AN OUT BREAK OF MORE THAN 1300 CASES OF ACUTE VIRAL HEPATITIS IN A TERTIARY CARE HOSPITAL IN RAWALPINDI IN SUMMER OF 2009

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ABSTRACT

Objective: To find out the short-term clinical course including common clinical features, laboratory parameters, treatment provided and outcome of cases of acute viral hepatitis hospitalized in a tertiary care hospital.

Study Design: Descriptive observational study.

Place and Duration of Study: Military Hospital in Rawalpindi from May to July 2009.

Patients and Methods: Patients hospitalized with acute viral hepatitis, both male and female, older than 12 years of age were included in the study. A detailed proforma including patients' particulars, clinical features; laboratory parameters, treatment provided, disposal/ outcome was designed and filled for each patient.

Results: During the study period a total 1334 patients were hospitalized, 1279 (95.87%) were male while only 55 (4.13%) were female. Majority of patients were young adults. Mean age was 26 years with a range of 12 to 85 years. Maximum serum bilirubin levels of 559 micromoles /l and serum alanine aminotransferas (ALT) levels of 7750 IU/L were observed. Maximum prothrombin time (PT) ranged from 105 seconds to failed to clot, against a control of 13 seconds. Thrombocytopenia was observed in some patients especially those with coagulopathy and encephalopathy but recovered with improvement in LFTs. Anti HEV serology was sent in a third of all admitted patients and was positive for IgM in patients tested. Five patients were pregnant ladies. Two patients also had laboratory proven malaria along with acute viral hepatitis. Majority of patients had uneventful recovery. A total of 13 patients went in to hepatic encephalopathy while three unfortunate patients died.

Conclusion: HEV has been an important cause of acute viral hepatitis in Pakistan, particularly in adults from lower socioeconomic groups. The problem is more serious for those living in military camps, residential institutions and in segregated areas who consume untreated water from a common source. Outbreaks like the one described have significant morbidity and not ignorable mortality for the affected persons.

Keywords: Acute viral hepatitis (AVH), Hepatitis E virus (HEV), HEV in Pakistan, Infectious hepatitis, Outbreak.

INTRODUCTION

Acute viral hepatitis is caused by many hepatotropic viruses. The so-called "infectious hepatitis" refers to cases thought to be caused by hepatitis A virus and hepatitis E virus (HEV). Hepatitis E is an important cause of acute clinical hepatitis in adults throughout Asia, the Middle East and Africa. In contrast, it is rare in industrialized countries, but antibody (Anti-HEV) is found worldwide[1]. The first major out break of infectious hepatitis due to HEV in our part of the world can be traced back to 1955; when about 29,300 clinical cases of the disease were reported from Delhi due to contamination of drinking water by the overflow of an open sewer[2]. In Pakistan, epidemics of acute viral hepatitis were reported as early as the 1950s and 1960s. An out break of acute viral hepatitis was reported from a military unit at Mardan, from August to October 1987. About 10% of the exposed personnel developed jaundice[3].

The causative agent of hepatitis E was characterized in 1988, when it was given its present name[4]. The genome of this virus, now named hepatitis E virus, was cloned in 1990 and fully sequenced shortly thereafter[5,6]. It is an RNA virus, excreted in feces and transmitted

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predominantly by the focal-oral route (usually through contaminated water). Infection occurs in epidemics during summer months and rainy seasons. It is considered a self-limiting illness having good prognosis, however, large outbreaks can have high morbidity and definite mortality associated with it.

