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HEPATOCELLULAR CARCINOMA;
CORRELATION OF SERUM ALPHA FETOPROTEIN AND TUMOR SIZE

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ABSTRACT… Background: Hepatocellular carcinoma (HCC) also known as malignant hepatoma, accounts for most of the liver cancers. Alpha fetoprotein (AFP) has been undoubtedly widely used as a marker for the detection and monitoring of HCC. This study aimed to find the correlation of serum alpha fetoprotein and tumor size in HCC in the tertiary care hospital. **Study Design:** This cross sectional descriptive study. **Setting:** Pathology Department of Allama Iqbal Medical College, Lahore (AIMC). **Materials and Methods:** The study was carried out on 45 HCC patients (13 females and 32 males) came to Jinnah Hospital Lahore. Five ml of venous blood was drawn aseptically from anterior cubital vein of patients and added into plain vial to clot. The samples were centrifuged, to get the plasma separated from blood cells. Serum AFP was measured by using Enzyme linked Immunosorbent Assay technique (ELISA). **Results:** There were 10 (22.2%), 19 (42.2%), 16 (35.6) cases in AFP group 1,2,3 respectively. While 10 (22.2%), 13 (28.8%), 22 (48.8%) cases in tumor size groups A,B,C. Group C with large tumor size got 48.8% raised AFP levels as compared to group B (28.8%) and group A (10%). **Conclusion:** This study shows there is significant correlation between serum AFP and tumor size in HCC (r=0.668). Serum AFP progressively increases with tumor size especially in larger size. Although AFP have suboptimal sensitivity but it is still proves a beneficial in early diagnosis and screening of HCC, when used in combination of USG/Imaging technique.

Keywords: Hepatocellular carcinoma, α-fetoprotein, HCV Infection, Hbs Ag

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INTRODUCTION

Hepatocellular carcinoma (HCC) also known as malignant hepatoma, accounts for most of the liver cancers. HCC is the most common liver cancer. It is 5th most common tumor and third leading cause of cancer deaths world wide1. Although this disease is prevalent in Asia and Africa but its incidence is continuously increasing throughout the rest of world.2 Patients with Hepatitis B or C are at higher risk to suffer from HCC, even without transition to cirrhosis. Most of patients with chronic liver disease may progress to HCC (70-90%).3 Early diagnosis of HCC could be done by regular surveillance of high risk population using biochemical markers and ultrasonography (USG). Up till now α-fetoprotein (AFP) has been widely used as tumor marker for detection and monitoring of HCC.[4]

AFP is a single chain glycoprotein. It is produced in early fetal life in the yolk sac, gastrointestinal tract and liver. AFP is as major serum protein during fetal life but its level decreases rapidly towards birth. Its level is increased during pregnancy and also in some benign and malignant conditions including HCC. Therefore it has been used as tumor marker of HCC. High AFP level in blood has been associated with larger size tumor, bilobar involvement, diffuse type tumors and portal vein tumor thrombus.

This study was aimed to verify the correlation between serum AFP level and tumor size in patients with HCC in a tertiary care hospital.

MATERIALS AND METHODS

Study Design

This cross sectional descriptive study was conducted in Pathology Department of Allama Iqbal Medical College, Lahore (AIMC). A total of

45 cases of HCC from attached Jinnah Hospital selected by non-probability purposive sampling. Patients included both men and women above the age of 30 years. Patients with secondary liver tumor or suffering from serious heart, lung, kidney or blood disease, autoimmune liver disorder or other malignant tumors were excluded from the study. The diagnosis of HCC was based on imaging and histopathology examination of liver biopsy.

The patients with HCC were recruited after written informed consent. Data was collected using semi pre-developed questionnaire. The study plan was approved by Institutional Ethical Review Board of AIMC. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) V. 21. Pearson correlation test was applied for determining correlation between AFP level and tumor size HCC. A p- value of less than 0.05 was taken as significant.

Methods

Five ml venous blood was drawn aseptically from anterior cubital vain and allowed to clot. Serum was obtained by centrifugation and refrigerated until tested. Serum AFP level, anti HCV and Hbs Ag were measured using standard ELISA kits. Manufacturers instructions were strictly followed during testing.

To study correlation between serum AFT level and tumor size, study population was divided into two groups based on tumor size and AFP level. For the purpose of statistical analysis each group was further divided into three subgroups depending on tumor size: Group I = < 5cm, Group II = 5-10 cm, Group III = > 10 cm.

RESULTS

A total number of 45 HCC cases were enrolled in the study. The majority of patients were men (32 males, 13 females). Mean age was 52.0±11.1 years (range 30-90). Thirty-three patients (73.3%) were seropositive for anti HCV, six (13.3%) for HBV and 2 (4.5%) had both HBV and anti HCV.

The serum AFP level was correlated with tumor size as depicted in Table I. Depending on increasing tumor size, three groups consisted of 10 (22.2%), 13(28.8%), and 22 (48.8%) patients respectively whereas on the basis of rising serum AFT level three groups had 10 (22.2%), 19 (42.2%), 16 (35.6%) respectively. With large tumor size Group A patients had got raised AFT level in 48.8%, whereas fewer cases had raised AFT in Group B and C (28.8% and 10.0% respectively). More patients had normal AFT level with lesser tumor size (Table II).

