Normalization of the Psychometric Encephalopathy Score in Cameroonian Population

Larissa Pessidjo Djomatcho

University of Yaounde I Faculty of Medicine and Biomedical Sciences: Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales

Mathurin Kowo (✉ kowomathurin@yahoo.fr)

faculty of medicine and biomedical sciences university of yaounde 1 <https://orcid.org/0000-0001-9055-6165>

Antonin Ndjitoyap Ndam

University of Yaounde I Faculty of Medicine and Biomedical Sciences: Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales

Sylvain Raoul Simeni Njonou

faculty of Medecine and Pharmaceutical Sciences University of Dschang

Gabin Ulrich Kenfack

University of Yaounde I Faculty of Medicine and Biomedical Sciences: Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales

Firmin Ankouane Andoulo

University of Yaounde I Faculty of Medicine and Biomedical Sciences: Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales

Servais Fiacre Eloumou Bagnaka

University of Douala Faculty of Medicine and Pharmaceutical Sciences: Universite de Douala Faculte de Medecine et Sciences Pharmaceutiques

Winnie Tatiana Bekolo

University of Douala Faculty of Medicine and Pharmaceutical Sciences: Universite de Douala Faculte de Medecine et Sciences Pharmaceutiques

Agnès Malongue

Douala General Hospital

Isabelle Dang Babagna

Cathedral Medical Center Yaounde Cameroon

Magloire Biwolé Sida

university of Yaounde 1. Faculty of medicine and biomedical Sciences

Henry Luma

University of Yaounde 1. Faculty of Medicine and Biomedical Sciences

Oudou Njoya

Research article

Keywords: Cirrhosis, Minimal Hepatic Encephalopathy, Psychometric Tests, Sub-Saharan Africa, Cameroon

Posted Date: October 29th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-97727/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published at BMC Gastroenterology on July 12th, 2021. See the published version at <https://doi.org/10.1186/s12876-021-01858-7>.

Abstract

Background: Minimal hepatic encephalopathy (MHE) is the presence of neuropsychological abnormalities detectable by psychometric tests. Psychometric Hepatic Encephalopathy Score (PHES) is a gold standard test for the early diagnosis of MHE in cirrhotic patients.

Aim: To standardize the PHES in a healthy Cameroonian population and to evaluate the prevalence of MHE among cirrhotic patients.

Methods: This was a prospective, multicentric study from December 1st, 2018 to July 31st, 2019 in two groups: healthy volunteers and cirrhotic patients without clinical signs of hepatic encephalopathy. The results of the Number Connection Test-A (NCT-A), Number Connection Test-B (NCT-B), Serial Dotting Test (SDT), Line Tracing Test (LTT) were expressed in seconds and those of the Digit Symbol Test (DST) in points.

Results: A total of 102 healthy volunteers (54 men, 48 women) and 50 cirrhotic patients (29 men, 31 women) were included. The mean age was 38.1 ± 12.55 years in healthy volunteers and 49.3 ± 15.6 years in cirrhotic patients. The mean years of education level was 11.63 ± 4.20 years in healthy volunteers and 9.62 ± 3.9 years in cirrhotic patients. The PHES of the healthy volunteer group was -0.08 ± 1.28 and the cut-off between normal and pathological values was set at -3 points. PHES of the cirrhotic patients was -7.66 ± 5.62 points and significantly lower than that of volunteers ($p < 0.001$). Prevalence of MHE was 74% among cirrhotic patients. Age and education level were associated with MHE.

Conclusion: PHES cut-off value in Cameroonians is -3 , with MHE prevalence of 74% among cirrhotic patients.

Introduction

The notion of minimal hepatic encephalopathy (MHE) was developed for the first time in the 1970s when cirrhotic patients with normal physical examination had pathological neuropsychological tests [1, 2, 3]. MHE is the earliest form of hepatic encephalopathy characterized by neurocognitive, alertness and integrative function involvement [4]. Most at times it is not diagnosed at the beginning due to its subclinical nature whereas it alters quality of life, increases the risk of domestic and car accidents, predisposes to clinical hepatic encephalopathy and reduces life expectancy [2, 3, 5].

