

Hepatitis E Virus Infection: A Neglected Problem in Our Region

Seyed-Moayed Alavian

Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL),
Baqiyatallah University of Medical Sciences & Tehran Hepatitis Center, Tehran, Iran
editor@hepmon.ir

Hepatitis E is one of the most important infectious problems in developing countries as other oral-fecal transmitted infections^(1, 2). Hepatitis E virus (HEV) infection is enterically transmitted and widely spread in many tropical and subtropical countries. Hepatitis E is an important public health concern in many developing countries of Asia and Africa where environmental sanitation facilities are poor⁽³⁾. Large outbreaks of hepatitis E were observed in, India, Pakistan, Nepal, Myanmar, China⁽⁴⁾, in East Africa which affecting the Ethiopian refugees in Somalia and Sudan⁽⁵⁾, and Central Asia⁽⁶⁾. Usually hepatitis E occurs in localities with a high population density, lowlands, and valley areas. The incidence and prevalence rate of HEV infection is underestimated due to unavailability of laboratory services in endemic territories. It is believed that in India at least one-half of acute sporadic viral hepatitis cases in adults are etiologically associated with HEV⁽⁷⁾.

In endemic areas general sanitation is poor, so HEV spreads through contaminated water sources frequently and non-human HEV reservoirs are very probable. Under natural conditions, fecally contaminated drinking water seems to be the principle vehicle of HEV transmission. Almost all large outbreaks or epidemics of hepatitis E were caused by the consumption of contaminated water. In particular, epidemic situations often arise during the rainy seasons or floods when sewage waters gain access to open water reservoirs⁽⁸⁾. Food-borne outbreaks occur less frequently and usually involve fewer people. Contact or person-to-person transmission is known to exist, particularly during or after big epidemics, but occurs at a lower rate

when compared with other enteric viral infections (e.g. hepatitis A)⁽⁹⁾. In non-endemic areas and in industrialized countries, travelers to endemic regions are at major risk of HEV infection (imported cases), but sporadic cases of acute hepatitis E without an implicated travel history have also been reported in Europe and the United States^(10, 11).

There are some reports regarding HEV infection in our region. Iran is located between Iraq and Turkey in the west and Afghanistan and Pakistan in east. On two sides of our border, we have war-like situation. Due to damage of water supply infrastructure and its contamination with sewage, the reported cases in general population and military personnel are a serious health problem. In 2004, there were some reports of HEV infection outbreaks in hundreds of Iraqi people in Sadr, Mahmodiya. The health condition in Iraq is catastrophic regarding low security and problems in social and water safety. WHO had reported thousands of cholera infected cases in September 2007 in Iraq which reveals the low access of people to safe water in Iraq. The infrastructure of water supply has totally damaged as a result of war.

Transmission of HEV occurs primarily by the fecal-oral route through contaminated water supplies in developing countries. Now, less than 40% of Afghans have access to safe drinking water. Soldiers from western countries are at risk of acquiring HEV infection in the region. Epidemic hepatitis E has been reported in military personnel in Pakistan and in this epidemic, 95% of patients with acute hepatitis had serologic evidence of acute hepatitis E whose source was fecal contamination of a water system, but the prevalence of anti-HEV in

this population before the outbreak was estimated to be 30%. On the other hand, military persons may drink unhealthy water in remote areas, therefore they had risk for hepatitis E infection⁽¹²⁾.

Iran is a developing country in Asia, which is expected to have a high probability of hepatitis E occurrence. In Iran, some outbreaks had been reported previously⁽¹³⁾. The first report of epidemic of HEV infection was reported by Hatami in 1991 from Kermanshah that had some mortality in pregnant. At the same time, there was another report from Fereidoon-Shahr, Isfahan with more than 100 cases. In 1992, about 154 cases were reported from Lordegan (Southwest of Iran) with a mortality of two pregnant cases⁽¹⁴⁾. In a study in blood donors, 7.8% were anti-HEV antibody positive⁽¹⁵⁾. The prevalence of more than 5% correlates with the prevalence of endemic areas. The obtained value is higher than that obtained in Israel (Jews: 2.8% and Arab: 1.8%)⁽¹⁶⁾ and Ankara, Turkey (3.8%)⁽¹⁷⁾, but less than values of Iraqi-Kurdish refugees (16.4%)⁽¹⁸⁾ and general population in Pakistan (17.5%)⁽¹⁹⁾.

