CLINICAL PRESENTATION IN AN OUTBREAK OF HEPATITIS E

WAQAR AZIM, WAJIHA FAROOQ, M. Q. ALAM KHAN, SAAD AZIM, AND NASIRA SHAHEEN

Department of Pathology, Army Medical College, National University of Sciences and Technology, Islamabad
Department of Medicine, Armed Forces Post Graduate Medical Institute, Rawalpindi

Introduction: In many cases of acute hepatitis, hepatitis E virus (HEV) is a common cause. Hepatitis E is a self limiting disease which shares many epidemiological, clinical and morphological similarities with hepatitis A. Both are enterically transmitted. Materials and Methods: The purpose of this study was to evaluate the clinical presentation of hepatitis E during an epidemic and correlate the clinical features with liver function tests (LFTs). It is a cross sectional retrospective study. The study was conducted at Army Medical College (National University of Sciences and Technology) and Military Hospitals Rawalpindi from July to December 2009. One hundred patients admitted to the hospital with clinical features of acute hepatitis including anorexia, nausea, vomiting, pain epigastrium, jaundice, raised serum total bilirubin (TBil) and serum aminotransferase (ALT) were included in the study. Hepatitis E in these patients was confirmed by detecting the presence of anti HEV IgM. The patients were monitored during their stay in the hospital and changes in their clinical condition were correlated with liver function tests (LFTs). Results: The most prominent symptoms in all patients were fatigue, nausea, anorexia, jaundice and dark urine, followed by pain epigastrium (50%), low grade fever (48%) and hiccups (2-3%). Jaundice developed when mean total bilirubin was 127µmol/L, mean ALT was 1527 U/L and mean ALP 127 U/L. Serum bilirubin correlates with the development of jaundice. Conclusion: Hepatitis E presents with varying clinical features. The presentation is acute with marked anorexia, nausea and fatigue coupled with sharp rise in LFTs. Any adult presenting with acute onset of these symptoms should be investigated for LFTs and anti HEV IgM.

Key Words: Hepatitis E, clinical features, total bilirubin, alanine aminotransferase, epidemic.

INTRODUCTION

In many cases of acute hepatitis, hepatitis E virus (HEV) is a common cause. Hepatitis E is a self limiting disease which shares many epidemiological, clinical and morphological similarities with hepatitis A. Both are enterically transmitted. Evidence for the existence of HEV was first provided in 1980. Mode of transmission of HEV is orofecal. The virus is shed in feces hence contamination of drinking water has given rise to epidemics in countries where conditions of inappropriate human waste disposal still prevail. Recently it has been highlighted that zoonotic transmission of the virus also occurs. HEV can be held responsible for more than 50% cases of acute viral hepatitis in the developing countries which are endemic to HEV. Out of these only 1-3% progress to hepatic failure, however the disease is more severe in pregnant females in whom the fatality rate may be up to 20%. HEV mostly affects young adults in the age group of 15 to 40 years. The incubation period is 3-9 weeks. The symptoms and signs include fatigue, anorexia, nausea, vomiting, pyrexia, jaundice, hiccups and hepatomegaly. The clinical course varies from mild anicteric attack to icteric and more severe attacks depending on a person's general health condition and previous immune status. The features of hepatic encephalopathy include neuropsychological features such as irritability, impaired coordination and disturbed sleep, which in severe cases may progress to somnolence and eventually coma. In intermediate stages there is characteristic jerking movements of limbs called flapping tremors.

HEV is endemic in Pakistan and many epidemics of HEV have been reported from here. In this particular epidemic which occurred last year in Rawalpindi, a huge population was affected. Patients of HEV constituted approximately 90% of total hospital admissions in the affected area's population during that period, and were the major cause of work loss and drain of hospital resources. Patients were admitted for several days and after discharge they were advised bed rest for a couple of weeks. From this it can be emphasized how big a burden hepatitis E can be in the form of epidemics. There were 2 mortalities in the same epidemic.

This study was aimed to evaluate the clinical features of hepatitis E during the epidemic that would be beneficial for not only the medical community but general public as well.
PATIENTS AND METHODS
It is a cross sectional retrospective study. A total of 100 patients were included in it. Among them 75 were males and 25 were females. Age range of the patients was 15-56 years. Patients presenting with anorexia, nausea, vomiting, abdominal pain, jaundice and testing positive for anti HEV IgM with raised serum ALT and TBil were included in the study.

Patients with hepatitis B, C and chronic liver disease were excluded from the study. Detailed history was obtained regarding the time of onset of illness, detailed account of symptoms along with their duration and severity were noted. Complete examination and LFTs were performed. Serum ALT, serum bilirubin and serum ALP were performed on automated clinical chemistry analyser Selectra E using Pioneer kit, USA. HEV diagnosis was confirmed by detecting Anti HEV IgM by enzyme linked immunosorbent assay (ELISA).

Patients were monitored during their stay in the hospital; improvement in their symptoms and signs was observed and correlated with changes in biochemical markers of liver function (serum ALT, serum TBil, serum ALP). The data was analysed using SP-SS version 17.

RESULTS
The age range of the patients was 15 to 56 years. Seventy five percent of the patients were males. They complained of non specific symptoms like malaise, fatigue, nausea and anorexia for 5-10 days before jaundice developed. The symptoms and signs of the patients are shown in figure 1.