Psychometric Hepatic Encephalopathy Score (PHES) is a series of 5 psychometric tests recommended as a first line diagnostic tool for MHE [1]. These include Digit Symbol Test (DST), Number connection Test-A (NCT-A), Number connection Test-B (NCT-B), Serial Dotting Test (SDT), Line tracing Test (LTT). They assess psychomotor retardation, attention deficit and executive functions [6]. The PHES is expressed as the number of standard deviation (SD) in a population matched with respect to age and educational level.

Studies on MHE in Sub-Saharan Africa are scarce. In Cameroon, MHE is an entity which is not well known and scarcely assessed. The aim of this study was to standardize the PHES in a healthy Cameroonian population and to evaluate the prevalence of MHE among Cameroonian patients with liver cirrhosis.

Material And Methods

This was a prospective, multicentric and cross-sectional study from December 1st 2018 to July 31st, 2019 in two study populations. On one hand, healthy volunteers and on the other hand cirrhotic patients who did not show clinical signs of hepatic encephalopathy (HE). This study was carried out in 5 hospitals in the cities of Douala and Yaoundé (Douala General Hospital, Gynaeco-Obstetric and Paediatric Hospital Douala, Yaoundé Central Hospital, University Teaching Hospital Yaoundé, Yaoundé General Hospital).

Group of Healthy Volunteers

Persons present at the hospital for non-medical reasons were selected as healthy volunteers: Excluded from this group were persons with: a risky alcohol consumption in the last three months ($>30\text{g/day}$ in males and $>20\text{g/day}$ in females), chronic liver disease, psychiatric or neurologic disease, renal failure, heart failure, use of psychotic drugs. For each volunteer socio-demographic data (age, gender, level of education) and past medical history were recorded. The volunteers were grouped by age (20-29,30-39,40-49,50-59, $>60\text{years}$), gender and level of education (less than or equal to 5 years, 6-12 years, $>12\text{years}$).

Group of cirrhotic patients

The diagnosis of cirrhosis was based on clinical, biological, morphologic and endoscopic evidence of portal hypertension and liver failure or elastography criteria (Fibrosis score 4). For each cirrhotic patient, socio-demographic data (age, gender, level of education), past history (alcohol consumption, smoking, past history of hepatic encephalopathy, gastrointestinal bleeding, spontaneous bacteria peritonitis in the last three months, presence of hepatocellular carcinoma and psychiatric follow up) were recorded. Clinical data included signs of clinical hepatic encephalopathy: mental confusion, asterixis; signs of portal hypertension and chronic liver failure: jaundice, splenomegaly, hepatomegaly, ascites and pedal edema. Para-clinical data included complete blood count, serum albumin, total bilirubin, prothrombin time, international normalized ratio, etiology of cirrhosis, ultrasound evidence of cirrhosis, endoscopic evidence of portal hypertension (esophageal varices, gastric varices). Patients were classified either using Child or MELD (Model for End Stage Liver Disease) score [7].

Psychometric Tests:

All healthy volunteers and cirrhotic patients had a series of 5 psychometric tests made up of:

1. Number Connection Test-A (NCT-A): It consists in connecting numbers in an arithmetic order (1-25) as quick as possible. Time taken to complete the test and time taken to correct any errors is expressed in seconds.

2. Number Connection Test-B (NCT-B): It consists in linking of numbers and letters in an alternative manner (1-A, 2-B, 3-C). Time taken to complete the test and time taken to correct any errors is expressed in seconds.
3. Serial Dotting Test (SDT): It consists in making dots at the centre of 10 circles as fast as possible from left to right. Time taken to complete the test and time taken to correct any errors is expressed in seconds.
4. Digit Symbol Test (DST): It consists in linking symbols to corresponding numbers as quick as possible. The time required to complete the test is 90 seconds. The result is expressed in points.
5. Line Tracing Test (LTT): It consists in drawing a dash between 2 lines 5mm apart without touching the borders as fast as possible. The LTT results is expressed in terms of time taken to complete the test (LTTt seconds) and error score (LTTe), $LTT = (1 + LTTe/100) \times LTTt$.

The tests were performed using a pencil. After an initial demonstration, participants performed the test following recommendations in a calm and lighted place between 8 AM to 3 PM.

