

INCIDENCE OF CIRRHOTIC LIVER AND HEPATOCELLULAR CARCINOMA IN PAKISTAN

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ABSTRACT

Hepatocellular carcinoma (HCC) is a rising cancer in Pakistan especially males have an increased incidence. The major risk factor for HCC is Hepatitis C and in Pakistan the prevalence rate of this cancer is also very high. In this article, different aspects of liver cancer are presented and highlighted the risk factors relating to HCC in Pakistan. This article will evaluate the prevalence of HCC and cirrhotic liver diseases with respect to etiological factors. In Pakistan there is a lack of general awareness regarding transmission of hepatitis virus, which is the main risk factor for HCC. There is lack in availability of proper treatments in the hospitals for the people with end stage of hepatic cancer. Regular checkup and early diagnosis can reduce the severity of disease. At this moment in Pakistan there is an immense need of detailed population-based studies and surveillance programs to estimate the exact burden of the HCC.

KEYWORDS: Alpha-fetoproteins (AFP), Chronic Liver Disease (CLD), Hepatocellular Carcinoma (HCC).

1. INTRODUCTION

Hepatocellular carcinoma (HCC) is a big health issue and the sixth common neoplasm globally, while the third most common cause of death. Prevalence, and transmission pathways of hepatitis is different across the world as well as within the countries. Liver cancer is more common in developing countries, around 80% of HCC occur in Asia and Africa. The most common transmission of viral hepatitis is through contaminated blood. Hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) leads to chronic hepatitis in the majority of cases. Hepatocellular carcinoma occurs when histology of liver get abnormal and chronic liver disorder represents the higher risk of Hepatocellular carcinoma (HCC).^[1] In Pakistan from 1970s till 1990s hepatitis B was the major etiology for HCC, nevertheless with the passage of time hepatitis C virus was also observed as a rising factor for HCC. The common risk factors regarding the HCC are chronic infection with hepatitis B and C, alcohol consumption, autoimmune hepatitis etc. There are numbers of HCC cases which are non-B, non-C (NBNC) hepatitis are also reported in Pakistan. According to some evidence, obesity and

diabetes can be linked to development of higher rate of HCC.^[2] The median subclinical time period of HCC is 3.2 years. During this time period highest impact on screening with early detection and treatment can be cured. There is significant difference among regional areas in the development of HCC globally. Even HCC has a very poor prognosis and low survival rate it can be cured at early stages including these strategies such as chemo-radiotherapy, surgery and chemotherapeutic drugs etc.

In the developing countries Hepatitis C is considered as the most common cause of HCC and its genotype varies globally. In Pakistan hepatitis C "genotype 3" is considered the most prevalent genotype. Till now there are only two studies were carried out at Pakistan level to find out association of HCV genotype to HCC.^[3] In a study 189 patients were evaluated with chronic liver disease, among them 82 patients were diagnosed with HCC, while in 76% "genotype 3a" was more dominant than 3b, 3k, 1a, 1c, 1b and 2a. Due to small sample size of this study it lacks the evidence of HCV genotype 3a correlation with HCC in Pakistani population. The important aspect of this study was that it provides

additional information about HCV genotype 3a, which contain polygenic cluster in Pakistan. Epidemic spread of HCV genotype 3a might be due to the increasing the HCC rate in Pakistan during the last few decades. Contrast to other research study HCV genotype 3a was 41%, while 3b was 16% and 1a, 1b was 10%, 2% respectively and the mixed genotype was 29% in HCC patients. However, two samples found to be undetectable genotype.^[4] In developing countries, the common cause for HCC is hepatitis C and the viral distribution as well as its genotypes differs across globally.

Epidemiology

Unfortunately, till now there is no comprehensive population-based study available in the Pakistan, which can tell the exact prevalence and the incidence rate of HCC in patients. So far, the most of reported studies were conducted at hospital level, containing small sample size. In Pakistan there have limited cancer registries. The first ever population-based cancer registry in Pakistan was founded in Karachi by the government of Sindh in 1995 with the collaboration of International Agency for Research on Cancer (IARC) WHO.^[5] Agha Khan university with 84 centers across the Pakistan in 2000 established cancer surveillance for Pakistan (ACSP). Through these registries incidence and prevalence of cancer were estimated. In Karachi cancer registry 4,268 cases were registered in 1995-1997, for HCC and age standardized rate (ASR) were found to be 3.7 per 100,000 in female and 5.7 per 100,000 in males.^[5] During 1998 – 2002 in Karachi ASR found to be in females 4.0 per 100,000 while in male were 5.3 per 100,000 respectively.^[6] During 2000-2002 from Larkana ASR for HCC patients were 2.0 per 100,000 persons in females 10.5 per 100,000 in male.^[7] Similarly, residents of Hyderabad, during 1998-2002, the cancer patients were registered in KCR and APCR, the patients ASR for HCC disease were reported to be 1.2 1.2 per 100,000 in females and 4.4 per 100,000 in males.^[8]

