Original Article

Hypoglycemic Episodes among Cirrhotic Patients Presenting with Hepatic Encephalopathy to Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of hypoglycemic episodes among cirrhotic patients presenting to tertiary care hospital.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine, Khyber Teaching Hospital from May, 2017 to October, 2017.

Materials and Methods: 150 male and female cirrhotic patients aged between 18 and 65 years, and fulfilling the inclusion criteria were recruited in the study. Patients were stratified into different grades of hepatic encephalopathy according to West Haven criteria. A random blood sugar level of 72mg/dl was taken as cut off level. Those presenting with levels less than 72mg/dl were labeled as having hypoglycemia. Data collected were entered in SPSS 23. Mean ± SD were calculated for continuous variables and categorical variables were expressed as frequencies and percentages. Effect modifiers were controlled though stratification. Chi square test was used by taking p-value less than or equal to 0.05 as significant for post stratification. Results were presented as tables.

Results: A total of 150 patients with hepatic encephalopathy due to liver cirrhosis were included in the study. Male to female ratio was 1.42:1. Average age of the patients was 52.24 years±10 SD. Average blood glucose level in patients with hepatic encephalopathy due to liver cirrhosis was 88 mg/dl± 6.32 SD. Majority (102 (68%)) of patients had more than or equal to 72mg/dl blood glucose level while 48 (32%) patients had less than 72mg/dl blood glucose level. Majority (48.66%) of the patients presented in Grade II hepatic encephalopathy. Among cirrhotic patients with hepatic encephalopathy that presented with hypoglycemia, 4 were aged <30 years, 10 were aged between 31 and 45 years, 26 were aged between 46 and 60 years and 8 were aged >60 years. 34.17% male and 29.57% female patients developed hypoglycemia. Slightly more hypoglycemic episodes were seen among patients with higher grades of encephalopathy

Conclusion: Hypoglycemia is seen among patients with hepatic encephalopathy due to liver cirrhosis. It is not yet clear whether hypoglycemia is jointly responsible for the increased short-term mortality of patients with hepatic encephalopathy due to liver cirrhosis or is only a consequence of the severity of the disease or the complications. Further multi-centered trials are recommended to prove this relationship.

Key Words: Hypoglycemic episodes; cirrhotic; hepatic encephalopathy; West Haven Criteria

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INTRODUCTION

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome which is manifested by altered and deteriorated mental status, psychomotor dysfunction, memory impairment, increased reaction time, inability to concentrate, stupor and in its most severe form - coma [1, 2].

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It may develop at an annual rate of 8% in cirrhotic patients according to a study conducted in Far East [3]. A past history of hepatic encephalopathy is associated with problems at work place, and also causes financial burden on the care givers of such patients. Financial burden can also lead to poor drug compliance, thereby reducing the chances of improvement. A multidisciplinary approach is needed to address this issue and to devise treatment modalities not only in accordance with patients' clinical situation, but also after taking into consideration the collateral issues especially of finances [4].

The clinical diagnosis of overt hepatic encephalopathy is based on two concurrent types of symptoms: impaired mental status, as defined by Conn's score (also called West Haven criteria) (on scale from 0 to 4,

with greater score indicating more severe impairment),[5] and impaired neuromotor function [2].

A very narrow line exists between decompensated chronic liver disease with and without hepatic encephalopathy, and insults like constipation, hypovolemia, infection, hypoglycemia, hypokalemia, gastrointestinal bleeding and tranquilizers can precipitate encephalopathy in predisposed patients [6]. Hypoglycemia is associated with increased mortality in patients with acutely decompensated liver cirrhosis. It is not yet clear whether hypoglycemia is jointly responsible for the increased short-term mortality of patients with acute decompensated liver cirrhosis or is only a consequence of the severity of the disease or the complications [7]. Severe persistent hypoglycemic states, however, may cause long-lasting coma, seizures, and a myriad of other global and focal neurologic deficits [8], some of which may be mistaken for cerebrovascular accidents or other acute neurological disorders [9]. In analogy to hypoxic encephalopathy, this syndrome has been named hypoglycemic encephalopathy. However, the underlying pathophysiologies in both entities are markedly distinct [10].

The pathophysiology of clinical deterioration in hepatic encephalopathy patients with hypoglycemia is not clear. Diabetic patients with chronic liver disease usually develop accelerated liver fibrosis. They are also more prone to bacterial infections [11]. In one study, about 80% of patients presenting with compensated liver cirrhosis had some type of glucose metabolism disorders [11]. In another study, 28.5% of patients had acute glucose disturbances out of which 15.7% were hypoglycemic and 12.8% were hyperglycemic [7]. In another study, out of 100 cases of HE due to liver cirrhosis, 39% were found to have hypoglycemia [12].

