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Hepatitis E outbreak in Nepal during 2014

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Abstract

Hepatitis E Virus (HEV) is prevalent in developing country like Nepal. There were many sporadic cases as well outbreak reported from Nepal. The first outbreak of hepatitis E reported in 1973 at Kathmandu, which affected more than 10,000 people, mostly young adults of the age group 25±8. The disease was associated with high incidence of acute hepatic failure and high mortality among pregnant women. There was a massive outbreak of HEV during 2014 infecting more than 6,000 individual with 11 deaths by hepatitis E in Biratnagar municipality in Morang district of Nepal. The outbreak occurs for two months from April-May 2014. The first case of HEV documented in first week of April, 2014 and reached to pick level in last week of April. For this study, serum sample was collected from 526 patients and were subjected for the detection of immunoglobulin M (IgM) classes of antibodies against HEV by indirect (sandwich) enzyme immunoassay. Among the 526 samples, IgM anti-HEV-positive percentage from different age groups were 43.84% for ≥25-≤50, 39.71% for >50 and 32.62% for <25 years of age. Our result shows HEV infection is mostly prevalence among the intermediate age group of population. Only two pregnant women out of 526 were infected with HEV. There was no reported death among the pregnant women during 2014 outbreak.

Keywords Hepatitis E; Hepatitis E in pregnancy; Epidemic; Nepal

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Introduction

Hepatitis E virus (HEV) is responsible for several outbreaks of waterborne hepatitis in tropical and subtropical countries and for sporadic cases of viral hepatitis in endemic and industrialized countries (3, 4). The virus is transmitted by faeco-oral route, most often through contaminated drinking water. The mortality rate among hepatitis E patients is usually 1-3 %, but it can reach up to 20% in infected pregnant women, especially during the third trimester (16). Hepatitis E Virus belongs to family *Hepeviridae and genus Hepevirus* which infect deer, boars, rabbits, mongooses, swine and humans (2). HEV is a non-enveloped virus having single-stranded, positive-sense RNA and capped at the 5' end and polyadenylated at the 3' end. The genome of HEV is approximately of 7.2 kbp with three open reading frames (ORFs: ORF1, ORF2 and ORF3) (2, 15). There are 4 genotypes of HEV have been reported till date and all the four genotypes belong to one serotype. The HEV genotypes which are transmitted human to human and cause for sporadic and epidemic are fall into group 1 and 2 (4,8) and HEV which are transmitted to human animal belongs to genotype 3 and 4 (8). The pattern of outbreaks is mostly seen in developing and underdeveloped countries of Asia and Africa whereas the sporadic cases observed worldwide (3, 9). Alternatively, the developed countries of Europe have been found to harbor autochthonous HEV (4).

Nepal is an endemic zone for Hepatitis E virus that causes epidemic and sporadic infections (5). The 2014 epidemic of hepatitis was with similar nature that occurred in the valley in 1981, 1985 (10). To the best of our knowledge, this is the first documented outbreak of hepatitis with HEV in Biratnagar city, Nepal, indicating that the city is an endemic zone for HEV infection with 11 deaths during 2014 outbreak. The purpose of this study is to figure out the number of case during 2014 outbreak in Biratnagar, Nepal.

Materials and Method

Patient and study design

The suspected Hepatitis E patients who visited to the three hospitals namely: Seti zone hospital, Biratnagar, Morang; Nobel medical college and teaching hospital, Biratnagar, Morang; and Biratnagar Hospital, Biratnagar, Morang; were enrolled in the study.

Collection of blood samples and serological assay

Blood samples (n=526) were collected from patients who visited to the respective hospital. The serum were separated and stored at 4°C for less than 24 hours at respective hospital and then transported to National Ayurveda Research and Training Center, Kirtipur, Kathmandu, Nepal by maintaining cold chain. The IgM antibody against HEV was detected by ELISA and remaining sample was stored at -40°C for molecular study.

Detection of Antibodies against HEV

The protocols used for detection of anti-HEV IgG and IgM were determined by an indirect (sandwich) enzyme immunoassay developed by Meng et al. with slight modification [6, 7]. Briefly, polystyrene plates were coated with antigens and stored at 4˚C until use. Test sera, with a 1:20 dilution, were added into the wells and incubated at 37˚C for 45 minutes. After washing, horseradish peroxidase-labeled goat-anti-human IgG or IgM was added to each well and then incubated at 37˚C for 45 minutes. The plates were washed five times with wash buffer after this incubation. After washing, TMB was added and incubated for 15 min. The reaction was stopped by adding H2SO4. The absorbance was read at 450 nm. The cutoff values for the assay of anti-HEV IgM was set at 0.386.

