Role of Serum Alphafetoprotein in Diagnosing Hepatocellular Carcinoma at the Hepatology Unit of A Tertiary Care Hospital

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Abstract

Background: Hepatocellular Carcinoma (HCC) is responsible for a large proportion of cancer deaths in Bangladesh. Alpha-fetoprotein (AFP) is a serum glycoprotein recognized as a marker for HCC, which is used to detect HCC. This study aimed to observe the level of AFP in the diagnosis of patients with HCC.

Materials and methods: This cross sectional observational study has been carried out in the Department of Hepatology, Chattogram Medical College Hospital, Chattogram, Bangladesh, from January 2017 to December 2019. A total of 169 patients were enrolled in this research after consent. Patients were admitted to the hospital based on ultrasonographic findings and ultrasonographic guided Fine Needle Aspiration Cytology (FNAC) was done. 19 patients were lost from follow-up and 150 patients had completed the procedure and were finally evaluated. AFP was measured by automated Chemiluminescent immunoassays.

Results: The age distribution of the study patients revealed that almost one-fourth (24%) of patients belonged to 51-60 years of age. The mean age was 55.6±16.64 years ranged from 25-80 years. The majority (90%) of patients were male and 15(10%) were female. It was observed that 64(42.7%) patients had HBsAg positive and almost one-third (29.3%) patients had Anti-HCV positive. Mean serum AFP was 8615.3 ±3629.3IU/ml and the range was 5.19-172000 IU/ml.AFP level was normal (<20 IU/ml) in 30 (20%) patients, moderately elevated (20-399 IU/ml) in 99(66%) patients and markedly elevated (>400 IU/ml) in 21 (14%) patients. Mean AFP was found 997.5±1813.8 IU/ml in multifocal HCC, 250.0±157.6 IU/ml in solitary HCC and 57455.7±82995.3 IU/ml in CLD with HCC. The mean AFP is statistically significant in different USG findings.

Conclusions: Serum AFP level used alone is sufficient enough for HCC diagnosis majority of patients. But sometimes confirmation by FNAC can be helpful when confused in HCC diagnosis.

Key words: Alpha-Fetoprotein (AFP); Fine Needle Aspiration Cytology (FNAC); Hepatocellular carcinoma.

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Introduction

Hepatocellular Carcinoma (HCC) is one the most common primary malignancy of the liver and represents the third leading cause of cancer-related deaths worldwide.[1] HCC incidence is the 12th but mortality was 10th highest in Bangladesh[2]. Incidence rates are highest in East Asia and Sub-Saharan Africa. Some evidence suggestsa possible role of Alpha-Fetoprotein (AFP) and another marker like Interleukin1(IL-1) Des-γ-Carboxyprothrombin (DCP) in the pathogenesis and diagnosis of Hepatocellular Carcinoma (HCC).

There are some risk factors for HCC such as chronic inflammation of theliver due to Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection.[3,4] HCC can be diagnosed histopathologically,but there are no satisfactory screening procedures for early detectionfor HCC is available in our settings. Serum AFP and an ultrasound scan are commonly recommended to decidethe diagnosis of HCC noninvasively.[5]

AFP is a major serum glycoprotein comprised of 591 amino and 4% carbohydrate residues, encoded by a gene on chromosome 4q11-q13 with a half-life of 5-7 days, which is synthesized by fetal liver cells, fetal yolk sac, and in trace amounts by the fetal gastrointestinal tract.[6]

AFP can be produced under many circumstances, including cancer of the stomach, pancreas, biliary tree, pregnancy and germ cell tumor. Chronic hepatitis or Cirrhosis raise AFP in 20% and 40% of patients respectively.[7] Therefore, the use of AFP as a primary screen for HCC has been questioned and more sensitive serum biomarkers for HCC are desired. So present study is designed to observe the usefulness of AFP in the diagnosis of HCC which was histopathologically confirmed.

Materials and methods

Present cross-sectional observational study was conducted inthe Department of Hepatology, Chittagong Medical College Hospital, Chattogram, Bangladesh during a three-year study period from January 2017 to December 2019. All patients suspected of HCC were evaluated by USG. AFP and USG guided FNAC were done after informed written consent. HBsAg and Anti HCV were also done. Levels of AFP were compared with histopathologically proved HCC. In that way, a total of 169 patients were enrolled in this study as per inclusion and exclusion criteria. Among them, 19 patients were lost from the study due to the unavailability of reports or unwilling to be included in the study. A total of 150 patients have completed the study and were finally evaluated. AFP was measured by automated Chemiluminescent immunoassays. ERB clearance was taken from the ERB of CMCH and data were analyzed by SPSS-20.

Results

Table I : Distribution of the patientsby age (in a year) (n=150)

Age (In years)	Number of patients	Percentage (%)
≤40	28	18.7
41-50	29	19.2
51-60	36	24.0
61-70	28	18.7
>70	29	19.4
Mean±SD	55.6±16.64	100.00
Range (Min-max)	25-80	

Table I above shows the age distribution of the study patients, it was observed that almost one-fourth (24.0%) of patients belonged to age 51-60 years. The mean age was 55.6±16.64 years, ranged from 25-80 years.

Table II : Sex of the patient(n=150)

Sex	Number of patients	Percentage (%)
Male	135	90.0
Female	15	10.0

It was observed that the majority 135(90.0%) of patients were male and only 15(10.0%) were female.