Iran was accounted as endemic country for hepatitis E and its seroprevalence increased significantly with age, from 3.3% in subjects less than 30 years of age to 37.5% in individuals of 50 years^(20, 21). In Iranian soldiers, the prevalence was 1.1% which was much lower than other evidence. What are the reasons? I believe that improvement in sanitation and water supply has decreased the prevalence of HAV and HEV infections in young people in Iran⁽²²⁾. A report from general population in Mazendaran (North of Iran) showed that 1.1% of children younger than 10 years old and 7.2% of population between 20 and 25 years old had anti-HEV IgG antibody. The prevalence was more common in rural areas, more dense families, and low educational level⁽²³⁾. In another study in blood donors from Tabriz (Northwest of Iran), in blood donors the prevalence of anti-HEV IgG was 7.8% (from 3.3% in subjects under 30 years of age to 13.7% in individuals of 50 years and higher)⁽²⁰⁾, which is generally higher than figures reported from developed countries (0.4-3.9%)^(24, 25); although lower than those from other countries of the Eastern Mediterranean region where reports of anti-HEV have been observed⁽²⁶⁾. In hemodialysis patients from Tabriz, 7.4% had anti-HEV IgG antibody⁽²¹⁾. The prevalence of anti-HCV IgG antibody in cirrhotic cases was 6% and in healthy controls was 5%⁽²⁷⁾. Another study from East Azerbaijan showed that 27.5% of patients with chronic liver disease and 19.7% of controls had anti-HEV IgG antibody that showed different epidemiology of

infection in the country⁽²⁸⁾.

Iran is a country with few suspected outbreaks of HEV [13]. A population-based study indicated that the prevalence rate of anti-HEV IgG among healthy population was 9.6%⁽²⁹⁾. In Iran, large cities have better public health services, such as clinics, municipal water and sewage systems, possibly explaining the reduced risk of infection.

I should emphasize here that HEV infection should be considered in any cases with viral hepatitis without evidence of HAV and HBV infections in our region. Traveling to Iraq, Pakistan, and Afghanistan will be important in approach to cases with clinical symptoms of acute viral hepatitis. Precautionary recommendation should be given to travelers to these countries. UN agencies should help these countries by funding and donating materials for health education campaign and provide water and sanitation measures.

References

1. Arankalle VA, Chadha MS, Tsarev SA. Seroepidemiology of water-born hepatitis in India and evidence for a third enterically-transmitted hepatitis agent. *Proc Natl Acad Sci U S A* 1994; **91**: 3428-32.
2. Chow WC, Lee AS, Lim GK. Acute viral hepatitis E: Clinical and serological studies in Singapore. *J Clin Gastroenterol* 1997; **24**: 235-38.
3. Smith JL. A review of hepatitis E virus. *J Food Prot* 2001; **64**: 572-86.
4. Zuang H. Hepatitis E and strategies for its control. In: Wemn YM, Xu ZY, Melnick JL, eds. *Viral Hepatitis in China: Problems and Control Strategies*. Basel: Karger, 1992.
5. Centers for Disease Control, Enterically transmitted non-A, non-B hepatitis: East Africa. *MMWR* 1987; **36**: 241-4.
6. Beliakov VD, Ovezov AO, Khozhimirzaev AKh, Rozina VF, Khozhimirzaeva DZ, Gasanov ELu, et al. Retrospective epidemiological diagnosis of viral hepatitis non-A, non-B with fecal-oral transmission. *Zh Mikrobiol Epidemiol Immunobiol* 1990; **3**: 44-8.
7. Khuroo MS, Rustgi VK, Dawson GJ, Mushahwar IK, Yattoo GN, Kamili S, et al. Spectrum of hepatitis E virus infection in India. *J Med Virol* 1994; **43**: 281-6.
8. Sreenivasan MA, Sehgal A, Prasad SR, Dhorje S. A seroepidemiological study of a water-born epidemic of viral hepatitis in Kolhapur City, India. *J Hyg Camb* 1984; **93**: 113-22.
9. Khuroo MS, Dar MY. Hepatitis E: evidence for person-to-person transmission and inability of low dose immune serum globulin from and Indian source to prevent it. *Indian J Gastroenterol* 1992; **11**: 113-6.
10. Dawson GJ, Mushahwar IK, Chau KH, Gitnick GL. Detection of long-lasting antibody to hepatitis E virus in a US traveller to Pakistan. *Lancet* 1992; **340**: 426-7.
11. Heath TC, Burrow JN, Currie BJ, Bowden FJ, Fisher DA, Demediuk BH, et al. Locally acquired hepatitis E in the Northern Territory of Australia. *Med J Aust* 1995; **162**: 318-9.
12. Bryan JP, Iqbal M, Tsarev SA, Malik IA, Duncan JF,