The results of cirrhotic patients were compared to those of healthy volunteers with the same age and educational level. Test results of (NCT-A, NCT-B, SDT, LTT) found between the mean $\pm$ 1SD were given a score of 0 points. Those between the mean, +1SD and + 2SD were given a score of -1 point, those between the mean +2SD and +3SD were given a score of -2 points, those above the mean+3SD were given a score of -3. Test results with the mean less than -1SD were given a score of +1 points. SDT results found between the mean $\pm$ 1SD were given a score of 0 points. Test results found between the mean-1SD and -2SD, -2 and-3 SD and less than -3SD were respectively given -1, -2, -3 points. Test results greater than the mean +1SD were given a score of +1 point. PHES was the sum of these 5 tests expressed in terms of the number of standard deviations. Patients were classified as having MHE when their PHES was less than -3.

Statistical analysis

Data was analysed using Statistical Package for Social Sciences (SPSS Inc, Chicago, Illinois, USA) version 23.0. Depending on quantitative data distribution, they were expressed as mean $\pm$ SD or median and interquartile range. Categorical data was expressed as numbers and proportions. Means and medians were compared using the *t* test and the Mann-Whitney *U*-test respectively. Proportions were compared using the chi-squared test or Fisher's exact test. Levene's test was used in the evaluation of differences in variance. Non-parametric tests were applied if homogeneity of variance assumptions were not met. The Shapiro–Wilk test was performed to test the hypothesis that the variables came from a normally distributed population. The regression equations were used to calculate scores for individual tests. Correlations were tested with Pearson's *r* or Spearman's *R*, as needed. A two-sided *P* value < 0.05 was considered significant.

Results

Standardization sample

One hundred and two healthy volunteers were enrolled, including 54 males (52.90%) and 48 females (48.10%). The mean age was 38.1 ± 12.55 years (range 20–72 years). The mean number of years of study was 11.63 ± 4.20 years (range 4–22 years). Data are summarized in Table 1.

Table 1
Distribution of volunteers (n = 102) in relation to age classes

Age	Gender (male/female)	Education (years, mean $\pm$ SD, range)
[20–30[years (n = 29)	18 (62.1%)/11 (37.9%)	12 ± 4 (7–21)
[30–40[years (n = 31)	16 (51.6%)/15 (48.4%)	13 ± 5 (4–22)
[40–50[years (n = 19)	8 (42.1%)/11 (57.9%)	11 ± 3 (5–16)
[50–60[years (n = 17)	9 (52.9%)/8 (47.1%)	10 ± 4 (4–15)
[60–72] years (n = 6)	3 (50%)/3 (50%)	6 ± 2 (4–6)

The results of NCT-A, NCT-B, SDT, DST, LTT tests were respectively 85.14 ± 30.78 seconds; 120.33 ± 64.63 seconds; 73.56 ± 20.55 seconds; 34.47 ± 10.40 points; 109.83 ± 33.93 seconds.

Age and education were significantly correlated with all test performance except for LTT with age (Table 2).

Table 2
Correlations between single psychometric tests results and PHES and studied variables in standardization sample subjects (n = 102)

	Age (years)	Education (years)
NCT-A	r = 0.30 (p = 0.002)	r = -0.67 (p < 0.001)
NCT-B	r = 0.33 (p = 0.001)	r = -0.70 (p < 0.001)
DST	r = -0.50 (p < 0.001)	r = 0.71 (p < 0.001)
LTT	r = 0.17 (p = 0.08)	r = -0.44 (p < 0.001)
SDT	r = 0.29 (p = 0.003)	r = -0.42 (p < 0.001)
PHES	r = -0.49 (p < 0.001)	r = 0.70 (p < 0.001)

After multivariate analysis, predictive equations were parameterized on age and education to compute the standard deviations and to calculate scores for each test (Table 3).

