Original Article

Frequency of Hepatocellular Carcinoma and Associated Factors in Patients Presenting to Mayo Hospital, Lahore

Samina Qamar, Shahid Mahmood, Ahmad Hameed and Sobia Ashraf

ABSTRACT

Objective: To determine the frequency of patients having Hepatocellular Carcinoma and major causative factors associated with it, presenting to Mayo Hospital Lahore.

Study Design: Observational / cross-sectional study

Place and Duration of Study: This study was conducted at the Oncology Department of Mayo Hospital, Lahore from Jan 2017 to Dec 2017.

Materials and Methods: This study enrolled clinical data of 151/207 Hepatocellular Carcinoma patients. Their age, sex, socioeconomic status underlying co-morbidity, presence or absence of liver cirrhosis, tumor size, single/multiple tumors, tumor stage, hepatitis serologies, serum AFP levels, and portal vein thrombosis.

Results: Out of 151, 106(70%) were males and 45 (30%) were females. Mean age of presentation was 57.1 ± 8.6 years. Patients with rural background were 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic strata while 15 (10%) were of middle social class. 104 (69%) patients were positive for Hepatitis C virus, 27 (18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses, 3 (2%) were alcoholic and 11(7%) patients had no known causative factor .Regarding levels of serum Alpha fetoprotein, 67 (44 %) of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (25%) had AFP levels below 20 ng/ml. Mean tumor size was 8.2 cm ± 2.9 cm. 3 (1.9%) patients were at Stage I, 16(10.7%) had stage II, 84 (55.7%) had stage III and 48(31.7%) of patients were at stage IV of disease., 48(32%) of patients had class A of Child classification, 71 (47%) class B, and 32(21%) had class C.

Conclusion: In our population, Hepatitis C virus is the main causative agent behind Hepatocellular Carcinoma and most of the patients present with large tumor size, multicentric tumor and portal vein thrombosis. Serum AFP levels are low in more than 50% of patients and is not reliable for detecting HCC.

We should implement effective screening programs of viral hepatitis and cirrhosis to save this precious organ and prevent the need of liver transplant.

Key Words: Cirrhosis, Hepatocellular Carcinoma, Serum AFP level, Hepatitis B and C

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common malignancy of liver. It is second commonest cause of cancer death around the world as its incidence is 5.4%[1]. Highest incidence is found in Asian (China, Taiwan, Korea) and Sub-Saharan African countries because of Hepatitis B virus that is transmitted to infants through vertical transmission. In Japan and Europe most important causative agent is Hepatitis C virus [2]. Other important causative factors of HCC are metabolic toxins like aflatoxin and alcohol, hemochromatosis, alpha1 antitrypsin deficiency and steatohepatitis.

Department of Pathology, King Edward Medical University, Lahore.

Correspondence: Dr. Samina Qamar, Assistant Professor of Pathology, King Edward Medical University, Lahore.
Contact No: 0346-4658931
Email: samnir@gmail.com

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All these agents infect and reside in hepatocytes, disturb their structure, function and genomic material resulting in a repitittive cycle of inflammation and regeneration of hepatocytes. Hepatocytes try to overcome the damage by dividing rapidly but become dysplastic and ultimately neoplastic as they accumulate structural and numeric chromosomal abnormality resulting in genomic instability[3]

Developed countries like United States, HCC is relatively uncommon. Pakistan and other under-developed countries harbors great number of HCC patients. Many remain undiagnosed due to lack of proper health care facilities and unawareness to risk factors. Pakistan has 2nd highest prevalence of chronic Hepatitis C infection in the world [4]. Approximately over 10 million people are infected with chronic Hepatitis virus in Pakistan. Hepatitis C prevalence is 6%-13% while Hepatitis B prevalence is 2-3%. According to Punjab cancer registry, it is the fifth most common cancer collectively in both genders (3.8%) and 3rd most common in men (6.6%) [5]. Viral hepatitis and excessive alcohol consumption are the top most causes

of HCC [6]. HCC can be treated by radioablation, chemoembolization, resection and transplant in advanced stages but has a dismal outcome [7].

The purpose of this study was to find out frequency of patients presenting with HCC and associated causative factors that play major role in development of carcinoma, so that we can plan proper screening methods to detect and prevent this menace. We collected data encompassing various fields like socioeconomic status and background, causative agent, stage and tumor size at presentation, cirrhotic changes, Child Pugh score (based on presence of encephalopathy, ascites, albumin, prothrombin time, bilirubin and divided into class A,B and C).

