International Journal of Medical and Health Research
ISSN: 2454-9142
www.medicalsciencejournal.com
Volume 4; Issue 8; August 2018; Page No. 211-213

Assessment of serological markers in children with hepatic encephalopathy

Dr. Ramanuj Sharma[1], Dr. Chhitiz Anand[2], Dr. JPN Barnwal[3]
[1] Junior Resident, Upgraded Department of Paediatrics, Patna Medical college and Hospital, Patna, Bihar, India
[2] Junior Resident, Department of Paediatrics, Darbhanga Medical college and Hospital, Laheriasarai, Darbhanga, Bihar, India
[3] Professor, Upgraded Department of Paediatrics, Patna Medical college and Hospital, Patna, Bihar, India
[*] Corresponding Author: Dr. Chhitiz Anand

Abstract
Hepatic encephalopathy (HE) refers to changes in the brain that occur in patients with advanced, acute (sudden) or chronic (long-term) liver disease. It is one of the major complications of cirrhosis. It can occur suddenly in people with acute liver failure but is more often seen in those with chronic liver disease.
The present study was planned to evaluate the clinical spectrum and indicators influencing the diagnosis of patients with hepatic encephalopathy. There is an inadequacy of data about the field of manifestation and prognosis of children with hepatic encephalopathy especially in developing countries.
The study was planned in the Upgraded Department of Paediatrics in Patna Medical College and Hospital, Patna from Jan 2014 to Feb 2015. Total 50 children below age of 18 years diagnosed with hepatic encephalopathy were enrolled in the present study. All the patients underwent complete neurological examination.
From our findings, it can be concluded that the there is significant variation in the serological markers found in children with hepatic encephalopathy. Also hepatic failure is a condition associated with high mortality primarily in absence of hepatic transplantation facilities. Hence focus of efforts should be in providing preventive steps such as immunization and society education.

Keywords: hepatic encephalopathy, liver disease, children, acute hepatic failure

Introduction
Hepatic encephalopathy (HE) refers to changes in the brain that occur in patients with advanced, acute (sudden) or chronic (long-term) liver disease. It is one of the major complications of cirrhosis. It can occur suddenly in people with acute liver failure but is more often seen in those with chronic liver disease. One of the most important things the liver does is to change potentially damaging substances that are either made by or taken in by the body and make them harmless. However, if the liver is badly damaged and unable to function properly, these 'toxins' can build up in the bloodstream. If they enter the brain, they can result in a condition called hepatic encephalopathy. As well as the build-up of chemicals and toxins that cause HE, other factors, such as dehydration, constipation or an infection can also trigger an episode [1].
HE symptoms can range from mild to severe and can vary from person to person. Symptoms can develop rapidly or slowly over a period of time. Patients with HE can have both physical symptoms and reduced mental function. Mild symptoms may include: confusion, forgetfulness, personality or mood changes, stale or sweet odour on the breath, poor judgement, poor concentration, change in sleep patterns and worsening of handwriting or small hand movements. Severe symptoms may include unusual movements or shaking of hands or arms, extreme anxiety, seizures, severe confusion, sleepiness or fatigue, severe personality changes, jumbled and slurred speech, slow movement.
HE can be an emergency, so it's important to seek advice from your doctor as soon as you notice worrying symptoms. If you've already been diagnosed with HE and feel as though your condition is worsening, seek medical help as soon as possible. HE is a treatable condition. The severity of the condition and potential triggers will determine the treatment given. The first step is to identify and treat any factors that have caused the HE episode. Once this has been addressed, your doctor may prescribe medication to help prevent future episodes. The long term aim of HE treatment is to reduce the production and absorption of toxins such as ammonia [2].
Classification. A simplified classification of hepatic encephalopathy is as follows:

1. Acute hepatic encephalopathy associated with acute liver failure and characterized by cerebral edema and raised intracranial pressure. This is likely to be manifested as hepatic coma.
2. Subacute or subclinical hepatic encephalopathy associated with hepatic cirrhosis and associated with abnormal findings on neuropsychological testing.
3. Chronic hepatic encephalopathy associated with hepatic cirrhosis. This classification of hepatic encephalopathy takes several forms. The most common form of presentation is "precipitant-induced encephalopathy" in which cirrhotic patients develop progressive changes of mental function with several precipitating factors. One type is called portal-systemic encephalopathy because of

extensive portosystemic shunting or surgical portacaval shunt. Another form is hepatocerebral degeneration, wherein patients present with dementia and extrapyramidal disorders [3].

Hepatic encephalopathy is a syndrome observed in patients with cirrhosis. Hepatic encephalopathy is defined as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction, after exclusion of brain disease [1, 2, 3]. Hepatic encephalopathy is characterized by personality changes, intellectual impairment, and a depressed level of consciousness [4]. An important prerequisite for the syndrome is diversion of portal blood into the systemic circulation through portosystemic collateral vessels [5]. Hepatic encephalopathy is also described in patients without cirrhosis with either spontaneous or surgically created portosystemic shunts. The development of hepatic encephalopathy is explained, to some extent, by the effect of neurotoxic substances, which occurs in the setting of cirrhosis and portal hypertension.

