Expression of Circulating Annexin A2 in Hepatic Diseases and Hepatocellular Carcinoma

Ebtesam El Gezawy , Laila Abdelbaki*, Mohamed Zeinel Deen, Sahar Eldeek***, Marwa I. Abdelgawad******

Assisstant Professor of Clinical Pathology,*Assistant Professor of Tropical Medicine and Gastroenterology., **Assistant consultant of internal Medicine, ***Assisstant Professor of Biochemistry , ****Lecturer Of Clinical Oncology , Faculty of Medicine-Assiut University

Introduction and Objectives:

Hepatocellular carcinoma (HCC) is the fifth most common malignancy and the third leading cause of cancer-related mortality worldwide. HCC develops as a result of chronic inflammation caused by either hepatotropic viruses, toxins, metabolic liver disease or autoimmunity. The up-regulation of annexin A2 in HCC was associated with malignant transformation of hepatocytes and not with liver tissue regeneration.

- This study was conducted to evaluate the serum level of the value of serum Annexin A2 as non-invasive tool in correlation with histopathology of the liver biopsy in prediction of hepatic fibrosis in chronic viral hepatitis "C"and prospective assessment of the predictive value of Annexin for the diagnosis of significant fibrosis.
- to assess weather serum Annexin A2 will be used as a prognostic biomarker for early diagnosis and monitoring of tumor recurrence of HCC.
- To prove the concept that serum levels of annexin A2 are also elevated in early stage HCC patients which are AFP-negative.

Patients and Methods:

- A total number of 40 who were recruited from the outpatient clinics of Tropical and Internal Medicine and Clinical Oncology Departments, Assiut University Hospital (Egypt) classified as follows (6 (15%) patients with chronic HCV, 8 patients (20%) with liver fiberosis, 6 patients (15%) with liver cirrhosis , 8 patients (20%) with early HCC and 12 patients (30%) with late HCC. The same number of age and sex matched healthy people as a control group with negative hepatitis viral markers [HBV surface antigen, and anti-hepatitis C virus (HCV)] and a normal alanine aminotransferase level obtained from the Central Blood Transfusion Services(CBTS), Assiut University Hospitals, were enrolled in this study.
- All patients and controls were subjected to full medical history, complete medical examination, abdominal sonography, laboratory investigations including liver function tests, alpha fetoprotein (AFP), complete blood pictures, Prothrombin time and concentration, HBsAg , anti-HCV and serum HCV RNA quantitation by real time PCR . Liver biopsies were done for all patients (Group I) after informed consent.
- Evaluation of serum Annexin A2 level **(ANXA2)** for all groups was detected by using a human ANXA2 ELISA kit (Glory Science Co., Ltd., USA)according to the manufacturer's instructions.
- Clinicopathological characteristics of circulating ANXA2 expression were analyzed, and its diagnostic efficiency and clinical values in HCC were evaluated. anti-annexin A2 antibody (Abcam, Cambridge, UK). ANXA2 staining was assessed using the immunoreactive score.

Results and Conclusions:

Table I: Patients demographic data:

ITEM	*Descriptive*
Age (years) (Mean ± SD) (min-max)	57.73 ± 12.45 (29.0-81.0)
Sex: Male Female	11(27.5%) 29(72.5%)
Serological tests: HBsAg (+ve) Anti-HCV (+ve) HCV –PCR (+ve)	4(10.0%) 22 (55.0%) 17 (42.5%)

Table II: Laboratory data of all studied group (n=40) compared to the control group:

Parameter	All studied groups N.=40	Control group N.=40	*P-value*
PT (sec)	10.01 ± 1.34	12.52 ± 1.04	P<0.01*
PC(%)	76.23 ± 3.12	98.34±1.23	P<0.000***
AST (U/L)	72.12 ± 29.94	28.32 ± 6.40	P<0.000***
ALT (U/L)	78.82 ± 28.63	26.60 ± 4.91	P<0.000***
GGT (U/L)	97.23 ± 8.56	32.12 ± 3.56	P<0.000***
ALK (U/L)	163.23 ± 12.56	74.34 ± 5.34	P <0.000***
Platelets (x10^9 /L)	165.70 ± 49.26	238.9 ± 79.41	P< 0.01*
AFP (IU/ml)	295.23 ± 23.67	3.21 ± 1.11	P<0.000***
Annexin A2 (ng/ml)	39.44±7.34	10.52±2.04	P <0.000***

PT: prothrombin time, PC: prothrombin concentration, AST: aspartate transaminase, ALT: alanine transaminase, GGT:gamma-glutamyltransferase, ALK: Alkaline phosphatase, AFP: alpha fetoprotein

Figure (1): Patients Classification and grouping:

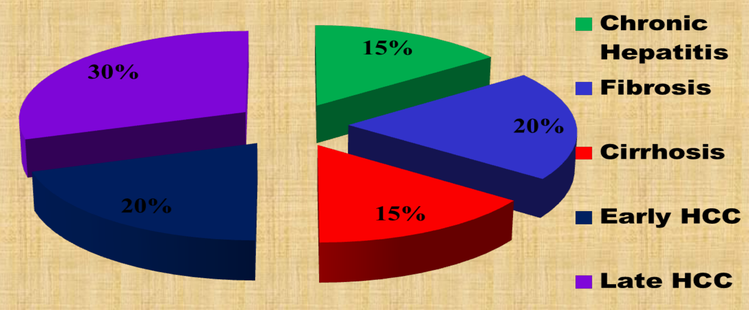


Table III: Serum Annexin A2 in different studied groups compared to the control group:

