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HEPATOCELLULAR CARCINOMA; DIFFERENT CHILD-PUGH CLASSES BASED ON α -FETOPROTEIN LEVEL

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ABSTRACT... Objective: To determine the frequency of hepatocellular carcinoma in different Child-Pugh classes based on Alfa fetoprotein level. **Study design:** Case series study. **Period:** Six months **Setting:** Medical Unit-I of Liaquat University Hospital, Hyderabad Sindh Pakistan. **Patients & Methods:** A total of 100 patients admitted (inpatients) in Medical Unit I with the diagnosis of cirrhosis were enrolled in the study. Patients with cirrhosis of liver (more than six month duration) of either gender were included. If patients had metastatic lesion of the liver, liver abscess, or acute liver failure then they were excluded. Child-Pugh score was calculated which included ascites, encephalopathy, prothrombin time, albumin and serum bilirubin. The levels of α -fetoprotein were measured and HCC was diagnosed. The primary outcome variable was presence of HCC in cirrhotic patients. **Results:** The proportion of males (53%) was higher as compared to females (47%). The mean age of the study patients was 40.47 years with a standard deviation of 11.5. At the beginning patients were categorized according to Child Pugh Classes (A= up to 6, B=7-9 and C=10-11), age groups (15-30 years, 31-50 years and 51-70 years respectively). The mean Child Pugh score was 6.83 with \pm 1.8 S.D. The majority of the cases of HCC (75.61%) occurred in the Child Class A, whereas 21.95% occurred in Child Class B and finally only one case of HCC (2.44%) was present in Child Class C. **Conclusions:** This study comprehensively demonstrated that hepatocellular carcinoma (HCC) is far more common in compensated cirrhosis (Child Pugh Class A) vs. decompensated cirrhosis (Child Pugh Class B and C).

Key words: Cirrhosis of liver - Hepatocellular carcinoma - Child Pugh Classes - α fetoprotein

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INTRODUCTION

Liver cirrhosis leads to regenerative nodules surrounded by fibrous bands in response to chronic liver injury and is responsible for portal hypertension and advance liver disease¹. Chronic viral hepatitis B infection is the major risk factor for hepatic cirrhosis and hepatocellular carcinoma (HCC)². Complications of liver cirrhosis include hepatic encephalopathy, variceal bleeding, spontaneous bacterial peritonitis SBP, ascites, hepato-pulmonary and hepatorenal syndrome and HCC³. Liver cirrhosis is a major risk factor for HCC with poor prognosis⁴⁻⁶.

Hepatocellular carcinoma is the fifth most common cancer of the world and the third most common cause of cancer related deaths^{7,8}. Incidence of HCC in south east Asia ranges from 150-500 /

100,000,⁹ while the annual global incidence is about one million patients with a male to female ratio of 4:1¹⁰.

There are several classification systems for staging HCC and the CLIP system is one of them. CLIP (cancer of the liver Italian program) has four components i.e. (i) child-Pugh score (class), (ii) alpha-fetoprotein (AFP) level, (iii) tumor size and (iv) portal vein thrombosis¹¹. The child-pugh classification is a good prognostic factor in HCC¹². The HCC is curative in early stage but still associated with increase mortality¹³.

Alpha (α) fetoprotein (AFP) is a useful tool in the diagnosis of HCC and the Level of AFP > 400-500ng/ml is considered diagnostic of HCC while computed tomography (CT) is a useful method in

identifying and characterizing HCC¹⁴⁻¹⁷.

Surgery including liver transplantation (LT) remains the most important treatment but survival is related to number of tumor foci, tumor size and underlying liver function (defined by child-Pugh class). Radiofrequency (RF) ablation of tumor is alternate option for subjects who are not eligible for resection or liver transplant (LT), a bridge therapy for cases waiting for hepatic transplant and is considered appropriate than ethanol injection¹⁸. Percutaneous ethanol is a option when tumors near major blood vessels not suitable for RF¹⁹. Transarterial chemoembolization (TACE) is another option for unrespectable tumors with improvement in survival²⁰.

Therefore, the focus of our study was to evaluate the frequency of hepatocellular carcinoma in different Child-Pugh classes based on Alfa fetoprotein level in patients presented at tertiary care teaching hospital Hyderabad / Jamshoro. Early evaluated, detection and management of the patients with hepatoma by AFP can save the patients to acquire life threatening complications in relation to severity (Child-Pugh) score is concerned.

