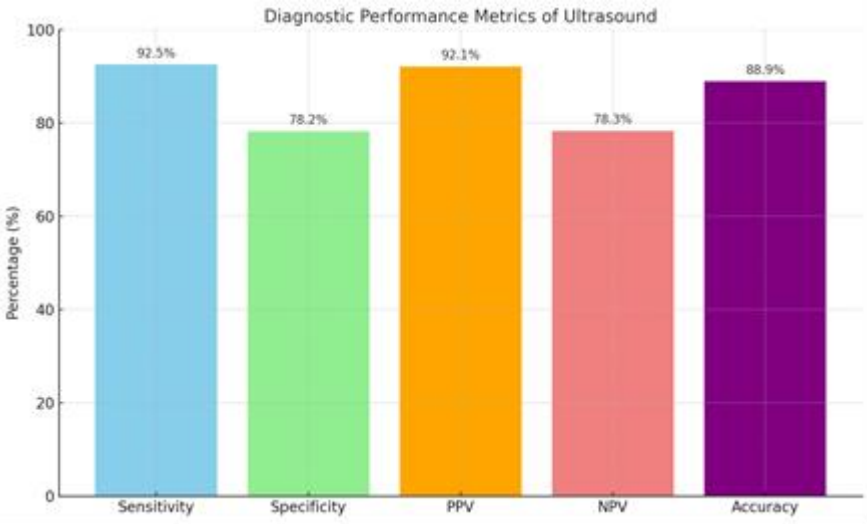
- **Mean ± SD:** 56.3 ± 9.4 years
- **Gender:** 56 (62.2%) males; 34 (37.8%) females

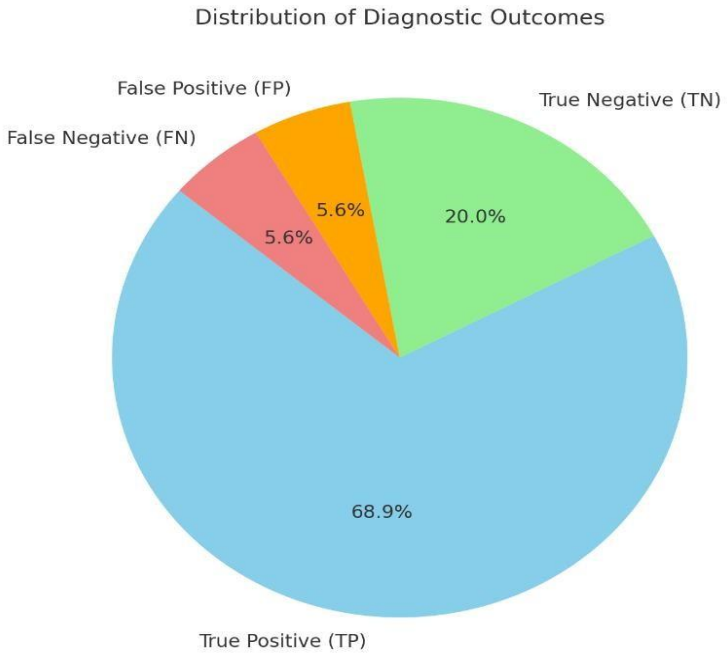
Table: Diagnostic Performance of Ultrasound in Diagnosis of Hepatocellular Carcinoma (HCC) Compared to Histopathology

Histopathology Result	Positive on Ultrasound (US)	Negative on Ultrasound (US)	Total
Positive	62 (True Positive - TP)	5 (False Negative - FN)	67
Negative	5 (False Positive - FP)	18 (True Negative - TN)	23
Total	67	23	90