Table 3
Predictors of psychometric tests on multivariate analysis (multiple regression models)

Test	Equation	SD
NCT-A	$125.62 + 0.3 \times \text{age} - 4.47 \times \text{education}$	11.69
NCT-B	$159.82 + 1.39 \times \text{age} - 7.96 \times \text{education}$	24.65
SDT	$78.89 + 0.35 \times \text{age} - 1.6 \times \text{education}$	9.39
LTT	$150.02 + 0.11 \times \text{age} - 3.82 \times \text{education}$	15.10
DST	$23.40 - 0.20 \times \text{age} + 1.63 \times \text{education}$	3.24

The mean PHES score in volunteers was -0.08 ± 1.28 (range - 3 to + 4) points. The limit between normal and pathologic PHES was calculated at mean-2SD and was set at -3 points. MHE was diagnosed at PHES score less than - 3 points. In the healthy volunteer group, the score PHES was correlated with education years and age (Table 2). There was no association between each test or PHES score with gender (p $\geq$ 0.05).

Phes Results In Patients With Cirrhosis

We recruited 70 cirrhotic patients among which 20 were excluded due to one or more exclusion criteria; illiterate (10), hepatocellular carcinoma (6), visual impairments (4). Fifty patients without clinical evidence of HE were retained including 29 males (58%) and 21 females (42%). Characteristics of cirrhotic patients are described in Table 4.

Table 4
Characteristics of cirrhotic patients

Variables	Patients with cirrhosis
Age (Years, mean $\pm$ SD, range)	49.3 $\pm$ 15.6 [21–78] (n = 50)
Gender (male/female)	29 (58%)/21 (42%)
Education (years, mean $\pm$ SD, range)	9.62 $\pm$ 3.9 (2–19) (n = 50)
Aetiology of cirrhosis	
Viral hepatitis B	33 (66%)
Viral hepatitis C	17 (34%)
Child-Pugh class	
A	26 (60.5%)
B	12 (27.9%)
C	5 (11.6%)
MELD score (score, mean $\pm$ SD, range)	10.7 $\pm$ 3.5 (6–18) (n = 22)
Ascites (yes/no)	17 (34%)/33 (66%)
Jaundice (yes/no)	9 (18%)/41 (82%)
Previous spontaneous bacterial peritonitis (yes/no)	1 (2%)/49 (98%)
Previous overt HE (yes/no)	1 (2%)/49 (98%)
Previous GI tract hemorrhage (yes/no)	8 (16%)/42 (84%)
Creatinine (mg/dl, mean $\pm$ SD, range)	9.1 $\pm$ 3 (3-17.5) (n = 42)
INR (Median, IQR)	1.19 [1.0-1.8] (n = 20)
Albumin (g/l, mean $\pm$ SD, range)	34.4 $\pm$ 7 (19–45) (n = 26)

MELD, model of end-stage liver disease; HE, Hepatic encephalopathy

Variables	Patients with cirrhosis
Bilirubin (mg/dl, Median, IQR)	9.4 [1.1–68.0] (n = 31)
ALT (IU/L, Median, IQR)	35.5 [11–155] (n = 32)
MELD, model of end-stage liver disease; HE, Hepatic encephalopathy	

NCT-A, NCT-B, SDT, DST, LTT means values were respectively 164.72 ± 169.93 seconds; 255.96 ± 203.69 seconds; 150.26 ± 93.26 seconds; 22.62 ± 11.36 points; 183.03 ± 134.54 seconds. The mean PHES in the cirrhotic group was -7.66 ± 5.62 (range - 14 to + 3). Thus, we had a prevalence of 74% (37/50) for minimal hepatic encephalopathy in cirrhotic patients. Patients with abnormal PHES score were older and less educated than normal subjects (Table 5 and Fig. 1). We did not observe any significant correlation between PHES score and biological parameters: ALAT, bilirubin, prothrombin time, albumin, creatinine, INR, platelets ($p \geq 0.05$). Comparisons of clinical and biochemical data of patients with normal and pathological PHES is presented in Table 5. We found significant difference in PHES score between cirrhotic patients and normal participants ($p < 0.001$).

