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Original Research Article

Validating Modified-ANT and Stroop Tests for Diagnosing Minimal Hepatic Encephalopathy (MHE) Patients in the Pakistani Population

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Abstract: *Minimal Hepatic Encephalopathy (MHE) is a subclinical cognitive impairment affecting a substantial proportion of patients with chronic liver disease (CLD). Early diagnosis remains challenging in resource-limited settings like Pakistan, where standard neuropsychological testing is not widely accessible. This study aimed to validate the Modified Animal Naming Test (ANT) and the Stroop Test as simplified tools for MHE screening in the Pakistani population.* ***Methods:*** *A case-control study was conducted at Holy Family Hospital, Rawalpindi, enrolling 196 participants—98 patients with CLD and 98 age- and gender-matched healthy controls. Participants underwent cognitive assessment using three psychometric tools: Psychometric Hepatic Encephalopathy Score (PHES), Modified ANT, and a smartphone-based Stroop Test. A PHES score ≥ -5 was considered diagnostic for MHE. ANT scores <14 and Stroop completion times >190 seconds were also indicative of MHE. Associations among test results and demographic variables were analyzed using SPSS version 26, with $p < 0.05$ considered statistically significant.* ***Results:*** *The Modified ANT was completed by all participants and revealed MHE in 51% of patients. PHES confirmed MHE in 31.6% of patients. A statistically significant association was found between Modified ANT and PHES scores ($p < 0.001$). Stroop Test completion was low, with only 8.2% of patients able to perform it, highlighting barriers related to low education and IT literacy. PHES was also significantly associated with age ($p < 0.001$) but not with gender or education level.* ***Conclusion:*** *The Modified ANT is a reliable and culturally appropriate tool for MHE screening in Pakistani patients with CLD, showing strong correlation with PHES. The Stroop Test, though theoretically valuable, demonstrated limited applicability due to educational and technological constraints. Incorporating low-literacy-friendly psychometric tests like the Modified ANT into routine hepatology practice can facilitate early diagnosis of MHE and help mitigate progression to overt hepatic encephalopathy.*

Keywords: Minimal hepatic encephalopathy, chronic liver disease, Modified Animal Naming Test, Stroop test, PHES

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Introduction

The diagnosis of Minimal Hepatic Encephalopathy (MHE) in cirrhotic patients poses a significant challenge, especially within the context of Pakistan's healthcare system. Hepatic encephalopathy, a disorder characterized by cognitive dysfunction due to liver insufficiency, encompasses a spectrum of manifestations ranging from mild cognitive impairment to overt psychosis. MHE, identified as the subclinical phase of this ailment, affects a considerable proportion of patients with liver cirrhosis, with estimates suggesting prevalence rates between 30% and 84% in this demographic Agarwal et al. (12). The symptoms of MHE often remain elusive, frequently escaping detection via conventional clinical evaluation methods, which can hinder both timely diagnoses and appropriate management strategies Agarwal et al. (12, 3).

In the Pakistani context, the burden of liver diseases, particularly hepatitis C, contributes significantly to the high incidence of cirrhosis and its complications, including MHE. Chronic liver disease is prevalent in Pakistan, primarily attributable to viral hepatitis, substance abuse, and socio-economic factors that impede access to healthcare (2, 4). As a result, many patients present with advanced liver disease, further complicating diagnosis and treatment endeavors. Psychometric testing, including the Modified Animal Naming Test (ANT) and the Stroop Test, could offer a quick and efficient means of detection since these tests are less resource-intensive than neuropsychological assessments Agarwal et al., (15).

Recent investigations highlight the utility of these modified tests in assessing cognitive function in cirrhotic patients at risk for MHE. The ANT, for instance, has shown promise due to its simplicity, ease of administration, and proven reliability in diagnosing MHE Agarwal et al. (1) while the Stroop Test has been validated in other populations for its ability to differentiate between MHE and overt hepatic encephalopathy (OHE) (6). Both tests could be incorporated into routine clinical practice in Pakistan to facilitate better screening and optimize therapeutic strategies for liver disease patients (7, 8).

