

STUDY OF ALPHA FETOPROTEIN, FERRITIN LEVELS AND LIVER ULTRASONIC FINDINGS IN HEMODIALYSIS PATIENTS POSSESSING HEPATITIS C VIRUS ANTIBODIES IN TABRIZ

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ABSTRACT

Background & Objectives: Alpha Feto Protein (AFP) is the most important tumor marker of Hepato Cellular Carcinoma (HCC) and ferritin is a quantitative marker of iron in storage compartments. In this study for early assessment of (HCC), anti-HCV positive patients were investigated with AFP and obtained results for ferritin levels and ultrasonic findings compared with each other.

Methods: Forty nine anti - HCV positive hemodialysis patients as case group and 41 anti-HCV negative hemodialysis patients as control group were randomly selected and studied for AFP and ferritin using EIA methods and liver ultrasonic findings.

Results: The mean of AFP level in case group (6.8 ± 0.9 ng / ml) was significantly higher than that of control group (3.1 ± 0.3 ng / ml) and by statistical analysis significant difference between the two groups was noticed ($p < 0.05$). Comparing serum ferritin level between the two groups, no significant difference was observed ($p > 0.05$). No significant correlation was found between age and sex with AFP or ferritin in the both groups. Sonographic findings in anti -HCV positive patients with high level of AFP showed 16.3% slight splenomegaly and 2% splenomegaly with vein dilation and 4.1% splenomegaly with cholelithiasis.

Conclusion: The results of this study emphasis on the necessity of routine AFP evaluation in anti - HCV positive patients for early assessment of hepatocellular carcinoma.

KEY WORDS: Alpha fetoprotein, Ferritin, Hemodialytic patient, Anti-HCV.

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INTRODUCTION

Alpha Feto Protein (AFP) is one of the most important tumor marker for Hepato Cellular Carcinoma (HCC), that increase considerably in more than 90% of patients.¹ AFP is a

non-specific tumor marker and may appear in certain malignant disease such as tumors of testis, ovary, bronchi and pregnancy but rises considerably (more than 500 ng/ml) in HCC.^{2,3} Ferritin is a marker for storage of iron and has important role in protection of cells against free iron toxic effects. In some malignant disease and chronic disorders ferritin levels is used for assessment of diseases.⁴

Knowing that chronic infections with Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are important causes of in HCC and some previous studies have shown no correlation between HBV and AFP,^{5,6} we studied the above mentioned parameters in hemodialysis patients who are at high risk for HCV in this area.

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Table-I: Level of AFP in anti – HCV positive and negative hemodialysis patients

AFP ng / ml	Anti – HCV (-)		Anti – HCV (+)		Total	
	%	N	%	N	%	N
0 – 2.9	56.1	23	18.4	9	35.6	32
3 – 5.9	34.2	14	38.8	19	36.7	33
6 – 8.9	7.3	3	24.48	12	16.7	15
9 – 11.9	2.4	1	6.1	3	4.4	4
12 – 14.9	0	0	6.1	3	3.3	3
15 – 17.9	0	0	2.04	1	1.1	1
> 18	0	0	4.08	2	2.2	2
Total	100	41	100	49	100	90

N = Number of samples studied

PATIENTS AND METHODS

Forty nine anti – HCV Hemodialysis patients as case group and 41 age and sex matched anti – HCV hemodialysis patients as control group were randomly selected and studied for AFP, Ferritin (using EIA methods) and liver ultrasonography from May 2002 to December 2003.

RESULTS

This study showed that the mean levels of AFP are 6.8 ± 0.9 and 3.1 ± 0.3 ng/ml in case and control groups, respectively (Table-I). Statistical analysis showed that there is significant difference between serum levels of AFP in case and control groups ($p < 0.0005$). The means of serum AFP level in different age groups in anti HCV patients and descriptive of these data are shown in Table-II. Statistical analysis didn't show significant correlation between serum AFP level and age. Measuring AFP levels in both sex, we found serum AFP

was 8.2 ± 2.3 ng/ml in males and 6.2 ± 0.8 ng/ml in females, but statistically no significant difference between the groups. The mean levels of serum ferritin in patients and control groups were 535 ± 0.59 ng/ml and 610 ± 0.61 ng/ml respectively and its distribution are shown in Table-III.

Ultrasonic finding showed 10.2% silent splenomegaly, 2% splenomegaly with vein dilation and 4.1% cholelithiasis in 17% of anti – HCV positive hemodialysis patients.