Table 5
Clinical and biochemical data of cirrhotic patients with MHE and no MHE

Demographic data	MHE	No MHE	OR [95% CI]	p value
Age (Years, mean $\pm$ SD)	54.3 $\pm$ 13.9 (n = 37)	35.2 $\pm$ 10.9 (n = 13)	/	< 0.001
Male gender	20 (54.1%)	9 (69.2%)	0.52 [0.1- 2.0]	0.51
Education (Years, mean $\pm$ SD)	7.9 $\pm$ 2.8 (n = 37)	14.3 $\pm$ 2.0 (n = 13)	/	< 0.001
CHILD-PUGH B/C	15 (48.4%)	2 (16.7%)	4.68 [0.8– 24.9]	0.08
A	16 (51.6%)	10 (83.3%)	1	1
Jaundice (Yes/no)	8 (21.6%)	1 (7.7%)	3.31 [0.3– 29.4]	0.41
Ascites (Yes/no)	14 (37.8%)	3 (23.1%)	2.02 [0.4– 8.6]	0.49
Previous GI hemorrhage (Yes/no)	6 (16.2%)	2 (15.4%)	1.06 [0.1- 6.0]	1.00
MELD score (Score, mean $\pm$ SD)	11.6 $\pm$ 3.7 (n = 15)	8.8 $\pm$ 2.6 (n = 7)	/	0.09
INR (Median, IQR)	1.2 [1.0-1.8] (n = 13)	1.1 [1.0-1.6] (n = 7)	/	0.75
Albumin (g/l, mean $\pm$ SD)	33.8 $\pm$ 7.0 (n = 21)	36.8 $\pm$ 7.3 (n = 5)	/	0.41
Creatinin (mg/dl, mean $\pm$ SD)	9.4 $\pm$ 3.4 (n = 31)	8.5 $\pm$ 1.8 (n = 11)	/	0.40
Prothrombin time (%)	65.7 $\pm$ 18.7 (n = 30)	59.6 $\pm$ 13.7 (n = 10)	/	0.35
Bilirubin (mg/dl, Median, IQR)	8.7 [1.1–68.0] (n = 24)	10.0 [8.0–41.0] (n = 7)	/	0.14
ALAT (IU/L, Median, IQR)	33 [15–155] (n = 20)	46 [11–76] (n = 12)	/	0.34

Demographic data	MHE	No MHE	OR [95% CI]	p value
Platelets (/ml, Median, IQR)	110.10 ³ [15.10 ³ - 421.10 ³] (n = 37)	91.10 ³ [42.10 ³ - 300.10 ³] (n = 12)	/	0.81

In patients with cirrhosis, we calculated PHES using the Spanish reference data

Using the online PHES score calculator for Spanish population available on www.redeh.org, we calculated PHES score for each cirrhotic patient and compared the obtained values with Cameroonians values. We found a correlation between the two scoring systems ($r = 0.36$; $p = 0.01$, Fig. 2)

Discussion

Minimal hepatic encephalopathy is the earliest form of hepatic encephalopathy. It alters quality of life, increases the risk of domestic and car accidents. Its diagnosis requires altered psychometric tests with normal clinical examination [2, 3]. The aim of this study was to standardize the PHES in a healthy Cameroonian population and to evaluate the prevalence of MHE among Cameroonian patients with liver cirrhosis. In order to achieve our objectives, we carried out a cross sectional prospective and multicentric study in two groups. This study showed that the PHES was significantly lower among cirrhotic patients than in health volunteers. The prevalence of MHE was 74% among cirrhotic patients. Age and education level were found to be associated with MHE in our study population.

We included 102 healthy volunteers including 52.9% males and 47.1% females in order to obtain normal values for the tests of the PHES among Cameroonian population. The mean age of healthy volunteers was 38.1 ± 12.5 years with a range (20–72) years. The mean number of years of study was 11.6 ± 4.2 years with extremes (4–22) years. These results are similar to those of Li et al. in China who found a male predominance of 67.8% with a mean age of 37.3 ± 10.5 years and mean number of years of study of 12 ± 4 years [9]. Coskun et al. in Turkey also found a male predominance of 51.6% with a mean age of 46 ± 10.30 years and mean number of years of study of 8.60 ± 3.03 years slightly lower than ours [10]. Seo et al. in Korea found an equal gender distribution (50%), mean age of 41.2 ± 12.9 years and a mean number of years of study 12.60 ± 3.10 years close to ours [11]. Badea et al. in Romania found a female predominance (53.5%), a mean age of 48.73 ± 14 years and a mean number of years of study of 12.37 ± 3.15 years [12]. All these differences could be explained by the sociocultural diversities of the different populations studied.