From the current study, we aim to determine the frequency of hypoglycemia in cirrhotic patients with hepatic encephalopathy. Blood glucose disturbances are a predisposing factor for hepatic encephalopathy, but at the same time, patients with HE and no prior glucose abnormalities can also develop hypoglycemia. Therefore, hypoglycemia seems to be having a cause and effect relationship with HE. Once local data is collected regarding this finding, we can then compare the results with other studies, and can come up with recommendations regarding routine monitoring of blood glucose in cirrhotic patients with HE.

MATERIALS AND METHODS

This Cross sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar from May, 2017 to October, 2017. 150 male and female patients aged 18-65 years and above, with hepatic encephalopathy were recruited in the study. Patients with concomitant chronic renal failure and who were on haemodialysis, patients with acute fulminant hepatitis, and patients having history of diabetes and taking anti diabetic drugs were excluded from the study. This study was conducted after approval from hospital ethical and research committee. All admitted patients meeting the inclusion criteria were included in the study. The diagnosis and severity of HE was based on West Haven Criteria [7]. The purpose and benefits of study were explained to the patients and a written informed consent was obtained.

All patients were subjected to detailed history and examination. 5 ml of blood was taken from all patients under strict aseptic technique and was sent to hospital laboratory on the same day. Blood glucose level for all patients was measured from the hospital clinical laboratory. Patient information including name, age, gender and address were recorded in the study Pro forma. Strict exclusion criteria were followed to control confounders and bias in study results. Patients with random blood sugar levels less than 72 mg/dl were labeled as having hypoglycemia [13]. Data collected were entered in SPSS 23. Mean ± SD were calculated for continuous variables like age and blood glucose levels and categorical variables like gender and hypoglycemia were expressed as frequencies and percentages. Effect modifiers like age, gender and level of severity of encephalopathy were controlled though stratification. Chi square test was used by taking p-value less than or equal to 0.05 as significant for post stratification. Results were presented as tables.

RESULTS

A total of 150 patients with hepatic encephalopathy due to liver cirrhosis were included in the study. There were 88 (58.66%) males and 62 (41.33%) females. Male to female ratio was 1.42:1. Average age of the patients was 52.24 years±10 SD with range 18-65 years. Patients' age was divided into four categories, out of which most common age group for liver cirrhosis was between 46 and 60 years. 15 (10%) patients were under 30 years of age; 41 (27.33%) patients were in the age group 31-45 years; 60 (40%) patients were in the age group 46-60 years, and the remaining 34 (22.66%) patients were older than 60 years (Table 1).

Table No.1: Age-Wise Distribution of Patients

Age Group (Years)	Frequency (n)	Percentage (%)	Mean ± SD
< 30	15	10	52.24 ± 10
31 – 45	41	27.33	
46 – 60	60	40	
>60	34	22.66	

Average blood glucose level in patients with hepatic encephalopathy due to liver cirrhosis was 88 mg/dl± 6.32SD. Majority (102 (68%)) of patients had more than or equal to 72mg/dl blood glucose level while 48 (32%) patients had less than 72mg/dl blood glucose

level (Table 02). Of these 48 patients, 41(27.33%) patients were symptomatic of hypoglycaemia.

Table No.2: Hypoglycemia Among Cirrhotic Patients with Hepatic Encephalopathy

Hypoglycemia	Number of Patients (n)	Percentage (%)
Yes	102	68
No	48	32

Majority (73 (48.66%) of the patients presented in Grade II HE (Table 03).

Table No.3: Hepatic Encephalopathy Grades Among Patients

Grade of Hepatic Encephalopathy	Number of Patients (n)	Percentage (%)
I	7	4.66
II	73	48.66
III	48	32
IV	22	14.66

Among cirrhotic patients with hepatic encephalopathy that presented with hypoglycemia, 4 were aged <30 years, 10 were aged between 31 and 45 years, 26 were aged between 46 and 60 years and 8 were aged >60 years (Table 04).

