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PROGNOSTIC FACTORS OF HEPATOCELLULAR CARCINOMA IN A TERTIARY CARE HOSPITAL

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Abstract

Objective: *To determine the prognostic factors of Hepatocellular carcinoma in a tertiary care hospital.*

Methodology: *A total of 88 diagnosed cases of HCC of aged between 18 to 75 years of either gender underwent for Surgery with no prior treatment for HCC were included via non-probability consecutive sampling technique. HCC diagnosed on the basis of clinical sign & symptoms were confirmed on CT scan. Blood samples were drawn preoperatively and centrifuged immediately at 1500× g for 10 min. Serum biomarkers were measured using an enzyme-linked immunosorbent assay (ELISA) kit. Data was analyzed through the statistical software SPSS. 26 version. Mean and standard deviations were calculated for the continuous data Frequency and percentage were calculated for categorical variables.*

Results: *In this study, a total of 88 patients of HCC were enrolled. The mean age of the patients was 62.35±13.10 years with mean BMI was 27±3.5 kg/n^2. HCC found more in male 70 (79.5%) as compared to female 18 (20.5%). The most common etiology of HCC found in this study was HCV 79 (90%). The assessment of serum levels in HCC patients revealed mean a-fetoprotein- AFP were 615.2 ±153.8 ng/ml, mean alanine transaminase were 47.15±17.7 U/L, mean Aspartate Aminotransferase were 45.85±23.9 U/L, mean total Bilirubin were 19.31±18.1 mg% and total protein were 67.35±5.20 g/L. Further elevated a-fetoprotein- AFP > 400 (ng/ml) found in 55 (62%) cases of HCC.*

Conclusions: *In conclusion, in patients with suspicious liver lesions, serum levels of AFP are useful to achieve the diagnosis of HCC. The use of an AFP cut-off value of 400 ng/ml may help clinicians to achieve a diagnosis.*

INTRODUCTION:

Globally, hepatocellular carcinoma (HCC) is becoming more common as a malignant tumor.[1] It is responsible for between 70% and 90% of primary liver cancer cases. Liver cancer drops from the fifth most common cancer in terms of mortality to the second due to its poor prognosis. Hepatitis B, exposure to chemicals, and Hepatitis C are risk factors for the development of HCC. Smoking, obesity, and alcohol use are other risk factors. Hepatocellular carcinoma was caused by hepatitis B and C in 44% and 21% of patients, respectively.[2] HCC increased risk is also associated with certain diseases such as antitrypsin deficiency Wilson and Alpha -1 and hemochromatosis.[3] Secondary to other causes, the majority of the hepatocellular carcinoma cases were already chronic liver disease patients.

In Pakistan, the epidemiology of hepatocellular carcinoma is extremely dispersed. The cancer registry did not provide an adequate estimate of the prevalence of HCC. According to the available data, the age-adjusted incidence rate for women is between 0.2 and 2.2 per one million, while the rate for men is between 0.7 and 7.5 per one million. HCC accounts for 4.8% of all malignancies, while the ratio of males to females is 4:1. The median age was 40 to 70 years. Liver cirrhosis has been observed in 70-90% patients treated in Pakistan-based tertiary care set-up.[4] In Pakistan, the majority causative agent for HCC development has been documented as Hepatitis B virus infection.[5]

Hepatomegaly, weight loss, and right hypochondrial abdominal pain are among the clinical signs of HCC. Atypical histopathology and laboratory screening, such as hepatic damage indicators (alanine aminotransferase and aspartate aminotransferase), cholestasis indicators (alkaline phosphatase and gamma-glutamyl transpeptidase), hepatic synthesis indicators (albumin, prothrombin time, bilirubin), and tumor markers and instrumental tests (hepatic ultrasonography, computed tomography (CT), nuclear magnetic resonance (NMR), and angiography) are typically used to diagnose HCC.[6,7]Transcatheter arterial embolization and chemoembolization (TACE), systemic chemotherapy, hepatic intra-arterial chemotherapy (HIAC), percutaneous ethanol injection (PEI), and hormone therapy are some of the treatments that may be used when surgical hepatic resection is not an option for HCC.[8]When paired with hepatic ultrasonography, alpha-fetoprotein is currently the most often used marker in clinical practice to detect HCC in patients with cirrhosis. Early detection of HCC is essential for improving patient survival. Identification of biological markers of metastasis and recurrence is necessary for the appropriate management of HCC.[9,10]

The present study was designed to determine prognostic factors of Hepatocellular carcinoma. HCC prognostic factors have been described by several investigations but limited data found in Pakistan. Due to scarcity of published data on Pakistani population HCC patient's, present study was planned.

