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Evaluation of Split Hand Syndrome in Early Diagnosis of Amyotrophic Lateral Sclerosis by Nerve Conduction Study as a Diagnostic Tool

A WAZIB[a], S RAHMAN[b], MR AHMED[c]

Abstract

Background: *Amyotrophic lateral sclerosis (ALS), a degenerative disease of the motor neurons that can present diversly. Needle electromyography (EMG) is the gold standard investigation for the diagnosis of ALS. Split hand syndrome (SHS) demonstrated by nerve conduction study (NCS); a noninvasive tool could be useful in diagnosing ALS. This study aimed to assess SHS by NCS in ALS.*

Materials & Method: *This diagnostic accuracy case-control study included 37 cases of ALS and 37 age and gender-matched controls. Compound muscle action potential (CMAP) and distal motor latency (DML) of median and ulnar nerves and the ratio of median and ulnar CMAP and DML were compared between study groups. The diagnostic validity testing of electrophysiological SHS was also done.*

Results: *The mean age of the ALS and control groups were similar, 39.8±2.7 and 39.3±2.6 years, respectively. Sixteen (43.2%) ALS patients were in 30-59 years age group. Male-female ratio was 5.2. In the ALS group, median-ulnar CMAP ratio was lower and median-ulnar DML ratio was prolonged than the control. The diagnostic efficacy of median-ulnar CMAP ratio and DML ratio were calculated. A median-ulnar CMAP ratio cut-off value d"1 showed 70% sensitivity, 97% specificity, 96% positive predictive value and 77% negative predictive value. A median-ulnar DML ratio cut-off value e"1.5 showed 48% sensitivity, 89% specificity, 82% positive predictive value and 65% negative predictive value.*

Conclusion: *NCS demonstrating SHS can be an important tool in the early diagnosis of ALS.*

Key words: *Amyotrophic lateral sclerosis, Nerve conduction study, Split hand syndrome*

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Introduction:

Amyotrophic lateral sclerosis (ALS) is suspected clinically with mixed upper & lower motor neuron signs and absence of sensory loss, ocular motor palsy and sphincter dysfunction[1]. MRI of the brain and/or relevant segments spinal cord and nerve conduction study (NCS) are done to exclude potentially curable alternative diagnoses[2]. Needle electromyography (EMG) is the cornerstone in the diagnosis of ALS. El Escorial criteria is currently used for the diagnosis of ALS, in which features of denervation (fibrillation, positive sharps or fasciculation) found in three in four of the bulbar, cervical, thoracic and lumbo-sacral segments establish the diagnosis[3].

Split-hand syndrome (SHS) is observed in early ALS cases, even before the fulfilment of El Escorial criteria in EMG in a few recent studies[4]. SHS is dissociated pattern of wasting of intrinsic hand muscles, more severe in the lateral hand group of muscles, predominantly affecting the thenar eminence - abductor pollicis brevis (APB) and first dorsal interosseous muscle (FDI), with relative preservation of the hypothenar muscles - abductor digit minimi (ADM). The pattern does not follow any nerve, trunk or root territories[5]. SHS of ALS is electrophysiologically expressed as Split-hand ratios, lower median-ulnar compound muscle action potential (CMAP) amplitude ratio and higher median-ulnar distal motor latency (DML) ratio while recording median and ulnar CMAP on APB and ADM, respectively[6,7].

An ADM-APB CMAP ratio >1.7 or absent APB CMAP showed a 51% sensitivity and 91% specificity in early

a. Dr. Amit Wazib, Professor & Head, Department of Medicine, Shaheed Monsur Ali Medical College, Dhaka, Bangladesh.
b. Dr. Shaila Rahman, Associate Professor, Department of Medicine, Shaheed Monsur Ali Medical College, Dhaka, Bangladesh.
c. Dr. Md. Rayhan Ahmed, Assistant Registrar, Department of Medicine, Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh.

Address of Correspondent: Prof. Dr. Amit Wazib. Professor & Head, Department of Medicine, Shaheed Monsur Ali Medical College, House-26 & 26A, Road-10, Sector-11, Uttara, Dhaka, Bangladesh. Mobile: 01979181182; Email: amit.bcps.2552@gmail.com
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ALS, irrespective of the site of onset[8]. A lower ulnar-median distal motor latency (DML) ratio was found in ALS patients with mean DML 0.7 and 0.8 mSec, in ulnar & median nerves, respectively[9].