China is one of the high epidemic areas and there have been 11 hepatitis E epidemics reported. The longest one in the world occurred in Xininang Uighur Autonomous Region, the Northwest of China, during 1986-1988, with a total number of 119280 cases and more than 700 death[7,8]. Similarly, in a study from Kathmandu-Nepal by Clayson *et al*[9] carried out in1992-93 infection and disease rates reported were as high as 99/1000 and 45/1000 person years respectively. Kathmandu Valley during last 30 years had three large epidemics and many focal outbreaks. About 50% of the sporadic cases of acute hepatitis in Kathmandu Valley are caused by hepatitis E.[10]

A large epidemic of hepatitis E occurred in one of the Army garrisons at Lahore in early 1995, when, more than 600 cases were treated as inpatients[11]. The present outbreak being reported in this paper in Rawalpindi Cantonment, a large outbreak of hepatitis E, occurred in summer 2009, when more than 1300 cases were treated as inpatients. Early on during the course of the outbreak a study was designed to find out the short-term clinical course including common clinical features, diagnostic laboratory parameters, treatment provided, complications and outcome of cases of acute viral hepatitis hospitalized in a tertiary care teaching hospital in Rawalpindi Cantonment.

PATIENTS AND METHODS

This descriptive study was carried out at a a tertiary care teaching hospital in Rawalpindi Cantonment. Convenience (non-probability) sampling was done. Patients hospitalized from May to July 2009 with acute viral hepatitis, both male and female, older than 12 years of age were included. Patients not admitted in hospital and less than 12 years of age were excluded. A detailed proforma including patients' particulars, clinical features both history and examination; laboratory parameters, treatment provided, disposal/ outcome was designed and filled for each patient. This included, patients' history of change in appetite, nausea, vomiting, weakness, fever, and pain abdomen. On examination consciousness level, vital signs, jaundice, asterexis, palpation for hepatosplenomegaly, change in liver span were documented. Laboratory investigations done included S.bilirubin, alanine aminotransferase (ALT), prothrombin time (PT); hemoglobin level; total leukocyte and platelet count, blood for malarial parasite and urine for bile salts and bile pigment, serology for hepatitis E virus in selected cases totaling a third of all admitted patients. Treatment provided and complications if any were documented. Data analysis was done using SPSS14.

RESULTS

During the study period a total 1334 patients were hospitalized, 1279 (95.88%) were male while only 55 (4.12%) were female. Majority of patients were young adults as shown in Fig I. Mean age of patients was 26 years with a range of 12 to 85 years.

Maximum patients admitted in one day were 60, and more than 400 patients remained admitted at a time with acute viral hepatitis. All this was in addition to ever increasing routine work load of our hospital, and the health care system, putting tremendous strain on the already constrained medical resources. A new acute viral hepatitis unit was established under direct supervision of first three authors and guidance of the remaining authors. The duration of hospitalization ranged from days to weeks.

There was a brief prodromal phase of anorexia, nausea, vomiting and abdominal pain, followed by jaundice in the majority. However, some patients were diagnosed in the prodromal phase on screening in early phase, as the awareness among people increased. This was achieved by programme of health education for troops and their families, in the form of lectures, pamphlets delivered at places of duty. Main presentation was with anorexia, dark coloration of urine and eyes, nausea and

vomiting. Examination revealed jaundice in most, followed by hepatomegaly and splenomegaly in minority. Laboratory investigations revealed deranged liver function tests. Serum bilirubin was raised to variable level as shown in Fig 2.

Maximum serum bilirubin levels of 559 micromoles / l and serum alanine aminotransferas (ALT) levels of 7750 IU/L were observed among two patients who went in to hepatic encephalopathy , remained in intensive care unit one needing ventilatory support but had a favorable ultimate outcome. Prothrombin time in patients is shown in Fig 2. Maximum prothrombin time ranged from 105 seconds to failed to clot against a control of 13 seconds.

Thrombocytopenia was observed in some patients especially those with coagulopathy and encephalopathy but recovered with improvement in LFTs. Test for the Hepatitis E Virus antibody (Ig M) was sent in a third of all admitted patients and was positive. Five patients were pregnant ladies. Two patients also had concomitant laboratory proven malaria.

Majority of patients were managed symptomatically and had uneventful recovery. However, those complicated by encephalopathy were shifted to ICU and HNC units and were managed jointly by gastroenterologists and intensivists. Some of them were given parenteral antibiotics, I/V mannitol, proton pump inhibitors, laxatives, fresh frozen plasma, vitamin K, nutritional and ventilatory support.