PHES has been validated in several countries including Germany, Spain, Italy, South Korea, Poland, India, Mexico and China and is globally influenced by age and level of education [1]. In this study, age and education were significantly correlated with all test performance except for LTT with age. The interpretation of the LTT test results is different from one study to another. This result could be explained

by the younger age of the volunteers and, the LTT examines visuomotor and visuospatial skills with attention given to speed and accuracy.

The mean results of NCT-A, NCT-B, SDT, DST, LTT tests were respectively 85.14 ± 30.78 seconds; 120.33 ± 64.63 seconds ; 73.56 ± 20.55 seconds ; 34.47 ± 10.40 points ; 109.83 ± 33.93 seconds. The mean PHES score in volunteers was -0.08 ± 1.28 points with extremes of (-3, + 4). Li et al. found mean results for NCT-A, NCT-B, SDT, DST, LTT tests respectively at 38.29 ± 13.69 seconds, 55.85 ± 17.80 seconds, 38.03 ± 5.77 seconds, 55 ± 14.30 points and 33.29 ± 8.29 seconds. The mean PHES score -0.6 ± 3.7 points [9]. Badea et al. found a mean PHES score of -0.23 ± 2.08 points while Seo et al. found a mean PHES score of -0.31 ± 2.06 [11, 12]. All these authors found age and level of education to influence psychometric tests results. This is consistent with our findings and could be explained by a decline in cognitive function with age and a certain degree of cognitive incapacity associated with low level of education.

We equally included 50 cirrhotic patients. Their mean age was 49.3 ± 15.61 years (21–78) with a male predominance (58%). The mean number of years of study was 9.62 ± 3.90 years (2–19). These findings are similar to those of Li et al. who included 53 patients with cirrhosis with a mean age of 45.0 ± 8.20 years, a male predominance (94.3%) and a mean number of years of study of 8.20 ± 3.60 years [9]. Coskun et al. included 60 cirrhotic patients with a mean of 54.20 ± 8.30 years and a mean number of years of study of 6.20 ± 2.50 years [10]. The few numbers of patients with cirrhosis included in these studies could be explained by the numerous exclusion criteria while the difference in mean ages could be explained by the difference in the aetiologies of cirrhosis which vary from one population to another.

The cut-off between the normal and pathologic values of the PHES was set at -4 according to the lower boundary of the 95% range between + 2 and - 2 SD [1, 7, 9, 13–14]. In our study we considered the same methodology and we found that the lower limit was set at -3 points. MHE was diagnosed at a PHES score less than - 3. The high cut-off value in this study may be due to the younger age of the population, the fact that most of them came from urban areas and probably the socio-cultural difference compared to other countries. We found 34 cirrhotic patients with a PHES score less than - 3 points giving a 74% prevalence for MHE in this population. Lower prevalences have been reported by Yoshimura et al., in Japan (46.15%) [5], Ennaifer et al., in Tunisia (44.4%) [13], Bale et al. (52.4%) and Dhiman et al. (48%) in India [14, 15]. This higher prevalence in our study could be explained by the age, the lower level of studies and the signs of decompensated cirrhosis which were more important in patients with MHE.

Among the patients with MHE, the mean age was 54.3 ± 13.9 years, with a male predominance (54.1%) and the mean number of years of study was 7.9 ± 2.8 years. When the two groups of cirrhotic patients with and without MHE was compared, MHE was found to be associated with age ($p \leq 0.001$) and number of years of study ($p \leq 0.001$). We didn't find any correlation between gender, Child Pugh score, MELD score, aetiology of cirrhosis and the onset of MHE. Several studies suggest that the level of education and Child Pugh score influence the onset of MHE. Coskun et al. found the number of years of study ($p \leq 0.03$) and Child score ($p \leq 0.03$) to be independently associated with MHE [10]. Seo et al. found the number of years of study, Child score and serum ammonia levels to be associated with the onset of MHE [11]. Bale et al.

reported Child score as the only variable associated with onset of MHE [14]. Li et al. found that the higher the Child score, the higher the number of cases of MHE [9]. Ennaifer et al. found a MELD score ≥ 15 as the only independent variable associated with the onset of MHE [13]. However, we noticed that more than half of patients with MHE was Child Pugh A in the group of patients with MHE. Through this observation, even cirrhotic patients with child Pugh A should be screened for the diagnosis of MHE.

