



“A Study of Minimal Hepatic Encephalopathy in Patients with Cirrhosis of Liver – A Hospital Based Study”

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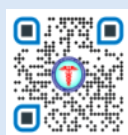
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ABSTRACT

Hepatic encephalopathy is a serious complication of chronic liver disease characterized by the presence of various states of altered mental status, ranging from mild alteration in sleep wake cycle to obtundation and deep coma.

Minimal hepatic encephalopathy is defined as early stage of hepatic encephalopathy without symptoms on clinical and neurological examination but with mild cognitive impairment and attention deficits.

Various combination of psychomotor test has been assessed for their use in diagnosis of minimal hepatic encephalopathy.

Aim: To study the Proportion of patients presenting with minimal hepatic encephalopathy in cirrhosis liver and also to find out the correlation between results of psychometric tests.

Result: Age Distribution of 120 patients showed majority of the patients were in age group of 31- 40 years and gender distribution showed 92.5% were males. Majority of the patients had alcoholic cirrhosis as the etiology (79.1%). Among the clinical features distension of the abdomen was the most common symptoms and among the clinical signs pallor (55%) was the most common, followed by splenomegaly (48.33%). On calculating Child Pugh's score it was seen that 44.17% patients were in Child Class B. Minimal hepatic encephalopathy was found to be highest in Child Pugh Class B (56.6%). Patients with minimal hepatic encephalopathy with gastro esophageal varices and was found to be statistically significant (P-value <0.001).

Conclusion: The single centered cross-sectional observational hospital-based study performed with 120 cases of cirrhosis of liver without overt hepatic encephalopathy showed majority of patients have abnormal psychometric test- number connection test (NCT A), digital symbol test etc.

Key Words: Minimal hepatic encephalopathy esophageal varices, Child Pugh.

INTRODUCTION

Hepatic encephalopathy is a serious complication of chronic liver disease which is characterized by presence of various states of altered mental status ranging from mild alterations in sleep wake cycle, changes in mood, forgetfulness to progressive degrees of lethargy, obtundation and deep coma that occurs due to portosystemic shunting which leads to accumulation of toxic materials and altered endogenous false neurotransmitters in the central nervous system.¹

Minimal hepatic encephalopathy (MHE) is defined as early stage of hepatic encephalopathy without symptoms on clinical/neurological examination but with mild cognitive symptoms and attention deficits that can be characterized by

response disinhibition, and with impairments of working memory and visuomotor coordination.³⁻⁵ These neurocognitive abnormalities are independent of sleep dysfunction or problems with overall intelligence² Ferenci et al, 2002. Bajaj et al 2009 suggested that these symptoms are considered to reduce the safety and Quality of life (QOL) of patients with cirrhosis and are considered to be a preclinical stage of overt Hepatic Encephalopathy. Minimal hepatic encephalopathy predicts the development of overt Hepatic encephalopathy and is associated with poor survival.⁶

There are no accurate data on the incidence of Hepatic Encephalopathy. However, several studies suggest that majority of patients with cirrhosis will develop some degree of hepatic encephalopathy at some point during the course of disease. Overt Hepatic Encephalopathy occurs in approximately 30% to 45% of cirrhotic patients.⁹⁻¹¹ Quero JC et al 1996, reported that the prevalence of Minimal Hepatic Encephalopathy has been found to vary between 10-40% in patients with cirrhosis of liver.¹²

The diagnostic approach to the assessment of Minimal Hepatic Encephalopathy is not uniform. Various combinations of psychometric test with or without neurophysiologic measures like EEG, Evoked Potential and Critical Flicker Frequency test have been assessed for their use in the diagnosis of Minimal Hepatic Encephalopathy.¹³

Hepatic encephalopathy is quite a common development in patients suffering from chronic parenchymal liver disease especially cirrhosis of liver which has a high incidence in our country.¹⁴ Hepatic encephalopathy is quite prevalent amongst the cirrhotic in the North-eastern part of the country.

BACKGROUND

Minimal hepatic encephalopathy is associated with impaired driving skills and increased risk of motor vehicle accidents and has been associated with increased hospitalizations and deaths. There is no single **gold standard test** for diagnosis of minimal hepatic encephalopathy, a combination of neuropsychological tests or psychometric hepatic encephalopathy score battery test and/or neurophysiological test is standard for diagnosis of minimal hepatic encephalopathy. It was found that, treatment for minimal hepatic encephalopathy improves neuropsychiatric performance and quality of life and decreases the risk of developing overt hepatic encephalopathy. The Psychometric Hepatic Encephalopathy score is composed of five tests, number connection test-A (NCT-A), number connection test-B (NCT-B), serial dotting test (SDT), line tracing test (LTT) and digit symbol test (DST). PHES can be used to assess motor speed, motor accuracy, concentration, attention, visual perception, visual-spatial orientation, visual construction and memory which are related to most of neuropsychological impairments in minimal hepatic encephalopathy. The PHES has been standardized in several countries, such as Germany, Italy, Spain, India, Korea and Mexico. Studies from India report a prevalence of 53%-62%. Prevalence of minimal hepatic encephalopathy is influenced by history of overt hepatic encephalopathy, severity of liver disease, age, alcoholic aetiology, and surgical portosystemic shunts. Furthermore, patients with minimal hepatic encephalopathy have a higher incidence of overt hepatic encephalopathy and mortality than those without minimal hepatic encephalopathy. Recognizing minimal hepatic encephalopathy at an early stage is important to initiate timely treatment to improve cognitive functions and prevent progression to overt hepatic encephalopathy. Diagnosis of minimal hepatic encephalopathy requires specialized neuropsychological and neurophysiological tests. As these are often impaired in patients with other causes of cognitive impairment, the minimal state examination (MMSE) is used for screening and excluding advanced cognitive impairment in high-quality studies before administering diagnostic tests for minimal hepatic encephalopathy is widely prevalent in patients with cirrhosis. Minimal hepatic encephalopathy is associated with impaired health-related quality of life, driving capability and can predict the development of overt hepatic encephalopathy. International consensus recommends use of the psychometric hepatic encephalopathy score (PHES) for diagnosing minimal hepatic encephalopathy.

AIMS AND OBJECTIVE

- To study the Proportion of patients presenting with minimal hepatic encephalopathy in cirrhosis of liver.
- To find out the correlation between results of psychometric tests.

MATERIALS AND METHODS

The present work **"A STUDY OF MINIMAL HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS OF LIVER – A HOSPITAL BASED STUDY."** At tertiary care hospital in Assam, consented consecutive patients attending the Department of Medicine diagnosed with cirrhosis of liver has been enrolled in the study. And the period of the study was one year duration. This was a cross sectional study, observational and hospital-based study, involving patients of cirrhosis of liver using primarily SMMSE along with two neuropsychological test, Number Connection Test (NCT-A) Digit Symbol Test (DST).