MATERIALS AND METHODS

This cross-sectional observational study enrolled clinical data base of 207 HCC patients and variables studied were age, sex, socioeconomic status (monthly income below 10,000 PKR = Low, or above =Middle class) underlying co-morbidity, presence or absence of liver cirrhosis, tumor size (Less or more than 10cm), single/multiple tumors, tumor stage, hepatitis serologies, serum AFP levels (Normal level= upto 44ng/ml), portal vein thrombosis, Child classification (Classified as A, B and C depending upon serum bilirubin, albumin, prothrombin, ascites and encephalopathy) of patients diagnosed with HCC between January 2017 till December 2017 were extracted from medical records of Oncology Department and outdoor of Mayo Hospital, Lahore with the help of participating investigators. Out of 207 patients, 151 cases fulfilled the inclusion criteria and were included in the study. All information was recorded in a predesigned proforma. All data was analyzed by SPSS 22 and descriptive statistics were used for variables. Mean and standard deviation was calculated for quantitative variables. Frequency and percentage was calculated for qualitative variables like gender, socioeconomic status, cirrhosis, stage of tumor, causes of HCC, serum AFP and portal vein thrombosis.

Inclusion Criteria: All patients presenting to Oncology department with diagnosis of HCC either biopsy proven or with radiological evidence of disease were included in the study.

Exclusion Criteria: Patients having insufficient diagnostic investigations to prove hepatic mass as HCC were excluded.

RESULTS

Total 151 patients were included in the study. Out of 151, 106(70%) were males and 45 (30%) were females. Mean age of presentation was 57.1 ± 8.6 years. Patients with rural background were 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic strata while 15 (10%) were of middle social class. (Table I)

According to our study 104 (69%) patients were positive for Hepatitis C virus, 27 (18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses, 3 (2%) were alcoholic and 11(7%) patients had no known causative factor for HCC (Figure I). Analysis of child-turcotte-pugh classification, our patient population showed that 48(32%) of patients had class A, 71 (47%) class B, and 32(21%) had class C (Figure II). Levels of serum Alpha fetoprotein showed that 67 (44 %) of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (25%) had AFP levels below 20 ng/ml (Figure III) Mean tumor size was 8.2 cm ± 2.9 cm. Tumor size was more than 10cm in 39(25.8%) patients. Multicentric tumor was present in 97(64.2%) and Portal Vein Thrombosis was seen in 56 (37%) of patients. Regarding stage of Hepatocellular carcinoma 3 (1.9%) patients were at Stage I, 16(10.7%) had stage II, 84 (55.7%) had stage III and 48(31.7%) of patients were at stage IV of disease.

Table No.1: Demographic features of HCC.

Males	106 (70%)
Females	45 (30%)
Rural	115 (76.2%)
Urban	36 (23.7%)
Lower class	136 (90%)
Middle class	15 (10%)

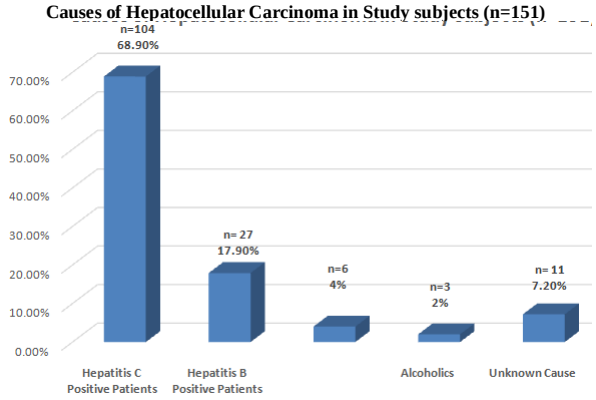

Figure No.I- Causative agent of Hepatocellular Carcinoma.

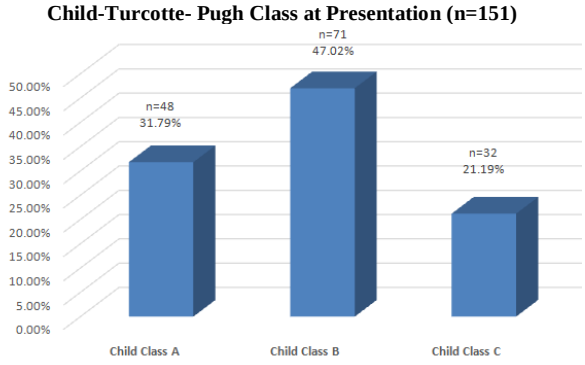

Figure No.2- Stage of cirrhosis at presentation.

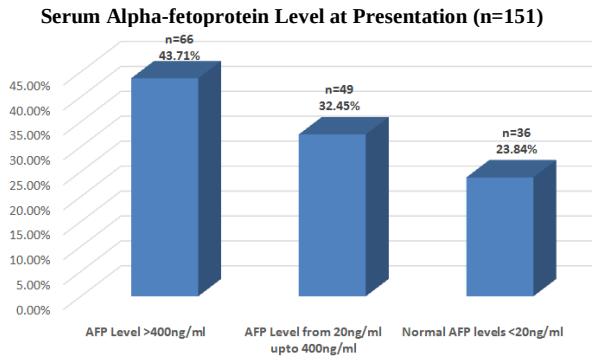

Figure No.3: Level of serum AFP (normal upto 44ng/ml).

