EDITORIAL

Hepatocellular Carcinoma in Pakistan

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Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and the third most common cause of death from cancer, and the second most common cancer in men.[1] This could be the reason why the World Gastroenterology Organization focused on HCC this year on World Digestive Health Day, held on the 29th of May. "Act today. Save your life tomorrow" was the theme of campaign as HCC is preventable by adopting adequate measures.

Though the hepatitis B virus (HBV) is still the main etiological agent for HCC in many Asian Pacific countries, hepatitis C virus (HCV) related disease is the single largest cause of HCC in Pakistan.[2-6] In a country of about 200 million, 4.8% of general population is positive for anti-HCV antibody and 2.5% for HBV surface antigen.[7,8] HCV HCC dominance appears to be related to this higher prevalence of hepatitis C. HCV related HCC is seen in about 60 – 70% of cases. Only about 20% of cases are positive for HBV and 10 – 15% are non-B non-C.[5,6,9,10] High contamination rates with aflatoxin in Pakistan also contribute to liver carcinogenesis.[11,12] The age-standardized rate of HCC in Pakistan is about 7.6 per 100,000 persons per year for males and 2.8 for females.[13-16] The male to female ratio for HCC is 3.6:1. Most of the patients present in their 5th and 6th decade.[6] Genotype 3a of HCV, and genotype D of hepatitis B, which are the most common genotypes in Pakistan, are also seen in the majority of HCC patients.[2,4,17] However, the duration of infection rather than the genotypes appears to correlate with HCC development. Moreover, there is an importance of mean HCV RNA levels which were found to be significantly higher in our HCC than in liver cirrhosis patients without HCC.[2] Other significant factors associated with HCC were older age, male gender and higher alkaline phosphatase.

The epidemic spread of HCV-3a occurred earlier in Pakistan than the other countries in which this genotype has been reported and this might be associated with rising incidence of HCC.[2] Molecular evolutionary analysis revealed a distinct phylogenetic cluster of HCV-3a in Pakistan and an estimation of the effective number of HCV infections indicated the appearance of HCV-3a in this region in the 1920s and a rapid exponential growth in the 1950s. The spread of hepatitis B and C is related to number of therapeutic injections received per year, reuse of syringes, improper sterilization of invasive medical devices, including surgical and dental instruments, circumcision and cord-cutting instruments and the re-use of razors by street barbers.

Compared with HBV, development of HCC in hepatitis C was less associated with rise in alpha-fetoprotein in Pakistani patients.[18] Comparing HCC in HBV mono-infection with HDV co-infection, latter was associated with smaller liver size and indirect evidence of more severe portal hypertension but earlier TNM stage.[19] The patients with viral marker negative HCC tend not to be under a surveillance program which ends up in a late diagnosis at a more advanced stage of disease.[5] They have larger tumour size, shorter duration between diagnosis of cirrhosis and HCC, and concomitant diabetes mellitus. Many of these cases are thought to be related to non-alcoholic fatty liver disease, which again has a rising trend in our population.

Surveillance for HCC is recommended in patients with compensated cirrhosis and in chronic active hepatitis B patients as it is cost effective and survival is improved by early intervention and treatment.[20] Many sonologists in Pakistan are practicing without enough training to pick up early lesions. Alpha-fetoprotein is now considered as an inadequate screening test for HCC.[21] However, considering the insufficient expertise to pick up early HCC by sonography, including alpha-fetoprotein for surveillance may still be suggested in our setting to increase the pick up rate. Though the Barcelona Clinic Liver Cancer (BCLC) is an excellent staging system to plan treatment, a majority of our patients present with advanced non-resectable disease in a cirrhotic liver when the simple staging system by Okuda predicts prognosis effectively.[18]

HCC is by and large a preventable disease. There is an urgent need to act today and implement measures to prevent the spread of hepatitis viruses. This appears to be the elemental step to save our lives tomorrow from cirrhosis and HCC. Health authorities should recommend and implement policies for preventing hepatitis B and C transmission. The mandatory hepatitis B vaccination program for new-borns was introduced in 2002 but it is covering less than 60% of new-borns.[22] Hepatitis control programs should focus on this aspect

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as well. In addition, early detection of these viral infections and treatment of cases to prevent cirrhosis is equally important. Awareness should be increased to get tested for hepatitis B and C. The risk of HCC is reduced among patients with hepatitis B and C who are successfully treated.[23,24] In cases with cirrhosis, facilities for screening HCC with ultrasound should be available. Sonologists should be properly trained to detect the early cancer.

It is encouraging that centres of excellence are being developed where proper facilities for the diagnosis and management of liver disease are becoming available. These facilities provide oral drug treatment, transarterial chemoembolization, radiofrequency ablation and resection. However, these services are insufficient and out of reach of an ordinary patient, which is an unfortunate aspect of the healthcare services in Pakistan as HCC is a disease more prevalent amongst the poor.

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