

Original Article

The prevalence of neurological complications among adult Sudanese patients with chronic liver disease.

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Abstract

Objective

We aimed to study the prevalence of neurological complications among adult Sudanese patients with chronic liver disease (CLD) seen in Ibn Sina Hospital (Sudan) (February 2005 - February 2006).

Patients & Methods

This is a prospective descriptive cross sectional hospital based study. Ninety six adult Sudanese patients with CLD were included in the study. All patients had been subjected to full detailed history, proper clinical examination and necessary investigations including EEG, Brain CT, MRI, NCS and EMG.

Result:

Male to female ratio was (2.5:1). Splenomegally was observed in 71 patients (74%), shrunken liver in 83 (86.5%), 74 (77.1%) had ascites.

Sixty percent had liver cirrhosis, 24% had cirrhosis with periportal fibrosis (PPF). Hepatocellular Carcinoma (HCC) was detected in 12 patients. Out of 96 patients

with CLD, neurological complications were detected in 44 (45.8%), acute hepatic encephalopathy ranging from grade I to grade IV was found to be the most common neurological complication (29 patients).

Conclusion

Neurological complications were common among adult Sudanese patient with chronic liver disease.

Keywords: hepatitis, ovulation, pituitary, dopamine

Introduction

The liver is the largest organ in the body weighs about 1500 g and receives about 1500 ml of blood per minute.⁽¹⁾ Chronic liver disease is marked by the gradual destruction of liver tissue over time.⁽²⁻³⁻⁴⁾ The most common chronic liver diseases are cirrhosis and hepatitis⁽⁵⁻⁶⁾. Cirrhosis is a chronic diffuse liver disease that is characterized by fibrosis and nodule formation. Nodule formation with disturbed architecture is essential for the diagnosis of cirrhosis.⁽⁷⁻⁸⁾ Known causes of cirrhosis account for about 90-95% of the cases. Most common etiologies include alcoholism, autoimmune chronic hepatitis and chronic viral hepatitis. Less common causes include hemochromatosis, primary biliary cirrhosis, sclerosing cholangitis, drug-induced liver disease and chronic biliary obstruction. Rare causes include α 1-antitrypsin deficiency,

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severe steatohepatitis in the morbidly obese and Wilson's disease.⁽⁹⁻¹⁰⁾ The remaining 5-10% of patients with cirrhosis of the liver has no known cause(s). Over the last 10 years, the rate of cryptogenic cirrhosis has fallen from 30% to current levels. The most likely cause for this fall has been the availability of testing for hepatitis C⁽¹¹⁾. The following neurological complications can occur in patients with CLD:

- 1) Encephalopathy (acute or chronic).
- 2) Myelopathy.
- 3) Abnormal movement e.g. Parkinsonism.
- 4) Cerebellar signs.
- 5) Paraparesis.
- 6) Hemiplegia.
- 7) Convulsion⁽¹²⁾.

The objective of this work is to study on the prevalence of neurological complications among adult Sudanese patients with chronic liver disease, seen in Ibn Sina Hospital (Khartoum) in the period from (February 2005 - February 2006).

Methods

This is a prospective cross sectional hospital based study conducted in Ibn Sina Hospital, a tertiary care hospital with 132 beds. A sample of 96 patients with CLD was enrolled in the study after taking informed consent. The study period was 1 year from February 2005 to February 2006.

Inclusion criteria

1. Sudanese nationality.
2. Age 18 years and above.
3. Liver disease for more than 6 months.

Exclusion criteria

1. Other nationalities.
2. Age below 18 years.
3. Acute liver disease.
4. Encephalopathy due to other causes.
5. Periportal fibrosis without cirrhosis.

Data were collected by the investigators through a fully-detailed history and physical examination for all patients.

Data collection: Data were collected by self administered questionnaire. This was constructed in sections to address the different aspects of the study including risk factors for developing CLD, in the following orders:-

- 1) Personal data.
- 2) Presentation.
- 3) Past history.
- 4) Physical examination.
- 5) Investigations.

The following investigations were done: - FBC, LFTs, Blood urea, RBS, U/S scan Abdomen, MRI, EEG, NCS, EMG, serum ceruloplasmin and alpha fetoprotein when indicated. All collected data was finally entered the computer using statistical package program for social science (SPSS) to analyze the data.

Results: Sixty eight (70.8%) patients were males with male to female ratio of 2.5:1. The age of patients on presentation was ranging from 18 years to 80 years with mean age of 52.3.

Thirty one patients (32.3%) were from Khartoum area, 29 (30.2%) from Algezira, 12 (12.5%) from the West, 10 from White Nile, while only 3 patients were from Blue Nile.