The results of this study which to the best of our knowledge is the first in Cameroon have to be analysed taking into consideration certain limits. Firstly, our population of cirrhotic patients was small due to our numerous exclusion criteria. Secondly due to the high cost of laboratory tests and the absence of universal health coverage in our setting, all laboratory tests (serum ammonia levels) couldn't be done reducing the quality of this study.

Conclusion

We standardized PHES in a Cameroonian population of healthy volunteers. This enabled us to make the diagnosis of MHE in 74% of cirrhotic patients with no clinical evidence of encephalopathy. Age and education level were identified as factors associated with MHE of this study. Cirrhotic patients with Child Pugh A should be screened for the diagnosis of MHE. Further studies on larger cohorts have to be done to confirm our results.

Declarations

Conflict of Interest

Authors declare no conflict of interest

What is known on the subject

- MHE is defined by the presence of neuropsychological anomalies diagnosed using psychometric tests in the presence of a normal clinical examination.
- It is the earliest form of hepatic encephalopathy characterized by impaired neurocognitive attention, alertness and integrative functions.
- It is rarely diagnosed due to its subclinical nature whereas it alters quality of life, increases the risk of car and domestic accidents and reduces life expectancy.

Novelty the topic brings

- The use of PHES score makes possible the diagnosis of MHE in Cameroon cirrhotic patients.
- A high prevalence of 74% of MHE was found.
- Age and fewer number years of study was found to be associated with the onset of MHE.

Ethics

This study received approval from the Institutional Review Board of the Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, number: 232/UYI/FMSB/VDRC/CSD. It was carried out following the declaration of Helsinki [8]. Patients were free to participate without any external pressure. An informed and written consent was obtained from each patient. There was no participant less than 16 in any of the groups.

Authors Contribution

Conception and study design: LPD, MPK, FAA, ON. Data collection: LPD, MPK, ANN, WTB, AM, IDB. Statistical analysis: SRSN, GUK. Administrative support: MBS, HL, ON. Data interpretation: LPD, MPK, SRSN, GUK, FAA, ON. Review of draft: SFEB, FAA, MBS, HL, ON. All the authors read and approved the manuscript.

Acknowledgements

We express gratitude to the healthcare workers in the various facilities in which the study was carried out.

References

1. Weissenborn K. Diagnosis of minimal hepatic encephalopathy. *J Clin Exp Hepatol*. 2015;5 (Suppl 1):S54–S59. [10.1016/j.jceh.2014.06.005](https://doi.org/10.1016/j.jceh.2014.06.005)
2. Jacques J, Carrier P, Debette-Gratien M, Sobesky R, Loustaud-Ratti V. Encéphalopathie hépatique. *Press Medicale*. 2016;45 (1):46–59. [10.1016/j.lpm.2015.02.021](https://doi.org/10.1016/j.lpm.2015.02.021)
3. Yoon Jeong J, Won Jun D, Bai D, Yean Kim J et al. Validation of a Paper and Pencil Test Battery for the Diagnosis of Minimal Hepatic Encephalopathy in Korea. *J Korean Med Sci*. 2017;32 (9):1484–90. doi: [10.3346/jkms.2017.32.9.1484](https://doi.org/10.3346/jkms.2017.32.9.1484)
4. Stinton LM, Jayakumar S. E. Minimal hepatic encephalopathy. *Can J Gastroenterol*. 2013;27 (10):572–574. doi: [10.1155/2013/547670](https://doi.org/10.1155/2013/547670)
5. Yoshimura E, Ichikawa T, Miyaaki H, Taura N et al. Screening for minimal hepatic encephalopathy in patients with cirrhosis by cirrhosis-related symptoms and a history of overt hepatic encephalopathy. *Biomed Reports*. 2016;5 (2):193–8. doi: [10.3892/br.2016.702](https://doi.org/10.3892/br.2016.702)
6. Weissenborn K, Ennen JC, Schomerus H, Rückert N, Hecker H. Neuropsychological characterization of hepatic encephalopathy. *J Hepatol*. 2001;34 (5):768–73. doi: [10.1016/s0168-8278\(01\)00026-5](https://doi.org/10.1016/s0168-8278(01)00026-5)
7. Peng Y, Qi X., Guo X. Child-Pugh Versus MELD Score for the Assessment of Prognosis in Liver Cirrhosis: A Systematic Review and Meta-Analysis of Observational Studies. *Med* 2016; 95 (8):1-29. doi:[10.1097/MD.0000000000002877](https://doi.org/10.1097/MD.0000000000002877)
8. Association Médicale Mondiale. Déclaration d'Helsinki de l'Association Médicale Mondiale: principes éthiques applicables aux recherches médicales sur des sujets humains. 2013. Disponible sur:

