

Does Value of Alpha Fetoprotein Matter in HCC?

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ABSTRACT

Aim: To determine whether value of Alpha Fetoprotein matter in HCC

Methods: A cross sectional analytical study was done at Departments of Medicine Lahore General Hospital and Ghurki Trust Teaching Hospital Lahore, from January 2012-2014. After informed written consent patients with biphasic CT scan proven hepatocellular carcinoma were included. History GPE and demographics were recorded on a preformed proforma AFP done and patients were divided according to alpha-fetoprotein levels i.e., Group I less than 20ng/dl, Group II 20-399ng/dl, Group III more than 400ng/dl and the size of tumor i.e., Group A less than 3cm, Group B 3-8cm, Group C more than 8cm results are analyzed. Data was analyzed by SPSS 18 by applying Spearman's rank correlation with p-values of 0.05 being considered significant.

Result: A total number of 253 patients were enrolled out of which there were 183 males (72.33%) and 70 females (27.66%), with the mean age of 52±11.51 ranging from 32 to 82 years. 138 (54.5%) patients were having HCV, 64 (25.29%) patients were HBV and 9 (3.55%) patients having both HBV&HCV. There were 25 (9.88%), 153 (60.47%), 75 (29.64%) cases in AFP group I, II, III respectively. While 22 (8.69%), 132 (52.17%), 99 (39.1%) cases in tumors size groups A, B, C respectively. Large tumor size Group C got 92.8% raised AFP levels as compared to group B (91.5%) and Group A (72.6%). Small Tumor size group A got 27% normal AFP, group B and C got 8.3% and 8% normal AFP respectively.

Conclusion: AFP levels correlates with HCC especially in large tumors and in early HCC. Its value should be co-related with sensitive imaging techniques so that early detection of tumor is not missed.

Keywords: Alpha-fetoprotein, Hepatocellular carcinoma, tumor size

INTRODUCTION

Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world. Risk factors include hepatitis B and C virus infections, alcoholism, cirrhosis, aflatoxins, hemochromatosis and Wilson's disease¹. The risk factors which are most important varies widely from country to country. In countries where Hepatitis B is endemic, such as China, Hepatitis B is the predominant cause of Hepatocellular Carcinoma. Whereas in countries, such as the United States, where Hepatitis B is rare because of high vaccination rates, the major cause of HCC is Cirrhosis (often due to alcohol abuse)². In Pakistan, the major cause of HCC is HCV related cirrhosis because 6-7% population is affected by HCV³. The annual incidence of developing HCC in hepatitis B and C positive patients is 3-5% and 75-90% of these patients have cirrhosis⁴.

Diagnosis of HCC is made usually by sensitive imaging of liver, biopsy or tumor markers like alpha-fetoprotein. AFP is a large glycoprotein, belonging to the class of onco-development protein comprising of 591 amino acids with a half life of 5-7 days. Normally

produced by the fetal yolk sac, liver, and intestine, elevated levels can be associated with HCC in the appropriate clinical settings and there are other causes of raised levels as well including cirrhosis, lung cancer, gastric cancer, biliary and pancreatic tumors and spherocytosis. Alpha fetoprotein has been considered for a long time the ideal serological marker for detecting HCC⁶. Clinical studies have shown that there is a close relationship between the level of serum AFP and HCC incidence, recurrence and metastasis and serum AFP levels has been used as the main index of prediction for HCC prognosis after hepatectomy⁷. The objective of this study is to find out the relationship of AFP with HCC and its co relation with tumor size so that we can plan effective management plan.

MATERIAL AND METHODS

This cross-sectional study was conducted at division of Gastroenterology, Medical unit 1, Post Graduate Medical Institute/Lahore General Hospital Lahore and Ghurki Trust Teaching hospital Lahore. It was carried out between January 2012 to January 2014. Patients enrolled in the study were known cases of chronic liver disease and were complicated by development of hepatocellular carcinoma proven by Biphasic CT

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scan abdomen .Written informed consent for each patient was given before participating in the study. Patients with serious heart, lung, kidney, or blood diseases, autoimmune liver disease, or the presence of other malignant tumors, were excluded. Demographic data such as age, gender, residence were recorded. Detailed clinical history and examination were carried out and recoded in proforma. Complete blood count, liver function tests, total protein, HBsAg and anti HCV and alpha fetoprotein were performed.

On the basis of alpha fetoprotein levels, the patients were divided into three groups. Group I with AFP less than 20ng/ml, Group II with AFP between 20-399ng/ml and group III with AFP more than 400ng/ml. Patients were also divided on the basis of tumor size as group A having tumor size less than 3, group B having size 3-8cm and group C having size more than 8cm. Data was analyzed by SPSS 18 by

applying Spearman's rank correlation with p-values of 0.05 being considered significant.

RESULTS

A total number of 253 patients were enrolled out of which there were 183 males (72.33%) and 70 females (27.66%), with the mean age of 52±11.51 ranging from 32 to 82 years. 138(54.5%) were having HCV, 64(25.29%) were HBV,9(3.55%) having both HBV&HCV. There were 25(9.88%), 153(60.47%), 75(29.64%) cases in AFP group 1, 2, 3 respectively. While 22(8.69%), 132(52.17%), 99(39.1%) cases in tumors size groups A, B, C respectively. Large tumor size Group C got 92.8% raised AFP levels as compared to group B (91.5%) and Group A (72.6%).Small Tumor size group A got 27% normal AFP, group B and C got 8.3% and 8% normal AFP level respectively.