DISCUSSION

Hepatocellular carcinoma is life threatening carcinoma with rising incidence worldwide. Despite improvement in HCC management multiple factors like lifestyle, metabolic syndrome, environmental factors, obesity, hepatitis viruses and many other are supporting its development. It is diagnosed at advanced stage and has many complications during and after treatment [8]. Males and females are affected differently from it. Zheng et al stated that estrogen /androgen signaling pathway is associated with decreased/increased transcription and replication of HBV genes that promote development of HBV infection by up/downregulating RNA transcription of viruses which in turn slows the progression of HBV induced HCC. Estrogen and androgen can also effect HBV related HCC by induction of epigenetic changes. This could be the reason behind different incidence among males and females [9]. In our study, out of 151, 106(70%) were males and 45 (30%) were females. Kao conducted multivariate analysis on HCC patients and results showed that HCC was associated with poor prognosis when accompanied by factors like age older than 65 years, Alpha fetoprotein (AFP) greater than 20 and multiple tumors [10]. Similarly, poor survival was seen in older patients, with advanced tumor stage and multiple tumors [7]. Kotewall's group of patients had median age of 58.5 with age range of 25-78 years [11].In our study, mean age of presentation was 57.1 ± 8.6 years Egyptian population also had median age of 58 years at diagnosis of HCC while African patients presented at median age of 46 years. Hepatitis C was leading cause of HCC in Egypt while Hepatitis B was major cause in African population[12]. We concluded that most of our patients were from rural background 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic (income below 10,000 PKR/ month) strata while 15 (10%) were of middle social class (income above 10,000 PKR). Similarly, in United States lower socioeconomic strata harbored more cases of HCC than higher class [13].

AFP level more than 400ng/mL is independent risk factor for overall survival, it is still not sensitive enough to predict the prognosis in patients with HCC diameter less than 3 cm [14]. Similarly, Kotewall found that AFP levels (more than 400ng/mL) were higher in HCV infected patients (78.2%) as compared to HBV infected group (67.1%) [12] . We found that (67) 44 % of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (24%) had AFP levels below 20 ng/ml. In our patients tumor size was more than 3cm and still more than 50% of patients had AFP below 400ng/mL. We conclude that AFP is not sensitive enough to detect HCC in our population as most of them are infected with HCV.

According to our study 104 (69%) of patients were positive for Hepatitis C virus, 27(18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses. However in United States, HCV is more common in HCC patients as compared to HBV[15]. Munaf A and studies in United States showed prevalence of HCV to be 66% and HBV as 34%. Patients with HCV were more likely to develop HCC at advanced age of 52 years as compared to HBV infected who developed HCC at the age of 40 years [15,16]. A study conducted in Iran on 1654 people (healthy) with mean age of 29.1 showed HCV infection in 0.42%(7/1654) of patient population. Among them 80% were males and 20% were females. Iran has very low prevalence of hepatitis virus infection [17]. So our data is consistent with these observations but different from China.

In our patients tumor size was more than 10cm in 39 (25.8%) patients. Kotewall's patients had median tumor size of 2.7 cm [12]. Tumor size was larger; more than 5cm in HCV group (66%) while less than 5cm in HBV group (59.3%). In our population, tumor size is much larger than seen in other studies. We found that multicentric tumor was present in 97 (64.2%) and Portal Vein Thrombosis was seen in 56 (37%) of patients. Contrastingly, Munaf states that portal vein thrombosis was seen in 8% of HCV patients and only 1% of HBV group. HCV-HCC group were more cirrhotic than HBV and had more than two times higher rate of solitary macrovascular involvement than HBV group (OR=0.245 and 2.533 respectively). Regarding stage of Hepatocellular carcinoma 3(1.9%) patients were at Stage I, 16 (10.7%) had stage II, 84 (55.7%) had stage III and 48 (31.7%) of patients were at stage IV of disease. Analysis of child-turcotte-pugh classification, our patient population showed that 32% of patients had class A, 47% class B, and 21% had class C. In West and China most patients are diagnosed with early resectable disease [18]. This probably is due to effective screening programs in high risk cirrhotic population which include ultrasound and serum AFP levels. While in our local population no such facility is available for cirrhotic patients and rural population is unaware of disease signs and symptoms. Lack of awareness among masses and ineffective screening leads to late disease presentation and diagnosis resulting in high morbidity and mortality due to HCC.

CONCLUSION

In our population, Hepatitis C virus is the main causative agent behind Hepatocellular Carcinoma and most of the patients present with large tumor size, multicentric tumor and portal vein thrombosis. Serum AFP levels are low in more than 50% of patients and is not reliable for detecting HCC.

We should implement effective screening programs of viral hepatitis and cirrhosis to save this precious organ and prevent the need of liver transplant.

Author's Contribution:

Concept & Design of Study:	Samina Qamar
Drafting:	Shahid Mahmood
Data Analysis:	Ahmad Hameed, Sobia Ashraf
Revisiting Critically:	Samina Qamar, Shahid Mahmood
Final Approval of version:	Samina Qamar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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