Acute liver failure is loss of liver function that occurs rapidly-in days or weeks-usually in a person who has no pre-existing liver disease. Acute liver failure is less common than chronic liver failure, which develops more slowly. Acute liver failure, also known as fulminant hepatic failure, can cause serious complications, including excessive bleeding and increasing pressure in the brain. It's a medical emergency that requires hospitalization. Depending on the cause, acute liver failure can sometimes be reversed with treatment. In many situations, though, a liver transplant may be the only cure.

Hence from the above documented literature the present study was planned to evaluate the clinical spectrum and indicators influencing the diagnosis of patients with hepatic encephalopathy. There is inadequacy of data about the field of manifestation and prognosis of children with hepatic encephalopathy especially in developing countries.

Methodology

The study was planned in the Upgraded Department of Paediatrics in Patna Medical College and Hospital, Patna from Jan 2014 to Feb 2015. Total 50 children below age of 18 years diagnosed with hepatic encephalopathy were enrolled in the present study. All the patients underwent complete neurological examination.

The study was approved from the Institutional Ethical committee. All the patients were informed and consent was taken. The aim and objective of the present study was conveyed to the patients.

The patients underwent diagnostic tests for assessment viz. blood cell counts, peripheral blood smear for malarial parasite, liver function tests [Serum Aspartate Aminotransferase, Alanine aminotransferase, Direct and Total Bilirubin, Serum Albumin, Prothrombin time (PT), Serum electrolytes, Blood urea, Serum creatinine and blood culture. Tests for Viral markers was done which included hepatitis B surface antigen (HBsAg) and antibodies against hepatitis A virus and hepatitis C virus (HCV).The end result was determined in form of survival (improvement and successful discharge after the encephalopathy has been resolved), death and leave against medical advice (LAMA).

The following was the inclusion and exclusion criteria for the present study:

Inclusion Criteria

- Age less than 18 years old.
- Onset of hepatic encephalopathy within 8 weeks of appearance of symptoms of jaundice. And/or.
- Elevated levels of ALT, AST, alkaline phosphatase, GGT, total bilirubin, albumin, Prothrombin time >30 sec. And/or.
- Viral hepatitis serologies: anti-HAV IgM, HBsAg, anti-HBcIgM, anti-HCV reactive.
- Non-reactive in viral hepatitis serologies.

Exclusion Criteria

- Known case of liver cirrhosis presenting with fulminant hepatic failure.
- Physical trauma to liver.
- Diagnosed case of Hepatocellular carcinoma presenting with fulminant hepatic failure.
- Patients not willing to give written informed consent.

Results & Discussion

The data from 50 children below age of 18 years diagnosed with hepatic encephalopathy were collected and is presented as below.

Table 1: Study of Different Parameters

Parameters	Mean
Age	**4-17**
Icterus (duration)	11.8-12.5
Declined level of consciousness(duration)	1.91.6-0
Hemoglobin Gm/dl	8.6-10.2
TLC ($\times 10^9$/L)	1.3-1.9
Platelet count ($\times 10^5$/L)	0.7-2.6
Prothrombin Time (sec)	25-87
international normalized ratio (sec)	2.2-6.1
SGPT mg/dl	750-893
SGOT mg/dl	672-749
Alkaline Phosphatase (IU/L)	462-1020
Bilirubin (serum) mg/dl	
Total	11.6-22.3
Direct	4.3-13.9
Proteins (serum)	
Total g/dL	5.1-7.3
Albumin g/dL	2.6-4.5
Sodium g/dL	121-129
Potassium g/dL	3.2-4.8
Blood Urea mg/dl	31.5-76.3
Serum Creatinine mg/dl	0.95-2.62

Table 2: Displaying course on the basis of Encephalopathy's stage

Stage	No. of Cases	Expire	Survival	Lama
One	11	0	5	0
Two	14	2	2	0
Three	12	4	5	3
Four	13	6	0	3

Acute hepatic failure is a life-threatening condition of varied causes. Clinical scenario of it involves icterus, coagulation abnormality and encephalopathy. Aetiology of it is varied in nature. Common agents are viruses and drugs. Hepatitis A

and Hepatitis E are common cause of Hepatic encephalopathy in underdeveloped nations [5, 6]. Hepatitis B virus is not a common agent nowadays, probably due to vast coverage of hepatitis B vaccination [7]. Evaluation of etiology could not be possible in most (75%) of patients due to scarcity of diagnostic modalities. Still it has been mentioned that etiology is not clear in 45-50% of acute hepatic failure even after detailed investigations [8]. These cases known as 'cryptogenic' cases [9] may be due to metabolic disorders or unknown viral agents.