Table No.4: Age Wise Distribution of Hypoglycemia Among Cirrhotic Patients with Hepatic Encephalopathy

Age (Years)	Hypoglycemia		Total	p-value
	Yes	No		
<30	4	47	51	0.184
	7.84%	92.15%	100%	
31-45	10	42	52	
	19.23%	80.76%	100%	
46-60	26	36	62	
	41.93%	58.06%	100%	
>60	8	25	33	
	24.24%	75.75%	100%	
Total	48	102	150	
	32%	68%	100%	

Table No.5: Gender-wise distribution of hypoglycemia among cirrhotic patients with hepatic encephalopathy

Hypoglycemia	Gender		Total	p-value
	Male	Female		
Yes	27 (34.17%)	21 (29.57%)	48 (32%)	0.265
No	52 (65.82%)	50 (70.42%)	102 (68%)	
Total	79 (100%)	71 (100%)	150 (100%)	

No difference was noted in incidence of hypoglycemia among male and female patients with encephalopathy. 34.17% male and 29.57% female patients developed hypoglycemia (Table 5).

Similarly, not much difference was noted in the occurrence of hypoglycemia among different strata of hepatic encephalopathy; however, slightly more hypoglycemic episodes were seen among patients with higher grades of encephalopathy (Table 06).

Table No.6: Distribution of Hypoglycemia over grades of hepatic encephalopathy

Grade of Encephalopathy	Hypoglycemia		Total	p-value
	Yes	No		
I	12	25	37	0.876
	32.43%	67.6%	100%	
II	9	36	45	
	20%	80%	100%	
III	15	18	33	
	45.45%	54.54%	100%	
IV	12	23	35	
	34.28%	65.71%	100%	
Total	48	102	150	
	32%	68%	100%	

DISCUSSION

Liver diseases affect millions of people worldwide. However, in the developing countries where cost of health care has always been an issue, chronic diseases such as liver cirrhosis and its complications are a major health problem and pose a big challenge to the health economy. Because of poverty, poor hygienic conditions, inadequate education and lack of counselling, the number of cirrhotic patients is increasing and most of them land up in medical wards with different complications. Most of these patients do not receive treatment at early stage; as a result of which they progress to decompensated cirrhosis with reduced chances of complete recovery.

Chronic liver disease is becoming an epidemic in Pakistan due to a very high prevalence of hepatitis B and C in our community. As a result increasing number of patients come with one or another complication of cirrhosis liver[13,14]. It is a major cause of mortality and morbidity worldwide[15]. It is also a common cause of mortality amongst Pakistani population and frequent cause of admission in our hospitals[16]. Cirrhosis develops in about 10-20% of the patients within 5-30 years. The most common cause of cirrhosis in our setup is viral hepatitis as compared to West where alcoholic liver disease is more common[17]. Majority of patients (90%) with chronic liver disease had evidence of HBV, HCV or coinfection. Severe disease is reported in patients with co-infection and cirrhosis is recorded in 74% of patients[18,19]. HCV is now more common as compared to HBV in our country, and there is high frequency of HCV seropositive individuals of both sexes among patients referred for management of chronic liver disease [20].

In a local study, results showed that out of 240 patients enrolled in the study, 148 were male (61.7%) and 92 were female (38.3 %)[21]. Another local study of 100 patients showed 67 (67%) males and 33 (33%) females[22]. In a local case series study conducted at Department of Medicine, Liaquat University of Medical & Health Sciences Jamshoro, Pakistan, which included 222 patients, 144 (65%) were male and 78 (35%) were female[23]. Male preponderance has also been reported in various international studies. In a study on seven patients, five were males admitted to the Unit of Gastroenterology and Hepatology of the "Hospital Português" of Salvador, BA, Brazil[24].

In our study, overall mean age was 52.24 years ± SD. Similar results have also been reported in a local study in which patients mean age was 53.09 with SD= 8.85 years[25]. The association between liver cirrhosis and alterations of glucose tolerance has been extensively documented[26]. They range from postprandial hyperglycemia to clinically overt, non-ketotic, non–insulin dependent diabetes mellitus (i.e., type 2 diabetes mellitus) [27-28]. The risk of hypoglycemia has been well demonstrated in clinical studies and in animal models. Unfortunately, the ideal method of preventing hypoglycemia and glucopenic brain injury has not been established. Certainly, following the onset of hypoglycemia, blood glucose levels require frequent monitoring and continuous infusions of 10–20% dextrose.

CONCLUSION

It can be concluded that hypoglycemia is a common finding among patients with hepatic encephalopathy due to liver cirrhosis. It is not yet clear whether hypoglycemia is jointly responsible for the increased short-term mortality of patients with hepatic encephalopathy due to liver cirrhosis or is only a consequence of the severity of the disease or the complications. Further trials are recommended to prove this relationship.

Author's Contribution:

Concept & Design of Study:	Aliena Badshah
Drafting:	Iqbal Haider
Data Analysis:	Main idea, Wazir Mohammad
Revisiting Critically:	Zahid Marwat
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