

# Hepatitis E infection in chronic liver disease patients causing acute on chronic liver failure: Vaccination is need of the hour

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Hepatitis E virus (HEV) infection is a serious global public health illness and one of the major causes of viral hepatitis worldwide. Its prevalence rate globally is under-reported. However, literature has documented an annual incidence of around 20 million people. Approximately 56 000 patients die of HEV-related illnesses every year.<sup>1</sup> HEV infection is acquired through the fecal-oral route secondary to the use of contaminated food and water.<sup>2</sup> Acute hepatitis secondary to HEV infection is usually a self-limiting disease with a similar clinical presentation to that of hepatitis A.<sup>3</sup> HEV infection is also the leading cause of Acute on chronic liver failure (ACLF) in endemic areas.<sup>1</sup> HEV-induced superimposed acute hepatitis in patients having underlying cirrhosis may complicate and worsen the primary disease and can develop a syndrome called ACLF. The sudden deterioration of liver functions in cirrhotic patients is the distinguishing feature of ACLF.<sup>4</sup> The ACLF may progress and involve the other organs, resulting in multi-organ dysfunction.<sup>2</sup> The 180-day mortality was showed significantly higher for cirrhotics patients having HEV-induced superimposed

infection compared with non-cirrhotics (22.7% vs 3.8%,  $p=0.013$ ).<sup>5</sup> The ACLF patients need treatment in intensive care units for supporting the failing organs and halting the disease progression.<sup>4</sup> Majority of these patients may need early transplantation and priority on the transplant waiting list to improve their survival.<sup>6</sup>

Pakistan has a major burden of liver disease and is considered an endemic region for viral hepatitis. In Pakistan, almost 12 million people suffer from either hepatitis B or C. Each year brings about 150 000 new cases.<sup>7</sup> Pakistan is also considered a highly prevalent area regarding HEV infections. HEV infection was found as one of the leading causes (14.1%) of acute hepatitis in patients admitted to the hospital.<sup>8</sup> Water contamination with sewage was labelled a major risk factor for HEV spread in the country. In Pakistan, HEV genotype 1 so far, has been reported as the dominant genotype.<sup>9</sup> One recent study in the urban population of Pakistan reported 20% of HEV seroprevalence in the general symptomatic population.<sup>10</sup>

Similarly, another study reported about 17.5% seroprevalence in cirrhotics patients. The authors also reported severe exacerbation of liver disease in these HEV-induced

superinfected cirrhotic patients leading to decompensation or death.<sup>11</sup> Also, exposure to Hepatitis E during pregnancy can be fatal to the mother as well as the baby, many Pakistan-based hospital studies show a prevalence of Hepatitis E to be as high as 10% during the first and 20% during the second and third trimesters respectively.<sup>12</sup>

Recombinant HEV vaccines have been developed, but to date, only a single brand, which is licensed in China since 2011, is commercially available.<sup>13</sup> This recombinant vaccine is increasingly recommended for immunocompromised patients, particularly chronic liver disease and pregnant and transplanted patients.<sup>3,13</sup> Probably, it's time to start HEV immunoprophylaxis in pre-existing CLD patients and immunocompromised patients. As it will decrease the burden on the transplant waiting list in the country. In Pakistan, almost more than five thousand CLD patients wait for liver transplantation annually and the capacity is almost up to five hundred.<sup>14</sup> General public health education is also important along with preventive measures like improvement of sanitary conditions, proper waste disposal, and the provision of clean water. These preventive measures and immunoprophylaxis will decrease the incidence of HEV-induced ACLF and will lessen the burden on the transplant waiting list. Public health measures are needed to vaccinate CLD patients to prevent HEV-induced ACLF in the Pakistani population.

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#### REFERENCES

- 1 WHO. *Hepatitis E* [Internet] 2016.
- 2 Kmush B, Wierzba T, Krain L, *et al*. Epidemiology of hepatitis E in low- and middle-income countries of Asia and Africa. *Semin Liver Dis* 2013;33:015–29.
- 3 Zaman K, Goyal K, Singh MP. *Hepatitis E vaccines—Current scenario*.
- 4 Laleman W, Verbeke L, Meersseman P, *et al*. Acute-On-Chronic liver failure: current concepts on definition, pathogenesis, clinical manifestations and potential therapeutic interventions. *Expert Rev Gastroenterol Hepatol* 2011;5:523–37.
- 5 Choi JW, Son HJ, Lee SS, *et al*. Acute hepatitis E virus superinfection increases mortality in patients with cirrhosis. *BMC Infect Dis* 2022;22:62.
- 6 Artru F, Louvet A, Ruiz I, *et al*. Liver transplantation in the most severely ill cirrhotic patients: a multicenter study in acute-on-chronic liver failure grade 3. *J Hepatol* 2017;67:708–15.
- 7 WHO. Prevention and control of hepatitis. Available: <https://www.emro.who.int/pak/programmes/prevention-a-control-of-hepatitis.html> [Accessed 12 Nov 2022].
- 8 Saeedi M I, Mahmood K A, Ziauddin M I. Frequency and clinical course of hepatitis E in tertiary care hospitals. *Journal of the College of physicians and Surgeons—Pakistan. JCPSP* 2004;14:527–9.
- 9 Butt AS. Epidemiology of viral hepatitis and liver diseases in Pakistan. *Euroasian J Hepatogastroenterol* 2015;5:43–8.
- 10 Nadeem M, Ahmad T, Kakar SJ, *et al*. Hepatitis E virus genotyping in Pakistan: a regional study to explore the implications for pregnant females. *Future Virol* 2021;16:611–7.
- 11 Hamid SS, Atiq M, Shehzad F, *et al*. Hepatitis E virus superinfection in patients with chronic liver disease. *Hepatology* 2002;36:474–8.
- 12 Khan AR, Waqar S, Rafiq Z, *et al*. Frequency of acute viral hepatitis A, B, C, and E in pregnant women presenting to Hayatabad medical complex, Peshawar, Pakistan. *Cureus* 2022;14:e24208.
- 13 Hindawi Biomed research International volume 2018. Article ID 5769201, 9 pages.
- 14 Ullah K, Dogar AW, Rehman IU, *et al*. Expanding the living liver donor pool in countries having limited deceased donor activity: Pakistani perspective. *Transpl Immunol* 2022;75:101683.