The rationale for validating these tests within the Pakistani population is imperative. Ethnic, cultural, and socio-economic factors could influence cognitive assessment performance. By examining the psychometric properties of the Modified-ANT and Stroop Tests in this unique demographic context, the study aims to address gaps in the existing research concerning the diagnosis of MHE. Establishing localized diagnostic criteria can enhance the identification of at-risk patients, allowing early intervention that can mitigate the potential progression to OHE and associated complications such as increased morbidity and mortality (9, 10).

Methodology

The present study was designed as a case-control investigation conducted at Rawalpindi Medical University, Pakistan, to evaluate the diagnostic performance of the Modified Animal Naming Test (ANT) and the Stroop test in identifying Minimal Hepatic Encephalopathy (MHE) among patients with chronic liver disease (CLD). Ethical clearance was obtained from the institutional review board of Rawalpindi Medical University,

Allied Hospital, and Holy Family Hospital, and written informed consent was obtained from all participants prior to enrollment. The study followed the ethical principles outlined in the Declaration of Helsinki and complied with Good Clinical Practice (GCP) guidelines.

A total of 196 individuals participated in the study, including 98 patients with clinically confirmed CLD and 98 age- and gender-matched healthy controls. Patients were recruited from the outpatient hepatology and gastroenterology clinics using a non-probability consecutive sampling strategy. The diagnosis of CLD was based on clinical assessment and supporting hospital records, including laboratory and imaging investigations. Individuals with a prior history of overt hepatic encephalopathy (OHE), known neurological or psychiatric disorders, substance abuse, or who were unable to comply with the testing procedures were excluded from the study. While literacy was not a criterion for exclusion from the ANT, participants who were illiterate or lacked technological familiarity were unable to complete the Stroop test.

All eligible participants underwent cognitive assessment using three psychometric tools:

- Psychometric Hepatic Encephalopathy Score (PHES),
- Modified Animal Naming Test (ANT), and
- Smartphone-based Stroop test.

The PHES, which is considered the gold standard for diagnosing MHE, includes five subtests: the number connection tests A and B, the digit symbol test, the serial dotting test, and the line tracing test. A composite PHES score of ≥ -5 was used to define the presence of MHE. This test was successfully completed by 94 patients and 94 controls. The Modified ANT required participants to name as many animals as possible within 60 seconds, assessing semantic fluency and executive function. A cut-off of fewer than 14 animals named was used as the diagnostic threshold for MHE. All 196 participants completed the ANT. The Stroop test, designed to assess cognitive interference and response inhibition, was performed on a smartphone platform. However, due to educational and technological barriers, only 8 patients (8.2%) and 24 controls (24.5%) completed this test. The time to complete the Stroop task was recorded, with durations under 190 seconds considered normal.

Demographic and clinical data, including age, gender, education status, ethnicity, and liver disease etiology (e.g., Non-Alcoholic Steatohepatitis, Hepatitis B, Hepatitis C, cirrhosis), were collected through structured interviews and medical records. The majority of patients were female and over 40 years of age, with a predominant representation from the Punjabi ethnic group. A significant proportion of the patient cohort was uneducated, contributing to challenges in performing certain cognitive assessments such as the Stroop test. Among the patients, the most common underlying etiologies were NASH and Hepatitis C.

All statistical analyses were conducted using SPSS version 26.0. Descriptive statistics including mean, standard deviation, frequencies, and percentages were calculated for baseline variables. Inferential statistics such as chi-square tests and independent sample t-tests were employed to evaluate associations between cognitive test performance and participant characteristics. Correlation analyses were used to assess relationships between the PHES, Modified ANT, and Stroop test scores. A p-value of less than 0.05 was considered statistically significant. Significant associations were observed between PHES scores and both the Modified ANT score and age, while no significant associations were found with gender, education level, or Stroop performance. Missing data from participants who were unable to complete the PHES or Stroop test were excluded using listwise deletion.