However, from Quetta, there were 1,077 cancer patients registered in KCR in 1998-1999. Where, HCC was found the third most common type of cancer in men (ASR) 12.3 per 100,000 whereas, the seventh most common type of cancer in females (ASR) 3.1/100 000.^[9] Except these registered data, other 29 studies reported evaluated epidemiological aspects of HCC. From these 29 hospital-based studies the numbers of sample sizes were gathered (n = 3319) with trends of HCC, like etiological factors and gender distribution were analyzed. Among 3,319 studied cases in another study reported that the gender information was available for 2,967, in that study 21.71% were women and 78.29% were male. Information regarding 2852 cases and their etiological factors for HCC was studied, it was reported that the co-infection such as HCV/HBV, HBV, and HCV was found in 5.26%, 25.35%, and 57.99%, cases respectively. The incidences of coinfection with hepatitis B/C/D were found in 0.63% cases, while coinfection with HBV and

HDV was reported in 1.09% cases. During study period, the majority reported HCC cases were male. Hepatitis B and C were the most common etiological factor for HCC.^[10] Viral hepatitis is the main contributing factor for HCC in Pakistan. Viral hepatitis, HBV/HCV and/or HBV/HDV coinfections are the most common cause that leads to HCC.

Risk Factors

Some important risk factors are responsible for prevalence of hepatitis which further lead to HCC when remain untreatable. In Pakistan mode of transmission is same like other countries worldwide like, history of dental treatment sexual contact history of blood transfusion, tattoo etc. A study was conducted in Peshawar (Pakistan) with sample size of 100 cases, the study identified the highlight risk factors involved in transmission of hepatitis and the cause HCC in the studied patients. The ratio of these risk factors was 4:1 for dental treatment, 3:9 for sexual contact, 2:1 for blood transfusion, drug abuse, tattoo and other contact sports were found not significant. The study concluded that the HCC is becoming endemic in Pakistan due to lack of awareness about transmission of viral hepatitis.^[11]

Clinical Presentation and Diagnosis of HCC

Most patients with liver disease stayed asymptomatic or may experience, weight loss, fever, jaundice right hypochondrial pain, hepatic encephalopathy, upper gastrointestinal bleeding hepatosplenomegaly, and ascites.^[12-17] Cirrhosis was also reported in 69-84% cases.^[12,15-19] In another study, where the sample size was 145 and the patients with HCC were found with elevated serum bilirubin (100%), alkaline phosphatase (ALP) (100%), aspartate aminotransferase (AST) (42.1%), alanine aminotransferase (ALT) (42.1%).^[19] Alpha-fetoprotein (AFP), a high molecular weight serum glycoprotein and considered as a screening marker to along with liver ultrasound for HCC detection. Elevated AFP was considered to >200 or > 400 ng/ml for detection of HCC. Similarly in another study with small sample size (n = 100), AFP was found to be 89% specific for detection of HCC.^[20] Diagnosis of HCC, there are different procedures available like; AFP, biopsy of liver, triphasic CT scan and abdomen ultrasound have been carried out in various reported studies. In other study with 584 samples size, used these different screening markers to measure the incidence of HCC, biopsy and liver ultrasound were performed in 26, 60 patients respectively. CT scan with AFP were performed in 365 patients.^[21]

Treatment and Survival of HCC

In Pakistan unfortunately, fewer data is available for HCC treatment. The study conducted in Larkana (Pakistan) with sample size 584 only 79 were eligible for different procedure of treatment. Only 48 patients used transarterial chemoembolization (TACE) with doxorubicin and lipiodol.^[7] Another study conducted in Karachi (Pakistan) with 129 cases, out of 129 only 41

patients of HCC underwent TACE modality.^[22] Generally, research studies on the topic of the treatment of HCC are scarce, while the existing data carries the limitations due to small sample size.

2. CONCLUSION

In Pakistan HBV and HCV are the major cause of CLD and HCC. Pakistan is considered an endemic county for HCC. There exists an immense need to carry out further epidemiological population-based studies and surveillance program to measure the exact prevalence of CLD and HCC. In Pakistan at country level the data regarding treatment of HCC with proper facilities are not available and the outcomes are rare. At this moment, it's important to diagnosed HCC at its early stage for better and proper treatment. And general population should vaccinate themselves against the viral hepatitis to stop the spread of HCC in Pakistan.

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