A total of 13 patients went in to hepatic encephalopathy, making 0.97%. Eleven of them were males (85%) while two were pregnant females (15%).Their ages ranged from 21 to 45 years with a mean of 28 years and 5 months. Their duration of hospitalization varied from 11 to 34 days with a mean of 20 days. Main symptoms at presentation were jaundice and fever in 69% each and vomiting among 38%. Biochemically they had serum bilirubin ranging from 74 to 559µ micro moles/L with a mean of 234µ micro moles/L. Similarly maximum serum ALT observed was between 1027 and 7750 U/L with a mean of 2699 U/L. One patient with hepatic encephalopathy also had Falciparum Malaria along with thalassemic trait and made uneventful recovery.

Three patients out of 1334 during study period ended fatally. Important clinical and biochemical parameters of these unfortunate patients are given in Table I.

LFTs were repeated at variable interval and mostly settled as expected but few patients had prolonged cholestasis with out any extrahepatic obstruction, one of them underwent ERCP as well. Patients and public awareness for preventive measures was increased by patients and attendants education during hospital stay and at discharge and distribution of public awareness pamphlets and delivery of lectures by doctors. A high level team including one of author was entrusted to find out the cause and suggest remedial measures. Most of the patients had been using drinking water coming from common source-

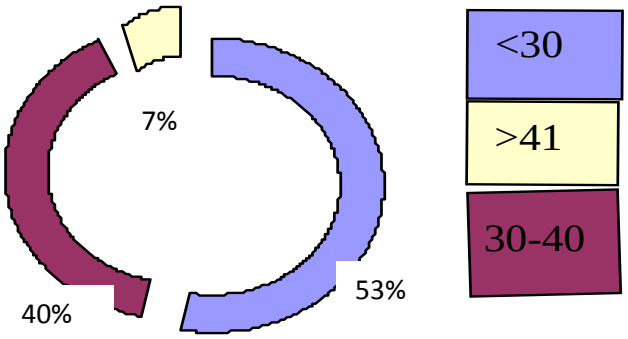

Fig.1: Age wise distribution of patients with acute viral hepatitis (n=1334)

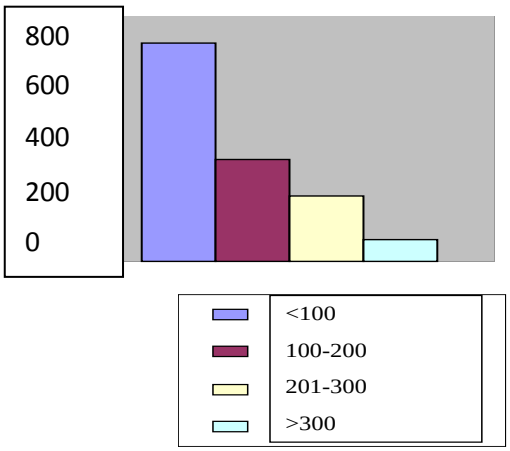

Fig.2: Number of patients, with different levels of elevation in Serum Bilirubin

Table I: Important clinical and biochemical features of patients with Hepatic Encephalopathy ending fatally

No	Age	Duration of hospitalization Days	Admission to Encephalopathy interval Days	Symptoms Fever (F) Jaundice (J) Vomiting (V)	Max S Bil µ moles / l	Max ALT U/L	Max PT Sec	Remarks
1	25	9	7	F, J, V	129	3295	20	Hepatorenal syndrome
2	25	12	3	F, J, V	355	1097	17	
3	36	7	4	F, V	329	3366	Failed to clot	Hepatorenal syndrome

Rawal Dam to filtration plants, contaminating at a pumping station which had been contaminated. Areas of Rawalpindi supplied from Khan pur Dam had been spared.

DISCUSSION

In Pakistan cases of acute viral hepatitis had been reported in the form of small outbreaks and epidemics from the various cities at different times. In 1987, 123 clinical cases of acute viral hepatitis were reported from a college campus at Sargodha[12]. All patients were hospitalized and had prolonged convalescence period. All of them were serologically negative for HAV and HBV, and ten out of 85 patients showed the presence of HEV particles. The affected students shared common water source. The epidemic ended on hygienic water supply.

