

Hematological changes associated with hepatitis by hepatitis E virus

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Abstract

The purpose of the study was to find out the changes in the common hematological parameters in patients (n=998) of acute viral hepatitis caused by hepatitis E virus from April to May, 2018. The mean hemoglobin level was 13.5 g/dL. However, seven patients were found to have hemoglobin level <11.0 g/dL. The mean red cell count was $4.5 \times 10^{12}/L$. The mean packed cell volume was 40.6%. The mean white blood cell count was $7.1 \times 10^9/L$. However, leucopenia was found in 8 cases. The mean platelet count was $186.2 \times 10^9/L$. Among the hematological changes associated with hepatitis E virus infection, thrombocytopenia is a notable finding.

Introduction

Hepatitis E virus is one of the five known hepatotropic viruses which causes inflammation of the liver and has fecal-oral transmission.¹ The letter “E” stands for ‘enteric’, ‘epidemic’ or ‘endemic’, all these terms are related to the epidemiological behavior of hepatitis E virus.² Hepatitis E virus is the most common cause of acute viral hepatitis in most regions with about 20 million hepatitis E infections worldwide.^{3,4} Phylogenetic analysis of many hepatitis E virus strains based on complete viral genome and a range of subgenomic regions leads to the identification of four major genotypes (HEV1, HEV2, HEV3 and HEV4).⁵ Human infection with hepatitis E virus has two distinct epidemiological patterns. In areas of poor sanitation, HEV1 and HEV2 are transmitted between humans by the fecal-oral route, usually via contaminated water.^{6,7} A massive outbreak of hepatitis E virus infection causing acute hepatitis had occurred in Chattogram from February to August 2012 affecting 698 individuals which was confirmed by third generation Enzyme Immune Assay.⁸

Hepatitis E virus infection usually leads to acute and self-limiting infection in the majority of patients with symptomatic and biochemical recovery within 4–6 weeks. In two groups of patients, the natural history and prognosis are different: Patients who have an underlying chronic liver disease have a poor prognosis and individuals who are immunosuppressed often develop chronic infections. A minority of patients present with neurological symptoms and when this occurs, the diagnosis may easily be overlooked because of the dominant

neurological features.^{9,10} Hepatitis E virus infection usually leads to low death rates in developed countries but it sometimes makes the infected individuals with high-risk of chronic hepatitis with significant death rates. Individuals who have undergone organ transplantation and are taking immunosuppressive medicines to prevent organ rejection are particularly susceptible to develop chronic hepatitis E.¹¹ Liver transplant recipients may develop graft hepatitis when contacted with hepatitis E virus. Besides fecal-oral transmission, hepatitis E virus can be transmitted by the transfusion of blood products especially for patients in the transplant setting. Liver or other solid organ transplant patients with hepatitis E virus infection rapidly progress to cirrhosis with 1–2 years of infection. In addition to the involvement of the liver by hepatitis E virus, a number of extra-hepatic manifestations have been reported with hepatitis E virus infection. Notable among these are severe thrombocytopenia and hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency, lymphoma, acute pancreatitis, thyroiditis, glomerulonephritis, mixed cryoglobulinemia, meningitis, Guillain-Barré syndrome, neuralgic amyotrophy. Such extra-hepatic manifestations may develop during or after acute or chronic hepatitis E virus infection. Pathophysiological links between hepatitis E virus infection and the mentioned extra-hepatic manifestations are yet to be established.¹²

In this study, hematological changes were analyzed among 998 patients who were IgM hepatitis E virus positive.



Materials and Methods

This retrospective study was carried out in Combined Military Hospital, Chattogram Cantonment, Chattogram, Bangladesh during the month of April and May, 2018. During this period, a massive outbreak of acute hepatitis by hepatitis E virus occurred in a military installation as well as the surrounding civil communities in Halisahar, Chattogram. In this study, only military personnel staying in this military installation were included. Total number of individuals staying in this installation was 3,010. During this outbreak, a total of 1,298 patients reported to the medical inspection room and then to the Combined Military Hospital, Chattogram. Among them, 998 patients were diagnosed as acute hepatitis caused by hepatitis E virus. The blood sample (2.5 mL) was taken in EDTA anticoagulant tube and mixed and labelled properly for hematological profile.

The variables taken to assess the hematological changes include hemoglobin level, red blood cell count, packed cell volume, white cell count, differentials of leucocytes and platelet count. The hematological parameters were carried out by automated hematology analyzer (ABX Pentra DF 120). The relevant findings of these patients were evaluated and data were entered into Microsoft excel and analyzed by SPSS.