Groups	Annexin A2(ng/ml)	*P-value*
Control	18.45 ± 3.27	
Chronic hepatitis	10.67 ± 2.89	P<0.03*
Liver Fiberosis	11.78 ± 1.40	P<0.000***
Liver Cirrhosis	16.34 ± 3.96	P=0.376n.s
Early HCC	33.85 ± 3.59	P<0.000***
Late HCC	36.89 ± 5.22	P <0.000***

HCC: hepatocellular carcinoma

Table IV: Serum AFP in different studied groups compared to the control group:

Group	AFP (IU/ml)	*P-value*
Control	4.02 ± 0.97	
Chronic hepatitis	17.45 ± 2.33	P<0.02*
Liver Fiberosis	21.65 ± 4.65	P<0.001**
Fibrosis	37.45± 2.92	P<0.000***
Early HCC	287.34 ± 4.57	P<0.000***
Late HCC	298.23 ± 3.68	P <0.000***

HCC: hepatocellular carcinoma

Figure (2 & 3): Annexin A2 Immunehistochemical study among those with healthy controls, liver cirrhosis, early stage HCC and late-stage HCC, Fig 2A showed negative liver tissue, Fig.2b liver cirrhosis and Fig 2C show HCC:

Fig. 1

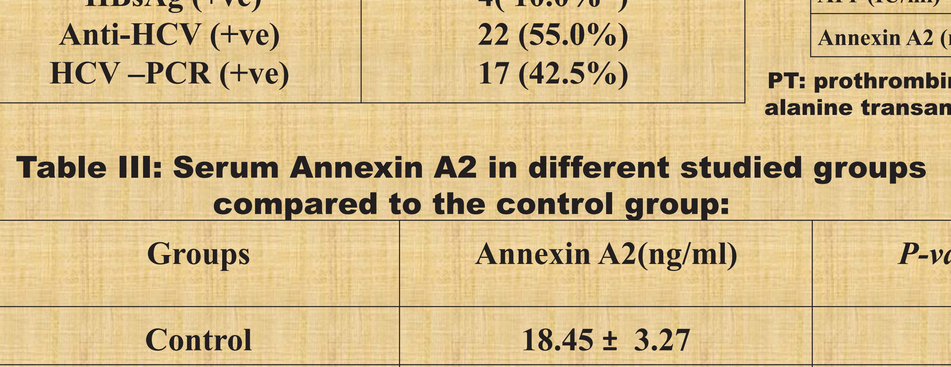
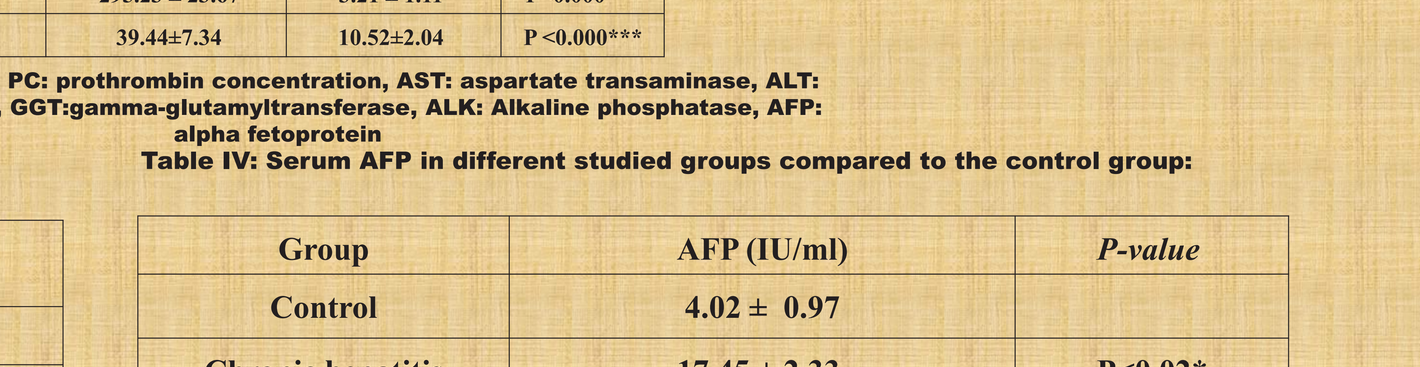


Fig.2



In our study we assess the complementary abilities for HCC diagnosis of annexin A2 and AFP. The serological examination showed that the annexin A2 levels significantly increased in early HCC compared to serum AFP, suggesting that the elevation of serum annexin A2 may serve as an index of hepatocarcinogenesis. In conclusion, our results demonstrated upregulation of annexin A2 in both of tissues and sera of HCC patients and also in both AFP-positive and -negative cases. Remarkably, Results of Annexin A2 was concomitant with Annexin A2 immunecytochemistry. Combination of conventional serum marker AFP with annexin A2 may complement and benefit for early HCC detection. Further validation with a larger sample size may help to systematical evaluation of annexin A2 and develop novel diagnostic and prognostic markers for liver cancer.

WCGC 2015
22-P
Basic Hepatocellular Cancer
Ebtesam Elgezawy
DOI: 10.3252/pso.eu.17wcgc.2015
Poster presented at: ESMO Imedex 17th World Congress on Gastrointestinal Cancer 1-4 JULY 2015 BARCELONA, SPAIN