All the patients who had attended the Department of Medicine, of the tertiary care hospital Assam with the diagnosis of cirrhosis of liver were included in this study after fulfilment of inclusion and exclusion criteria.

Taking the prevalence of 70% of minimal hepatic encephalopathy in cases of cirrhosis of liver, with a relative precision of 15% at 95% confidence level, we calculated the sample size to be one hundred and twenty (120). A total of 120 patients who had attended the Department of Medicine, at the tertiary care hospital in Assam with Cirrhosis of liver has been selected for the study.

Every patient included in the study signed an informed consent form to undergo the Psychometric Tests. The study was approved by the Ethics Committee of the tertiary care hospital in Assam.

CRITERIA FOR INCLUSION:

- Age more than or equal to 18 years of age.
- Diagnosed as having cirrhosis of liver by history, clinical examination, laboratory investigations,
- ultrasonography abdomen and fibro scan of liver.

EXCLUSION CRITERIA:

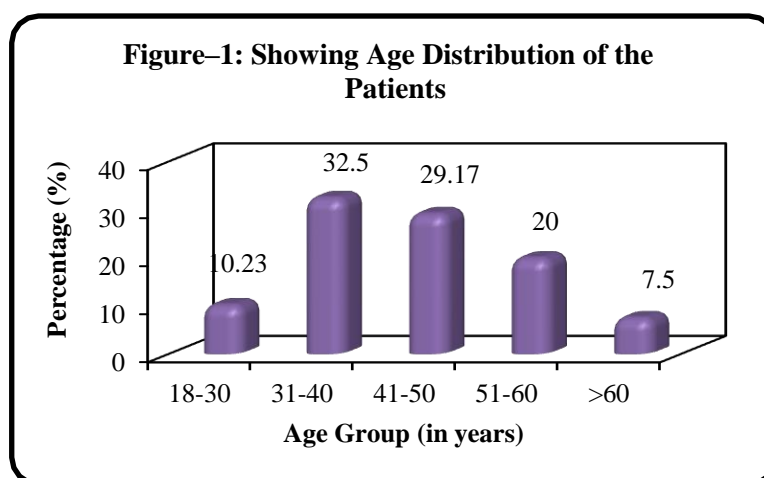
- Patient having overt hepatic encephalopathy.
- Presence of other psychiatric and neurological diseases causing cognitive dysfunction.
- Patient having difficulty in performing psychometric tests such as with bad vision.
- Patients on hepatotoxic drugs: like diclofenac, fluconazole, or ketoconazole, rifampicin, isoniazid, pyrazinamide, carbamazepine, ritonavir, nevirapine, amiodarone, and methotrexate.
- Patients with primary neoplasm and secondaries in liver recognised by ultrasonography.
- Patients who did not give consent for the study.

RESULT AND OBSERVATIONS

All cases included in the study after fulfillment of the inclusion and exclusion criteria's. were subjected to a thorough history, clinical examination and laboratory investigations as per the requirement. None of the patients had evidence of neurological and /or psychiatric abnormalities on global clinical examination.

Table 1: Age Distribution of the Patients

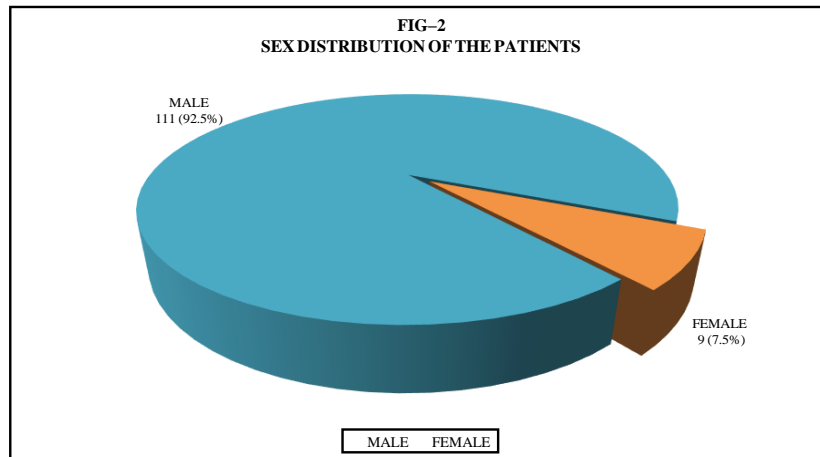
AGE GROUP (in years)	NUMBER (n)	PERCENTAGE (%)
18—30	13	10.83
31—40	39	32.50
41—50	35	29.17
51—60	24	20.00
>60	9	7.50
TOTAL	120	100.00



The study group comprised of 120 patients with mean age 44.19 ± 11.10 years, minimum age of 18 years and maximum of 70 years. In the case group majority were in the age group of 31—40 (n= 39).

Table 2: Sex Distribution of the Patients

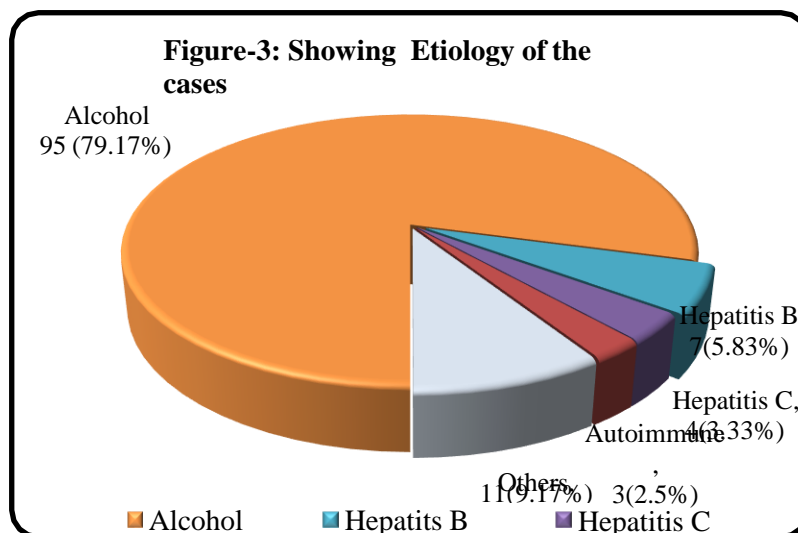
SEX	NUMBER (n)	PERCENTAGE (%)	RATIO (Male : Female)
Male	111	92.50	12.33 : 1
Female	9	7.50	
TOTAL	120	100.00	



It was observed that the study group 92.5 % (n=111) were males and 7.5% (n=9) were females. A male preponderance was observed.