Table III : Alpha-fetoprotein levels of respondent's patients (n=150)

Alpha-fetoprotein	Numberof patients	Percentage (%)
Normal (<20 IU/ml)	30	20.0
Moderately elevated (20-399 IU/ml)	99	66.0
Markedly elevated (≥400 IU/ml)	21	14.0
Mean±SD	8615.3±3629.3	
Range (Min-max)	3.19-172000	

It is revealed from the above table that alpha-fetoprotein of the study patients, it was observed that two-third (66.0%) patients had moderately elevated AFP level (20-399IU/ml). The mean alpha-fetoprotein was 8615.3±3629.3 IU/ml, ranged from 3.19 to 172000 IU/ml.

Table IV : HBsAg categorization of the respondents (n=150)

HBsAg	Number of patients	Percentage (%)
Positive	64	42.7
Negative	86	57.3
Total	150	100.0

It was revealed from the above table that that 64(42.7%) of the patients were HBsAg positive and the rest 86(57.3%) were HBsAg negative.

Table V : Distribution of the study patients by Anti-HCV (n=150)

Anti-HCV	Number of patients	Percentage (%)
Positive	44	29.3
Negative	106	70.7
Total	150	100.00

It was found that almost one-third 44(29.3%) of patients had Anti-HCV positive and 106(70.7%) were negative.

Table VI : Types of patients based on USG diagnosis (n=150)

USG findings	Number of patients	Percentage (%)
Multifocal HCC	47	31.3
Solitary HCC	69	46.0
CLD with HCC	34	22.7

From the above table,USG diagnosis disclosed the types of patients. The majority of 69 (46.0%) patients had Solitary HCC and 47(31.3%) were multifocal HCC.

Table VII : Association between USG findings with Alpha-fetoprotein (n=150)

USG findings	n	Alpha-fetoprotein (IU/ml)		
		Mean ±SD	Range (Min, max)	p value
Multifocal HCC	47	997.5±1813.8	3.5, 4230	
Solitary HCC	69	250.0±157.6	10.3, 364.0	0.001[s]
CLD with HCC	34	57455.7±82995.3	3.2, 172000	

s=significant, p-value reached from ANOVA t-test.

The mean alpha-fetoprotein was found 997.5±1813.8IU/ml inmultifocal HCC, 250.0±157.6 IU/ml in solitary HCC and 57455.7±82995.3 IU/ml in CLD with HCC. The mean alpha-fetoprotein is statistically significant (p<0.001) in different USG findings.

Discussion

This study was carried out to determine the usefulness of AFP for the evaluation of Hepatocellular Carcinoma (HCC) and correlation with histopathological examinations. Subjects of this study were taken from Chittagong Medical College Hospital, Chattogram during the study period from January 2017 to December 2019. A total of 150 cases were studied who had undergone histopathological examinations and the finaldiagnosis of HCC was made by histopathology.

Age distribution of the study patients revealed that almost one-fourth (24.0%) of patients belonged to age 51-60 years. The mean age was found 55.6±16.64 years with ranged from 25-80 years. The majority135(90.0%) of patients were male and 15(10.0%) were female. In Britain, Hepatocellular Carcinoma (HCC) was found over 50 years of age. In Japan age distribution of HCC was found from 5 years to 100 years with a mean age of 55.5 years. In Bangladesh, HCC was found to be common between the 41 to 50 years of age group. In this study, the age of the youngest patient with HCC was 25 years and that of the eldest one was 80 years. The diseases were found to be common between 41 to 50 years of the age group which correlated with the above study done in Bangladesh.[8]

It was observed that 64(42.7%) patients had HBsAg positive and almost one third (29.3%) patients had Anti-HCV positive. The principal reason for the high incidence of HCC in parts of Asia like Bangladesh is due to the increased frequency of chronic infection with Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV). These chronic infections frequently lead to cirrhosis, which itself is an important risk factor for HCC.

Studies in regions of Asia where HCC and HBV infection are prevalent have shown that the incidence of this cancer is about 100-fold higher in individuals with evidence of HBV infections man in non-infected controls.[9]

Alpha-fetoprotein of the study patients, it was observed that 20% had normal AFP level, two-third (66.0%) patients had moderately elevated (20-399IU/ml). Oka et al found a similar observation.[10] So, this group of patients needs FNAC / Liver biopsy for confirmation of HCC and HCC confirmed by FNAC in this study. The mean alpha-fetoprotein was 8615.3±3629.3 IU/ml with ranged from 3.19 to 172000 IU/ml. Mean AFP level 250.0±157.6 IU/ml insolitary HCC, 57455.7±82995.3 IU/ml in CLD with HCC and 997.5+_1813.8 IU/ml in multifocal HCC. The mean AFPis statistically significant ($p<0.001$) in different USG findings. AFP levels greater than 500 IU/ml are found in about 70 to 80 percent of patients with HCC. The presence of persistence of high levels of serum AFP over 500 to 1000 IU/ml in an adult with the liver disease without an obviousgerm cell tumor strongly suggests HCC. Imaging procedures used to detect HCC include ultrasound,CT-scan, MRI, hepatic artery angiography and radionuclide scans.[2]

Limitations

The limitations of the study are, the sample size was small.Newer markers like Desgamma Carboxy Prothrombin (DCP) are not done.

Conclusion

AFP shows a diagnostic marker for the evaluation of HCC. This may assistclinicians in selecting high-risk patients for the HCCsurveillance program. Combining the markerscan provide a new perspective on the diagnosis andprognosis of HCC.But in a group of patients,FNAC is needed for confirming the diagnosis of HCC.

Recommendation

Multicenter with large size study is recommended.

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Contributions of authors

AKR- Conception, design, acquisition of data, drafting and final approval.
SN- Analysis, critical revision and final approval.

Disclosure

The author declared no conflicts of interest.

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