There is no published study of the electrophysiological SHS of ALS on the Bangladeshi population. The study was aimed at studying the SHS with NCS in the diagnosis of ALS.

Methods:

This diagnostic accuracy case-control study was conducted in the Neurology outpatient of Shaheed Monsur Ali Medical College Hospital from January 2018 to December 2023. Inclusion criteria for cases were established cases of ALS, as per El-Escorial criteria[10], aged e"18 years. Inclusion criteria for controls were persons aged e"18 years without any muscles weakness, wasting, absent reflexes or fasciculation. Exclusion criteria for both cases and controls were co-existing radiculopathy, neuropathy and/or myopathy, and incomplete data. Forty-two patients of ALS were enrolled in the Neurology outpatient. Thirty-seven of them could be contacted and included as cases considering ALS as a rare disorder. Thirty-seven age and gender-matched controls were selected by purposive sampling for comparison. Ethical clearance was obtained from the Institutional Ethical Review Board (IERB) of Shaheed Monsur Ali Medical College Hospital. All procedures followed the ethical rules and the principles of the Declaration of Helsinki.

Motor NCS of median and ulnar nerves was performed in all seventy-four (74) study participants by the first author, who is a neurologist with experience in electrophysiology. NCS was conducted with standard surface stimulation and recording techniques on a Neuropack S1 four-channel electromyograph with standard filter settings and a surface stimulator using a 0.1 ms square-wave pulse. The temperature of the electrophysiology laboratory was kept at 25-28p C during the NCS procedure.

MEB-9400 EMG/EP measuring system software was used to measure and calculate the motor NCS parameters. Abductor pollicis brevis (APB) and abductor digiti minimi (ADM) were used to assess median and ulnar motor nerves, respectively. The CMAP amplitude was measured from the baseline to the peak of CMAP. Distal motor latency was measured from the time of stimulus to the onset of CMAP. Motor nerve conduction velocity (NCV) was calculated by dividing the distance with the latency differences between CMAPs obtained with distal and proximal stimuli. F-waves and sensory NCS were not performed.

Data on the Needle electromyography (EMG) of the ALS cases were available from the patient records. Needle EMG was not performed on the controls.

Data were collected in a pre-designed case record form. The following data were collected from all 74 study subjects: age, gender, CMAP amplitude and DML of median and ulnar motor nerves. Motor NCV was not assessed in this study. Microsoft Excel and Statistical Package for the Social Sciences (SPSS) 22 were used for the final analyses. Median-ulnar CMAP amplitude ratio and DML ratio were calculated, and compared between the ALS and control groups. The diagnostic validity of these ratios was calculated and presented as sensitivity, specificity, positive predictive value and negative predictive value.

Results:

The mean age of the ALS and control groups were similar, 39.8±2.7 and 39.3±2.6 years, respectively. The number of ALS patients in <30 years, 30-59 years and e"60 years age groups were 15(40.5%), 16(43.2%) and 6(16.2%), respectively (Figure-1). The numbers of males and females were 31 & 6, respectively in both groups (male-female ratio 5.2).

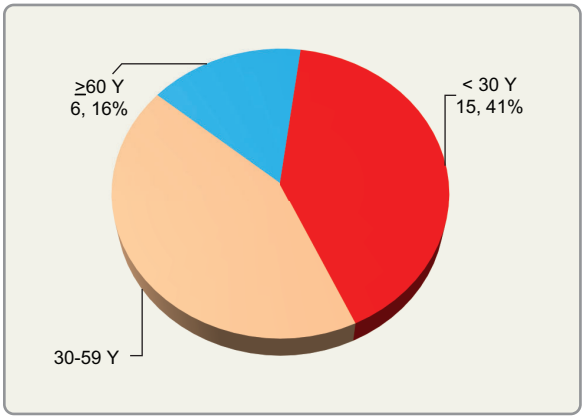

Figure-1: *Age distribution of ALS patients in the study*

Median & ulnar CMAP amplitude in the ALS group were 5.2±0.6 (0.1-11.4) mV and 5.8±0.5 (0.3-13.8) mV. In the healthy control group, these were 11.4±0.5 (6.5-16.3 mV) mV and 6.9±0.4 (2.6-16.3) mV, respectively (Table-I).