Table 3: Etiology of the Cases

ETIOLOGY	NUMBER (n)	PERCENTAGE (%)
Alcohol	95	79.17
Hepatitis B	7	5.83
Hepatitis C	4	3.33
Autoimmune	3	2.50
Others	11	9.17
TOTAL	120	100.00

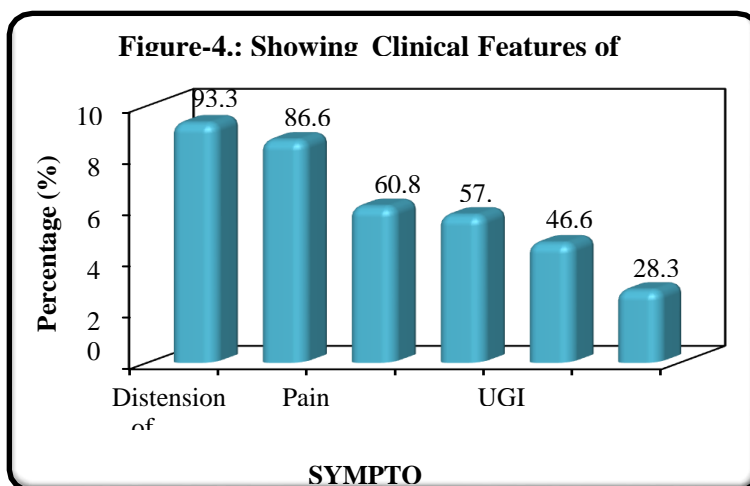


The maximum number of patients had alcoholic cirrhosis 95 (79.17%) followed by hepatitis B 7 (5.83%) and hepatitis C 4 (3.33%) and 3 (2.5%) patients had autoimmune hepatitis. Other 11 (9.17%)

Table 4: Clinical Features of the Cases

AETIOLOGY	
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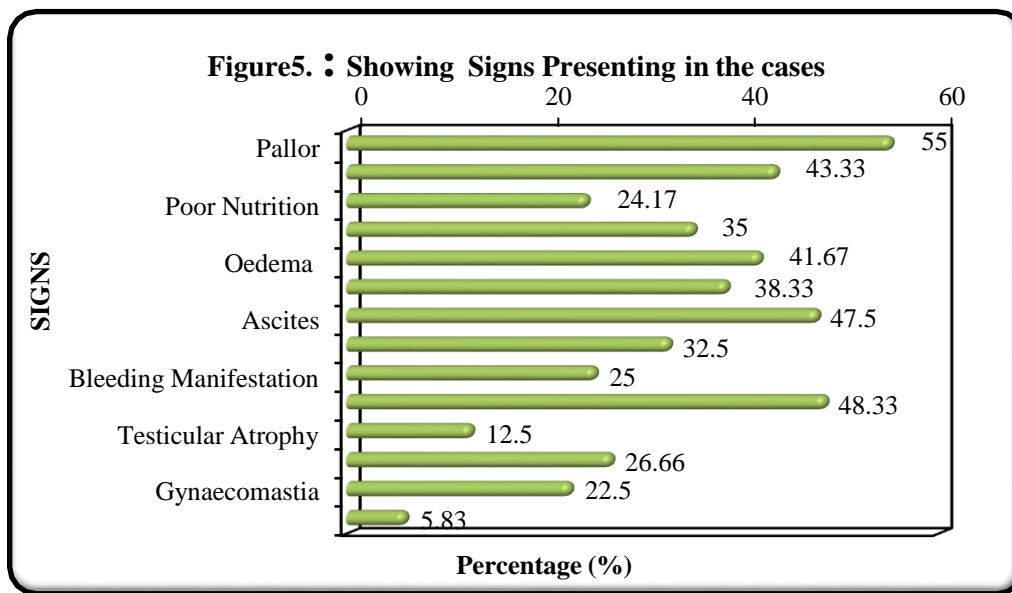
SYMPTOMS	AETIOLOGY					(n)	Total(%)
	Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others		
Distension of Abdomen	90	5	4	3	10	120	100%
Constitutional Symptoms	83	6	4	2	9	104	86.67%
Pain Abdomen	63	9	3	1	7	73	60.83%
Constipation	53	3	33	2	8	69	57.50%
UGI Bleed	48	2	2	1	3	56	46.67%
Jaundice	22	4	4	0	4	34	28.33%



Distension of abdomen (93.33%) was the most common symptoms followed by constitutional symptoms like easy fatigability, weakness, malaise, anorexia which were other symptoms frequently presented (86.67%).

Table 5: Signs Present in the Cases

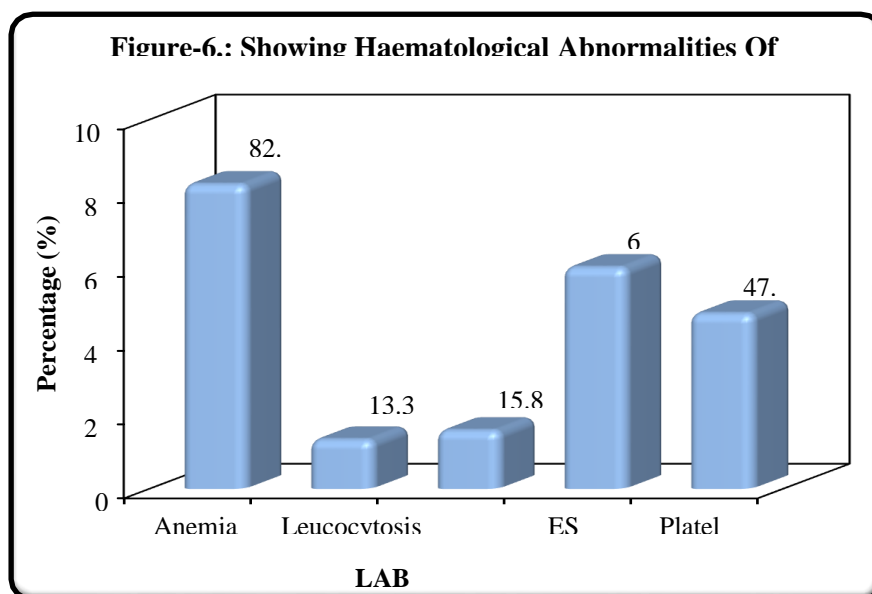
SIGNS	AETIOLOGY					Total(n)	Percentage(%)
	Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others		
Pallor	56	2	2	2	4	66	55.00%
Icterus	39	5	4	1	3	52	43.33%
Poor Nutrition	24	2	2	0	1	29	24.17%
Spider Naevi	35	4	3	0	0	42	35.00%
Oedema	37	2	4	2	5	50	41.67%
Palmar Erythema	37	2	3	1	3	46	38.33%
Ascites	40	5	3	3	6	57	47.50%
Pigmentation	32	2	2	1	2	39	32.50%
Bleeding Manifestation	23	2	2	1	2	30	25.00%
Splenomegaly	52	2	1	1	4	58	48.33%
Testicular Atrophy	14	0	1	0	0	15	12.50%
Hepatomegaly	27	2	1	1	1	32	26.66%
Gynaecomastia	25	0	1	0	1	27	22.50%
Caput Medusa	6	0	0	0	1	7	5.83%



Pallor was present in (55%) patients. Splenomegaly in (48.33%) Ascites (47.5%), Icterus (43.33%) Oedema (41.67%) poor Nutrition (24.7%), palmar erythema (38.33%), and Hepatomegaly were present in 26.66% patients.

