STUDY OF ALPHA-FETOPROTEIN LEVELS IN CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA

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ABSTRACT

Objective: To investigate the serum alpha-fetoprotein (AFP) levels in cirrhotic patients with and without hepatocellular carcinoma (HCC).

Subjects and methods: A cross-sectional descriptive study was conducted on 53 cases of cirrhosis at Military Hospital 175. We recorded 32 cases with HCC and 21 cases without HCC from January 2022 to January 2024.

Results: AFP levels in the group of cirrhotic patients with HCC were significantly higher compared to those without HCC ($p < 0.01$). The AUROC of AFP levels for diagnosis of HCC in cirrhotic patients was good with an AUC of 0.841, $p < 0.001$. The AFP cut-off threshold ≥ 25.88 ng/ml had the highest value for diagnosing HCC in cirrhotic patients, with a sensitivity of 68.75% and a specificity of 95.24%. Conclusion: Serum AFP level was a commonly used test, and with a cut-off threshold ≥ 25.88 ng/ml, AFP had a sensitivity of 68.75% and a specificity of 95.24% in diagnosing HCC in cirrhotic patients.

Keywords: Alpha-Fetoprotein (AFP), Hepatocellular Carcinoma (HCC), cirrhosis.

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1. Introduction

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for about 85-90% [1]. According to Globocan 2020, HCC ranks seventh among all cancers and is the second leading cause of cancer-related death [2]. Most HCC patients are related to chronic liver disease, typically developing HCC on a cirrhotic liver background. According to Coskun M.'s study (2017), the incidence of HCC in cirrhotic patients is between 2-6.6% [3]. Among the biomarkers present in the blood, AFP (alpha-fetoprotein) is commonly used for diagnosing and monitoring HCC treatment outcomes. Some studies report that AFP has a sensitivity of 39-45%, a specificity of 76-94%, and a positive predictive value of 9-50%. AFP is also used as a prognostic factor [4]. However, besides HCC, AFP levels can also be relatively high in hepatitis and cirrhosis [5], [6]. To determine the diagnostic threshold of AFP in HCC patients with cirrhosis, we conducted this study with the objective: "Surveying serum alpha-fetoprotein levels in cirrhotic patients with and without HCC."

2. Subjects and methods

*2.1. Subjects

***Selection Criteria**

- Patients meeting the diagnostic criteria for cirrhosis

- Underwent multi-phase contrast-enhanced CT scan

- AFP-level quantification tests available

***Exclusion Criteria:**

- Patients diagnosed with cancer at other sites (lung, colon, stomach, etc.)

2.2. Methods

***Study Design**: A Cross-sectional descriptive study combined with retrospective review.

***Sample Size:** All patients meeting the inclusion criteria and not meeting the exclusion criteria.

***Data Collection**: We collected data from inpatient and outpatient records of the Gastroenterology Department - Military Hospital 175. A retrospective review was conducted on all inpatients treated at the Gastroenterology Department and Gastroenterology Clinic from January 2020 to January 2024, meeting the inclusion criteria and not violating the exclusion criteria. Data were recorded using a data collection form.

***AFP Testing:**

- Location: Biochemistry Department - Military Hospital 175.

- Testing equipment: Unicel DxI Access II system by Beckman Coulter

- Testing principle: AFP was

measured on the Unicel DxI Access II system according to the principle of chemiluminescence immunoassay.

***Data Analysis:**

Data were analyzed using SPSS 20.0 software.

Differences between the two mean values were tested using the t-test for normal distribution and the Mann-Whitney test for non-normal distribution.

Differences between the two proportions were tested using the Chi-squared (X^2) test.

The difference is statistically significant with $p < 0.05$.

3. Results

From January 2022 to December 2023, we collected a total of 53 patients who met the criteria for inclusion in the study.