The main CLD symptoms were found as follows: abdominal pain was observed in 50 (52.1%) patients, abdominal distention in 44 (45.8%), yellowish discoloration of the sclerae in 26 (27.1%), vomiting of blood in 24 (25%), black stool in 23 (24%), lower limbs swelling in 13 (13.5%), itching in 2 (2.1%), while 5 (5.2%) patients were asymptomatic. Twenty-two (22.9%) patients had intellectual impairment, 21 (22.9%) had personality changes, 21

(22.9%) had impaired level of consciousness (Table 1).

Table 1: Neurological symptoms among 96 Sudanese patients with CLD.

%	Number of patients	Presenting neurological symptoms
22.9%	22	Intellectual impairment
21.9%	21	Personality changes
21.9%	21	Impaired level of consciousness
12.5%	12	Sleep abnormality
9.4%	9	Speech abnormality
8.3%	8	Sphincteric symptoms
8.3%	8	Motor symptoms
6.3%	6	Un steadiness
5.2%	5	Convulsion
2.1%	2	Sensory symptoms
44.8%	43	No symptoms

The study showed that forty six patients (47.9%) had past history of jaundice, 31 (32.3) had past history of intestinal schistosomiasis, past history of surgical operations was detected in 18 (18.8%), 7 (7.3%) had past history of blood transfusion and 21 patients (21.9%) had no relevant past history. It was observed that 23 patients were alcohol consumers. Abdominal examination revealed abdominal distention in 73 (76%) patients, surgical scars in 11 (11.5%), loss of pubic hair in 35 (36.5%), dilated veins in 24 (25%), 25 (26%) had abdominal tenderness, splenomegally was observed in 71(74%), shrunken liver in 83 (86.5%), hepatomegally in 7 (7.3%), normal liver span in 6 (6.3%), 74 (77.1%) had ascites, venous hump was hearted in 5 (5.2%) while hepatic bruit was detected in 4 patients.

Regarding extra abdominal manifestations of CLD, 17 patients had parotid enlargement, 12 had finger clubbing, 9 had gynaecomastia, 4 had palmer erythema, 3 had dupuytren contractions, 2 leuconaeikia, one had breast atrophy while 61 patients had no extra abdominal manifestations. Nervous system examination revealed no abnormality in 52 patients, 28 had impairment of higher function, 8 had motor signs, 5 had cerebellar signs, 4 had cranial nerves palsies, 3 had parkinsonian signs and 2 patients had sensory signs (peripheral neuropathy). Twenty three patients were disoriented, loss of concentration was seen in 14 (14.6%), impaired consciousness in 14 (14.6%), mood disturbance in 13 (13.5%), memory disturbance in 9 (9.4%), speech disorders in 8 (8.3%), reduced intelligence in 6 (6.3%)

while constructional apraxia was demonstrated in 8 patients (Table2).

Table 2: CNS examination findings among 96 Sudanese patients with CLD

%	Number of patients	CNS examination findings
%54.2	52	No abnormalities
29.2%	28	Higher function
%4.2	4	Cranial nerves
%8.3	8	Motor signs
%2.1	2	Sensory signs
%5.2	5	Cerebellar signs
%3.1	3	Parkinsonian signs

The liver function tests showed that eighty three patients had serum albumin level below 3.5 mg/dl, 7 had high SGOT, 6 had high SGPT and only 4 patients had high ALP. Ultra-sound examination findings were as follows: liver cirrhosis was detected in 90 patients, splenomegally in 83, ascites in 77, shrunken liver in 75, PPF in 23, hepatomegally in 12 while HCC was

detected in 12 patients.

Regarding the pattern of CLD distribution among our studied group, sixty percent had liver cirrhosis, 24% had cirrhosis with PPF, 11.5% had HCC on top of cirrhosis, 2.1% had Wilson's disease and 1% had HCC. The prevalence of neurological complications among our study group can be seen in Table 3.

Table 3: Neurological complications among 96 adult Sudanese patients with CLD.

