

Liver Diseases in Nepal

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Geo-cultural factors influence the prevalence liver disease of public health importance in any country. Liver disease may vary from country to country and in the same country in different cultural groups and at different periods of time. Whereas alcohol accounts for 80% of cirrhosis in the United States (1) the predominant cause of cirrhosis in China, South-East Asia and Africa is hepatitis B (2,3). In Japan in last 25 years the hepatitis B related liver cancer have remained steady, but the incidence of hepatitis C related liver cancer have rapidly increased- making it now a major health problem (4). Despite geographical proximity the pattern of liver disease in India and Nepal are different. Indian childhood cirrhosis and non-cirrhotic portal fibrosis, common in India does not occur in Nepal. The prevalence of hepatitis B in Nepal is much lower than in India, however certain ethnic groups in Nepal have very high incidence of this infection (5). A brief comment about the pattern of acute and chronic liver disease in Nepal is given below.

Acute Hepatitis in Nepal. Acute hepatitis (AH) is common in Nepal (6). In Kathmandu valley, its incidence is high during the rainy season. Hepatitis E, a water-borne infection is the common cause of acute hepatitis in Nepal. It was responsible for all epidemics and small focal outbreaks of hepatitis and much of sporadic hepatitis (7). Study done in 1997 showed that 56% of AH in the valley was caused by hepatitis E; and hepatitis A, hepatitis B and hepatitis C accounted for 3 % each only (8). Hepatitis E, though is a self-limiting disease, may cause cholestatic symptom with prolonged jaundice and itching in about 8% of the patients, and fatal acute hepatic failure in some, especially women with advanced pregnancy (7).

Hepatitis A, the common cause of AH in the West and Japan, is a rare in Nepalese adults. It is a highly infectious and all most all Nepalese acquire this infection by the age of 5 years usually asymptotically and develop life long immunity against this infection (9). Similarly, the incidence of acute hepatitis B in Nepal is low compared to other Afro-Asian countries. In 1997, though 20 (13%) patients with AH were HBsAg positive, only 3% had acute hepatitis B (anti-HBc IgM positive), the

remaining were hepatitis B carriers with acute hepatitis E (anti-HEV IgM positive). Incidence of acute hepatitis C is also low, and in Nepal it is confined to drug addicts. In injecting drug abusers in Nepal it is the commonest chronic viral infection - 90% are anti-HCV positive and 60% HCV RNA positive (10).

The cause of acute hepatitis in 34% of the patients in 1997 was not known. The incidence of this group, labeled as non A-E hepatitis have varied and increased recently (11). Clinical and epidemiological features of non A-E hepatitis was similar to hepatitis E. Bacterial hepatitis caused by Gram-negative organisms commonly *E. coli*, *Klebsiella* and *Salmonella* group of organisms was found to be responsible for some cases of non A-E hepatitis. It may occur alone or as co-infection with hepatitis E. And recently it has emerged as an important cause of acute hepatitis in Nepal. Thus it is important to recognize it, not only because there is specific treatment for it, but delay in treatment may be associated with high incidence of complications like septicemia, ascites due to acute hepatic outflow obstruction and renal failure.

The diagnostic work up a case of acute hepatitis in adult in Nepal thus should include tests for bacterial hepatitis and hepatitis E. Diagnostic serological tests for hepatitis E are anti-HEV IgM and HEV RNA. Tests to identify bacterial infection are total and differential white blood cell count and blood culture for aerobic organisms. C-reactive protein may be used as an additional surrogate test. These tests should be done in all patients of acute hepatitis presenting with fever.

It is important to remember that diabetic, elderly and very young and immune suppressed patients, who are more likely to have bacterial hepatitis may not present with fever and they may have normal or even low WBC count. Routine tests for acute hepatitis A (anti-HAV IgM) and C (anti-HCV and HCV RNA) in

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Nepalese adult is not cost-effective, except in certain specific groups like test for hepatitis C in drug addicts, and hepatitis A in children and persons of high socio-economic status. Doing these tests and missing to look for bacterial infection would be considered a serious mistake.

Chronic Liver Diseases in Nepal. The common causes of chronic liver diseases the world over are infection with hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol abuse. The community prevalence of both HBV and HCV infections in Nepal is low. Prevalence of HBsAg, a marker of HBV infection is 0.9%, and anti-HCV, a marker of past exposure to HCV is 0.4% (12,13). However, HBV and HCV accounted for 40% and 14% respectively of the liver cirrhosis in Nepal (14). Study of 430 liver biopsies, performed in the period 1990 to 1997 showed that alcohol and Hepatic IVC Disease (HVD) were the two predominant causes of liver diseases in Nepal (15). Alcohol was responsible for 44.6% of the cirrhosis and 20.4% of the other liver diseases and HVD for 34% of cirrhosis and 29.3% of other liver diseases.

Hepatic IVC Disease. Japanese investigators in early 1950s first drew attention to liver disease due to obstruction of the hepatic portion of the inferior vena cava (16). The disease now is very rare in Japan and in the West. But it is a common cause of liver diseases in Nepal ((17).

As hepatic IVC disease is not usually mentioned in medical textbook, a brief account follows. HVD is a clinical syndrome caused by obstructive lesion of the hepatic portion of the inferior vena cava. Much confusion in the past occurred as it was lumped together with hepatic vein thrombosis (HVT) under the eponym Budd-Chiari syndrome (18). It is now recognized clinically and epidemiologically as a distinct disease, different from HVT (19,20). Whereas HVT is an acute disease due to hypercoagulable conditions, common in the West; HVD is a chronic disease with insidious onset seen in developing countries. Studies in Nepal indicate that it is caused by bacterial infection (15,17,21). In the past HVD was recognized only at autopsy (22), later it was diagnosed clinically and by cavogram. Ultrasonography is specific and sensitive in the diagnosis of the disease (23,24). Its diagnosis depends upon being aware of the condition and use of USG.

Patients of HVD may present with symptoms of caval obstruction like dilated superficial veins in the body trunk with cephalad flow, pedal edema,

varicose veins and poorly healing ulcer in leg or albuminuria; or hepatic outflow obstruction like ascites and hepatomegaly or splenomegaly. The disease commonly presents as acute exacerbations, usually precipitated by surgery or infection, with clinical features like acute ascites, pedal edema, jaundice or digestive bleeding. It is the commonest cause of ascites in Nepal, and is usually associated with bacterial peritonitis (20). Delayed complications of HVD include liver cirrhosis (LC) and hepatocellular carcinoma (HCC). It is an important cause of LC and HCC in Nepal.

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