Table 6: Haematological Abnormalities of the Patients

LAB TEST	AETIOLOGY					(n)	Total(%)
	Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others		
Anemia	82	5	3	3	6	99	82.50%
Leucocytosis	13	1	0	0	2	16	13.33%
Leucopenia	14	1	0	3	1	19	15.83%
Raised ESR	61	3	2	3	3	72	60.00%
Thrombocytopenia	49	2	2	2	2	57	47.50%



Anaemia (82.5%) was the most common haematological abnormality present in the study. Leucocytosis was present in (13.33%) of the patients whereas (15.83%) of the patients at Leucopenia. ESR was elevated in 60% of patients. Thrombocytopenia was present in (47.5%) patients.

Table 7: Biochemical Abnormalities in the Patients

LAB TESTS		AETIOLOGY					Total	
		Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others	n=120	(%)
Albumin	Normal	19	2	1	2	3	27	22.50
	Abnormal	76	55	3	1	8	93	77.550
TBIL	Normal	26	1	4	2	4	37	30.83
	Abnormal	69	6	0	1	7	83	69.17
AST	Normal	18	2	3	0	4	27	22.50
	Abnormal	77	5	1	3	7	93	77.50
ALT	Normal	37	1	2	1	5	46	70.00
	Abnormal	62	6	2	2	6	78	30.00
ALP	Normal	70	5	2	2	5	84	70.00
	Increased	25	2	2	1	6	36	30.00
GGT	Normal	23	5	1	2	4	35	29.17
	Increased	72	2	3	1	7	85	70.83
ProthrombinTime	Normal	32	2	1	3	6	44	36.67
	Increased	63	5	3	0	5	76	63.33

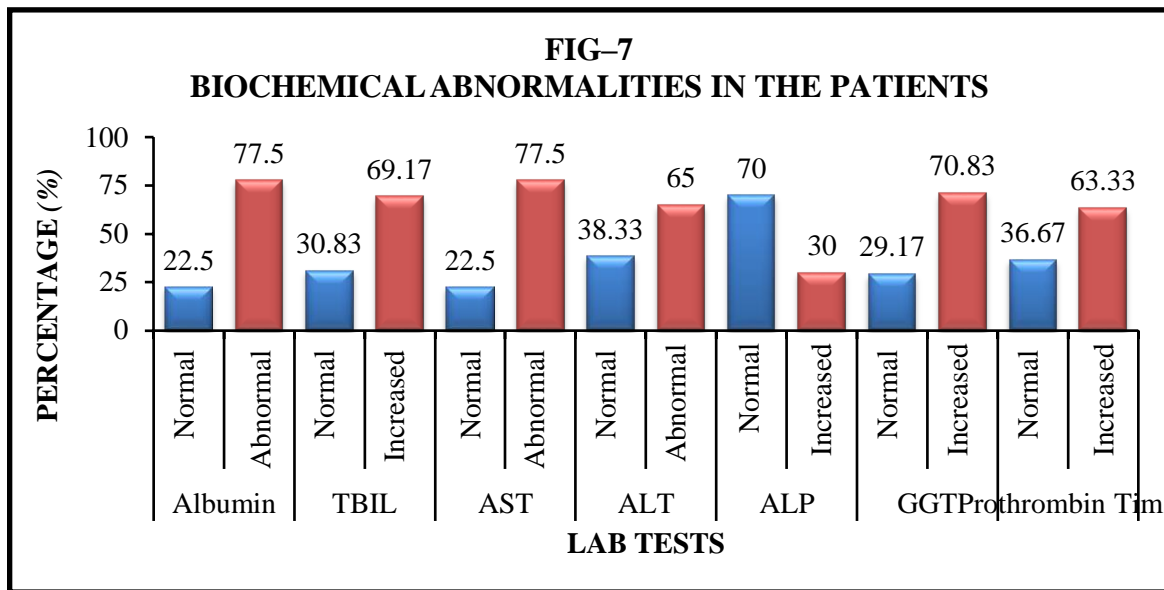
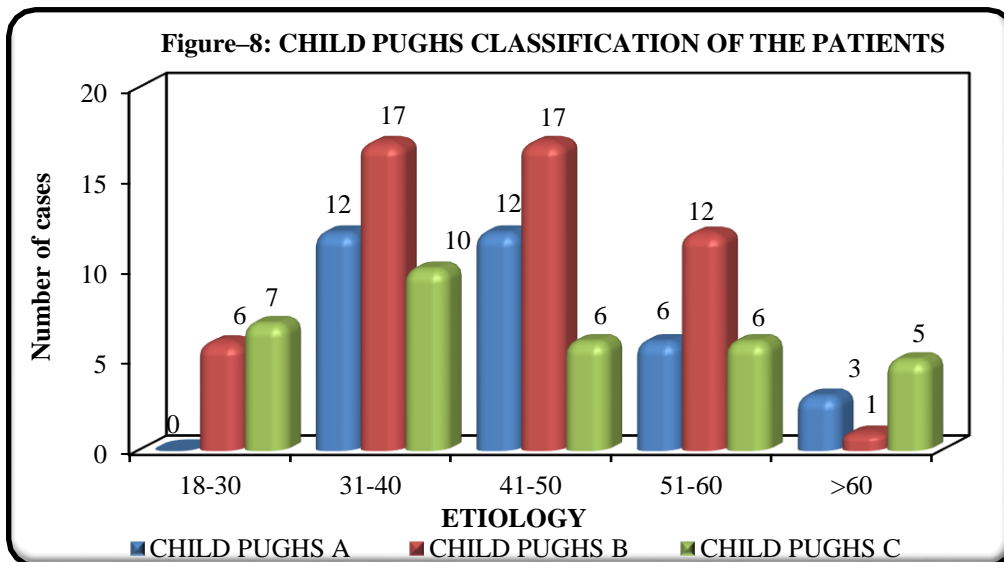


Table 8: Child Pughs Classification of the Patients

CHILD CLASS	AGE GROUP (in years)					TOTAL	
	18-30	31-40	41-50	51-60	>60	n	%
A	0	12	12	6	3	33	27.51
B	6	17	17	12	1	53	44.16
C	7	10	6	6	5	34	28.33
TOTAL	13	39	35	24	9	120	100%



Most of the patients were in Child Pugh's Class B (44.17%) followed by the Child Pugh's Class A (37.51%) and Child Class C (28.33%) respectively.