METHODOLOGY:

This study was carried out in the department of the Internal Medicine, Peoples University of Medical and Health Sciences, Nawabshah. A total of 88 diagnosed cases of HCC of aged between 18 to 75 years of either gender underwent for Surgery with no prior treatment for HCC were included via non-probability consecutive sampling technique. Patient with palliative hepatic resection and with history of other malignant tumors were excluded. The sample size was calculated by using W.H.O sample size calculator using the incidence of AFP) >400 ng/ml i.e. 35.4%[8], confidence interval = 95%, margin of error = 10% then the estimated sample was n = 88. HCC was diagnosed on the basis of clinical sign & symptoms like jaundice (pale skin), abdominal pain and ascites (shifting dullness and U/S) and was confirmed on CT scan triphasic showing focal nodule and appeared as either hypoattenuating or isoattenuating relative to the surrounding parenchyma *with delayed washout.* A written informed consent was taken after explaining the purpose and procedure of the study. After taking baseline data age, gender, BMI, Alcohol consumption, smoking, DM, HTN and etiology. Blood samples were drawn preoperatively and centrifuged immediately at 1500× *g* for 10 min. The sera was aliquoted and stored at −80 °C for batch analysis. Serum biomarkers were measured using an enzyme-linked immunosorbent assay (ELISA) kit.

Data was analyzed through the statistical software SPSS. 26 version. Mean and standard deviations were calculated for the continuous data like age, BMI, mean serum levels [Alanine Transaminase (ALT U/L), mean Aspartate Aminotransferase (AST U/L), mean Total Bilirubin (TB mg%) and mean Total Protein (TP g/L)]. Frequency and percentage will be calculated for gender, alcohol consumption, smoker (yes/no), DM, HTN and outcome variable i.e. (a-fetoprotein (AFP) ≤ 400 ng/ml and a-fetoprotein (AFP) >400 ng/ml.

RESULTS:

In this study, a total of 88 patients of HCC were enrolled. The mean age of the patients was 62.35±13.10 years with mean BMI was 27±3.5 kg/m^2. HCC found more in male 70 (79.5%) as compared to female 18 (20.5%). The most common etiology of HCC found in this study was HCV 79 (90%) followed by HBV 7 (7.9%) and combination of both found in 2 (2.2%). Moreover, 21 (24%) were smokers, 8 (9%) were consuming alcohol, 24 (27.2%) were diabetes and 33 (38%) were hypertensive, as shown in (Table – 1). The assessment of serum levels in HCC patients revealed mean a-fetoprotein- AFP were 615.2±153.8 ng/ml, mean alanine transaminase were 47.15±17.7 U/L, mean Aspartate Aminotransferase were 45.85±23.9 U/L, mean total Bilirubin were 19.31± 18.1 mg% and total protein were 67.35±5.20 g/L, as shown in (Table - 2). Further elevated a-fetoprotein-AFP > 400 (ng/ml) found in 55 (62%) cases of HCC, as shown in (Figure – 1).

Table 1: Baseline Characteristics of the Patients (n = 88)

Baseline Data	(mean ± sd)/ n (%)
Age (Years)	62.35 ± 13.10
BMI (kg/m^2)	27 ± 3.5
Gender • Male • Female	 70 (79.5%) 18 (20.5%)
Smoker • Yes • No	 21 (24%) 67 (76%)
Alcohol consumption • Yes • No	 8 (9%) 80 (91%)
Diabetes Mellitus: • Yes • No	 24 (27.2%) 64 (72.7%)
Hypertension: • Yes • No	 33 (38%) 55 (62%)
Etiology: • HBV • HCV • HBV + HCV	 07 (7.9%) 79 (90%) 02 (2.2%)

Table 2: Mean Serum Levels

Serum Levels	mean ± sd
a-fetoprotein- AFP (ng/ml)	615.2 +153.8
Alanine Transaminase (U/L)	47.15 +17.7
Aspartate Aminotransferase (U/L)	45.85 +23.9
Total Bilirubin (mg %)	19.31 + 18.1
Total Protein (g/L)	67.35 + 5.20