<https://www.wma.net/fr/policies-post/declaration-dhelsinki-de-lamm-principes-ethiques-applicables-a-la-recherche-medicale-impliquant-des-etres-humains/>. Consulté le 12/12/2019.

9. Li SW, Wang K, Yu YQ, Wang HB, Li YH, Xu JM. Psychometric hepatic encephalopathy score for diagnosis of minimal hepatic encephalopathy in China. *World J Gastroenterol*. 2013;19 (46):8745–51. doi: [10.3748/wjg.v19.i46.8745](https://doi.org/10.3748/wjg.v19.i46.8745)
10. Coskun BDO, Ngim OE, Gursoy S, Ozbakir OK et al. Normalization of the psychometric hepatic encephalopathy score for diagnosis of minimal hepatic encephalopathy in Turkey. *Niger J Clin Pract*. 2017;20 (4):421–6. doi:[10.4103/1119-3077.204375](https://doi.org/10.4103/1119-3077.204375).
11. Seo YS, Yim SY, Jung JY, Kim CH al. Psychometric Hepatic Encephalopathy Score for the detection of minimal hepatic encephalopathy in Korean patients with liver cirrhosis. *J Gastroenterol Hepatol*. 2012;27 (11):1695–704. Doi: [10.1111/j.1440-1746.2012.07217.x](https://doi.org/10.1111/j.1440-1746.2012.07217.x)
12. Badea MA, Drug VL, Dranga M, Gavrilescu O et al. Diagnosis of minimal hepatic encephalopathy in a tertiary care center from eastern Romania: validation of the psychometric hepatic encephalopathy score (PHES). *Metab Brain Dis*. 2016;31 (6) :1463–71. doi: [10.1007/s11011-016-9878-y](https://doi.org/10.1007/s11011-016-9878-y)
13. Ennaifer R, Cheikh M, Hefaiedh R, Romdhane H, Ben Nejma H, Hadj NB. Encéphalopathie hépatique minime : un diagnostic précoce pour améliorer le pronostic. *Presse Med*. 2014;43 (5) :27–33. doi: [10.1016/j.lpm.2013.09.016](https://doi.org/10.1016/j.lpm.2013.09.016)
14. Bale A, Pai CG, Shetty S, Balaraju G, Shetty A. Prevalence of and Factors Associated With Minimal Hepatic Encephalopathy in Patients With Cirrhosis of Liver. *J Clin Exp Hepatol*. 2018;8 (2) :156–61. doi : [10.1016/j.jceh.2017.06.005](https://doi.org/10.1016/j.jceh.2017.06.005)
15. Dhiman RK, Kurmi R, Thumburu KK, Venkataramarao SH et al. Diagnosis and Prognostic Significance of Minimal Hepatic Encephalopathy in Patients with Cirrhosis of Liver. *Dig Dis Sci* **55**, 2381–2390 (2010). doi : [10.1007/s10620-010-1249-7](https://doi.org/10.1007/s10620-010-1249-7)

Figures

$$y = -0,2391x + 4,1378$$

$$R^2 = 0,4408$$

$$y = 1,312x - 20,281$$

$$R^2 = 0,8286$$

Figure 1

Correlations between psychometric hepatic encephalopathy score (PHES) and age and education in patients with cirrhosis: age (A) and education (B)

$$y = 0,5248x - 3,3986$$

$$R^2 = 0.1606$$

Figure 2

Relationship between psychometric hepatic encephalopathy score (PHEs) calculated by Spanish and Cameroonian reference data in patients with cirrhosis (n =50)