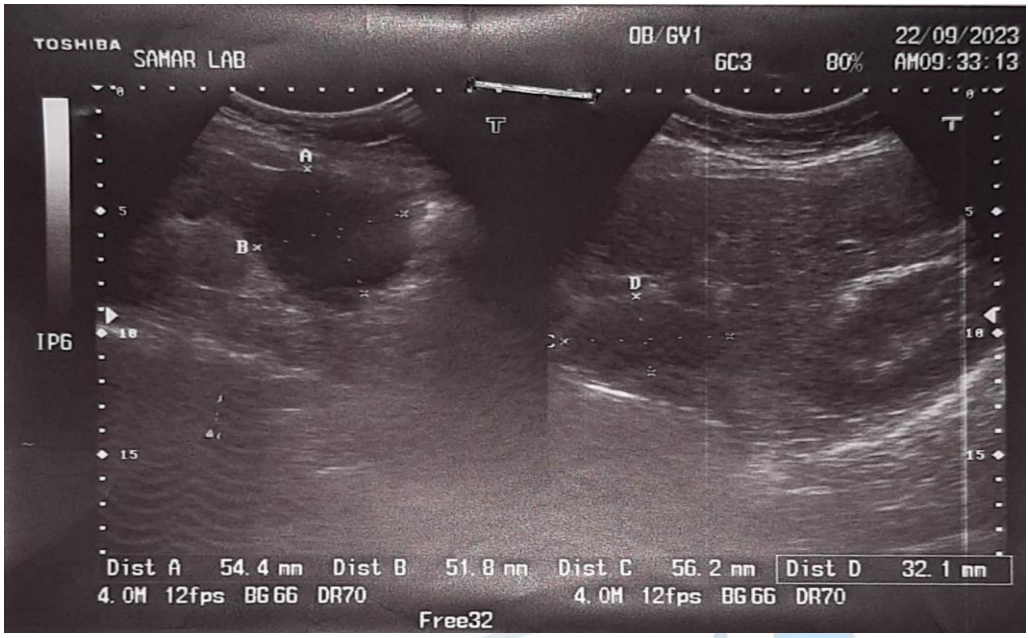
Diagnostic Metrics

- **Sensitivity:** 92.5%
- **Specificity:** 78.2%
- **Positive Predictive Value (PPV):** 92.1%
- **Negative Predictive Value (NPV):** 78.3%
- **Diagnostic Accuracy:** 88.9%
- **P-value:** <0.001





A hypoechoic mass (51x37mm) and a hyper echoic mass (29x24mm) were seen in RT lobe



A hypoechoic mass (54x51mm) in RT lobe and a (56x32mm) mass seen in RT lobe

Discussion

The results of this study support the use of ultrasound (US) as a primary screening method for hepatocellular carcinoma (HCC), particularly for monitoring high-risk population. The high sensitivity of 92.5% highlights US's strong ability to detect true cases of HCC, aligning with findings from studies by Esfeh JM et al. (2019) (10) and Morgan TA et al. (2018) (11). These studies demonstrated similar sensitivity levels, confirming US's role in the early detection and monitoring of HCC. However, the relatively moderate specificity of 78.2% underscores the challenge of distinguishing HCC from benign hepatic lesions, a limitation also noted by Dobek A et al. (2023) (12).

Advances in imaging modalities, such as contrast-enhanced ultrasound and magnetic resonance imaging (MRI), have shown improvements in specificity and overall diagnostic accuracy. Zhang Z et al. (2017) emphasized that contrast-enhanced US reduces false positive rates (13), while Roberts LR et al. (2018) concluded that MRI outperforms CT in detecting early-stage HCC in patients with cirrhosis (14). Despite these advancements, the affordability and widespread availability of traditional US make it indispensable, especially in resource-limited settings.

Conversely, Park HJ et al. (2020) highlighted the limitations of standard US, advocating for multimodal imaging protocols to improve diagnostic outcomes. Their findings suggested that combining US with other modalities, such as CT or MRI, enhances diagnostic accuracy, particularly in complex cases (15).

Future research could focus on integrating artificial intelligence (AI) with US technology to further enhance diagnostic precision. AI algorithms trained on large datasets could standardize operator– dependent variability, improve lesion characterization, and reduce false positive and false negative rates.

Conclusion

Our study highlights the use of ultrasound (US) as an effective tool for diagnosing hepatocellular carcinoma (HCC), suggesting significant implications for earlier detection and interventions. Although histopathology remains the gold standard for diagnosis, US serves as a crucial initial non-invasive modality and a useful first step in many clinical pathways. It has the potential to become the foundation of liver cancer diagnostics in both low-resource and advanced settings, with the ability to improve diagnostic outcomes through integration with advanced imaging modalities and artificial intelligence.

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