

The value of serum Glypican-3 in aided diagnosis of patients with primary hepatocellular carcinoma

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Summary: This study evaluated values of serum Glypican-3 for the diagnosis of primary hepatocellular carcinoma. This study from Department of laboratory, Fudan University Cancer Hospital, Department of oncology, Shanghai Medical College, Fudan University included a total of **166 HCC** (hepatocellular carcinoma) patients (85.5% male and 14.5% female), diagnosed with HCC from March 2018 to May 2019. These 166 HCC patients were further grouped based on staging (72 cases with Stage I-II and 94 cases in Stage III-IV) and number of lesions (121 cases with single lesion and 45 cases with multiple lesions). The study also included **94 HC** (healthy controls) collected from May to June 2019, and **50 patients** with benign liver disease (**BC= Benign Control**) - 15 of which had liver cirrhosis and 35 had chronic Hepatitis B- collected between March to June 2019. The study was approved by the Ethic Committee of Fudan University Shanghai Cancer Center.

Results: In the HCC group the measured median Glypican-3 concentration was 210 pg/mL. This value was higher than the values detected for both the HC group and the BC group, that were respectively 29 pg/mL and 33 pg/mL. Furthermore, these differences were statistically significant ($Z = -7.69, P < 0.001$).

	HC	BC	HCC	P value
Serum Glypican- 3 Median (interquartile range Q1, Q3)	29 pg/mL (19,52)	33 pg/mL (21,43)	210 pg/mL (48,801)	<0.001

Furthermore, the analysis of serological features within the three subgroups (HCC, BC and HC) showed a significant difference in Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alpha fetoprotein (AFP).

Clinical Serological Features of the Study Population

Group	N of cases	AST (U/L)	ALT (U/L)	ALP (U/L)	TB (mol/L)	AFP (U/L)
HCC	166	31.5 (21.9,46.2)	26.4 (20.0,38.9)	90.4 (74.7,114.1)	11.2 (8.9,16.0)	20.4 (3.8,556.3)
BC	50	22.0 (18.0,27.5)	28.0 (20.7,48.3)	96.5 (68.3,125.6)	11.1 (9.2,15.8)	3.2 (2.4,11.3)
HC	94	17.1 (14.9,19.8)	11.3 (7.4,16.2)	81.1 (49.9,107.4)	10.7 (8.2,12.7)	2.9 (1.9,5.6)
Z value		-7.02	-6.85	-0.82	-1.26	-8.36
P value		<0.001	<0.001	0.457	0.197	<0.001

Note: HCC (Primary hepatocellular), BC (Benign Control), HC (Health Control), AST (Aspartate aminotransferase), ALT (Alanine aminotransferase), ALP (Alkaline phosphatase), TB (Total Bilirubin), AFP (Alpha fetoprotein). Serum marker results are expressed by median (quartile Q1, Q3).

To evaluate possible differences in serum Glypican-3 concentrations, HCC patients were divided based on age, tumor stage, number of lesions and relevant serological indicators. The results showed that serum Glypican-3 concentration in HCC patients correlated with the two serological indicators ALT and AST but did not correlate with other factors such as age, tumor stage and number of lesions.

Furthermore, the diagnosis of HCC with serum Glypican-3 alone resulted in a sensitivity of 59.0% and a specificity of 86.0%. AFP on the other hand had a lower sensitivity of 57.8% and a specificity of 91.7%. The performance of Glypican-3 in combination with AFP resulted in a higher sensitivity of 87.8%, and a specificity of 77.9%.

Performance of joint detection of Glypican-3 and AFP of the diagnosis of HCC

Serum marker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Glypican-3	59.0	86.0	85.2	60.5
AFP	57.8	91.7	57.8	91.7
Glypican-3+AFP	87.8	77.9	82.5	84.3

In addition, a follow-up analysis was carried out on 119 out of 166 HCC patients. Specifically, serum was collected a week before and a week after surgery. The results showed that Glypican-3 serum concentrations in 111 patients (93.2%) after surgery were lower than the levels prior to surgery (454 pg/mL vs 608 pg/mL). It was also found that a $\geq 20\%$ decrease in serum Glypican-3 concentration levels after surgery compared to levels before surgery, may be a good predictor for successful surgical treatment.

Conclusions:

- Serum Glypican-3 concentration was higher in the HCC group compared to the HC and the BC group.
- The combination of Glypican-3 and AFP can improve the diagnostic efficiency of HCC.
- Glypican-3 may also be a good predictor of surgical outcome in HCC.