PATIENTS AND METHODS

This descriptive case series study of six months (October 2012 to March 2013) was conducted in department of Medicine at Liaquat University Hospital Hyderabad / Jamshoro. All the subjects with liver cirrhosis of liver (more than six month duration) of either gender were enrolled and entered in the study whereas the exclusion criteria of the study were the patients with metastatic lesion of the liver, non cirrhotic liver disease such as liver abscess and acute liver failure. The detail history was taken, relevant clinical examination was done and all the routine and relevant / specific investigations were advised. The informed consent was taken from the every patient / attendant to participate in the study. The child pugh score was calculated which included the presence of ascites, encephalopathy, albumin, prothrombin time and serum bilirubin. The ascites was detected by clinical examination (shifting

dullness and fluid thrill) and was confirmed on ultrasound. The severity of ascites was graded mild ascites by ultrasound, moderate ascites with symmetrical distention of abdomen (shifting dullness and fluid thrill positive), and huge (severe) ascites with marked abdominal distention (fluid thrill positive and shifting dullness negative). The serum albumin, PT/INR and bilirubin were evaluated by taking 3cc blood sample whereas the α -fetoprotein (AFP) were checked (cut off >200 ng/mL) based on which the diagnosis of HCC was confirmed by taking the 3cc venous blood sample. All the relevant blood samples were sent to laboratory for analysis. The data was collected on pre-designed proforma and all the maneuvers performed by the cooperation of whole research team and were under medical ethics while the sample size was calculated according to the prevalence of hepatocellular carcinoma 7.9%²¹ with 8% margin of error, thus total one hundred patients were recruited for the study. The data was entered, saved and analyzed in SPSS version 16 and the frequency and percentage was calculated for categorical variables. The mean \pm SD was calculated for numerical variables. The primary outcome variable would the presence of HCC in cirrhotic patients. No statistical test of significance was applicable for this descriptive study.

RESULTS

A total of one hundred (100) patients were selected for this study. Fifty three (53) males and 47 females were selected. The mean age of the study patients was 40.47 years with a standard deviation of 11.5.

At the very beginning patients were categorized according to Child Pugh Classes (A= up to 6, B=7-9 and C=10-11), age groups (15-30 years, 31-50 years and 51-70 years respectively). The mean Child Pugh score was 6.83 with \pm 1.8 S.D. Table No: 1 shows the means \pm S.D of continuous variables of this study. Mean bilirubin was 33.5 mmol/L with \pm SD of 5.4, whereas mean albumin was 36.08 g/L with \pm 5.4 SD. Mean Prothrombin time was 3.2 seconds prolonged than normal subjects with \pm 1.5 SD. The mean \pm SD for α -fetoprotein was 442.4 \pm 156.8ng/mL. Chart

No. 01 shows the frequency of hepatocellular carcinoma (HCC) in different child-pugh classes. In class A (up to 6 points) a total of 53 patients were present. Out of these 31 (58.5%) had HCC, whereas 22 (41.5%) were not having HCC. In child class B (7-9 points) had a total of 33 patients within which 09 (27.2%) were having HCC. In child-pugh class C (10-11 points) only 14 patients were present and only one (7.1%) patient had HCC.

Chart No. 02 shows the stratification of HCC via different age group categories. The majority of cases were clustered in the 31-50 year age group (32 out of 69 or 46.37%). In 51-70 year age group five out of 19 patients had HCC (26.31%), whereas 15-30 year age bracket had four cases of HCC in 12 patients (33.33%).

Chart No: 03 presents the relative frequency of HCC cases in different child-pugh classes. The majority of the cases (31 out of 41, 75.61%) occur in the child-pugh class A, whereas 21.95% (9 out of 41) occur in child-pugh class B and finally only one case of HCC (2.44%) was present in child-pugh class C.

Variable	Mean	Std. Deviation
Age (years)	40.47	11.519
Child Score	6.83	1.826
Bilirubin (mmol/l)	33.560	5.4334
Albumin (g/l)	36.08	5.456
PT / INR	3.29	1.533

Table-I. Mean ±SD for numerical variables

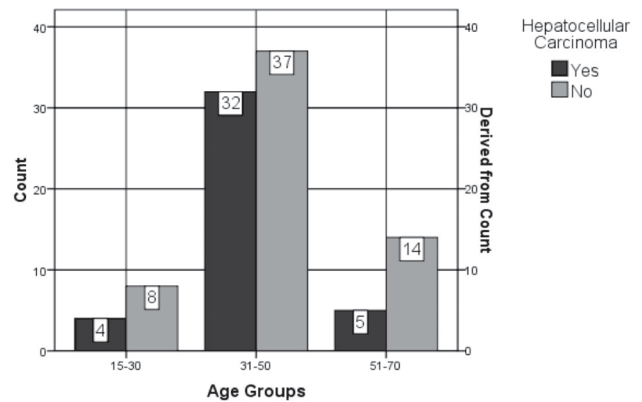


Fig-2. Bar chart showing stratification of hepatocellular carcinoma via age groups