In Islamabad, the capital of Pakistan with ample supply of potable water and good drainage system, a massive outbreak of acute viral hepatitis due to HEV was reported between December 1993 and March 1994 and created a lot of concern in the general population. A total of 3827 cases were recorded from sectors G/9,G/10 and H/11 areas mainly along Leh Nullah[11-13]. Faecal pollution and improper chlorination of drinking water was the cause of outbreak. Adjacent sectors with independent water supply were not affected. The disease affected the people mostly in their second and third decades of life mainly. The epidemic subsided after rectification of suspected water supply. These features of affecting part of city with common drinking water and sparing of adjacent parts with different water supply were also observed in our study. Similarly in both epidemics people in their second and third decade of life were mainly affected.

Acute viral hepatitis especially due to HEV has been a threat to Pakistan Army functioning, with sporadic outbreaks in different garrisons. One of the oldest outbreak was reported from Mardan in 1987, from a polluted water supply[3]. Another outbreak occurred in Lahore Garrison in December 1994 with 283 cases admitted to the army hospital at one time and a total of 600 cases were treated as inpatients[11]. On investigation, the pipes of the water supply, rusted with holes, were found to be practically submerged in the open drains. As a short-term measure, the troops were provided with boiled water until the total replacement of the existing water supply system could be undertaken along with the modification of the drainage system in the cantonments. Food and water discipline was enforced, and the epidemic was finally controlled. However, after three months hundreds of fresh cases of AVH were reported. The probable reason for this increase was a relaxation in water and food discipline, which occurred due to the influx of fresh troops from other stations, who were not accustomed to the strict water and food discipline enforced previously in the Lahore cantonment. The problem was gradually brought under control, and the outcome of efforts to supply pure water to troops was soon obvious.The same strategy adopted early on and rigorously implemented helped in overcoming the present crises, reported in our study. There was no significant increase in cases of acute viral hepatitis during six months of follow up of our study.

In another similar study reported in 2004, from Peshawar, acute viral hepatitis was responsible for 14% of hospitalizations for acute hepatitis. A total of 21 patients were admitted, 17 out of them (80.95%) were below the age of 40 years and there were increased number of cases during the late summer. Majority of patients had uneventful recovery, two patients had fulminant hepatitis and one pregnant female died of her illness despite intensive treatment[14].

In our study females were less than 5% and only 5 of them were pregnant and two of them went in to hepatic encephalopathy but fortunately recovered. HEV has a fatality rates reported as high as 25% in pregnant women[15]. In a recent large retrospective study conducted over a 20 years span, it was shown that HEV related acute liver failure was independent of the gender or the pregnancy status of the patients[16,17].

However no effective treatment currently exists for hepatitis E and the only cure is prevention. So far there are no commercial vaccines for Hepatitis E available. A cell culture system for the propagation of the virus has been described, and a very successful phase 2 vaccine trial has been completed[18]. The vaccine had been tested for safety and efficacy among US Army volunteers at Walter Reed Army Medical Hospital and Nepalese Army volunteers in the Kathmandu valley of Nepal respectively[19].

From these studies referred and our study it had been apparent that acute hepatitis E virus had been gradually becoming a threat to Pakistan army personnel because of the pressure of increasing population on the existing sewerage system and the rusting of pipelines of old water supply systems. These epidemics could have been avoided if proper measures had been followed in true spirit. Investigations of possible sources of spread have always led to the same conclusion: that someone's faeces find their way to someone's mouth. The seed (virus) is present, the soil is fertile and the environment is conducive to epidemics of hepatitis E in much of the developing world.

The number of cases included in this study could be the tip of iceberg, as majority of cases remained subclinical[20]. Further more, as expected, dependants especially females had not been keen for inpatient treatment as against male counterparts on active duty, expecting rest/sick leave. There is no specific immunoglobulin that can act prophylactically. This means that the existing civic amenities need improvement and the chlorination and supply of water must be consistent and uninterrupted.

