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Precipitating Factors of Hepatic Encephalopathy Among Sudanese Patients with Liver Cirrhosis

Siddig Omer Handady[1], Maiada Abbas Ahmed[2], Amira Abbas Fadl[3], Awad Ali M. Alawad[4, *]

[1]Department of Obstetrical and Gynecology, Imperial Hospital, Khartoum, Sudan
[2]Department of Internal Medicine, Khartoum North hospital, Khartoum, Sudan
[3]Department of Internal Medicine, Alribat University Hospital, Khartoum, Sudan
[4]Department of Surgery, Faculty of Medicine, University of Medical Sciences and Technology, Khartoum, Sudan

Email address

awadali82@hotmail.com (A. A. M. Alawad)

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Abstract

Background: Hepatic encephalopathy is a challenging complication of advanced liver disease causing significant morbidity and mortality worldwide. *Objective:* To determine the precipitating factors of hepatic encephalopathy (HE) in Sudanese patients with liver cirrhosis. *Methodology:* It was cross sectional study, descriptive, prospective and hospital based study, conducted at Khartoum state hospitals in Sudan over a period of six months from November 2013 to April 2014. One hundred and twenty (n=120) adults, diagnosed cases of liver cirrhosis were included in this study. *Results:* Ninety one (n= 91, 75.8%) were male and twenty nine (29, 24.2 %) were females. The mean age was 50.23 years with STD ± 16.2. The common precipitating factors identified in this study were as follows, (n= 50,) (41.7%) had infection (n= 43,) (36.4%) had constipation, (n=33, 27.5%) had hypokalemia, (n=32, 26.7%) had hematemesis and Melina, (n=26, 21.7%) had hyponatremia, hepato-renal syndrome, hepatocellular carcinoma and recent excessive paracentesis were seen in (21.7%), (13.3%) and (11.7%) of patients respectively. *Conclusion:* This study concluded that most common precipitating factors of hepatic encephalopathy in our patients are infection, constipation electrolyte imbalance and upper gastrointestinal bleeding. These are potentially preventable and reversible.

Keywords

Liver Cirrhosis, Hepatic Encephalopathy, Precipitating Factors

1. Introduction

Chronic liver disease and cirrhosis result in about 35,000 deaths each year in the United States [(1)], and worldwide end-stage liver disease accounts for one in forty deaths [(2)]. Hepatic encephalopathy is a challenging complication of advanced liver disease occurs in 30%-45% of patient with liver cirrhosis. It is an important complication of liver disease causing significant morbidity and mortality worldwide [(3)]. About 30% patients of chronic liver disease die of hepatic encephalopathy [(4,5)], and it is found in 19% of cirrhotic patients in a Sudanese study conducted to determine the aetiology, complications, and preventive measures of liver cirrhosis in 2007 in Elobeid Hospital; West Sudan [(6)].

The pathogenesis of hepatic encephalopathy is either due to inability of the hepatocytes to detoxify nitrogenous compounds or these compounds bypass the liver through collateral circulation, the result is accumulation of the nitrogenous waste products in the systemic circulation. The most important waste product is ammonia (NH_3) which crosses the blood-brain barrier and is absorbed and metabolized by the astrocytes, this lead to swelling of them (brain edema) also there is increase activity of inhibitory γ-aminobutyric acid (GABA) system, and the energy supply to other brain cells is decreased [(7)].

The hepatic encephalopathy is a diagnosis of exclusion [(8)]. The symptoms range from subtle personality changes to deep coma [(9)]. The present paper focus to determine the precipitating factors of hepatic encephalopathy (HE) in Sudanese patients with liver cirrhosis

2. Material and Methods

It was cross sectional study, descriptive, prospective and hospital based study, conducted at Khartoum state hospitals, which includes Ibnsina, Alribat and Khartoum North teaching hospitals over a period of six months from November 2013 to April 2014. One hundred and twenty (n=120) adults, diagnosed cases of chronic liver disease were included in this study. Hepatic encephalopathy was diagnosed clinically on the basis of history, physical examination and relevant laboratory and radiological investigations.

Detailed history was taken and a proper clinical examination was carried out. Biochemical and hematological tests were requested which included complete blood picture, urea, creatinine and electrolytes, liver function tests, prothrombin time and international normalized ratio, serum protein, albumin and globulin ratio, hepatitis B and C serology by ELISA technique.

Statistical analysis was performed via SPSS software (SPSS, Chicago, IL, USA). Continuous variables were compared using student's t test (for paired data) or Mann–Whitney U test for non-parametric data. For categorical data, comparison was done using Chi-square test (X2) or Fisher's Exact test when appropriate. A P value of <0.05 was considered statistically significant.

Ethical clearance and approval for conducting this research was obtained from the general manager of the hospitals and informed written consent was obtained from every respondent who agreed to participate in the study. Of course, the respondents informed that the study is not associated with experimental or therapeutic intervention, while information was collected from them.