DML was 3.8±0.2 (2.9-7.3) mSec in the median nerve and 2.8±0.2 (1.9-5.9) mSec in the ulnar nerve in ALS group. It was 3.3±0.1 (2.7-3.8) mSec and 2.7±0.1 (1.9-4.0) mSec in median and ulnar nerves, respectively, in the control group (Table-I).

Table-I

Basic NCS parameters in study subjects.

Nerve	Parameter	ALS	Control
Median	CMAP (mV)	5.2±0.6	11.4±0.5
	DML (mSec)	3.8±0.2	3.3±0.1
Ulnar	CMAP (mV)	5.8±0.5	6.9±0.4
	DML (mSec)	2.8±0.2	2.7±0.1

Expressed as Mean±Standard error

Median-ulnar CAMP ratio in the ALS group was 1.0±0.2 (0.2-2.8). In healthy controls, this was higher, 1.8±0.1 (0.9-3.3). This difference of median-ulnar CAMP ratio between ALS and control groups was statistically significant (p-value<0.001) (Table-II, Figure-2).

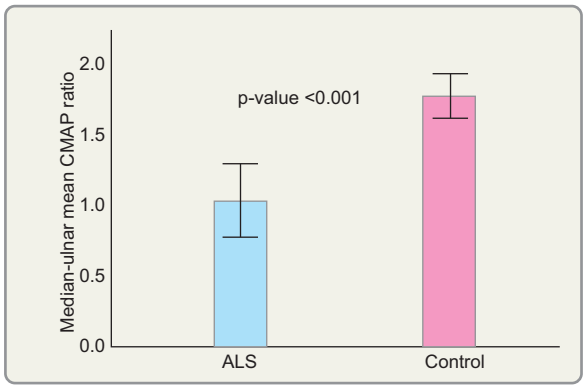

Figure 2: *Median-ulnar CMAP ratio in the study participants (n=74)*

Median-ulnar DML ratio in the ALS & control groups were 1.43±0.1 (0.9-2.2) and 1.27±0.1 (0.8-1.7), respectively. This difference was also statistically significant (p-value 0.01) (Table-II, Figure-3).

Table-II

Median-ulnar CMAP and DML ratio in study subjects.

Parameter	ALS	Control	p-value
Median-ulnar CMAP ratio	1.0±0.2	1.8±0.1	<0.001
Median-ulnar DML ratio	1.4±0.1	1.3±0.1	0.01

Expressed as Mean±Standard error

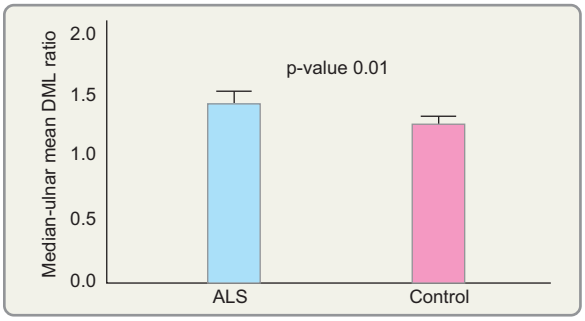

Figure 3: *Median-ulnar DML ratio in the study participants (n=74)*

ROC curves were produced for both median-ulnar CMAP ratio and median-ulnar DML ratio, with area under curve (AUC) 0.83 and 0.64, respectively (Figure-4 and 5).

