Research Article

Study role of C-reactive protein in early detection and prognosis of HCV-related HCC

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Abstract
Background: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer in adults, and it is the most common cause of death in people with cirrhosis. CRP values may be elevated in cancer patients. **Aim**: To investigate the diagnostic and prognostic values of CRP in patients with HCV-related HCC. **Patients and methods**: 60 cirrhotic patients with HCC, 30 patients with chronic hepatitis C infection Without HCC, 30 cirrhotic patients without HCC and 50 healthy controls were subjected to history, clinical examination, laboratory investigations. The serum levels of CRP and AFP were measured in the 4 groups. **Results: CRP** was significantly higher in HCC patients. And also, AST and age were significantly higher in HCC patients. **Conclusion:** This study indicated that Serum CRP could be a potential serum marker due to its high sensitivity and specificity in early detection of HCC. It also can predict the response to treatment of HCC after RFA.
Keywords: Hepatocellular carcinoma, C-reactive protein

Introduction
HCC is one of the major health problems worldwide and 600000 patients dying from this disease annually[1] (Forner et al., 2012). CRP values may be elevated in cancer patients. In fact, several studies have reported a prognostic value of elevated CRP levels in different types of cancer including resectable HCC. Also, It has been investigated the prognostic value of CRP levels in nonsurgical HCC patients with respect to the BCLC classification (Bataille R et al., 2002).

Patients and method
This study was conducted in Internal Medicine department and outpatient clinic EL-Minia University Hospital from May 2017 to April 2018. This cross section observation study included 60 cirrhotic patients with HCC, 30 patients with chronic hepatitis C infection Without HCC, 30 cirrhotic patients without HCC and 50 healthy controls. We excluded from our study patients who were younger than 18 years of age, Patients with liver cirrhosis due to any cause rather than HCV and patients with chronic renal insufficiency. All patients subjected to clinical assessment, complete blood count, renal function tests, liver function tests, International Normalized Ratio (INR), viral markers (HCV-Ab and HBsAg) HIV antibodies, Alpha-fetoprotein using enzyme immunoassay serum alpha fetoprotein. Serum hsCRP ELISA was assessed using immune-assay based on Principle of a solid phase enzyme-linked immunoscrbent assay adapted two-site sandwich ELISA. In this assay, standards and patient samples are simulta-neously incubated with the enzyme labeled detection antibody and is allowed to react simultaneously with the two antibodies, resulting in the CRP molecules being between the solid phase and enzyme linked antibody.

Results
Demographic and clinical date of the patients and control groups shows no significant difference between all groups as regard age, gender (Table 1). As regard hepatic encephalo-pathy there was statistically significant differ-ence between HCC group 88% compared to 66% of patient in liver cirrhosis group ($p<0.001$).

Also there was no statistically significant difference between both groups as regard percentage of patients with hematemesis (85% vs 83.3% $p=0.92$), while there was significantly higher percentage of patient as regard ascites, edema and jaundic in HCC group compared to all 3 control groups ($p=0.004$), there was significantly lower hemoglobin and TLC level in patient with HCC compared to chronic

hepatitis and healthy control (p= <0.001) and there was significant difference between HCC and liver cirrhosis groups (p=0.004 & 0.006) respectively. Platelet count was found to be significantly lower in HCC groups compared to all 3 controls (p< 0.001). There was no significant difference between HCC and cirrhotic groups as regard INR (p=1), while there was significantly higher INR in HCC group compared to both chronic hepatitis and healthy control groups (p<0.001). There was significantly higher bilirubin level in patient with HCC compared to chronic hepatitis and healthy control (p= 0.006) while there was no significant difference between HCC and liver cirrhosis groups (p=0.09).

No significant correlation was found between the mean serum CRP and age, sex, but significant correlation was found between the mean serum CRP and tumor size, number of lesions (P-value <0.001). There was a significant correlation between the mean AFP and age (r= 0.2 & p= 0.01) while there were no significant correlation between the mean AFP and sex, tumor size and tumor number of lesions

Our study detect that CRP at cut-off value of 1.3 mg/dl had superior sensitivity than AFP at cut-off values of 250ng/ml (88.5% and 78%, respectively). Combined use of both markers improved the sensitivity to 90.3% . There was significant decrease in serum level of CRP in patients with HCC after radiofrequency ablation compared to those before treatment (0.9±0.23vs 1.6±0.3, p< 0.001). Also there was significant decrease in serum level of AFP after compared to before RFA (985±393.7 vs1532.9 ±434, p< 0.001). There was significant decrease in serum level of creatinine patients with HCC after radiofrequency ablation compared to those before treatment (0.91±0.09 vs 1.13±0.19, p< 0.001).