Variable	Overall	Group I AFP=/<=20 (ng/dl)	Group II AFP= 21-399 (ng/dl)	Group III AFP >/= 400 (ng/dl)	r- value	P- value
Total number	45	10 (22.2%)	19 (42.2%)	16 (35.6%)		
Tumor size group A (<5cm)	10 (22.22%)	5 (50%)	2 (20%)	3 (30%)	0.644	0.044
Group B (5-10 cm)	13 (28.89%)	3 (23.1%)	7 (53.8%)	3 (23.1%)	0.575	0.040
Group C (> 10 cm)	22 (48.9%)	3 (13.6%)	8 (36.4%)	11 (50%)	0.622	0.002

Table-I. Correlations of serum AFP Level with Tumor Sizes

Tumor size group	N	%age of normal AFP levels
Group A (<5 cm)	5	50.0%
Group B (5-10 cm)	2	15.4%
Group C (>10 cm)	3	13.6%

Table-II. Distribution of patients with normal AFP according to tumor size

DISCUSSION

The main aim of this study was to verify the correlation of serum AFP level and tumor size in HCC. .In present study it was observed that HCV is the major cause of HCC in Pakistan. Etiology of HCV infection varies world-wide and it has replaced HBV as a major cause of HCC in Pakistan. Men are more susceptible to suffer

from HCC than women due to their tendency to consume more cigarettes, alcohol and tobacco. In our series, men were in a larger proportion in the HCC (predominantly HCV related HCC) than HBV related HCC. The result of this study is similar to findings of study by Abbasi and his co-worker.[5]

Early diagnosis of HCC is very important for successful potential treatment. Therefore, regular screening for HCC is recommended for high risk patients, including those with cirrhosis of any etiology, chronic liver disease patients due to HCV infection who had advanced liver disease and chronic HBV patients even without cirrhosis.[6] Some researchers have observed that high AFP levels in cirrhotic as well as viral infected patients precede the development of HCC.7 Combining both strategies i.e. serum AFP and ultrasound imaging every 6-12 months have been preferred as a method of screening for a long time.[7,8] The optimal frequency and method of surveillance remain debatable.[9]

Serum AFP is frequently increased in HCC. Our study revealed 77.8% positivity in HCC cases. AFP positivity among HBV and HCV co- infected and HBV alone HCC cases is 4.4% and 13.3% respectively, while HCV infected HCC cases it is 73.3%. Further, when AFP level were measured in carcinoma patients, the HCC infected group had elevated levels of AFP and we found a significant correlation (p value is < 0.05).

In the present study we have analyzed correlation serum AFP level with the tumor size in HCC. In spite of sub optimal sensitivity AFP is still a valid screening tool for HCC. Our study also shows that majority of patients (77.78%) had raised AFP levels (> 8.5ng/ml). Out of 45 patients 33 (73.33%) were having HCV related to HCC 6 (13.33%) patients were HBV and 2 (4%) patients having both HBV and HCV related HCC. While 4 (18.18%) HCC patients were not HCV and HBV infected. It is mainly due to the high incidence of HCV infection in general population (6-7%) in Pakistan.

In our study majority of patients had a tumor size of more than 5cm i.e Group B and C having 13 (28.8%) and 22 (48.8%) as compared to Group A (10 (22.2%). It shows that if the patients have bigger tumor size there are more chances of raised AFP levels. In present study normal AFP is found in group A (50.0%) and group B (15.4%) and group C (13.7%). This finding is in agreement with other studies.[10,11] Therefore it is not wise to depend on AFP level alone for assessing tumor size. Finding of sensitive USG should be taken into consideration for tumor size. Local and international data support our findings that there is significant correlation between tumor size and AFP levels in HCC.[12,13]

Our study is in agreement with other studies on AFP levels in patients with HCC and other benign and malignant liver diseases as serum AFP is greater than 400 ng/ml in 69% of patients with hepatoma.[14] A north Indian study showed that 65% of HCC cases have elevated AFP level, The highest level recorded was 580 ng/ml.[15] In another south Indian study, elevated AFP levels were observed in 47.4% of HCC cases.[16] Some clinical researches have suggested that the simultaneous determination of supplementary markers especially glypican-3 along with serum AFP and USG could significantly increase the sensitivity of AFT to detect HCC.[17,18] However, clinicians should be aware that some patients with primary hepatic cancer could have normal AFP levels, so normal or moderately elevated levels may not be considered a strong evidence to exclude the presence of HCC.

CONCLUSION

This study concludes that there is a significant correlation between serum AFP and tumor size in HCC. Serum AFP progressively increases with tumor size especially in larger size tumors. In spite of suboptimal sensitivity, AFP still proves a beneficial in early diagnosis and screening of HCC, when used in combination of USG/ imaging technique.

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PREVIOUS RELATED STUDY

Wasim Amer, Muhammad Akram, Muhammad Ashraf Majrooh. HEPATOCELLULAR CARCINOMA; CHARACTERISTICS A RETROSPECTIVE STUDY OF 34 PATIENTS AT JHL, LAHORE (Original) Prof Med Jour 16(3) 364-369 Jul, Aug, Sep, 2009.

AUTHORSHIP AND CONTRIBUTION DECLARATION

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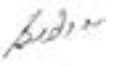
3	Sidra Sharif	Sample collection, Laboratory Analysis, Literature Search, Manuscript writing	
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