Table 9: Ultrasonography Findings in Patients

USG	AETIOLOGY						Total(%)
	Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others	(n)	
Chronic Hepatic Parenchymal Changes	91	4	3	3	10	111	100%
Splenomegaly	67	6	3	3	4	83	69.17%
Hepatomegaly	31	3	1	1	1	37	30.83%
Ascites	60	1	3	2	8	74	61.67%
Prominent Portal Vein	27	1	1	1	2	32	26.67%
Cholelithiasis	4	1	1	0	1	7	5.83%
Renal Stone	3	1	1	0	0	5	4.17%

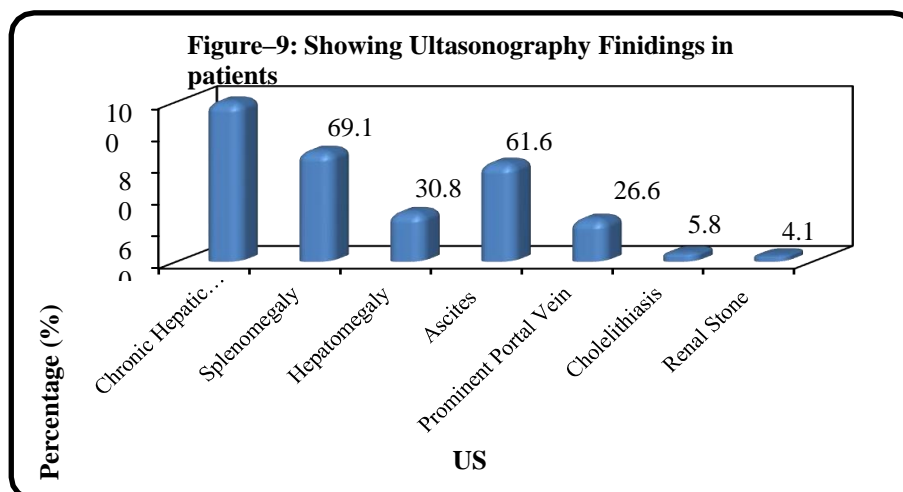
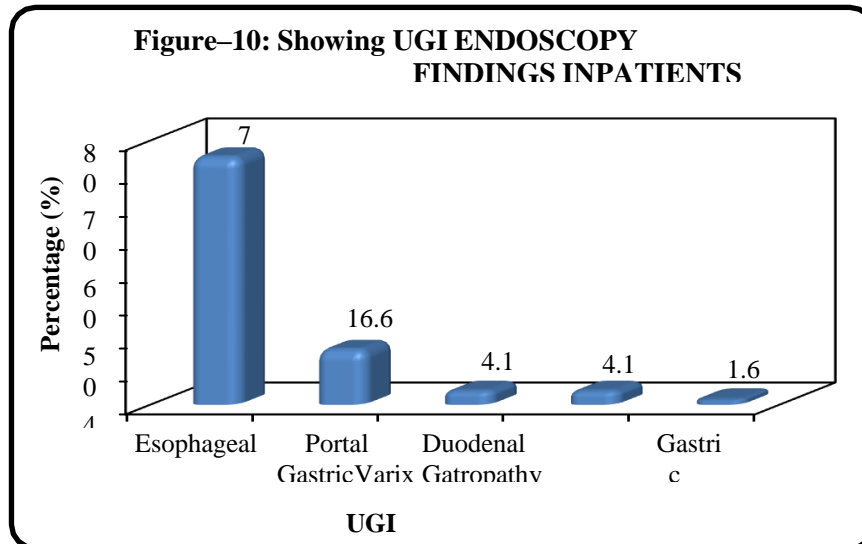


Table 10: Ugi Endoscopic Findings in Patients

UGI ENDOSCOPY	AETIOLOGY						Total(%)
	Alcohol	Hepatitis B	Hepatitis C	Autoimmune	Others	(n)	

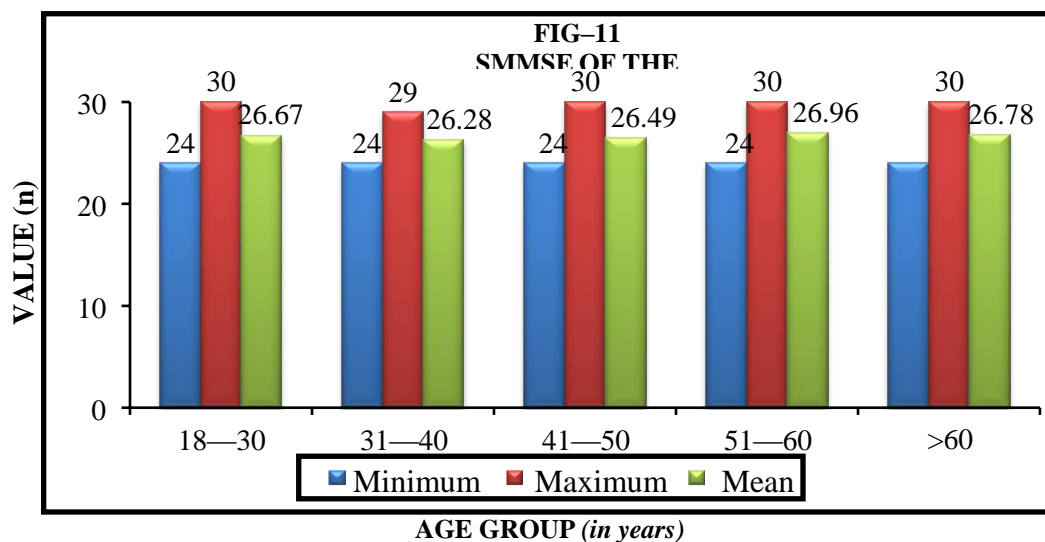
Esophageal Varix	72	6	4	2	6	90	75.00%
Portal Gatropathy	16	2	0	0	2	20	16.67%
Duodenal ulcer	4	1	0	0	1	6	4.17%
Gastric erosion	2	1	0	1	1	5	4.16%
Gastric ulcer	1	0	0	0	1	2	1.67%



Upper GI endoscopic findings had esophageal varices, in 75% patients, portalgastropathy presents in (16.67%).

