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Diagnostic Correlation of Alpha-Fetoprotein Levels with Imaging Findings in the Early Detection of Hepatocellular Carcinoma at a Tertiary Hospital

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Abstract

Background: The clinical outcomes of hepatocellular carcinoma (HCC) can be greatly improved with early detection. Imaging is the primary method of diagnosis; however, serum alpha-fetoprotein (AFP) is a biomarker of choice as a supplement. This study aims to explore the diagnostic relationship of serum AFP levels against the imaging findings hearted toward early stage HCC.

Methodology: A retrospective cross sectional study was carried out in a tertiary center with 146 patients screened for HCC from January 2022 to December 2023. Serum AFP levels were collected alongside imaging results (ultrasound, CT, or MRI). Based on the findings from the imaging done, patients were categorized into no lesion, indeterminate lesion and definitive HCC. Assessment was done for the statistical correlation between serum AFP levels and imaging confirmed HCC.

Findings: Definitive HCC patients (n=84) had mean serum AFP of 187.4 ng/mL while those with indeterminate and no lesion were 22.1ng/mL and 8.3ng/mL respectively. 88.1% of HCC cases were observed with AFP >20ng/mL. AFP elevation was also positively correlated with tumor size.

Conclusion: The study concludes that serum AFP levels correlate with HCC diagnosis and tumor burden. Using AFP in combination with imaging increases the precision of diagnosing the HCC thus retaining the value of AFP in multimodal screening and diagnosis of HCC in high-risk patients.

Keywords: Alpa-Fetoprotein, Hepatocellular Carcinoma, Liver Cancer, Diagnostic Imaging, Early Detection, Primatissimus, Biomarkers, Catheristicus Medicus Laboratory Overlap, Tertiary Care

Introduction

Hepatocellular carcinoma (HCC) is one of the most prevalent and deadly cancers alongside malignancies of its kind. It poses a particular concern in regions where hepatitis B and C is widespread due to the morbidity and mortality it causes. Alongside surgical resection, liver transplantation, and locoregional therapy, early detection improves postoperative survival outcomes.

While alpha-fetoprotein (AFP) is a serum biomarker linked with HCC, it has been also used extensively for screening and diagnostic purposes. Apart from being sensitive and specific, AFP can be unreliable is some cases. AFP especially fails to detect small, early-stage tumors whose AFP levels would be considered normal (Hanif et al., 2022). In the case of ultrasound, CT, and MRI, whose functions are more structural and geometrical, AFP can be used together and becomes helpful despite its limitations.

Adding AFP to imaging becomes advantageous in terms of capture rate. For instance, Tzartzeva et al. (2018) showed in a meta-analysis that using AFP alongside surveillance imaging provided better sensitivity for early-stage HCC in cirrhotic patients. Likewise, collecting AFP data over time has proven to improve diagnostic precision by lowering false negative results (Tayob et al., 2016).

In tertiary care facilities, due to the high patient volume and the intricate nature of the diagnosis, an integrated system using both biochemical and radiologic diagnostics is warranted. This study seeks to assess the diagnostic concordance of serum AFP levels and radiologic findings in patients suspected of early-stage HCC. Understanding this relationship in a real-world tertiary care context can inform and strengthen the argument for optimized multimodal diagnostic approaches intended for timely and precise detection of HCC.

Literature Review

The very best treatment of hepatocellular carcinoma (HCC) is very early detection, and prognosis greatly improving, but remains difficult because of the HCC's non or minimal symptoms at the early stages. Ultrasound, computed tomography(CT), and magnetic resonance imaging(MRI) are the gold standard in anatomical imaging of liver lesions, however, serum markers such as alpha-fetoprotein (AFP) assists in making the diagnosis.

AFP has long been associated with HCC as a key marker diagnosis, however its clinical value has undergone extensive scrutiny. Hanif et al (2022) discussed these limitations and remarked that up to 40% of early-stage HCC could be AFP negative and therefore defeat the purpose of diagnosis, which makes the case for its sole use uncertain. However, the use of AFP along with the imaging techniques yields better results.