Also there was significant decrease in serum level of T. bilirubin after compared to before RFA (2.3±1.4vs 2.88±2.1, p< 0.001). there was significant decrease INR after compared to before RFA (1.4±0.43vs1.7±0.34, p< 0.001). No significant decrease was found in serum albumin after compared to before RFA (2.24±0.45vs.2.37±0.5, p=0.066).there was significant change in MELD score after compared to before RFA (30.33±4.26vs, 26.22 ±4.87, p< 0.001). Also there was significant change in CHILD score after compared to before RFA (8.2 ±3.5vs. 9.5 ± 2.3, p=0.03).

Table (1): Laboratory data of the studied groups

Variables	Group I HCC (n=60)	Group II LC (n=30)	Group III CHC (n=30)	Group IV Control (n=50)	P-value		
					I vs II	I vs III	I vs IV
Hb (mg/dl)					<0.001*		
Range	(8-12)	(6-12)	(10-13)	(11-15)	0.004*	<0.001*	<0.001*
Mean ± SD	9.9±0.96	9.2±1.6	11.4±0.96	12.8±1.1			
T. Bilirubin					<0.001*		
Range	(0.7-9.9)	(0.5-6.6)	(0.8-1.4)	(0.3-1)	0.094	0.006*	<0.001*
Mean ± SD	2.9±2.4	2.2±1.6	1.1±0.17	0.60±0.2			
Albumin					<0.001*		
Range	(1.5-3.4)	(1.4-2.9)	(3.8-5.5)	(4.3-5.2)	0.272	<0.001*	<0.001*
Mean ± SD	2.4±0.44	2.3±0.43	4.46±0.5	4.74 ±0.3			
ALT					<0.001*		
Range	(25-92)	(13-76)	(28-43)	(11-25)	<0.001*	<0.001*	<0.001*
Mean ± SD	51.9±13.7	32.7±16.8	36.4±4.2	17.5±3.8			
AST					<0.001*		
Range	(36-115)	(14-107)	(31-43)	(18-28)	<0.001*	0.003*	<0.001*
Mean ± SD	65.3±20.3	50.7±27	37.5±3.6	22.2±3			
Creatinine					<0.001*		
Range	(0.5-1.5)	(0.5-3.7)	(0.5-0.9)	(0.4-1)	0.621	0.004*****	0.003*
Mean ± SD	0.99±0.28	1.03±0.75	0.68±0.13	0.66±0.18			
INR					<0.001*		
Range	(1.2-2.1)	(1.2-4)	(1-1.2)	(1-1.1)	1	<0.001*	<0.001*
Mean ± SD	1.65±0.34	1.65±0.68	1.04±0.06	1.03 ±0.05			
AFP					<0.001*		
Range	(27-2500)	(15-400)	(10-60)	(5-20)	0.007*	0.033*	0.002*
Mean ± SD	1090±741	97.3±94.2	39±14.6	8.8±7.25			
CRP					<0.001*		
Range	(0.8-2)	(0.4-1.6)	(0.2-0.4)	(0.15-0.2)	0.005*	0.002*	<0.001*
Mean ± SD	1.6±0.3	0.95±0.29	0.29±0.1	0.16±0.07			

Discussion

In Our study there was no significant difference between patients with solitary and multiple hepatic focal lesions as regard AFP .However there was significant difference as regard CRP serum levels. Similar date were reported with Wan-Long Chuang et al., 2000 who found that 55% of patients with single nodular SN-type, 81.5% (22/27) of patients with multible nodular MN-type, 87.8% (43/49) of patients with massive M-type and 94.1% (16/17) of patients with diffuse D-type HCC showed elevated CRP. Our results shows that there was a statistically significant decrease in both CRP and AFP after RFA with p value < 0.001 which implies good response to treatment whereas in recurrent cases there was non-significant decrease in both markers after treatment.

We found that MELD score as well as Child score was significantly decreased after succe-ssful RFA whereas there was no significant change in both scores after treatment in recurrence cases, this may be explained by that significant improvement of liver function test namely bilirubin and INR as well as serum creatinine after successful ablation therapy so it can be used as predictor of response to therapy.

In the present study, we observed non-significant difference of serum bilirubin in HCC in comparison to cirrhotic patients. However, our data showed a higher significant levels of serum bilirubin in both the HCC and the cirrhotic patients compared to the chronic hepatitis patients (p<0.001). Bilirubin is the most important measure of liver failure,

reflecting the dual causes of death from HCC being from either tumor aggressiveness or liver destruction. This is supported by Carr et al., 2014 who found association between abnormal bilirubin level and HCC aggressiveness. We also investigated serum CRP level in our patients and found a significant higher level of serum CRP in patients with HCC.

Conflict of interest

None

Acknowledgment

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