CONCLUSION

The HEV is an important cause of acute viral hepatitis in this part of Pakistan, particularly in adults from lower socioeconomic groups. The problem is more serious for those living in military camps, residential institutions and in segregated areas who consume untreated water from a common source. Outbreaks like the one described have significant morbidity and not ignorable mortality for the affected persons. Fortunately, increased awareness of the problem and effective management has reduced mortality, but further efforts are needed to prevent water contamination.

REFRENCES

1. Purcell RH, Emerson SU. Hepatitis E : An emerging awareness of an old disease. Journal of Hepatology 2008,48:494-503.
2. Vis wanath R. infectious hepatitis in Delhi (1955-1965) a critical study of epidemiology. Indian journal of medical research 1957, 45 (suppl) 1- 30
3. Qureshi M et al. Hepatitis non-A, non-B report of a water born out break. Journal of Pakistan medical association, 1988, 38 203-4.
4. Purcell R H Ticchurst JR. Enterically transmitted non-A, non-B hepatitis = epidemiology and clinical characteristic. In Zukerman AJ, ed Viral hepatitis and liver disease. New York, Alan R Liss Inc, 1988: 131-7.
5. Reyes GR, Purdy MA, Kim JP, et al. Isolation of a cDNA from the virus responsible for enterically transmitted non-A, non-B hepatitis, Science 1990;247: 1335-39
6. Tsarev SA, Emerson SU, Reyes GR, characterization of a prototype strain of hepatitis E virus, proc Natl Acad Sci USA 1992; 89: 559-63.
7. Zhuang H, Cao XY, Liu CB, Wang GM. Epidemilogy of hepatitis E in China Gastroenteral Jpn 1991;26 (suppl)=135-8
8. Zhuang H, Zhu WF, Lif, Zhu XJ, LiK, Cui, YH, Zhu YH. Studies on hepatitis E. Chin Med Sci J 1999; 14 (suppl) : s 47-50
9. Clayson Et, Shrestha Mp, Vaughn DW, Snithbhan R, Shrestha KB, longer CT Innis BL. Rates of hepatitis E virus infection and disease

among adolescents and adults in Kathmandu, Nepal. J infect Dis 1997; 176 (3): 763-6

10. Shrestha SM. Hepatitis E in Nepal. Kathmandu Univ Med J (KUMJ) 2006; 4(S) : 530-44.
11. Malik IA, Tariq WUZ.Hepatitis E in Pakistan. Eastern Mediterranean Health Journal, 1996;2(1):121-8.
12. Ticehurst J et al. Association of hepatitis E virus with an outbreak of hepatitis in Pakistan. Serological response and pattern of virus excretion. Journal of medical virology, 1992; 36:84-92.
13. Rab MA, Mubarik MM. Report on the hepatitis E epidemics in Islamabad Pakistan, Feb – Mar 1994. Unpublished report, 1994.
14. Saeedi MI, Mehmood K, Amanullah, Ziauddin M, Ilyas N, Zarif M. Frequency and clinical course of hepatitis E in tertiary care hospitals. J Coll Physicians Surg Pak 2004;14(9):527-29.
15. Myint KS, Gibbons RV, Hepatitis E: a neglected threat. Trans R SOC. Trop Med Hyg 2008; 102(3) : 211-2
16. Meng X.J. Recent advances in Hepatitis E virus. Journal of viral hepatitis 2010;17:153-61
17. Bhatia V.singhal A, Panda SK. Acharya SK. A 20 year single – centre experience with acute liver failure during pregnancy: is the prognosis really worse ? Hepatology 2008; 48 (5):1577-85
18. Mushahwar IK. Hepatitis E virus. Molecular Virology clinical features, diagnose, transmission, epidemiology and prevention. J Med Virol 2008 : 80(4) : 646-58
19. Shrestha MP, Scott RM, Joshi DM, Mammen Jr MP, Thapa GB, Thapa N.et al. Safety and efficacy of a recombinant hepatitis E vaccine. N Engl J Med 2007;356:895-903.
20. Usman J. Yet again Hepatitis E. (Editorial) Pak Armed Forces Med J 2009; 59: 257-8.

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