Table 3.1. General Characteristics of the Study Subjects

Characteristic	Total (n = 53)
Age	57.98 ± 11.44
Group with HCC	56.91 ± 11.28
Group without HCC	59.62 ± 11.76
Gender	
Male	50 (94.34%)
Female	3 (5.66%)
HCC	
Yes	32 (60.37%)
No	21 (39.62%)
Cirrhosis cause	
Viral hepatitis	36 (67.92%)
Alcohol	17 (32.08%)
Liver function (Child-Pugh)	
Child A	30 (56.60%)
Child B	17 (32.07%)
Child C	6 (11.33)

There was no significant difference in age between the group of cirrhosis with HCC and the group without HCC ($p > 0.05$). HCC accounted for a high rate of 60.37% of the cases, while 39.62% did not have HCC. The main cause of cirrhosis was viral hepatitis, accounting for 67.92%. Assessing liver function according to the Child-Pugh, Child A accounted for the highest rate of 67.92%.

Table 3.2. Characteristics of tumor location and size

Characteristic		Number (n)	Percentage (%)
Tumor location	Right lobe	21	65.63
	Left lobe	5	15.62
	Both lobes	6	18.75
Tumor Size	≤ 2 cm	10	31.25
	2 – 3 cm	11	34.37
	3 – 5 cm	7	21.88
	≥ 5 cm	4	12.50
Number of Tumors	1 tumor	14	43.75
	2 tumors	12	37.50
	3 tumors	6	18.75

Evaluation using contrast-enhanced CT scan: patients with liver tumors in the right lobe accounted for the highest proportion (65.63%). Assessing tumor size, liver tumors ≤ 3 cm accounted for the highest rate of 65.62%. Patients with one and two tumors accounted for the highest proportions, at 43.75% and 37.50%, respectively.

Table 3.3. AFP Values in Patients with and without HCC

Group	Median	Minimum	Maximum	p-value
Without HCC (ng/ml)	6.67	2.27	110.04	< 0,01 (Man Whitney test)
With HCC (ng/ml)	2272.41	3.44	47657.36	

Observation: Characteristics of AFP in cirrhotic patients with HCC and without HCC. In our study, there was a statistically significant difference in AFP levels between the group of cirrhosis with HCC and the group of cirrhosis without HCC ($p < 0.01$).

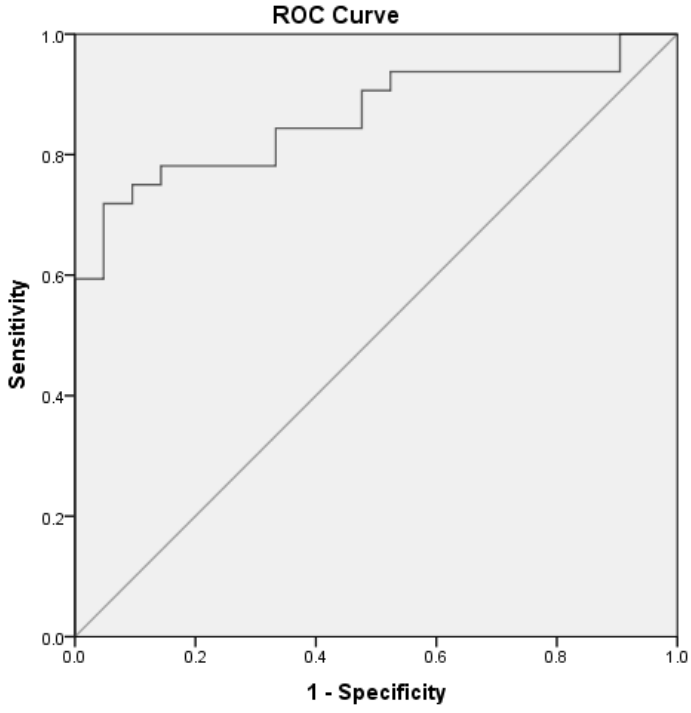

Figure 3.1. ROC Curve for AFP Levels in Diagnosing HCC in Cirrhotic Patients

When evaluating the value of AFP in diagnosing HCC, the results showed that the area under the ROC curve (AUC) for AFP levels in diagnosing HCC in cirrhotic patients was good, with an AUC of 0.841 and $p < 0.05$.