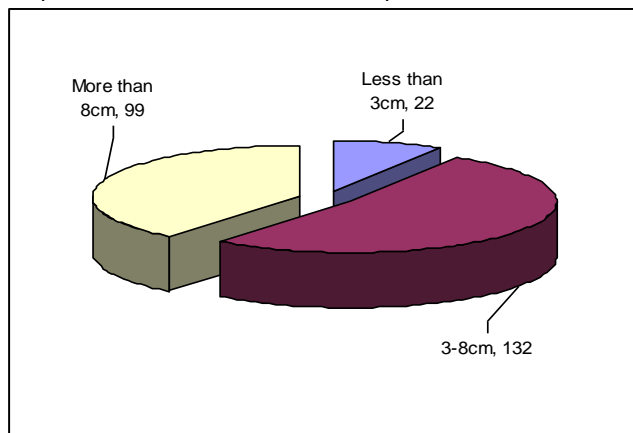
Table 1.Co relation of AFP levels with tumor size

Variables	Overall	AFP level≤20ng/ml (group I)	AFP 21-399 ng/ml (group II)	AFP ≥400ng/ml (group III)	P value
Total number	253	25(9.88%)	153(60.4%)	75(29.6%)	
Tumor size Group A (≤3cm)	22(8.69%)	6(27.2%)	12(54.5%)	4(18.1%)	0.004
Group B (3-8cm)	132(52.17%)	11(8.3%)	102(77.2%)	19(14.3%)	0.001
Group C (≥8cm)	99(39.1%)	8(8.1%)	39(39.3%)	52(52.5%)	0.003

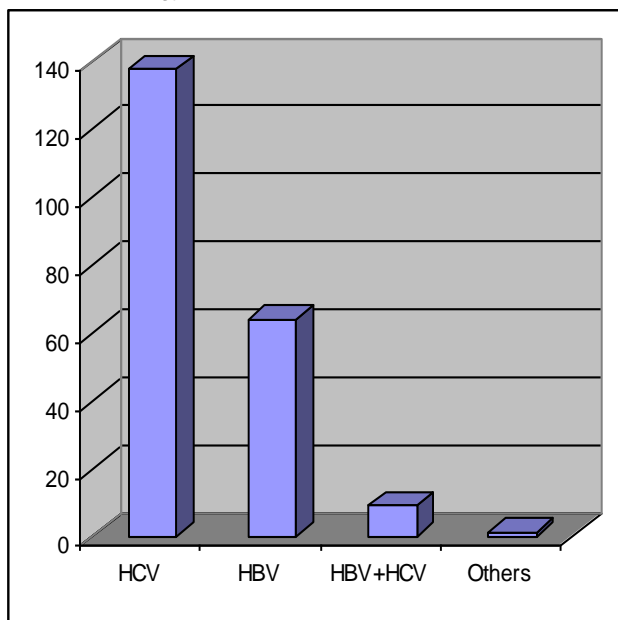
Table 2: %age of pts with normal AFP according to tumor size

Tumor size group	n	%age of normal AFP levels
Group A(≤3cm)	6	27%
Group B(3-8cm)	11	8.3%
Group C(≥8cm)	8	8%

Graph 2: Tumour size vs number of patients



Graph 1: Etiology of HCC



DISCUSSION

For diagnosing HCC, biopsy, biphasic CT scan and alpha fetoprotein are widely used. Biopsy is usually not done due to complications such as bleeding and needle track seeding of tumor cells and failure to achieve accuracy in differentiating between high grade dysplastic nodules and early HCC⁸. So basically two modalities are left that include imaging and alpha fetoprotein. AFP is not an ideal tumor marker for all HCC. Fluctuations of AFP can be due to exacerbation of underlying cirrhosis. Early HCC

(10-20%) may present with abnormal values only. Our study also shows 9.88% patients with normal AFP levels were CT scan confirmed cases of HCC. Majority of patients (90.2%) have got raised AFP levels (more than 20ng/ml).

High incidence of HCC in males in our study is supported by various international studies but with a comparatively less percentage (72.33%). In Western studies, it is mainly due to alcoholism, cigarettes, raised iron stores and genetic reasons⁹. Etiology of HCC in our study is mainly HCV related (54.5%) as compared to HBV(25.2%) as the cause in western studies¹⁰. It is mainly due to the high incidence of HCV infection in general population(6-7%) in Pakistan.

In our study majority of patients are having a tumor size of more than 3cm i.e., group B and C having 132(52.17%) and 99(39.1%) patients respectively, while only 22(8.69%) patients had tumor size less than 3cm i.e., group A. This represents a fact that majority of patients in our setup are detected late and very few treatment options are left in this advanced scenario^{11,12}.

In small tumors (group A) majority of patients have got high AFP levels i.e., 12(54.5%) and 4(18.1%) in group II and III respectively in contrast larger tumor size groups (group B and C) shows higher values of AFP in majority of patients 102(77.2%) and 19(14.3%) for group B, and 39(39.3%) and 52(52.5%) respectively for group C¹³. It shows that if the patient has bigger tumor size there are more chances of raised AFP levels. Local and international data support our finding that if the size of HCC is more AFP levels become significant^{14,15}. In various studies AFP above 400ng/dl should be considered specific for HCC regardless of the size of tumor although a normal AFP level does not exclude HCC^{16,17}. In present study normal AFP levels are found in group A 27% group B 8.3% and group C 8%¹⁸. So normal AFP levels should always be supported by sensitive imaging before excluding HCC specially in suspected small tumors^{19,20,21}.

CONCLUSION

AFP levels correlates with HCC especially in large tumors and in early HCC its value should be correlated with sensitive imaging techniques so that early detection of tumor is not missed.

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