

# FREQUENCY OF HEPATOCELLULAR CARCINOMA IN CIRRHOSIS

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**ABSTRACT... Objective:** To find the frequency of hepatocellular carcinoma in cirrhotic patients of our population. **Design:** Prospective observational study. **Setting:** Medical A Unit Hayat Abad Medical Complex Peshawar. **Period:** 1<sup>st</sup> January 2010 to 31<sup>st</sup> July 2011. **Material & methods:** All patients were screened for presence of Hepatocellular carcinoma (HCC) by performing Alpha fetoprotein and ultra sound (U/S) abdomen. Contrast enhanced computed tomography scan (CT) of abdomen was done in selective cases. European Association for the Study of Liver Diseases (EASLD) Noninvasive criteria (limited to patients with underlying cirrhosis) was used for diagnosis of HCC i.e. Two coincident imaging techniques that identify a focal lesion more than 2 cm showing arterial hypervascularization or one imaging modality that identifies a focal lesion more than 2 cm in diameter showing arterial hypervascularization and serum AFP levels greater than 400 ng/ml. **Results:** A total of 370 patients cirrhotic patients were enrolled in this study. Thirty nine patients (10.5%) were diagnosed as having HCC. Male patients were 30 (77%) and 9(23%) were female. Mean age was 49.2% (range 18 to 72 years). Abdominal discomfort was predominant symptom present in 94% patients, followed by anorexia present in 90% patients, abdominal distension in 76%, weight loss in 62%, jaundice was present in 46% patients, altered mental status was notice in 36% patients and history of upper gastrointestinal (GI) bleed and malena was extracted from 26% patients. Ultrasound abdomen and CT abdomen showed unifocal lesion in 48.7% patients, multifocal lesion in 30.7% patients and massive lesion in 20.5% patients. Alpha fetoprotein ranged from 45ng/dl to 630ng/dl. Hepatitis C (HCV) was the commonest cause present in 51% patients, Hepatitis B (HBV) in 15.3% patients and HBV and HCV co-infection in 10.25% patients, history of alcoholism was revealed in 5% patients and in 2.5% patients alcoholism was present along with HCV and HBV each, while in 10% cases the cause of cirrhosis remained unknown. **Conclusions:** Hepatocellular carcinoma is the most common primary hepatic tumor and one of the most common cancers worldwide. It is concluded that HCC is more common in males compared to female cirrhotic patients. Hepatitis C followed by HBV are the leading causes of HCC related cirrhosis in local Population of Khyber pakhtoonkha.

**Key words:** Hepatocellular Carcinoma, Cirrhosis. Frequency

## INTRODUCTION

Hepatocellular carcinoma is the commonest primary cancer of the liver and accounts for more than 90% of all primary liver tumours. Hepatocellular carcinoma is the sixth most common cancer and the third most common cause of death from cancer worldwide<sup>2</sup>. Hepatocellular cancer is a major health problem, more than half a million cases are reported yearly worldwide<sup>3</sup>.

Cirrhosis is the strongest and the most common known risk factor for HCC particularly cirrhosis related to HCV and HBV infections<sup>4</sup> with annual HCC incidences 2-6%<sup>5</sup>. An estimated 75% of all HCC cases are due to chronic infection with HBV or HCV<sup>6</sup>. Hepatitis B carriers are 100 times more likely to develop HCC than the uninfected<sup>7</sup>.

Early detection is highly desirable, patients with early disease are often asymptomatic<sup>8,9</sup> and consequently HCC is frequently diagnosed late, by which time it is often untreatable<sup>10</sup>.

The combination of regular measurement of tumor markers and ultrasound of the liver is used for surveillance of HCC<sup>11</sup> it was shown that HCC surveillance with testing of serum Alpha fetoprotein (AFP) and performance of U/S abdomen at repeated 6-month intervals improves survival<sup>12,13</sup>. Though liver biopsy is gold standard for definitive diagnosis of HCC<sup>14</sup>, characteristic triphasic CT and or dual contrast MRI features and elevated serum alpha fetoprotein (more than 200ng/ml) may Obviate the need for confirmatory

biopsy<sup>15</sup>. The rising incidence of HCC in Pakistan and especially in N.W.F.P requires evaluation of predisposing factors so that preventive measures can be taken<sup>16</sup>.

### MATERIAL AND METHOD

We conducted this prospective observational study in medical A unit Hayatabad Medical complex Peshawar from 1st January 2010 to 30th July 2011.

After detailed history examination and investigations review all diagnosed patients of liver cirrhosis were included in this study after informed consent. All patients were screened for presence of HCC by performing Alpha fetoprotein and U/S abdomen. Computed tomography scan of abdomen was done in selective cases where U/S abdomen was showing suspicious of HCC.

European Association for the Study of Liver Diseases (EASLD) Noninvasive criteria (limited to patients with underlying cirrhosis) mentioned below was used for diagnosis of HCC.

- (a) Radiologic criteria: Two coincident imaging techniques that identify a focal lesion more than 2 cm showing arterial hypervascularization.
- (b) Combined criteria: One imaging modality that identifies a focal lesion more than 2 cm in diameter showing arterial hypervascularization and serum AFP levels greater than 400 ng/ml<sup>17</sup>.

### EXCLUSION CRITERIA

Patients with other tumours of live and metastatic disease else where in body were excluded from study.

Patients were managed along the standard guidelines.

Demographic characteristics were recorded. Data was entered in objectively structured Performa. Chi-square test and P-values were retrieved wherever needed and applicable. SPSS 14 version was used for statistical analysis.