Table 11: Table of Standardized Mini Mental Score

AGE GROUP (in years)	Minimum	Maximum	Mean	S.D.	Total (n=120)	Percentage (%)
18-30	24	30	26.67	1.88	13	10.835
31-40	24	29	26.28	1.34	39	32.50%
41-50	24	30	26.49	1.80	35	29.17%
51-60	24	30	26.96	1.94	24	20.00%
>60	24	30	26.78	2.39	9	7.50%

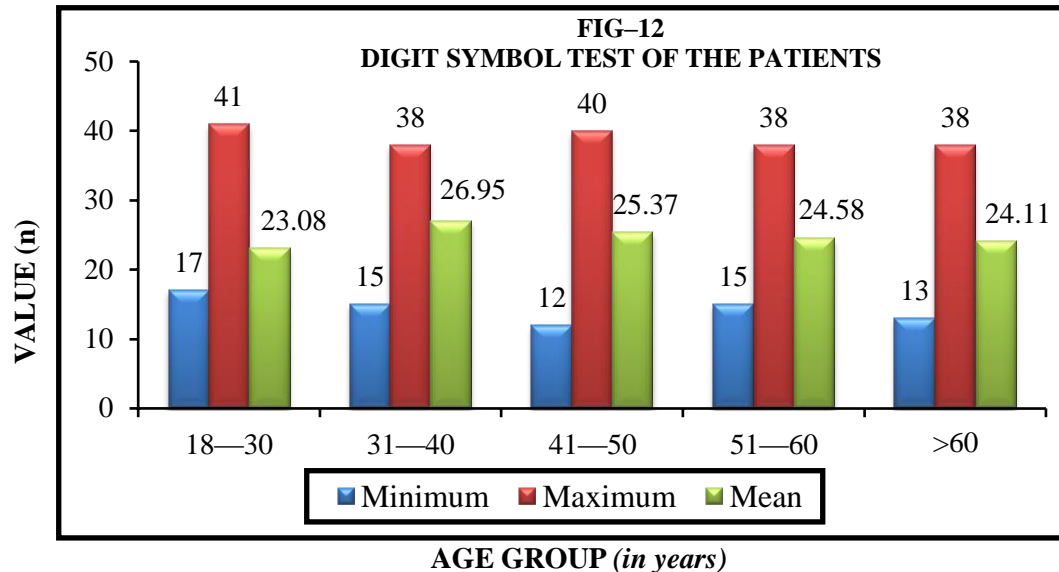


All Patients had a SMMSE score of 24 and above

Table 12: Digit Symbol Test in Subjects

AGE GROUP (in years)	Minimum	Maximum	Mean	S.D.	Total (n=120)	Total Abnormal Score (%)
18-30	17	41	23.08	7.42	13	11(84.61%)
31-40	15	38	26.95	7.73	39	21(53.84%)

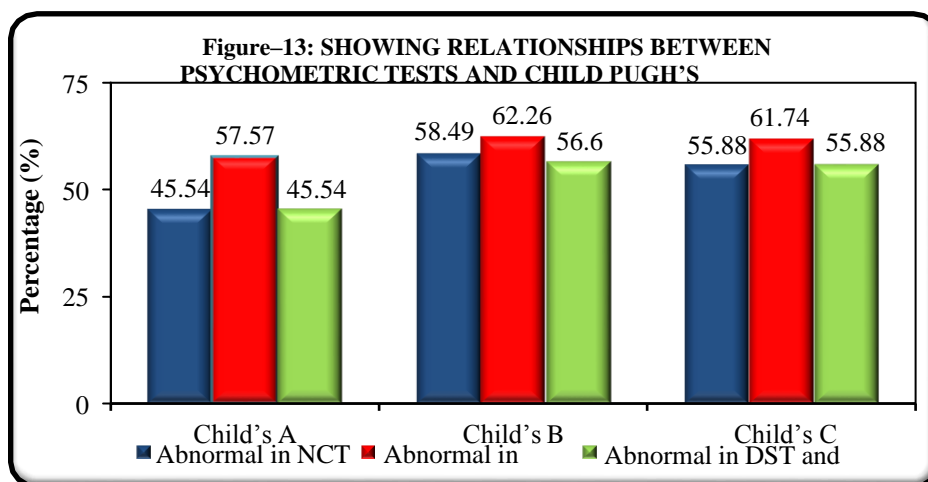
41-50	12	40	25.37	8.52	35	19(54.28%)
51-60	15	38	24.58	8.16	24	16(66.67%)
>60	13	38	24.11	8.08	9	6(66.67%)



60.83% of patients had abnormal DST test. The age group of 31-40 has highest number of abnormal test n=21 (54.28%) followed by age group 41-50, n=19 (66.67%)

Table 13: Relationships between Psychometric Tests and Child Pugh's Grade

	Child's A	Child's B	Child's C	Total (n, %)	P-Value
Number (n)	33	53	34	120	
Abnormal in NCT	15 (45.54%)	31 (58.49%)	19 (55.88%)	65 (54.16%)	0.485
Abnormal in DST	19 (57.57%)	33 (62.26%)	21 (61.74%)	73 (60.83%)	0.903
Abnormal in DST and NCT	15 (45.54%)	30 (56.60%)	19 (55.88%)	64 (53.33%)	0.566



54.17% of patients had abnormal NCT tests overall. The highest percentage of abnormal tests was seen in the age range of 41 to 50. Age group 31-40, n=19 (48.71%), came next, with n=21 (60%) in the lead.

Number connection test in subjects

Age Group	Abnormality	Percentage
18-30	10	16.95

31-40	18	30.51
41-50	14	23.73
51-60	12	20.34
>60	5	8.47
Total	59	100

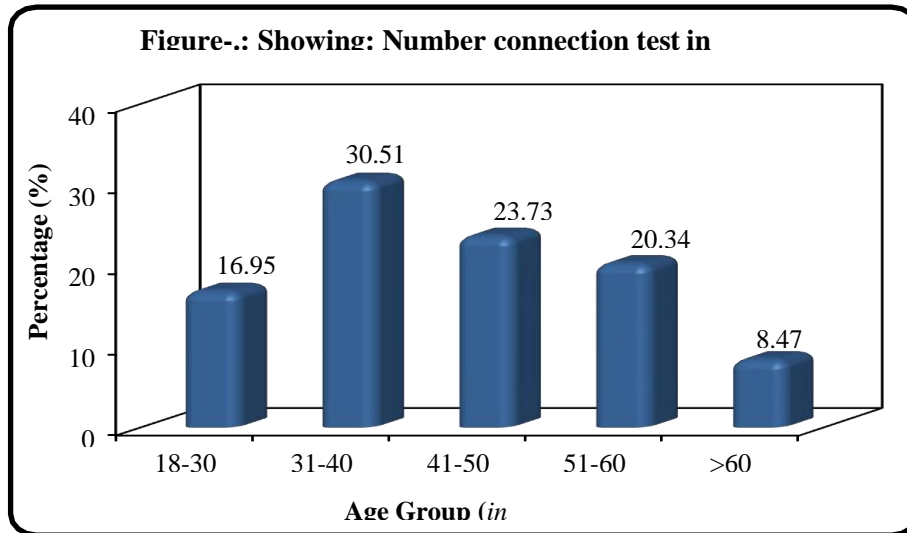


Table 14: Presence of Minimal Hepatic Encephalopathy According to Child PlugsClass