Statistical Methods

Chi-Square tests were used to compare the anti-HEV positive proportions between different age groups. Statistical analysis was carried out by using SPSS version 15.0 for Windows.

Result

Geographical distribution and seasonality

Hepatitis E virus is an emerging disease in Nepal. Though, the first documented outbreak of hepatitis E of Nepal that is in Kathmandu in in1973 .Subsequent outbreak occurs in 1981 and 1987. To our knowledge this is one of the major outbreak infecting more than 6000 people in the same city. Till second week of April, there were 1621 suspected individual visited to different hospital in the Biratnagar city, Says national daily Kantipur on 26 April 2014. According to Kantipur daily more than 200 suspected individual used to visit Seti zone Hospital, Novel Medical College and Biratnagar hospital.

This epidemic was spread over a 2 month period from April to May and reached a sharp peak during last week of April. At the peak of the epidemic, very low number of pregnant women was hospitalized with acute hepatitis, indicating surprisingly low prevalence of HEV infection among pregnant women during this outbreak.

Clinical symptoms study

During our visit at Biratnagar, the major symptoms we have seen were jaundice, anorexia, hepatomegaly, abdominal pain and tenderness, nausea and vomiting, fever during 2014 outbreak.

Serological prevalence

A total of 526 serum samples collected and investigated using ELISA for HEV; and 35.78% were found to be positive to HEV. The number of cases was found to be varied on the basis of collection pattern among Nobel Medical College and Teaching Hospital, Seti Zonal Hospital and Biratnagar Hospital. There was no significant difference between the age group, [< 25 (p= 0.30), ≥25-≤50 (p= 0.15),] and the gender (Figure 1) between the two seropositive and seronegative groups. But, there was significant correlation between gender and serostatus in the age group >50 (p= 0.90); (Figure 1).

Discussion:

Over the years, the Terai belt of Nepal, located on the south of the outer foot hills of Himalayan ranges, have become Hepatitis E virus established regions in Nepal. The 2014 outbreak that we studied was also predominantly confined to this region, affecting the districts of Morang. The maximum number of positive HEV cases detected was in Biratnagar City, the gateway to India. Apart from the plains, the 2014 outbreak also affected the highlands such as Kathmandu. One of the major factor enhancing the establishment and spread of Hepatitis E in Nepal is poor sanitation. The majority of the infected patients in the 2014 disease outbreak belonged to the age group of 25-50 years with a higher number of female patients. The disease broke out for two months in the town. The cause of the disease is drinking polluted water and stale food. Hepatitis E was found in 400-500 people who visited the hospital and various nursing homes for undergoing tests in the last two months. The epidemiology study from 1999-2000 shows that the prevalence of anti-HEV IgG is 38% and according to age group it varies as 16% in 1-9 year which then rises to 42% for 40-49 years then decreases(11). As in correlation with the above finding, we provided that, the seroprevalence is high up to 39.71% for the age group of ≥25-≤50 years compared to 32.62% for <25 years but there was peculiar cases regarding the seroprevalence of >50 years old subjects which was 43.84%. This may provide the case description that most elderly people are more susceptible to the virus thus acknowledging the degradative immune status of the subject due to increasing age factor. Due to HEV infection during 1982 to 1986, 86% of the sporadic hepatitis as 88% in adults and 58% children was seen (10). Relatively high prevalence of HEV for the age group ≥25-≤50 in this study as compared to subjects <25 years, is in correlation with the reporting done by Shrestha SM *et al* (10,14) but the new finding for elderly age group of >50 years old with high seropositive cases is reported first in Nepal through this study. Molecular assay of HEV in 1994 confirmed for the presence of 88% for acute hepatitis in Kathmandu valley (5). In another study, among of 144 sporadic cases, 50% were positive for IgM antibodies to HEV (anti- HEV IgM) and among 86 patients, 9 HEV-viremic patients without anti- HEV IgM along with 56% of subjects were diagnosed with hepatitis E (11). In Nepal, the most common HEV genotype to be observed was 1a, but during 1996 to 1998, genotype 1c was seen (12). According to local population the drinking water distributed by Nepal Water Supply Corporation was proved to be unsafe and one of the causes behind this is pollution at the water source, the administration failed to take action against the guilty. Another problem is that leaky drinking-water pipes runs close to sewer systems which leads to mixing of fecal material. Sewer contamination of the drinking water is very high especially during rainy season and this is one of the major causes for the outbreak of HEV case in Nepal.

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Annex

Figure 1: Seroprevalence of HEV in different age group