DISCUSSION

Hepatocellular carcinoma is one of the most common tumors in certain areas, and more than 250000 new cases are diagnosed every year in the world.² Brown and colleagues reported that more than 20-30% cases of HCC are found in some areas of Asia and Africa.⁷ The etiology and prevalence of the HCC differ in different parts of the world, but results of

Table-II: Comparison of the serum AFP level in different age groups in anti – HCV Hemodialysis patients

Age group (years)	N	Max	Min	AFP (mean)
10 – 19	1	7.3	7.3	7.3
20 – 29	6	16.0	3.3	$7.1 + 1.8$
30 – 39	6	7.9	2.6	$5.6 + 0.8$
40 – 49	16	26.9	1.1	$6.9 + 1.6$
50 – 59	9	5.4	2.9	$4.4 + 0.4$
60 – 69	7	35.5	3.1	$10.5 + 4.3$
70 – 79	4	14.0	0.8	$6.7 + 3.3$

N = Number of samples studied

Table-III: Distribution of the serum Ferritin level in case and control groups

<i>Ferritin ng / ml</i>	<i>Anti – HCV (-)</i>		<i>Anti – HCV (+)</i>		<i>Total</i>	
	N	%	N	%	N	%
< 199	10	24.4	13	26.5	23	25.6
200 – 399	3	7.3	10	20.4	13	14.4
400 – 599	9	22	7	14.3	16	17.8
600 – 799	1	2.4	3	6.1	4	4.4
800 – 999	6	14.6	4	8.2	10	11.1
> 1000	12	29.3	12	24.5	24	26.7
Total	41	100	49	100	90	100

N = Number of samples studied

many investigations show that alcohol, certain viruses and some toxins have crucial effect on this malignancy.⁸

Many studies from different countries have shown that the probability of HCC in patients with HBV and HCV was 20 times more than other individuals and serum levels of AFP in these patients was more than 400–500ng/ml.^{2,7} Results of some studies have shown that the rate of serum AFP increases in HBsAg positive carriers with HCC is not higher than that in Anti-HCV positive patients, and today role of HCV oncogenesis in HCC induction have been recognized.^{2,9}

Certain factors such as age, sex, infection with HBV and HCV, cirrhosis and acute liver necrosis specially size and form of tumor pathology can influence AFP level.² Serum AFP rises in hepatic and extra hepatic can be different by Foscusilation index.⁶

Kobayashi, Solmi and colleagues emphasized that AFP assessment and liver ultrasonic simultaneously can be a crucial diagnostic factor in screening and follow up of the patients at risk of HCC.¹⁰ Application of these two methods increases the probability of diagnosis and is very useful in initial screening method for the case of tumors less than 2 cm.¹¹ The AFP sensitivity differs very much on the basis of selected cut-off level in many countries. Results of many studies showed that serum AFP level more than 400-500 ng/ml is specific for HCC, but its range between 20-200 ng/ml is nonspecific in diagnosis, but in HCC individuals should be followed up and paid attentions as a high risk

groups for HCC.¹¹ Tsai and colleageus studied serum AFP level in anti-HCV positive and negative patients and they found meaningful difference ($p<0.0005$) in serum AFP level in two groups.⁵ The results of the serum AFP level in this study showed a meaningful difference ($p<0.0005$) in anti-HCV positive and negative patients. In our study the average of serum AFP level in patients and control groups were 6.8 ng/ml and 3.1 ng/ml respectively, and in the 26.5% of the anti-HCV positive hemodialysis patients the rate of the AFP was higher than that of the average. No meaningful difference ($p=0.4$) was noticed in comparison of serum AFP level in different sex and age groups with anti-HCV positive and these results were completely in agreement with Tsai et al findings.⁵

Dibiscegli and colleagues reported considerable increase in the levels of ferritin in 30% of 80 patients with viral chronic hepatitis and its increase in males was higher than females.¹² Albert and colleagues also reported increase in serum ferritin in about 31% of HCV positive patients.¹³ Comparing serum ferritin level no meaningful difference was noticed between two groups.

AFP assessment (whose relative risk is 14 times higher than that of patients with normal AFP levels) and liver ultrasonic are crucial parameters in primary diagnosis of HCC. In case the size of cancers is less than 1 cm, ultrasonic method is not helpful, but in these cases serum AFP assessment and CT-scan and MRI are very helpful.^{6,14}

As HCV, in long term, has crucial role in HCC induction, in anti-HCV positive patients and other high risk groups AFP assessment will be helpful and liver ultrasonography should be done every six months.⁹

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