%	Number of patients	Neurological complications
54.2%	52	No encephalopathy
8.3%	8	Grade I encephalopathy
6.3%	6	Grade I I encephalopathy
9.4%	9	Grade I I I encephalopathy
6.3%	6	I V encephalopathy Grade
4.2%	4	Para paresis
3.1%	3	Hemiplegia
3.1%	3	Cerebellar
%2.1	2	Cerebellar + Parkinsonism
1%	1	Parkinsonism
%1	1	Hemiplegia + P neuropathy
%1	1	Peripheral neuropathy
100%	96	Total

Discussion

The study showed that males are affected more than females, this is similar to what was described by Strauss, but it differs from what was mentioned by Pereira, where there was no gender variation.⁽¹³⁻¹⁴⁾ The male predominance is due to the fact that, twenty three of our male patients used to consume alcohol while no females used to consume alcohol, as we know that alcohol consumption is considered as one of the major cause of CLD in addition to viral hepatitis and autoimmune hepatitis.^(15,16,17) The age of our patients on presentation was ranging from 19 to 80 years and most of them were 40 years and above, this is similar to what was mentioned in the literature. This is due to the fact that most of the etiological factors take time to cause CLD.^(18,19) Most of our patients were from Khartoum and Algezira, this is due to the fact that the study was conducted at Khartoum area and as we know, the incidence of PPF in Algezira is very high. It appeared that abdominal pain and distention were the most common gastrointestinal symptoms among our patients, considerable number had yellowish discoloration of sclerae, hematemesis and malena and this is most probably due to late presentation of our patients. 47.5% of our patients had past history of jaundice while 31.3% had past history of intestinal schistosomiasis. The past history of jaundice reflects the previous exposure to liver disease such as viral hepatitis. The increased incidence of CLD in patients with intestinal schistosomiasis correlate with the study done by Zaki in Egypt which showed increased incidence of cirrhosis following hepatitis C infection in patients already having PPF secondary to intestinal schistosomiasis. Pereira also described the strong association between

hepatitis C infection and PPF, moreover Melo & Pereira described the same association between hepatitis B infection and PPF.^(20,21,22) Strikingly 18.8% of our patients had past history of surgical operations, this raise the possibility of hepatitis transmission (B&C) through contamination as mentioned by Prati and Kircheis.^(23,24) The study revealed that shrunken liver, splenomegally, ascites and abdominal distention were the most important clinical signs detected on abdominal examination. The high percentage of signs of CLD in our patients may be due to the fact that Ibn Sina is a tertiary hospital, most of the patients referred from different areas and they came late. Regarding extra abdominal examination, most of the patients had no stigmata of CLD (63.5%), while parotid enlargement (17.7%), finger clubbing (12.5%) and gynaecomastia (9.4%) were the most important signs. The study showed that intellectual impairment, personality changes and impaired level of consciousness were the most common neurological symptoms while sensory symptoms were the least (2.1%). This is similar to what was mentioned by Zaki in Egypt.⁽²⁰⁾ Regarding the nervous system examination, 54.2% of our patients had no positive findings, in fact subclinical encephalopathy was not assessed in our study because it needs more complicated psychomotor tests. The higher functions involvement was the commonest neurological disorder associated with CLD, it is due to the fact that acute hepatic encephalopathy is the commonest neurological complication associated with CLD.^(25,26,27) Out of 96 patients with CLD, neurological manifestations were detected in 44, this is similar to what was mentioned in the literature, but it is less than what was

reported by Barbara, because subclinical encephalopathy was included in his study.^(28,29) Most of our patients had grade III & I encephalopathy, this is due to the fact that patients with CLD easily went to decompensation and encephalopathy when exposed to predisposing factors, part of which needs follow-up and patients education (e.g. GI bleeding & infections) needs facilities for prevention. The rest of neurological complications like cerebellar, hemiplegia, myelopathy, parkinsonism, and peripheral neuropathy were less common. Hemiplegia was found in 4 patients, 3 due to intra cranial hemorrhage and one due to infarction. As mentioned by Melato and Kiyohara, CLD is associated with hemorrhagic stroke, but the presence of infarction raise the possibility of other underlying causes.^(30,31,32) Paraparesis was found in 4.2% this is a little bit higher than what was reported by Weissenborn⁽³³⁾, the difference is due to the fact that 3 patients in our study had shunt surgery which associated with higher incidence of

myelopathy as mentioned in the literature.⁽³⁴⁻³⁵⁾ Parkinsonism was observed in 3.1%, this is less than the results obtained by Burkhardts and his colleagues, because they included only patients with clinically overt encephalopathy.⁽³⁶⁾ In our study parkinsonism was associated with cerebellar signs in 2 patients, this is more or less similar to Klos, Ahloskog study.⁽³⁷⁾

However, the typical MRI findings described by Spahr (signal hyper intensities primarily in the globus pallidus) was not detected in our patients.⁽³⁸⁾ Three patients had cerebellar disease, two of them had Wilson's disease. Peripheral neuropathy was observed in 2 patients, it can be due to alcohol consumption rather than part of complication of CLD as mentioned in the literature.^(39,40)

In conclusion intellectual impairment and personality changes were the most common neurological symptoms. Acute hepatic encephalopathy was the commonest form of neurological complications (30.2%) in our studied group.

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