	Child's ClassA	Child's ClassB	Child's ClassC	P-Value
MHE	15(45.45%)	30(56.60%)	19(55.88%)	p-0.393
Non MHE	18(54.55%)	23(43.40%)	15(44.12%)	p-0.947
TOTAL	33	53	34	

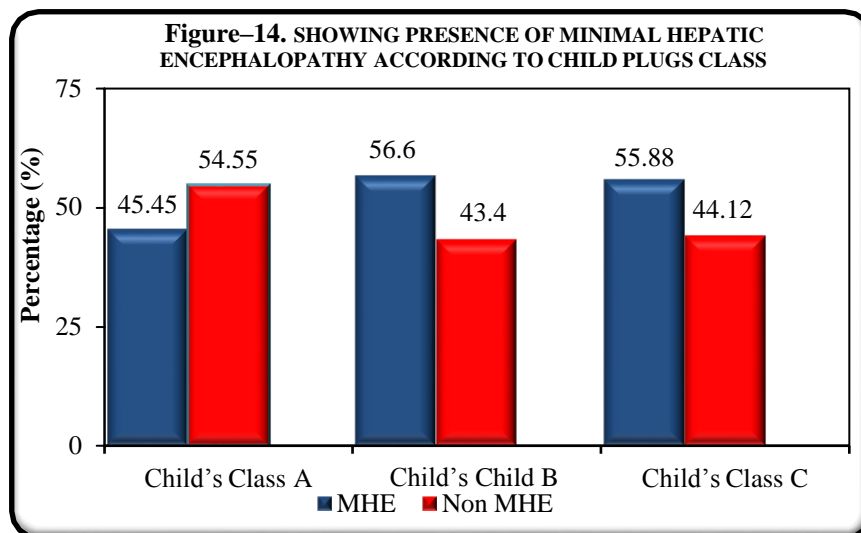
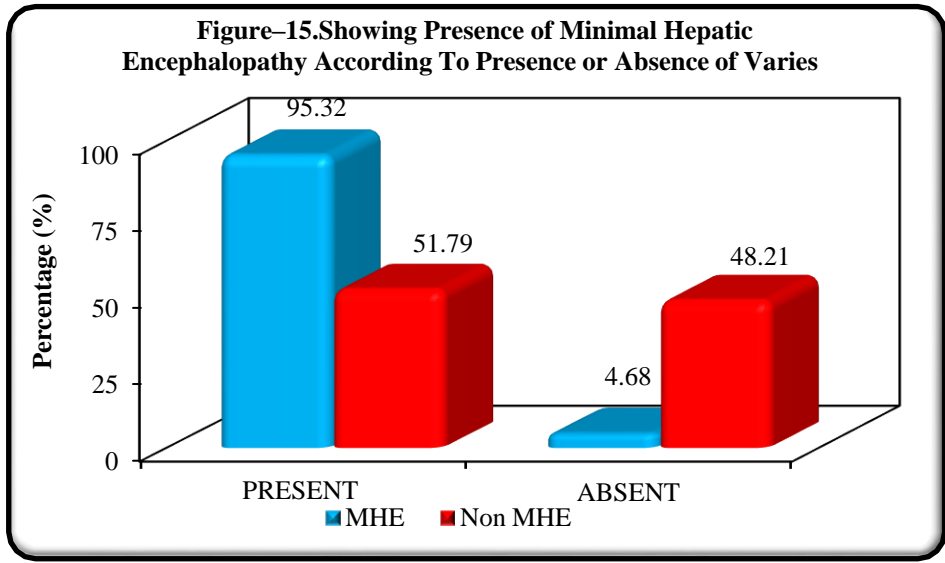


Table 15: Presence of Minimal Hepatic Encephalopathy According to Presence or Absence of Varices

VARICES	PRESENT	ABSENT	P-Value
MHE	61(95.32%)	3(4.68%)	<0.001
Non MHE	29(51.79%)	27(48.21%)	
TOTAL	90	30	



Minimal Hepatic Encephalopathy is present in different child classes, with Class B having the highest percentage (56.60%), followed by Class C (55.88%) and Class A (45.45%).

DISCUSSION

Every case met the study's inclusion and exclusion criteria. The Number Connection Test (NCT) and the Digit-Symbol Test were utilized to identify MHE in liver cirrhosis patients who had normal SMMSE results. The current study attempted to ascertain the percentage of liver cirrhosis patients who exhibit minimal hepatic encephalopathy in addition to establishing a relationship between the outcomes of psychometric tests. The maximum number of participants in our study were in the age range of 31 to 40 years old. Maximum age range of 31–60 years was also found by Zeegan et al. in 1970 and Yen CL et al. in 1990. There were 111 men and 9 women in our study, making up 92.5% and 7.5% of the sample, respectively. This result was consistent with Rikkers et al.'s findings. 1978, Groeneweg M et al. 2000, Amodio P et al. 1999, and so on, all with a comparable male majority. There was a male to female predominance in every aetiology. According to our research, alcohol is the most common aetiology of cirrhosis. This finding is consistent with the findings of Rikkers et al. (1978), Gitlin et al. (1985), and Dhiman RK et al. (2000). The majority of patients in our study had abdominal distension (93.33%) and constitutional symptoms (86.7%), such as easy fatigability. The second most typical symptom reported by the patients was weakness, malaise, and appetite loss. Our study's results were consistent with those of Maskey et al., who discovered that abdominal distension (100%) was the most frequent presenting symptom. and 84.5% jaundice. Based on a review of the clinical signs that patients presented with, pallor (55.0%) was found to be the most common sign, followed by splenomegaly (48.33%) and ascites (47.3%). Our research aligned with the findings of Jepsen Per et al, 2010 study, which found that ascites (55%) was the most frequently occurring presenting symptom, followed by jaundice and variceal bleeding. The most prevalent hematological abnormality among the patients' abnormalities was anemia (82.5%). There was thrombocytopenia in 47.5% of the patients. In line with our findings, Ahmad Hameed et al. (2006) discovered thrombocytopenia and anemia in the majority of the cases. Hypoalbuminemia was the most prevalent biochemical abnormality, present in 77.50% of patients. Increased levels of AST and total bilirubin were then observed in 77.5% and 69.17% of patients, respectively. Raised Prothrombin Time (63.33%) was one of the study's other biochemical anomalies. Gitlin et al. (1985) discovered increased levels of alkaline phosphates, total bilirubin, and AST. In 2000, Krammer et al. discovered hypoalbuminemia in every patient they looked at. The majority of the study's patients (44.16%) belonged to Child Class B, which is consistent with Amodio Petal's 1999 findings. In 2001, Das A et al. discovered that the majority of patients belonged to Child Class B and that 92.5% of patients had chronic hepatic parenchymal alterations. Ascites was present in 61% of patients, while splenomegaly was present in (69, 17%) of patients. Hepatomegaly was present in 20% of patients, and 26.67% of patients had a prominent portal vein. According to Gibson et al., 41% of patients with chronic liver disease and portal hypertension showed splenomegaly on ultrasound. The study's most frequent finding was esophageal varices (75.00%). For 16.67% of patients, portal gastropathy was present. Gomez et al. (2007) and Dhiman RK et al. (2010) found gastro-esophageal varices in 71.8% and 71% of patients, respectively, which is consistent with our findings. In our investigation, Child class B had the highest prevalence of Minimal Hepatic Encephalopathy (56.60%), followed by Child class C (55.88%) and Child class A (45–45%). Child C had a higher prevalence of MHE, according to Amodio P et al. (1999) and Groeneweg M et al. (2000). The child grade and the prevalence of minimal hepatic encephalopathy did not significantly correlate, according to our research (p=0.087). The reason for this could be that the study period was too short to allow for a thorough examination of the patients' lifestyle and quality of life. According to our research, gastro- esophageal varices were present in 95.32% of patients with minimal hepatic encephalopathy. Patients with Minimal Hepatic Encephalopathy had a significantly higher presence of gastro- esophageal varices (p value = <0.001). This finding aligned with the studies of Groeneweg M et al. (2000) and