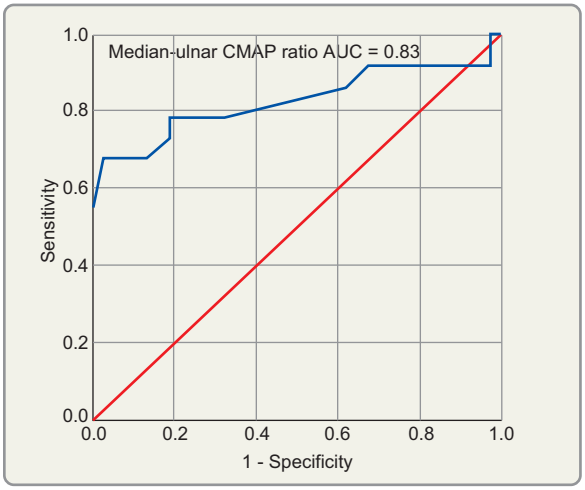

Figure 4: *ROC curve in median-ulnar CMAP ratio in the diagnosis of ALS*

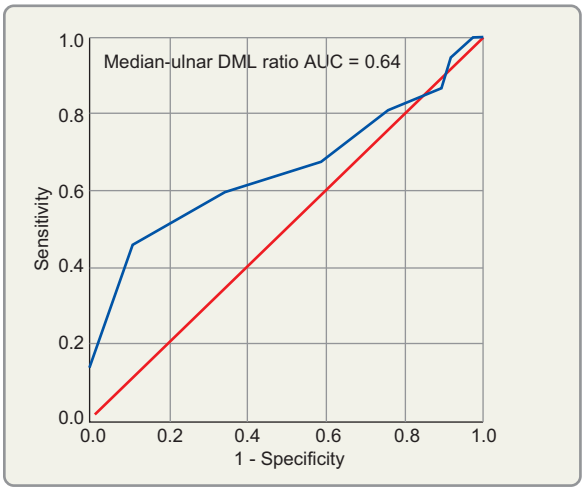

Figure 5: *ROC curve in median-ulnar DML ratio in the diagnosis of ALS*

The diagnostic efficacy of median-ulnar CMAP ratio and DML ratio were calculated. A Median-ulnar CMAP ratio cut-off value ≤1 showed 70% sensitivity, 97% specificity, 96% positive predictive value and 77% negative predictive value. (Table-III)

A median-ulnar DML ratio cut-off value ≥1.5 showed 48% sensitivity, 89% specificity, 82% positive predictive value and 65% negative predictive value. (Table-III)

Table-III

Diagnostic efficacy of NCS in ALS

Parameter	SEN	SPE	PPV	NPV
M-U CMAP ratio ≤1	70%	97%	96%	77%
M-U DML ratio ≥1.5	48%	89%	82%	65%

SEN–Sensitivity, SPE–Specificity, PPV-Positive predictive value, NPV- Negative predictive value

Discussion:

The age of the ALS patients in this study was nearly 40 years, which is lower than the global mean age of 75 years in ALS patients[11]. Recent two studies in India found a mean age of 46 and 42 years, respectively[12,13], similar to the age distribution of this study. The male-female ratio of this study was 5.2 which was different from the global gender ratio of ALS (1.2-1.5). However, Indian ALS patients showed a higher than the global male-female ratio (3-3.7) [12,13]. The ethnic similarity of Bangladeshi people to the Indians can explain the higher ratio than that of the global found in this study.

Split hand syndrome has been demonstrated in ALS patients in numbers of studies. A case-control study in Iraq showed a significantly lower Median-ulnar CMAP ratio among ALS patients than the healthy controls[14]. A decreased Median-ulnar CMAP ratio was found in 41% ALS patients and 5% healthy controls in Japan[6]. A Korean study also revealed a lower Median-ulnar CMAP ratio in ALS patients[15]. In this study, median-ulnar CMAP ratio was found to be lower in the ALS group than in the control group.

Median-ulnar DML ratio was higher in the ALS group than in the control group in this study. A recent Turkish study had a similar DML ratio among ALS patients and controls[9].

The sensitivity and specificity on median-ulnar CMAP ratio and DML ratio in the diagnosis of SHS in ALS were assessed in this study. A Median-ulnar CMAP ratio, with a cut-off value d"1 showed reasonable sensitivity (70%) with very high specificity (97%) for ALS. A median-ulnar DML ratio cut-off value ≥1.5 showed good specificity (89%), with a relively low sensitivity (48%).

Conclusion:

Although needle EMG is the specific diagnostic test for ALS, NCS demonstrating split hand syndrome can be used as an additional diagnostic tool, particularly in difficult cases.

Author contribution:

The first author designed the study and performed the NCS on the study participants. The statistical analyses were done by the second author. The third author collected all the data.

Conflict of interest:

The study did not receive any research grant and none of the authors got any financial aid for this study.

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