Table 3.4. Diagnostic threshold values of AFP

Diagnostic Threshold of AFP (ng/ml)	Sensitivity	Specificity	Youden's Index
≥ 10.03	78.13	71.43	0.496
≥ 10.07	75.00	71.43	0.464
≥ 11.04	75.00	76.19	0.512
≥ 13.14	71.88	76.19	0.481
≥ 14.39	71.88	80.95	0.528
≥ 15.41	71.88	85.71	0.576
≥ 17.61	71.88	90.48	0.624
≥ 20.46	68.75	90.48	0.592

≥ 25.88	68.75	95.24	0.640
≥ 44.45	65.63	95.24	0.609
≥ 63.08	62.50	95.24	0.577
≥ 68.58	59.38	95.24	0.546

The optimal cut-off threshold was determined based on the maximum Youden's index. The AFP cut-off threshold of ≥ 25.88 ng/ml had the highest value for diagnosing HCC in cirrhotic patients, with a sensitivity of 68.75% and a specificity of 95.24%.

4. Discussion

Male individuals have a higher prevalence of cirrhosis than females, with male-to-female ratios ranging from 2/1 to 4/1 in most regions [7]. Our study results were consistent with those of Thai Doan Ki (2015) [8] and Vu Thi Hanh Nhu et al. (2011) [9]. This could be explained by males having more risk factors than females such as higher rates of hepatitis B and C virus infections, alcohol consumption, smoking, higher body mass index, and higher iron reserves compared to females [7]. The causes of cirrhosis in our study were viral hepatitis in 67.92% of cases and alcohol consumption in 32.08%.

Studies by Best J. et al. (2016) [10], Thai Doan Ki (2015) [8], and Vu Thi Nhu Hanh et al. (2011) [9] also indicated that the leading causes of cirrhosis and liver cancer were viral hepatitis and alcohol. In our study, the proportion of cirrhotic patients with hepatocellular carcinoma (HCC) was 60.37%, higher than the group without HCC at 39.62%. Our ratio was similar to the study by Vo Duy Thong et al. (2021), but higher than the study by Coskun et al. (2017) with an HCC rate of approximately 2-6.6% [3]. This was because the main research subject in our study and Vo Duy Thong (2021) was HCC on a background of cirrhosis. When evaluating liver function according to Child-Pugh criteria, our results were similar to the study by Best J. et al. (2016) with Child A at 67.6% and Child B at 25.9%; Vo Duy Thong (2021) with Child A at 70.7%, Child B at 22.7%, and Child C at 6.6% [11].

When evaluating AFP levels in cirrhotic patients with and without HCC, our study results were similar to those of Best J. (2016) with AFP values of 39.35 ± 12329.26 (ng/ml) and Vo Duy Thong (2021) at 4197.1 (2.2;160250) (ng/ml) in cirrhotic patients with HCC being higher than those in the cirrhotic group without HCC ($p < 0.01$) [10],[11].

AFP was one of the diagnostic criteria for liver cancer; HCC diagnosis was made when there was a typical upper

tumor image on contrast-enhanced CT and AFP ≥ 400 ng/ml. Meanwhile, in other liver disease groups, AFP levels only increased moderately or transiently; however, in approximately 26% of cases, AFP increased above 200 ng/mL, and about 9% increased sustainably over a period of a long time [1].

In our study, the AFP cut-off threshold ≥ 25.88 ng/ml had the highest value for diagnosis of HCC in cirrhotic patients with a sensitivity of 68.75% and specificity of 95.24%. Some other studies such as Best J. et al. (2016), at a threshold of ≥ 20 ng/ml, had a sensitivity of 58.2% and specificity of 94% [10]; Research by Vo Duy Thong et al. (2021) with a cut-off threshold of 10.9 ng/ml, AFP had a sensitivity of 80.43% and specificity of 75.86% in diagnosing HCC in cirrhotic patients [11].

5. Conclusion

Serum AFP concentration was a simple test that helps in predicting the progression of HCC. With an AFP cut-off threshold of ≥ 25.88 ng/ml, AFP had a sensitivity of 68.75% and a specificity of 95.24% in diagnosing HCC in cirrhotic patients.

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