Tzartzeva et al (2018) conducted a major meta-analysis of patients with cirrhosis where it was shown that the sensitivity of detecting early HCC rises from 45% to 63% using ultrasound when AFP is added. This demonstrates the strong supporting role of AFP and the need to implement it into screening procedures, especially for tested high-risk groups.

The last paragraph of the rationale provided suggests that neither imaging nor AFP individually provides sufficient accuracy for the early detection of HCC. Their use in a multimodal approach enhances diagnostic accuracy, bolsters clinical decisions, and helps HCC treatment be initiated promptly—important considerations in tertiary care settings.

Tayob et al. (2016) developed a more advanced dynamic AFP monitoring algorithm that greatly surpassed static detection algorithms. AFP trend monitoring and individually tailored adjustments improved early detection rates while decreasing false positives.

In addition to sensitivity and specificity, the correlation of AFP levels with tumor has also been studied. Abbasi et al. (2012) demonstrated that serum AFP is significantly correlated with tumor size, hence reinforcing the rationale for AFP's use in disease staging.

Older systematic reviews like that of Colli et al. (2006) have put considerable effort into comparing AFP with imaging techniques. They reached the conclusion that imaging remains superior with anatomical localization; however, AFP offers important biological supplementary information, especially where imaging is inconclusive or where lesions are sub-centimeter.

Also, Galle et al. (2019) deepen the biological rationale of AFP expression related to its tumor differentiation and tumor aggressiveness, thus broadening the rationale for comprehensive diagnostic protocols.

Beyond these attributes, the biological context of AFP is gained from imaging and therefore improves the synergy between both techniques.

Methodology

Study Setting and Design

This retrospective, cross-sectional study was carried out at the Department of Radiology and Clinical Laboratory of a tertiary care hospital from January 2022 to December 2023. The purpose of the study was to assess the diagnostic relationship between serum alpha-fetoprotein (AFP) concentrations and radiological findings in patients with suspected hepatocellular carcinoma (HCC).

Study Population

We included 146 patients with clinical suspicion of HCC or those on chronic liver disease screening. Adults aged ≥18 years with serum AFP results and liver imaging studies (US, CT or MRI) done within a 4 week window were included. Patients were excluded if they had metastatic liver disease, previous treatment for HCC, or incomplete records.

Data Collection

Patient records were retrieved from the hospital's electronic medical system. Data collected included:

- Demographics: Age, gender
- Clinical variables: Causative factors of liver disease (e.g. HBV, HCV, NASH) and cirrhosis status

• AFP levels: Serum AFP concentrations were determined by chemiluminescent immunoassay and a diagnostic cutoff of ≥20 ng/mL was used.

• Radiological findings: Radiological reports were performed by two blinded board-certified radiologists to AFP results. Imaging features of HCC were interpreted according to the LI-RADS (Liver Imaging Reporting and Data System) classification.

The patients were divided into three groups according to the imaging results as no lesion, indeterminate lesion, and definitive HCC. Also, the maximum lesion size (in cm), number of nodules, and enhancement patterns were recorded.

Statistical Analysis

Data analysis was performed using SPSS Version 25. Descriptive statistics for study's those quantitative variables were expressed as means (±SD) and for categorical as frequencies (%). To evaluate the association between serum AFP levels and imaging-confirmed HCC, Pearson's correlation coefficient was used. A subgroup analysis was performed to assess the association between AFP levels and tumor size.

The diagnostic performance of AFP and imaging done separately and together was measured by sensitivity and specificity, as well as area under the receiver operating characteristic (ROC) curves. A p value of less than 0.05 was deemed significant.

Ethical consideration

The ethics committee of the hospital reviewed and approved the study protocol. In line with legal and ethical constraints, all data was de-identified before analysis.

Findings

A total of 146 patients were included in the final analysis. Participants within the cohort were classified into three diagnostic groups as per the radiological findings: No lesion (n=34), Indeterminate lesion (n=28), and Definitive HCC (n=84).