Results

Among the total 998 patients, 950 were males and 48 were females. The mean (\pm SD) age was 22 ± 7.6

years.

The mean hemoglobin level was 13.5 g/dL (Table I). However, seven patients were found to have hemoglobin level <11.0 g/dL. The mean red blood cell count and packed cell volume were $4.5 \times 10^{12}/L$ and 40.6%, respectively. The mean white blood cell count was $7.1 \times 10^9/L$. However, leucopenia was found in 8 cases. The platelet count was primarily measured by the hematology analyzer but in cases of thrombocytopenia which was found in 35 cases were checked microscopically. The mean platelet count was $186.2 \times 10^9/L$.

Discussion

The mechanisms by which hepatitis E virus can cause extra-hepatic manifestations are mostly unknown but may be either due to direct viral effects from the Hepatitis E virus replication in affected tissues or immune-mediated mechanisms.¹³ Thrombocytopenia may be associated with hepatitis E virus infection. Data from this study revealed the mean platelet count $186.2 \times 10^9/L$ but thrombocytopenia was observed in 35 cases. In a study conducted by Woolson et al, thrombocytopenia was found in 12 cases out of 102 cases.¹⁴ Severe thrombocytopenia ($<30 \times 10^9/L$) was found in one case, platelet count in between $30 \times 10^9/L$ to $\leq 100 \times 10^9/L$ was found in 10 cases and count in between $>100 \times 10^9/L$ to $<150 \times 10^9/L$ was found in 24 cases. The difference of finding low platelet count between this study and Woolson's study may be due to variation of sample size in these two studies. Mechanism of development of thrombocytopenia in hepatitis E virus infected individuals is not known. Two possible mechanisms are suspected: immune mediated thrombocytopenia and development of fibrosis and splenomegaly.¹⁵ Therefore, thrombocytopenia in hepatitis E virus infection may be either due to immune mediated platelet destruction with or without immune mediated megakaryocyte damage or alternatively direct toxicity to megakaryocytes resulting from viral infection of this cells.^{16,17}

Leucopenia was found in 8 cases and mild to moderate neutropenia was found in three cases in this study. Pancytopenia and hepatitis-associated aplastic anemia is an uncommon but a distinct variant of aplastic anemia which usually appears two to three months after acute viral infection. Such type of marrow failure may be severe and is typically fatal if untreated. Shah et al. (2012) reported a case of 32-year-old male who developed severe aplastic anemia after an acute attack of hepatitis by hepatitis E virus in Pakistan.¹⁸ In the present study, no patient presented with either pancytopenia or clinical features of pancytopenia.

Table I

Hematological changes in HEV positive hepatitis patients (n=998)

Parameters	
Gender	
Male	950
Female	48
Age (years)	22.0 ± 7.6
Hemoglobin (g/dL)	13.5 ± 1.26
Red blood cell count ($\times 10^{12}/L$)	4.5 ± 0.42
Packed cell volume (%)	40.6 ± 3.9
White blood cell count ($\times 10^9/L$)	7.1 ± 2.3
Neutrophils (%)	58.6 ± 9.3
Lymphocytes (%)	31.8 ± 8.8
Monocytes (%)	7.3 ± 2.8
Eosinophils (%)	2.1 ± 2.1
Platelet count ($\times 10^9/L$)	186.2 ± 57.4
Data are mean \pm SD	

In this study, seven patients had anemia with hemoglobin level less than 11.0 g/dL. HEV infected patients usually develop hemolytic anemia, particularly those who are glucose-6-phosphate dehydrogenase deficiency. In the present study, those who were anemic were not investigated to find out the cause of anemia. However, the causative relationship between hepatitis E virus infection and anemia is difficult to establish. It is possible that less severe cases have remain unnoticed and thus underreported.¹⁹

Monoclonal gammopathy of undetermined significance is another hematological abnormality detected in 26.2% patients with hepatitis E virus hepatitis.¹⁸ It is a clinically asymptomatic lymphoplasmacytic malignant disorder. Its approximate incidence is more than three percent in general Caucasian individuals and occurs usually over the age of 50 years.²⁰ In this study, the mean age of the patients was 22 years and therefore, protein electrophoresis was not done in these cases.

Henoc-Schonlein purpura may sometimes be associated with hepatitis E virus infection. In the present study, no such case was found. There is a one case report from India where a six-year old girl suffering from acute hepatitis E developed Henoch-Scholein purpura.²¹

Conclusion

The finding of abnormal platelet count in patients with hepatitis E virus hepatitis alerts the physicians to manage accordingly and may be of one among other markers in endemic region of hepatitis E virus hepatitis.

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