Clinical Strategy of Diagnosing patients with Hepatocellular Carcinoma based on Latent Transforming Growth Factor-Beta Binding Protein 1

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common liver cancer and a leading cause of cancerrelated death

worldwide. The latent transforming growth factor-beta binding protein 1 (LTBP-1) is a secreted protein and considers as a part of the extracellular matrix (ECM). LTBP-1 targets transforming growth factor-beta 1 (TGF-β1) and localizes it to ECM by interacting with integrin and fibronectin. It has been reported that in human malignant gliomas, the expression of LTBP-1 was gradually increased. Also, previous studies showed that the immunohistochemistry staining of LTBP-1 was extremely strong in the tumor stroma of malignant mesothelioma, pancreatic ductal adenocarcinoma and ovarian carcinoma. To date, only one publication is known about the serum level of LTBP-1 in cancer patients.

AIM

The current study aims to evaluate the diagnostic role of LTBP-1 as a biomarker to distinguish HCC from patients with liver cirrhosis.

METHOD

The current study was conducted as a cross-sectional and casecontrol based study in National Liver Institute,
Menoufia University, Egypt. It was approved by the Institutional Review Board National Liver Institute (IRB number 00003413). The participants provided written informed consent to participate in this study. The IRB approved this consent procedure. The current study included 90 individuals; 40 HCC patients (11 female and 29 males with the mean age of 53 years), 30 patients with cirrhosis (7 female and 23 males with the mean age of 54 years), and 20 healthy volunteers as a control group (1 female and 19 males with the mean age of 49 years).The serum level of LTBP-1 was measured by enzyme-linked immunosorbent assay (ELISA). Receiver operating characteristics (ROC) curves and area under the curve (AUC) were calculated.

RESULTS

The level of LTBP-1 was significantly higher in HCC patients than healthy and patients with cirrhosis. Furthermore, there was a significant ($p<0.001$) association between the level of LTBP-1 and CLIP and BCLC in HCC patients. Moreover, LTBP-1 levels were significantly ($p=0.01$) associated to child pugh grade in patients with cirrhosis and HCC. ROC curve analyses revealed that LTBP-1 showed a better diagnostic performance (AUC=0.970, Sensitivity: 82.50%, Specificity: 96.67%, PPV: 97.06%, NPV: 80.56%) in distinguishing HCC from cirrhosis patients, compared to AFP (AUC=0.810, Sensitivity: 62.50%, Specificity: 93.33%, PPV: 92.59%, NPV: 65.12%). the level of LTBP-1 in HCC patients was significantly ($p<0.001$) associated with CLIP score. Because, the LTBP-1 was gradually increased with CLIP score increasing, where LTBP-1 concentration in score 5 recorded 49.1 against to 19.4 in score 0. Conversely, AFP was not significantly ($p=0.098$) associated with CLIP score. Concerning to BCLC, There was a significant ($p<0.001$) association between the serum level of LTBP- 1 and BCLC score in HCC patients. The LTBP-1 level was gradually increased with the progress in BCLC score, where, the level was 46.8 in score 4 against 26.6 in score 0. On the contrary, AFP level was not significantly ($p=0.172$) associated with BCLC score.]

CLIP score		AFP		LTBP-1	
	N	*Mean + SD*	*P- value*	*Mean + SD*	*P- value*
0	7	117.8 ± 106.1	0.098	19.4 ± 0.7	< 0.001
1	8	593.5 ± 1004.3		26.0 ± 8.3	
2	5	1337.6 ± 2325.2		26.5 ± 2.4	
3	11	15791.6 ± 32407		31.9 ± 3.6	
4	5	949.4 ± 1218.7		38.2 ± 6.8	
5	4	33403.0 ± 39891.9		49.1 ± 5.7	

CONCLUSIONS

The serum levels of LTBP-1 exhibited gradually increased trend in healthy individuals, liver cirrhosis and HCC patients. Serum LTBP-1
might be a potential serum marker to discriminate HCC from liver cirrhosis patients due to its high sensitivity and specificity, compared to AFP. LTBP-1 was significantly associated with CLIP, BCLC, and child pugh grade. LTBP-1 might be a promising diagnostic biomarker for HCC although; we recommended that future studies on large number of patients are required to validate these results.

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CONTACT INFORMATION

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