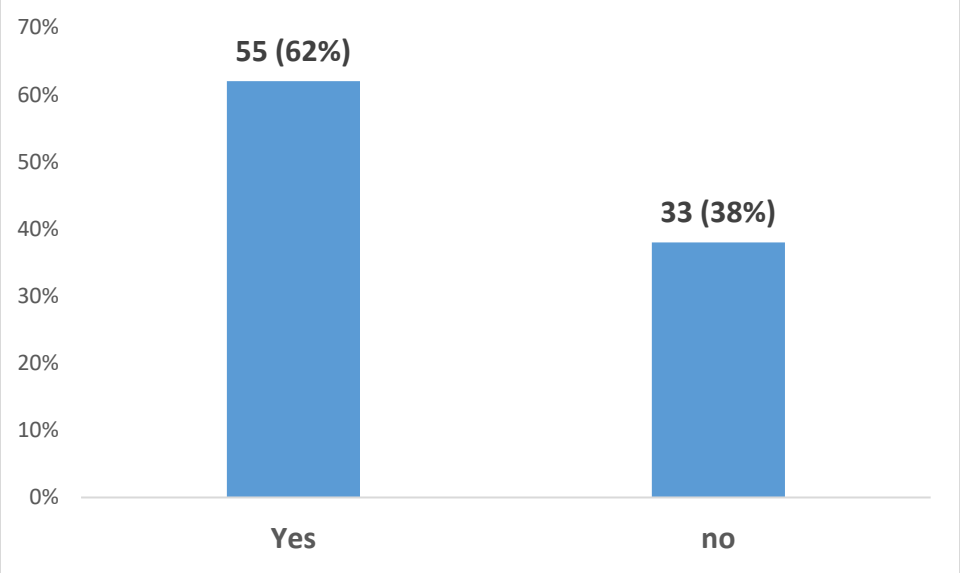

Figure 1

Elevated a-fetoprotein- AFP in Hepatocellular Carcinoma Patient's

DISCUSSION:

As a result of better management of liver cirrhosis-related comorbidities and longer survival times, the number of individuals with HCC is rising. Finding a sensitive screening test is essential for early, curable HCC diagnosis. It is important to remember that 66.4% of these patients were diagnosed with HCC at a stage where there is currently no treatment available in Pakistan for tumors larger than 5 cm[11,12].

In this study, we demonstrated that overall, 62% of patients with HCC had elevated AFP levels. 62.6% of HCC patients had elevated AFP levels (i.e., ≥20 ng/mL) at the time of diagnosis, according to a recent US study. The proportion of HCC patients with increased AFP levels decreased from 2010 to 2017 (68.2% vs. 57.5%). Additionally, patients with early-stage cancers (i.e., seventh edition AJCC stage 1) had the biggest reduction, going from 55.7% in 2010 to 40.7% in 2017. The authors did not, however, look into the possible reason for these findings. They believed that the transition from viral to nonviral etiology and the growing tendency in early-stage tumor diagnosis were probably the causes of these findings.[13]

Further, in current study, it has been found that mean alanine transaminase was 47.15±17.7 U/L, mean Aspartate Aminotransferase were 45.85±23.9 U/L, mean total Bilirubin were 19.31 ± 18.1 mg% and total protein were 67.35±5.20 g/L.

A study was conducted by Wei S, et al to assess the prognostic factors of HCC and revealed that AFP ≤ 400 ng/ml was in 64.5% cases, AFP >400 ng/ml was 35.4%, mean ALT (u/L) was 43.89 ±44.24, AST (u/L) was 47.77±46.12, TB (mmol/L) was 19.96± 23.67, TP

(g/L) was 66.54±6.40 and ALB (g/L) was 37.55±6.12.[14]

According to Marrero et al., AFP is most helpful for liver tumors that are in the early stages. Additionally, they determined that AFP remains a superior serum biomarker after comparing it to other novel biomarkers such as lectin-bound alpha fetoprotein (AFP-L3) and des-gamma carboxyprothrombin (DCP).[15]

According to Stefaniuk et al., AFP has a high specificity but a sensitivity of only 20 to 30% when the cutoff value is greater than 100 ng/ml. This suggests that 70 to 80% of patients with HCC will not receive therapy when it is necessary.16 According to a different study, AFP has a 60% sensitivity at a cutoff value of 20 ng/ml and a positive predictive value that varies from 9 to 50% according on the disease's etiology.17 According to Pervaiz et al., AFP has an 89% specificity and 72% sensitivity for diagnosing HCC.[18] This limitation of AFP is most likely due to the fact that a number of small tumours may not secrete AFP resulting in normal levels despite the presence of HCC.[19]In his review, Gupta came to the conclusion that AFP is not very useful in detecting hepatocellular carcinoma in hepatitis C patients.[20] According to Coon et al.'s economic research, the most economical method of screening for cirrhosis in patients is to employ both AFP and abdominal ultrasonography.[21] According to Baig et al., AFP is a practical and affordable method for identifying people in the area who may have HCC.[22] The most recent APASL guidelines state that serum alpha fetoprotein and ultrasonography should both be used to screen for HCC. According to EASL guidelines, consistently high AFP levels can be utilized to identify at-risk groups and are a risk factor for the development of HCC.[23]

CONCLUSION:

In conclusion, in patients with suspicious liver lesions, serum levels of AFP are useful to achieve the diagnosis of HCC. The use of an AFP cut-off value of 400 ng/ml may help clinicians to achieve a diagnosis. However, further studies to find out the cut-off value of AFP for optimal sensitivity and specificity of AFP in the diagnosis HCC patients.

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