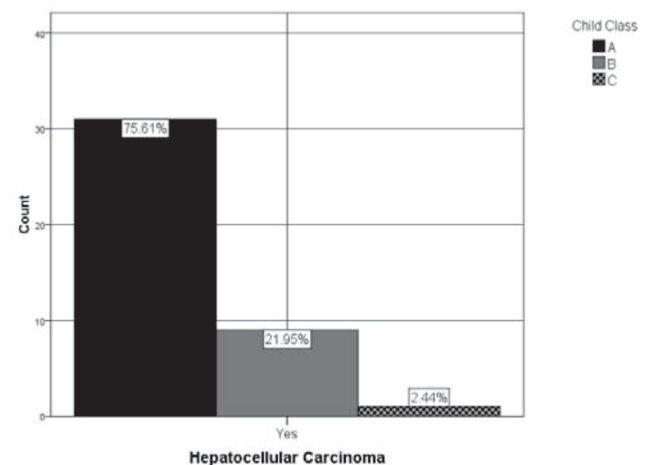


Fig-3. Bar chart showing the relative frequency of hepatocellular carcinoma in different child-pugh classes (n = 41)

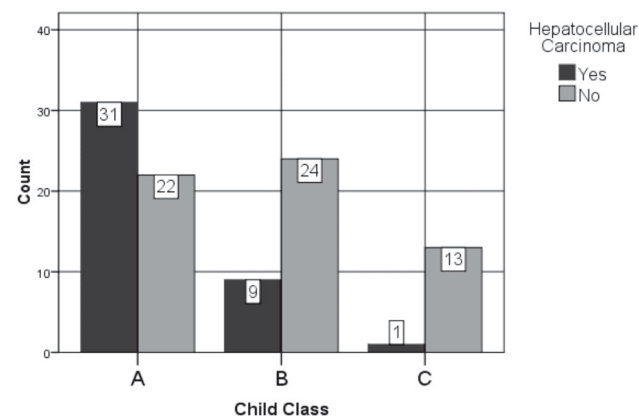


Fig-1. Bar chart showing frequency of Hepatocellular carcinoma in each child-pugh class

DISCUSSION

Hepatocellular carcinoma (HCC) is one of the leading causes of death in cirrhotic subjects. In the Orient, HCC commonly arises in the absence of cirrhosis in patients with hepatitis B or toxins whereas the hepatitis C and alcohol are the most common causes for liver diseases in the West leads to hepatocellular carcinoma^{22,23}. Although this study not related to etiology of cirrhosis but a majority of cases were due to viral etiology and were present in compensated as well as decompensated cirrhosis. The mean age of the subject in present study was 40.47 years with a standard deviation of 11.5 and it is consistent with the study by Pradat P, et al²⁴. The mean ±SD of serum α-fetoprotein (ng/mL) 442.4±156.8 and it

was reported as 460.73 ± 78.52 in the study by Oka H, et al²⁵.

In our study 75.61% of HCC cases belonged to compensated cirrhosis category (Child Class A) whereas 24.39% of HCC cases were present in decompensated cirrhosis category (Child Class B and C). The study conducted by Arrieta O et al, frequency of hepatocellular carcinoma (HCC) in child-pugh class A was 47% in child-pugh class B has 37.3% and in child-pugh class C was 15%,²⁶ whereas study conducted by Farinati et al, frequency of HCC in child-Pugh class A was 60%²⁷. In one study on 389 patients of HCC conducted by Greten et al, frequency of HCC in child-pugh in class A was 15% in class B was 79% and in class C was 35%²⁸. In another study conducted by Fong et al on patients of HCC, 342 were in child-pugh class A, 54 were in child-pugh class B and 16 were in class C²⁹.

In a study conducted by Marrero JA et al, on HCC patients frequency of HCC in child-pugh class A was 70.4% in class B was 27.7% and in class C was 1.9%²². while in the study conducted by Kirchner et al, frequency of HCC in class A was 40.2%, in class B was 45.4% and in child class C was 12.7%³⁰. In one study conducted by Garieco et al,³¹ 268 patients of HCC, 80.5% were in child-Pugh class A 19.4% were in child class B while the study conducted by Dhanasekaran R, et al³² frequency of HCC in child class was 48%, in class B was 28%, and in class C was 24% whereas in a study conducted by Cucchetti A et al,³³ frequency of HCC in child pugh class A was 94.1% and in class B was 5.9%.

CONCLUSIONS

It was concluded that hepatocellular carcinoma (HCC) is far more common in compensated cirrhosis (Child Pugh Class A) vs decompensated cirrhosis (Child Pugh Class B and C). Early detection and intervention are the main goals to treat this malignancy successfully.

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