3. Results

During the study period a total of 120 patients with underlying HE was included. Mean age was 50.23 years (±16.2). (75.8%) were males and (24.2 %) were female with male to female ratio of 3:1. Regarding etiology of liver cirrhosis, 50 (41.7%) of cases had viral hepatitis, alcoholic liver disease (heavy alcohol consumer) were 15 (12.5%), autoimmune diseases were 13 (10.8%) and in 38 (31.6%) of cases the cause was unknown. 34 (28.3%) of cases had hepatitis B and 16 (13.4%) had hepatitis C. Mean duration of disease was 3.26 years (±18.5). Common types of infections noted were spontaneous bacterial peritonitis in 23 (19.2%), Malaria in 10 (8.3%), chest infection in 6 (5.0%) and GE in 5 (4.2%). Majority of the patients were in stage II hepatic encephalopathy 52 (43.3%), while 16 (13.3%) stage IV, 14 (11.7%) stage I and 38 (31.7%) stage III coma. Majority of the patients had advanced liver disease according to Child Pugh score as no patient in score A, 82 (68.3%) patients in score B and 38 (31.7%) of cases in score C. (Table 1).

Amongst the precipitating factors, infection was found in 50 (41.7%), constipation in 43(36.4%), hypokalemia in 33 (27.5%), GIT bleeding in (26.7%), hyponatremia in 26 (21.7%), hepato-renal syndrome in 26 (21.7%) high protein diet in 15 (12.5%), use of sedative drugs in 4 (3.3%) and hypoglycemia found in 5 (4.3%) (Table 2).

Table 3 shows the nonparametric correlation between precipitant factors and gender. A strong correlation between precipitant factors and gender was found in infection, GI bleeding, hyponatremia and hepato-renal syndrome. Table 4 shows the nonparametric correlation between demographic data and past history of hepatic encephalopathy, significant correlation was found between past history of hepatic encephalopathy and age, gender and HCC.

Table 1. *Demographic data among respondents (N = 120).*

Items	Frequency	Percent
Age in years		
<20	2	1.7
20-29	2	1.7
30-39	15	12.5
40-49	34	28.3
50-60 and above	67	55.8
Mean ± SD 50.23±16.2		
Gender		
Male	91	75.8
Female	29	24.2
Duration of chronic liver		
<1 years	39	32.5
1-5 years	61	50.8
6-10 years	14	11.7
> 10 years	6	5
Mean ± SD 3.26 ±18.5		
Etiology of chronic liver		
Viral hepatitis	50	41.7
Unknown	38	31.6
Alcoholic liver disease	15	12.5
Autoimmune diseases	13	10.8
Wilson's disease	2	1.7
Heamochromatosis	2	1.7
Type of viral hepatitis		
Hepatitis B	34	28.4
Hepatitis C	16	13.4
No hepatitis	70	58.2
Type of infection		
Spontaneous bacterial peritonitis	23	19.2
Malaria	10	8.3
Chest infection	6	5
Gasteroenteritis	5	4.2
Urinary tract infection	6	5
No infection	70	58.3
Type of grade		
Grade 1	14	11.7
Grade 11	52	43.3
Grade 111	38	31.7
Grade IV	16	13.3
Child's class	0	0
Class A		
Class B	38	31.7
Class C	82	68.3
Total	500	100%

Table 2. *Distribution of the patients according to the precipitant factors for hepatic encephalopathy.*

Item	Frequency	Percent
Infection		
Yes	50	41.7
No	70	58.3
Conctipation		
Yes	43	36.3
No	77	63.7
Hypokalemia		
Yes	33	27.5
No	87	72.5
GI bleeding		
Yes	32	26.7
No	88	73.3
Hyponatremia		
Yes	26	21.7
No	94	78.3
Hepato-renal syndrome		
Yes	26	21.7
No	94	78.3
Hepatocellular carcinoma		
Yes	16	13.3
No	104	86.7
Recent excessive paracentesis		
Yes	14	11.7
No	106	88.3
High Protein Diet		
Yes	15	12.5
No	105	87.5
Hypoglycemia		
Yes	05	04.3
No	115	95.7
Use of sedative drug		
Yes	04	03.3
No	116	96.7

Table 3. *Distribution of the patients according to the precipitant factors in relation to gender.*

Precipitant factors	Male	Female	Total	P value
Infection	32(26.7%)	18(15.0%)	50(41.7%)	0.00*
Constipation	24(20.0%)	19(16.4%)	43(36.4%)	0.096
Hypokalemia	14(11.7%)	19(15.8%)	33(27.5%)	0.134
GI bleedin	19(15.9%)	13(10.8%)	32(26.7%)	0.05*
Hyponatremia	16(13.4%)	10(8.3%)	26(21.7%)	0.00*
Hepato-renal syndrome	18(15.0%)	08(6.7%)	26(21.7%)	0.04*
Hepatocellular carcinoma	09(07.5%)	7(05.8%)	16(13.3%)	0.09
Recent excessive paracentesis	08(06.7%)	6(05.0%)	14(11.7%)	0.23
High Protein Diet	09(07.5%)	06(05.0%)	15(12.5%)	0.06
Hypoglycemia	03(02.5%)	02(01.8%)	05(4.3%)	0.13
Use of sedative drug	02(01.7%)	02(01.7%)	04(3.4%)	0.17