Results

A total of 196 participants were included in the study, comprising 98 patients with chronic liver disease and 98 healthy controls. The diagnostic performance of the Modified Animal Naming Test (ANT), Stroop test, and PHES score was assessed to evaluate Minimal Hepatic Encephalopathy (MHE) in the Pakistani population. The gender distribution showed a female predominance in both patient and control groups. Among patients, 72 (73.5%) were female and 26 (26.5%) male, while in the control group, 76 (77.6%) were female and 22 (22.4%) male. The majority of patients were aged between 41–60 years (74.5%). A large proportion of patients were uneducated (58.2%), whereas the control group had a relatively higher literacy rate (58.2%). The dominant ethnic group was Punjabi in both populations. Among patients, common etiologies for liver disease included NASH (42.9%), Hepatitis C (39.8%), Hepatitis B (12.2%), and Liver Cirrhosis (5.1%). (Table 1)

Table 1. Demographic and Clinical Characteristics of Patients and Controls

Variable		Patients (n=98)	Controls (n=98)
Gender	Male	26 (26.5%)	22 (22.4%)
	Female	72 (73.5%)	76 (77.6%)
Age (Years)	<18	1 (1%)	1 (1%)
	18–30	6 (6.1%)	16 (16.3%)
	31–40	9 (9.2%)	28 (28.6%)
	41–50	33 (33.7%)	27 (27.6%)
	51–60	40 (40.8%)	21 (21.4%)
	61–70	9 (9.2%)	3 (3.1%)
	71–80	0	2 (2.0%)
Education	Educated	41 (41.8%)	25 (25.5%)
	Uneducated	57 (58.2%)	73 (74.5%)
Ethnicity	Punjabi	56 (57.1%)	97 (99.0%)
	KPK	20 (20.4%)	1 (1.0%)
	Balochi	19 (19.4%)	0
	Kashmiri	3 (3.1%)	0
Etiology	NASH	42 (42.9%)	-
	Hepatitis B	12 (12.2%)	-
	Hepatitis C	39 (39.8%)	-
	Liver Cirrhosis	5 (5.1%)	-

All 98 patients and controls underwent the Modified ANT. Among patients, the mean score was 13.03 (SD ± 2.94), compared to 15.78 (SD ± 3.20) in controls. Using a cut-off of <14 animals/minute for MHE diagnosis, 50 patients (51%) were identified with MHE and 48 without. In the control group, 16 individuals fell below the threshold. (Table 2)

Table 2. Distribution of Modified ANT Scores Among Patients and Controls

ANT Score	Patients (n=98)	Controls (n=98)
4–9	15 (15.3%)	4 (4.1%)
10–13	38 (38.8%)	20 (20.4%)
14–16	38 (38.8%)	41 (41.8%)
17–22	7 (7.1%)	33 (33.7%)

The Stroop test was completed by only 8 patients (8.2%) and 24 controls (24.5%). The mean Stroop time for patients was 164.5 seconds (SD ± 20.0) and for controls was 139.3 seconds (SD ± 19.47). The limited performance of this test among patients was mainly due to lack of education or IT literacy. (Table 3)

Table 3. Stroop Test Participation Among Patients and Controls

Stroop Test	Patients (n=98)	Controls (n=98)
Performed	8 (8.2%)	24 (24.5%)
Not Performed	90 (91.8%)	74 (75.5%)

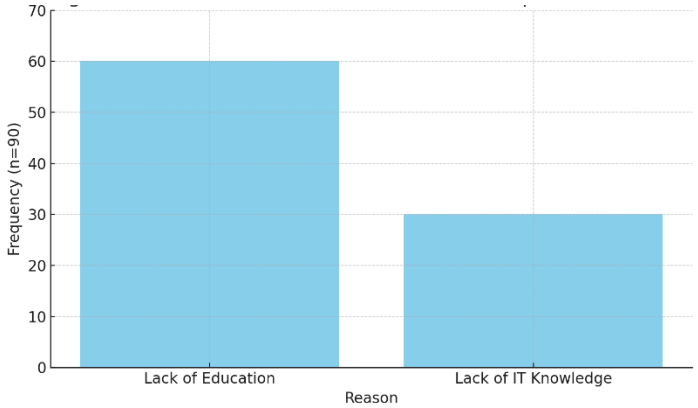

Figure 1. Reasons for Non-Performance of Stroop Test in Patients

The PHES test was conducted on 94 participants in each group. Based on the PHES score, ≥ -5 was considered as indicative of MHE. Among patients, 31 (31.6%) were classified as having MHE, whereas 63 (64.3%) did not. Among controls, only 9 (9.2%) had MHE-level scores. PHES showed statistically significant association with Modified ANT score ($p < 0.001$), Modified ANT encephalopathy status ($p < 0.001$), and age ($p < 0.001$), but not with gender, Stroop test results, or educational status. (Table 4)