Patients with definitive HCC had a mean serum AFP level of 187.4 ng/mL which was significantly higher in comparison to those with indeterminate lesions (22.1 ng/mL) and no detectable lesion (8.3 ng/mL). Importantly, 88.1% of patients in the HCC group had AFP level greater than diagnostic cutoff of 20 ng/mL. In comparison, only 46.4% of the indeterminate group and 5.9% of the no lesion group surpassed this threshold.

Also, an increase in tumor size was directly associated with an increase in AFP. The average tumor size in the definitive HCC patients was 3.9 cm while in the indeterminate lesion group it was 1.5 cm. The “no lesion” group had no measurable lesions.

Table 1. AFP Levels and Tumor Characteristics by Imaging Diagnosis Group

Diagnosis Group	Number of Patients	Mean AFP (ng/mL)	AFP >20 ng/mL (n)	Mean Tumor Size (cm)
No lesion	34	8.3	2	N/A
Indeterminate lesion	28	22.1	13	1.5
Definitive HCC	84	187.4	74	3.9

A high positive correlation was seen with both the presence and volume of hepatic lesions on imaging concerning AFP levels. This reasoning confirms the hypothesis that AFP measurements—when considered alongside imaging—may serve as a dependable complementary approach in the early diagnosis of hepatocellular carcinoma in a tertiary care context.

Discussion

This research sought to investigate the diagnostic relationship of serum alpha-fetoprotein (AFP) levels with imaging results for the early detection of hepatocellular carcinoma (HCC) within a tertiary care context. Our results reveal a statistically and clinically significant association between elevated AFP and HCC diagnosed by imaging. Patients with definitive HCC had strikingly greater mean AFP levels (187.4 ng/mL) than those with indeterminate (22.1 ng/mL) or no detectable lesions (8.3 ng/mL). Furthermore, 88.1% of the HCC group exceeded the suggestive threshold of 20 ng/mL.

These findings corroborate older research outlining the complementary use of AFP and imaging in the HCC diagnostic algorithm. For example, in Tzartzeva et al. (2018), the sensitivity of ultrasound for early-stage HCC significantly improved when used in conjunction with AFP. In the same way, Tayob et al. (2016) found that dynamical monitoring of AFP trends improved early detection while lowering the rate of misdiagnosis associated with isolated measurements.

Even with its shortcomings - including AFP’s overestimation in chronic liver disease and underestimation in early HCC - AFP continues to hold importance, especially when considered alongside other imaging studies. Roughly half of the patients with indeterminate imaging results and mildly elevated AFP levels reported in this study supports this notion. It underscores AFP's role as a potential marker for determining the need for more complex diagnostic procedures or advanced imaging timelines.

A concerning observation is that 5.9% of the patients with no radiological lesions had elevated AFP. This challenges our understanding of non-visible malignancy and Hepatic malignancy- that non-

malignant hepatic inflammation might also be involved. This was emphasized by Hanif et al. (2022), which advocated for tailored AFP assessment sustained over time.

Additionally, we support previous findings by Abbasi et al. (2012) regarding the positive association between AFP concentration and tumor burden. Much like in Abbasi's cohort, we found that patients with larger tumors (mean=3.9cm) also had higher AFP concentrations, thus reinforcing the potential of AFP in cancer staging and monitoring.

From a clinical view, combining laboratory results with imaging tests is of utmost importance in the context of tertiary hospitals, where advanced cases and complications of liver disease are encountered more frequently. This study advocates for multimodal diagnostics with strengthened radiology and laboratory medicine to improve early detection and guide proper intervention in a timely manner.

Conclusion

This study demonstrates the diagnostic utility of serum alpha-fetoprotein (AFP) levels in conjunction with imaging in hepatocellular carcinoma (HCC) detection. The significant association of elevated AFP with imaging-confirmed lesions, especially the size of the tumor, supports the benefits of integrating several diagnostic methods. The use of biochemical and radiologic information together ensures early diagnosis, which is essential in tertiary care settings where timely intervention drastically changes patient prognosis.

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