Hartman et al. (2000), which also reported a significant relationship between Varix and Minimal Hepatic Encephalopathy.

CONCLUSION

This short-term, single-centred, cross-sectional, observational study was conducted in a small number of hospital cases. Consequently, it was not possible to draw a definitive conclusion from this study. Despite these technological challenges, a study of 120 cases of liver cirrhosis led to the following findings and observations. Our study's average participant age was similar to other studies', with a male preponderance across all age groups. Due to the widespread availability of alcohol and the widely accepted social and traditional norms surrounding its consumption, the prevalence of alcoholic cirrhosis was found to be a high 79.17%. The individuals with liver cirrhosis who do not exhibit overt hepatic encephalopathy clinically reveal noteworthy irregularities in the psychometric examination. These psychometric assessments follow a recognized protocol for assessing cognitive impairment in patients with liver cirrhosis who have minimal hepatic encephalopathy. It is sensitive, easy to use, dependable, affordable, convenient, and readily repeatable when combined with two or more other factors to detect Minimal Hepatic Encephalopathy in liver cirrhosis.

REFERENCES

1. Hepatic Encephalopathy, Netter's Gastroenterology, 2nd Edition, Martin H Floch, MD, Editor, Publisher: Saunders, Publishing year: 2010, chapter no 225, page no.485.
2. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy-definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. *Hepatology*. 2002 Mar; 35 (3): 716-21
3. Bajaj JS, Saeian K, Schubert CM, Hafeezullah M, Franco J, Verma RR, Gibson DP, et al. Minimal hepatic encephalopathy is associated with motor vehicle crashes: the reality beyond the driving test. *Hepatology* 2009, 50: 1175-83.
4. Kappus MR, Bajaj JS. Covert hepatic encephalopathy: not as minimal as you might think. *Clinical Gastroenterology Hepatol* 2012; 10: 1208-19.
5. Zhan T, Stremmel W. The diagnosis and treatment of minimal hepatic encephalopathy. *Dtsch Arztebl Int* 2012; 109: 180-7.
6. Dhiman RK, Chawla YK. Minimal hepatic encephalopathy. *Indian J Gastroenterology* 2009, 28: 5-16
7. Summerskill W.H.J. et al (1956) The Neuropsychiatric symptoms associated with Hepatic cirrhosis and an extensive portal collateral circulation. *Quart. J. Of Med. New Series XXV*, No, 98, April 1956
8. Sherlock et al (1954), portal systemic encephalopathy, Neurological Complications of liver disease. *The Lancet* Sept. 4, p 6836, 1954 Quoted by summer skill et al (1956).
9. Amodio P, Del Piccolo F, Pettenu E, et al. Prevalence and prognostic value of quantified electroencephalogram (EEG) alterations in cirrhotic patients. *J Hepatol* 2001; 35: 37-45.
10. Note W, Wihang & Schindler Cetatea cirrhosis: clinical, laboratory, Popkic investigations. *Hepatology* 1998, 28 1215-25
11. Beyer TD, Hoskal 21, American Association for the Study of Liver Dieesses. The role of transjogstar intrahepatic portosystemic shunt in the enragenen of portal hypertension. *Hepatology* 2005, 41: 386-400
12. Quero JC et al, Subclinical Hepatic Fincephalopathy, *Seminars in liver disease*. Vol16, No1996
13. Weissenborn K, Ennen IC. Schonens Het of Nephelial characterization of hepatic encephalopathy. 1 Hepeint 20051, 34: 解773.
14. ittal VN et al, 1967. Hepatic Encephalopathy - A clinical study, the tadion Practitioner April 1967, p-263 Anand BS. Cirrhosis of liver. *West J Med* 1999; 171: 110-5.
15. Summerskill WHJ, Davidson EA, Sherlock S, Steiner RE. The neuropsychiatric syndrome associated with hepatic cirrhosis and an extensive portal collateral circulation. *QJ Med* 1956, XXV: 245-66.
16. Poh Z, Chang PE. A current review of the diagnostic and treatment strategies of hepaticencephalopathy. *International Journal of Hepatology* 2012, 2012: 480309
17. Souheil AZ, Reno V. Metabolic consequence of cirrhosis often is reversible *Postgraduate medicine* 2001; 109 (2): 521-6. Bright R. (1836), *Gay's Hosp Resp*. 1.604. Quoted by Summerskill er al (1956).
18. Ferrichs F.T. (1860), *A Clinical Treatise on diseases of liver*. Trans C. Murchison, London, New Sydenham Society. Quoted By Summerskill et al (1956)
19. Jenkins EJ (1884) *Briz Med J*. T. 357. Quoted by Summerskill er af (1956)
20. Rolleston H.D. (1912) *Diseases of the liver, Gall bladder and Bile Ducts* 2 edition London. Quoted by Summerskill et al (1956)
21. Wilcox WH (1919) *Trans Med Sec Lond* 42.14. Quoted by Summerskill et al (1956).