*statistically significant at 0.05 level

Table 4. *Shows the nonparametric correlation between demographic data and past history of hepatic encephalopathy.*

Demographic data	Past history of HE Yes		Past history of HE No		P value
	Count	%	Count	%	
Age in years					
<20 years	0	00.0%	02	01.7%	
20-29 years	0	00.0%	02	01.7%	
30-39 years	5	04.2%	10	08.3%	0.001*
40-49 year	10	08.3%	24	20.0%	
50-60 and above	35	29.2%	32	26.6%	
Total	50	41.7%	70	58.3%	
Gender					
Male	29	24.2%	62	51.6%	0.038*
Female	21	17.5%	08	06.7%	
Total	50	41.7%	70	58.3%	
HCC					
Yes	11	09.2%	05	04.2%	0.000*
No	39	32.5%	65	54.1%	
Total	50	41.7%	70	58.3%	
Grade					
Grade 1	06	05.0%	08	06.7%	
Grade11	20	16.7%	32	26.7%	0.153
Grade111	17	14.2%	21	17.4%	
Grade1V	07	05.8%	09	07.5%	
Total	50	41.7%	70	58.3%	
Type of hepatitis viral					
HCV	14	11.7%	20	16.7%	
HCV	05	04.2%	11	09.2%	0.125
No viral hepatitis	31	25.8%	39	32.4%	
Total	50	41.7%	70	58.3%	

*Statistically significant at 0.05 level

4. Discussion

The current study showed male dominance (75.8%) and male to female ratio was 3:1, reflect the male preponderance. This result is in keeping with other studies which reported male dominance [10], male predominance is also reported by other study in which the male to female ratio was 2.85:1 [11]. The study revealed that most of the patients were between the ages of 40-70 years. Similar finding was also reported by other studies [10,12,13]. The study revealed that Hepatitis B infection was found in (28.4%) of cases. Similarly Intekhab Alam et al [11] show 28% Hepatitis B positive patients in their study. To the contrary, detection of Hepatitis B infection was lower by Maqsood S etal [10] found 8%, Zikariaetal [15] found hepatitis B just in 10%, Bikha [16] found 15%. The discrepancy between these studies and our study may be explained by multiple factors, such as race discriminations between regions of Sudan, as well as a population difference and decreasing knowledge concerning vaccination against Hepatitis B virus among our patients. Regarding factors precipitant for HE, infection was the first common precipitating factor in our study, present in 41.7% of patients, more common in males than females. Previous study conducted in Nigeria have shown infection in 29% [17]. Chinese study [18], showed infection was the most common precipitating factor (40.2%), which in the same line of our study. Additionally they found that the type of infection was: respiratory tract infection (56.6%), intestinal tract infection (20.7%), peritoneal infection (17.0%) and urinary tract infection (5.7%)[18] which support the finding of current study. Constipation was the second precipitating factor, found in 36.4%. Our result is comparable with previous studies that have shown percentage from (18.3% - 38%) [10,19]. Other study conducted in Pakistan 2006 found amongst the precipitating factors, 30% had constipation [20].

Gastrointestinal bleeding is the precipitant factor in 26.7% of the patients in the current study, was found in 36.7% of the populations in Egyptian study [21] and almost all studies found it in varying percentages [18 , 21].

Also high protein intake was noted in our patients in 12.5%, this figure is comparable to the result of many studies [11, 18 &21]. Additionally, our study revealed that nearly one third of our patients (27.5 %) had hypokalemia, hyponatremia was (21.7%) and only (4.3%) had hypoglycemia as precipitating causes of hepatic encephalopathy. These figures are lower than previously reported results (hypokalemia 79.4% [22], hyponatremia 50% [10], this can be justified by excessive diuresis contribute to electrolytes disturbances and none of the patients in this study found on high diuretic dose.

In 3.3% of patients included in this study , the precipitating factor for hepatic encephalopathy was use of sedatives drugs

this can be comparable with the study mentioned in the literature found that use of sedatives is least common precipitant [11], other study showed relatively high percentage 10.5%[13]. Hepatorenal syndrome was found in 21.7% of patients, Atif Sitwat et al [11], have shown 6% .The high figure in our study may be due to racial variation.

In this study, the majority of patients were in stage II coma 41(45.6%) while 22(24.4%) stage IV, 18(20.0%) stage I and 9(10.0%) stage III coma. Different studies shows encephalopathy from grade I to grade IV with diverse frequency [10,16]. Limitation of our study is that, outcome of HE were not evaluated. Further studies should be done with proper involvement of outcome of HE. Another limitation is no interrogation of herbal and traditional medicine that may be a precipitant of hepatic encephalopathy.

5. Conclusion

This study concludes that most common precipitating factors of hepatic encephalopathy in our patients are infection, constipation electrolyte imbalance and upper gastrointestinal bleeding. These are potentially preventable and reversible. Finally hoping this will be the beginning for further general health education aiming to improve the community awareness about precipitating factors of hepatic encephalopathy

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