Table 4. PHES Score Classification Indicating Encephalopathy Status

PHES Classification	Patients (n=98)	Controls (n=98)
≥ -5 (With MHE)	31 (31.6%)	9 (9.2%)
< -5 (Without MHE)	63 (64.3%)	85 (86.7%)
No Test Done	4 (4.1%)	4 (4.1%)

Discussion

The findings from this study provide valuable insights into the diagnostic efficacy of the Modified Animal Naming Test (ANT), Stroop Test, and Psychometric Hepatic Encephalopathy Score (PHES) for identifying Minimal Hepatic Encephalopathy (MHE) in a Pakistani cohort. Our sample consisted of 196 participants, equally divided between patients with chronic liver disease and healthy controls, revealing a predominance of females across both groups—a reflection that aligns with broader literature highlighting gender disparities in health outcomes in Pakistan (11). The demographic characteristics noted, particularly the higher percentage of uneducated patients (58.2%), underscore significant socio-economic challenges that likely impact health literacy and access to healthcare, closely mirroring patterns observed in other developing contexts, such as in Bangladesh (12).

The observed MHE prevalence of 51% among chronic liver disease patients, as identified by the Modified ANT, is consistent with global findings that posit a high rate of MHE in cirrhotic patients, with prevalence rates often exceeding 30% (13). Comparisons to studies, such as that by Nardelli et al. (14), which highlighted a correlation of increased MHE rates with the use of Proton Pump Inhibitors, suggest that environmental and pharmacological factors could exacerbate neurocognitive impairments in susceptible populations.

Our results indicate significant challenges regarding participation rates in the Stroop Test, with only 8.2% of patients able to complete this assessment compared to 24.5% of controls. This discrepancy likely reflects barriers such as educational deficits and inadequate IT literacy, which have been observed in similar studies exploring cognitive testing in patients with liver disease (15). The limitation of the Stroop Test's utility in our cohort could reinforce the necessity for developing simpler, more accessible cognitive assessment tools tailored for low-literacy populations.

Further examination of the PHES, performed on only 94 participants, indicated that 31.6% of patients met criteria for MHE. This aligns closely with results from research such as that by Gairing et al. (11), who concluded a strong predictive value of PHES for identifying patients at

risk for more severe forms of hepatic encephalopathy. Notably, despite the significant association found between PHES and Modified ANT scores, the absence of correlation with educational status raises questions about the interpretation of cognitive testing outcomes in populations with varying literacy levels.

The findings from our research not only affirm the robustness of psychometric tests like the Modified ANT in diagnosing MHE but also highlight broader public health implications. The obtained data suggest a pressing need for education and awareness campaigns focused on liver health in Pakistan, akin to efforts that have been beneficial in other regions affected by similar burdens (16).

Thus, the findings of this study advocate for the integration of culturally and linguistically appropriate cognitive testing into routine hepatological assessments in Pakistan. Moreover, they emphasize the necessity for future research to incorporate longitudinal elements that can better elucidate the relationship between MHE and the progression of liver disease, thereby improving clinical strategies for management and patient outcomes in this vulnerable population.

Conclusion

This study underscores the diagnostic utility of the Modified Animal Naming Test (ANT) in identifying Minimal Hepatic Encephalopathy (MHE) among patients with chronic liver disease in Pakistan. The strong correlation between Modified ANT scores and PHES outcomes validates its role as an effective, low-cost, and easily administrable screening tool suitable for low-resource and low-literacy settings. In contrast, the Stroop Test showed limited practical value due to poor participant completion rates, largely influenced by educational and technological barriers.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC -24)

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The authors declared the absence of a conflict of interest.

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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