- Ahmed A, *et al.* Epidemic of hepatitis E in a military unit in Abbotabad, Pakistan. *Am J Trop Med Hyg* 2002; **67**: 662-8.
13. Ariyegan M, Amini S. Hepatitis E epidemic in Iran. *J Med Council I R Iran* 1998; **15**: 139-43.
14. Hatami H. Epidemic report of hepatitis E in Kermanshah. *Nabz Journal* 1991; **9**: 23-31.
15. Aminiafshar S, Alimagham M, Gachkar L, Yousefi F, Attarchi Z. Anti-hepatitis E virus seropositivity in a group of blood donors. *Iranian J Publ Health* 2004; **33**: 53-6.
16. Karetnyi YV, Favorov M, Khudyakova NS. Serological evidence for hepatitis E virus infection in Israel. *J Med Virol* 1995; **45**: 316-20.
17. Cesur S, Akin K, Dogaroglu I, Birengel S, Balik I. Hepatitis A and hepatitis E seroprevalence in adults in the Ankara area. *Mikrobiyol Bul* 2002; **36**: 79-83.
18. Abdelaal M, Zawawi TH, Al Sobhi E, Jeje O, Gilpin C, Kinsara A, *et al.* Epidemiology of hepatitis E virus in male blood donors in Jeddah, Saudi Arabia. *Ir J Med Sci* 1998; **167**: 94-6.
19. Hamid SS, Atiq M, Shehzad F, Yasmeen A, Nissa T, Salam A, *et al.* Hepatitis E virus superinfection in patients with chronic liver disease. *Hepatology* 2002; **36**: 474-8.
20. Taremi M, Gachkar L, MahmoudArabi S, Kheradpezhoh M, Khoshbaten M. Prevalence of antibodies to hepatitis E virus among male blood donors in Tabriz, Islamic Republic of Iran. *East Mediterr Health J* 2007; **13**: 98-102.
21. Taremi M, Khoshbaten M, Gachkar L, EhsaniArdakani M, Zali M. Hepatitis E virus infection in hemodialysis patients: a seroepidemiological survey in Iran. *BMC Infect Dis* 2005; **5**: 36.
22. Ghorbani GA, Alavian SM, Esfahani AA, Assari S. Seroepidemiology of hepatitis E virus in Iranian soldiers. *Hep Mon* 2007; **7**: 121-4.
23. Safar MJ, Khalilian A, Farhadi R, Babamohmoodi F. Seroepidemiology of HEV infection in 2-25 years of saravi in 2004. *J Mazandaran Univ Med Sci* 2005; **75**: 82-5.
24. Mast EE, Kuramoto IK, Favorov MO, Schoening VR, Burkholder BT, Shapiro CN, *et al.* Prevalence of and risk factors for antibody to hepatitis E virus seroreactivity among blood donors in Northern California. *J Infect Dis* 1997; **176**: 34-40.
25. Mateos ML, Camarero C, Lesa E, Teruel JL, Mir N, Baquero F. Hepatitis E virus: relevance in blood donors and risk groups. *Vox Sang* 1999; **76**: 78-80.
26. Ritter DA. Seroprevalence study of hepatitis E in Europe and the Middle East. *Viral Hepat Liver Dis* 1994; **12**: 432-4.
27. Shavakhi A, Esteghamat F, Sharifian A, Mohamad Alizade AH, Khodadostan M, Somi MH, *et al.* Evaluation of hepatitis E in cirrhotic patients, a case control study. *Govaresh* 2007; **12**: 27-9.
28. Somi MH, Farhang S, Majidi G, Shavakhi A, Pouri AA. Seroprevalence of hepatitis E in patients with chronic liver disease from East Azerbaijan, Iran. *Hep Mon* 2007; **7**: 125-8.
29. Zali MR, Taremi M, Arabi SMM, Ardalan A, Alizadeh AHM, Ansari SH. Seroprevalence of hepatitis E in Nahavand, Iran: A population-based study. In Proceeding of the Digestive Diseases Week, 15-19 May 2004; New Orleans, USA.