### RESULTS

A total of 370 patients cirrhotic patients were enrolled in this study. Thirty nine patients (10.5%) were diagnosed

as having HCC. Male patients outnumbered female. Male patients were 30 (77%) and 9(23%) were female. Mean age was 49.2% (range 18 to 72 years).less then 20 years was 1 (2.5%) patient, 21 to 30 years were 3(7.6%) patients, 31 to 40 years were 10(25.6%) patients, 41 to 50 years were 7(17%) patients, 51 to 60 years were 10(25.6%) patients and >60 years were 5(12.8%) patients.

Abdominal discomfort was predominant symptom present in 37 (95%) patients, followed by anorexia present in 35(90%) patients, abdominal distension in 29 (74%), weight loss in 24 (62%), jaundice was present in 18 (46%) patients, altered mental status was notice in 14(36%) patients and history of upper gastrointestinal (GI) bleed and malena was extracted from 10 (26%) patients. (Table I).

**Table-I. Symptoms of HCC patients**

	No. of patients	%age
Abdominal discomfort	37	95%
Abdominal distension	29	74%
Anorexia	35	90%
Weight Loss	24	62%
Jaundice	18	46%
Altered Mental Status	14	36%
Upper G.I Bleed	10	26%

Ultrasound abdomen and CT abdomen showed unifocal lesion (<50% of liver size) 1n 19(48.7%) patients, multifocal lesion (<50% of liver size) in 12(30.7%) patients and massive lesion (<50% of liver size) in 8(20.5%) patients. (Table II)

**Table-II. Radiological finding HCC patients**

	No. of patients	%age
Uninodular lesion <50% of liver	19	48.7%
Multinodular lesion <50% of liver	12	30.7%
Massive lesion <50% of liver	08	20.5%

Alpha fetoprotein ranged from 45ng/dl to 630ng/dl.

Hepatitis C infection was the commonest cause present in 20(51%) patients, HBV in 6(15.3%) patients, HBV and HCV co-infection in 4(10.25%) patients, history of alcoholism was revealed in 2(5%) patients and in 1(2.5%) patient alcoholism was present along with HCV and HBV each, while in 4(10%) cases the cause of cirrhosis remained unknown. (Table III).

Table-III. Causes of cirrhosis

Cause of cirrhosis	No. of patients	%age
Hepatitis C	20	51%
Hepatitis B	06	15.3%
Hepatitis B and C	04	10.25%
Hepatitis C and alcoholism	01	2.56%
Hepatitis B and alcoholism	01	2.56%
Alcoholism	02	05%
Unknown cause	04	10.25%

## DISCUSSION

Chronic liver disease is responsible for over 1.4 million deaths annually and is characterized by permanent inflammatory processes that predispose to liver cancer and in particular HCC is the first cause of death in cirrhotic patients<sup>18</sup>.

Male patients are more commonly affected than female in the ratio of 3:1 to 9:1<sup>19</sup>. Seventy seven percent of our patient were male while Mumtaz MS et al<sup>20</sup> and chowdhury OB et al<sup>21</sup> reported 89% and 97% respectively. The reasons for the higher proportion of male patients with HCC might be the possibility that more men are infected with HBV and HCV, consume alcohol, smoke, have increased iron stores, higher body mass index, and a possible involvement of male sex hormones in the onset of HCC<sup>22</sup>.

The mean age of presentation of HCC in Europe and the United States is approximately 60 years. This is in contrast with patients in Asia and Africa, where it is between 20 and 50 years<sup>23</sup> in our study the mean age was

49.2 years while Das et al<sup>24</sup>, chowdhury et al<sup>20</sup> and Khokhar et al<sup>25</sup> reported 49years, 48.5years, and 58.4years respectively.

Abdominal discomfort, abdominal distension and anorexia were the leading symptoms in our study matching the results from chowdhury et al<sup>20</sup> and Iqbal et al<sup>26</sup> (Table I).

In Pakistan, HCC accounts for 1.55% of all malignant tumors<sup>27</sup>.

Various researchers from Pakistan have reported variable figures about prevalence of HCC in cirrhosis, ranging from 3.7% to 16.7%<sup>28</sup> in our study we found frequency of HCC 10.5%. Some latest studies conducted in cirrhotic patients have reported 10.96% prevalence of HCC in North Western Frontier Province, 9.1% in Lahore and 8.25% in Karachi. This prevalence rate is high when compared to Spain (6.6%) but low when compared with Italy (19.7%) and Japan (39%)<sup>29</sup>.

It is believed that HCV infection is a major etiological factor for HCC<sup>30</sup>. Some other studies have reported positivity for HCV infection in up to 80% of patients with HCC<sup>31</sup>. We found alone HCV in 51% patients and in 10% HCC patients as co-infection with HBV. While it was reported 87% and 74% by Chohan et al<sup>32</sup> and Iqbal S et al<sup>26</sup> (Table III).

Hepatitis B has several cancer promoting actions including insertional mutagenesis and p53 inhibition that explain its potential to induce HCC in noncirrhotic liver<sup>33</sup>. Pakistan is highly endemic with HBV<sup>34</sup> with nine million people infected with HBV<sup>35</sup> and its infection rate is on a steady rise<sup>36</sup> we reported HBV in 15.3% HCC patients matching local studies by Rehman et al<sup>31</sup> and Qureshi et al<sup>37</sup> (Table III)

Chronic alcohol use of greater than 80 g per day for more than ten years increases the risk of hepatocellular cancer 5-fold. Furthermore, chronic alcohol use in HBV or HCV infection doubles the risk of hepatocellular cancer over either infection alone<sup>38</sup> In our study 5% patients were pure alcoholics and 5% had HBV or HCV along with

alcohol abuse. (Table III).  
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