The disease was first recognized as a distinct clinical entity in the 1980s when sera from persons affected during a large water-borne epidemic of viral hepatitis during 1955-56 in Delhi [10] and another epidemic in Kashmir were found to lack serological markers of acute hepatitis A and B [11]. It is an enterically transmitted disease that spreads through fecal contamination of drinking water. HEV infection, a common cause of waterborne epidemics, is endemic and frequently responsible for acute viral hepatitis in developing countries [12]. According to the South-East Asia Regional Office of the World Health Organization (WHO), hepatitis E is widespread in developing countries, accounting for upto 30-70% of all sporadic cases of acute viral hepatitis [10]. HEV causes high mortality in pregnant women, 20-30% as compared to 0.2-1% in general population [13, 14]. It has been implicated as an important etiological agent for sporadic fulminant hepatic failure (FHF) in developing countries. The classic epidemiological studies by Viswanathan [13] and recent serological studies by Wong *et al*. [14] and Khuroo *et al*. [10] have convincingly demonstrated that HEV is an important cause of non-A non-B viral hepatitis. Our data correspond with the existing epidemiological features of HEV.

Seventy percent of study patients were expired or taken leave against medical advice therefore, survived were thirty percent. This proportion is similar to evidences from other institutions where there is absence of facility for liver transplantation [15]. In majority of cases, there were markedly increased PT (INR > 4), which is well known factor to assess prognosis and very long prothrombin time is linked with high mortality [16]. At INR >4, there is the indication for the liver transplantation, especially in small children. Chances of Survival after liver transplantation is 60% to 80% which depends on patient's conditions and facilities and infrastructure which are available [16-17]. The study evaluated the indicators which influences end result of liver failure. Higher the stage of encephalopathy poorer the outcome. Hemorrhage was common in expired. Coagulation derangement is a common picture associated with acute hepatic failure. There was not an important difference in serum bilirubin ranges, hepatic enzymes and Prothrombin time between survived and expired. This may be due to small sample size. In a from Turkey based study, stage of encephalopathy, serum bilirubin levels were significantly greater in expired patients [15]. In this study, Sodium levels were lesser in expired patients as compared to those who survived, which may be explained by syndrome of inappropriate secretion of antidiuretic hormone.

Conclusion

From the above findings, it can be concluded that the there is significant variation in the serological markers found in the children with hepatic encephalopathy. Also hepatic failure is a condition associated with high mortality primarily in absence of hepatic transplantation facilities. Hence focus of efforts should be in providing preventive steps such as immunization and society education.

References

1. https://liverfoundation.org/for-patients/about-the-liver/diseases-of-the-liver/hepatic-encephalopathy/
2. https://www.britishlivertrust.org.uk/liver-information/liver.../hepatic-encephalopathy/
3. http://www.medlink.com/article/hepatic_encephalopathy
4. https://www.mayoclinic.org/diseases-conditions/acute-liver-failure/symptoms-causes/syc-20352863
5. Blei AT, Córdoba J. Practice Parameters Committee of the American College of Gastroenterology. Hepatic Encephalopathy. Am J Gastroenterol. 2001; 96(7):1968-76.
6. Rehm J, Samokhvalov AV, Shield KD. Global burden of alcoholic liver diseases. J Hepatol. 2013; 59(1):160-8. doi: 10.1016/j.jhep.2013.03.007. Epub 2013 Mar 16.
7. Liaw YF, Chu CM, Hepatitis B. virus infection. Lancet. 2009; 373(9663):582-92. doi: 10.1016/S0140-6736(09)60207-5.
8. Bernuau J, Rueff B, Benhamou JP. Fulminant and subfulminant liver failure: definitions and causes. Semin Liver Dis. 1986; 6(2):97-106.
9. Dhawan A, Cheeseman P, Mieli-Vergani G. Approaches to acute liver failure in children. Pediatr Transplant. 2004; 8(6):584-8.
10. 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(3):281-6.
11. Navaneethan U, Al Mohajer M, Shata MT. Hepatitis E and pregnancy: understanding the pathogenesis. Liver Int. 2008; 28(9):1190-9.
12. Goumba CM, Yandoko-Nakouné ER, Komas NP. A fatal case of acute hepatitis E among pregnant women, Central African Republic. BMC Res Notes. 2010; 3:103.
13. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK. Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. Ann Intern Med. 2007; 147(1):28-33.
14. Wong DC, Purcell RH, Sreenivasan MA, Prasad SR, Pavri KM. Epidemic and endemic hepatitis in India: evidence for a non-A, non-B hepatitis virus aetiology. Lancet. 1980; 2(8200):876-9.
15. Bernuau J, Rueff B, Benhamou JP. Fulminant and subfulminant liver failure: definitions and causes. Semin Liver Dis. 1986; 6(2):97-106.
16. Williams R, Wendon J. Indications for orthotopic liver transplantation in fulminant liver failure. Hepatology. 1994; 20(1Pt2):S5-10S.
17. Devictor D, Desplanques L, Debray D, Ozier Y, Dubousset AM, Valayer J, *et al*. Emergency liver transplantation for fulminant liver failure in infants and children. Hepatology. 1992; 16(5):1156-62.