Fig. 1: Frequency of symptoms and signs of 100 patients.

Mean serum bilirubin at admission was 127 µmol/L, mean serum ALT 1527 U/L while mean serum ALP was 275 U/L. Mean bilirubin at the time of discharge was 41.6 µmol/L and mean ALT was 212 U/L. Serum ALP was within reference range at the time of discharge. We have also worked out how the clinical features correlate with biochemical findings. Degree of jaundice correlates positively with bilirubin (p value <0.01, r value = 0.639) whereas no correlation could be established between the biochemical markers and other clinical features.

The duration of admission in hospital also varied among the them. The average duration of admission was 17 days and the longest was 37 days. The patients were discharged on the basis of improvement in their clinical condition despite mildly elevated LFTs. Clinical features at the time of discharge were jaundice and fatigability on exertion, whereas other symptoms like anorexia, nausea, fever and vomiting had subsided. Patients were advised complete bed rest for 2-4 weeks.

DISCUSSION
HEV is now recognized as the major causative agent of enterically transmitted non A, non B hepatitis in tropical and sub tropical countries. Sporadic cases are also reported in industrialised countries. Hence hepatitis E is more wide spread than previously considered. There is a diffuse and extensive spread in the dependent population in the form of epidemic. HEV exposure is influenced by local environmental and living conditions. It is believed that frequent low dose exposure to HEV confers immunity to people living in unhygienic conditions. Features that are most commonly linked to HEV include; water borne outbreaks caused by fecal contamination of drinking water, low rate of person to person transmission, no chronic sequelae and complete resolution in majority of patients. HEV causes asymptomatic or mild illness in children. This is in contrast to other feco orally transmitted agents like HAV and polio. Reasons for this need to be studied.

Many HEV epidemics have been reported in Pakistan. The source of infection in all had been contamination of drinking water by human waste. Apart from these, sporadic cases also occur throughout the year. According to Bryan et al, who studied hepatitis E epidemic in Abbottabad, approximately 50% of the cases of acute viral hepatitis admitted to military hospitals can be presumed to be due to hepatitis E.

The exact pathogenesis of HEV and the host defence mechanisms against the virus are not known. After ingestion, hepatocytes are targeted by HEV and multiplication occurs within the hepatocellular cytoplasm. There is leakage of ALT from the damaged hepatocytes into the extracellular space from where it enters the circulation. Total bilirubin is elevated due to biliary stasis.
The clinical picture varies depending on the grades of severity from mild asymptomatic or anicteric attacks to more severe icteric attacks. The mildest attack is either asymptomatic or the patient may suffer from non-specific gastrointestinal symptoms including anorexia, nausea and pain abdomen. Some patients may even experience flu like illness. This condition may be marked by raised serum aminotransferase only. This picture is usually seen in children.

The icteric attack is marked by a prodromal period in which the patient suffers from non-specific systemic symptoms including lethargy, anorexia, nausea, malaise, fatigue, arthralgias, myalgias, headache, photophobia, cough and coryza. Low grade fever may also accompany both hepatitis A and E. This phase lasts for a few days to weeks. The patients may notice darkening of urine and lightening of stools a few days before the onset of clinical jaundice. Appearance of jaundice marks the icteric phase which lasts for about 1 to 4 weeks.

After this phase patients recover fully in uncomplicated cases. The LFTs however, take several weeks to return to within reference range.2,8 Hepatic encephalopathy is a serious complication that can lead to fatality.

In this study we see a similar pattern of initial prodromal period followed by icteric phase and then recovery of the clinical condition. The clinical features vary. According to Worm et al the clinical features of hepatitis E are non specific. Jaundice, malaise and anorexia are reported by 100% patients.1 These findings are consistent with the present study. According to a study by Bashir et al, 80% patients complained of pain epigastrum, malaise and anorexia while 60% complained of arthralgias.7 In another study 56% patients complained of abdominal pain, 16% complained of pruritis, 17% constipation, and 12% diarrhoea.8 In our cases none of the patients complained of arthralgias, pruritis, constipation or diarrhoea. On the other hand nausea and vomiting a prominent feature in our cases was seen in 76% patients in a study by Saeedi et al.9 The same study reported 33% patients with pruritis and 66% arthralgias which were not reported by our patients.

Due to variable immunity, resistance and continuous mutations, clinical behaviour keeps changing from time to time and from region to region. Current study highlights the clinical and biochemical pattern that prevailed in the study region at a particular time which has similarities as well as differences from other studies. There is no definitive treatment for hepatitis E. Patients are managed symptomatically only. In case of hepatic failure patients are managed in intensive care unit, it is important that the airway should be maintained, monitoring for vital signs and for biochemical profile is important.

It is concluded that Hepatitis E can present with varying clinical picture. Symptoms of nausea, anorexia and fatigue are important pointers to HEV in an epidemic setting. However there is no set of symptoms that can be attributed specifically to hepatitis E. Any adult presenting with acute onset of lethargy, fatigue, anorexia should be suspected of hepatitis E and work up should be done to confirm otherwise the diagnosis of hepatitis E. The epidemic can be accompanied with peaks in clinical features such as encephalopathy and mortality therefore early diagnosis and optimal treatment should be instituted for prompt recovery.

ACKNOWLEDGEMENTS
We are thankful to the administration of NUST, Army Medical College and AFPGMI, Rawalpindi.

REFERENCES
