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# Study of Protein Level of Cerebrospinal Fluid (CSF) in Motor Neuron Disease

M A HAYEE[a], A HAQUE[b], QD MOHAMMAD[c]

**Summary:**

***A prospective study of cerebrospinal fluid (CSF) protein level of motor neuron disease (MND) patients was carried out in Medicine Department of Sir Salimullah Medical College, Dhaka and Sher-e-Bangla Medical College, Barisal. The duration of study was from July 1, 2000 to December 31, 2002. One hundred forty MND patients between 25 to 82 years were studied. Among them 89 were male and 51 were female. The mean age (with SD) of the patients was 53.12(±13.94) years (male 54.90(±12.32) and female 53.40(±14.52)). Clinical typing showed 67 (47.85%) had amyotrophic lateral sclerosis (ALS), 58 (41.42%) had amyotrophic lateral sclerosis with probable upper motor neuron signs (ALS-PUMNS), 11 (7.85%) had progressive muscular atrophy (PMA) and four (2.88%) had progressive bulbar palsy (PBP). Maximum patients were between 36 and 60 years and only 14% patients presented before 35 years of age. Cerebrospinal fluid was collected from each subject and protein was estimated. Ninety- eight patients (70%) had cerebrospinal protein level less than 50 mg/dl, 35 (25%) had protein between 50 to 74 mg/dl and seven (5%) had more than 75 mg/dl.***

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**Introduction:**

Motor neuron disease is one of the important debilitating diseases of mankind. It is a neurodegenerative disease. Motor neuron disease can briefly be described as a complex condition resulting in muscular weakness and wasting without sensory changes[1]. Motor neurons, grouped as upper and lower motor neurons, are nerve cells that transmit signals for movement from the brain and spinal cord to muscle fibres. Motor neuron disease is characterized by progressive deterioration of and loss of these neurons. The loss of nerve stimulus to specific muscle results in atrophy and progressive weakness leading to paralysis. Progressive muscular wasting disease was first described in 1850 by Aran and in 1860 by Duchenne. In 1869, the French neurologist Jean-Martin Charcot described a unique condition characterized by deterioration of both upper and lower motor neurons and this condition was termed amyotrophic lateral sclerosis[2]. If only lower motor neuron involvement is evident, the condition is termed progressive muscular atrophy[3]. Clinical manifestations of amyotrophic lateral sclerosis are largely dependent on the degree to which the upper or lower motor neurons are affected[4].

Amyotrophic lateral sclerosis is nearly always progressive and eventually leads to death. Common cause of death is respiratory failure or cardiac arrythmias. There are some rare reports of patients in whom the disease is stable[5]. There are three types of ALS – (i) Sporadic, (ii) Familial and (iii) Western Pacific variant. Individuals who have no family member with this condition are said to have sporadic or classic ALS. It constitutes 90% of all ALS cases. The age of onset of sporadic ALS commonly between 55 and 75 years[6,7] and more in females than males[8] (M:F = 1:1.6), but recent studies have suggested that the sex difference is decreasing[9]. Familial ALS can be defined as two or more cases occurring in the same family. About 5% to 10% of ALS cases are familial[10] and related to mutation in Cu/Zn superoxide dismutase gene[11]. There is little information about total CSF protein content in several important general reviews of CSF of MND[12-15].

Many fields of MND had been explored by many researchers. Till now we do not know it's etiology. Several simple facts are not yet known. How often is the total CSF protein content abnormally increased? This simple question is not satisfactorily answered till this moment. No work had been done in this field in our country. This has stimulated to do this study among the Bangladeshi MND patients.

a. Dr. Md Abdul Hayee, FCPS, MD, PhD, Associate Professor and Head of the Department of Neuromedicine, SSMC, Dhaka.

b. Dr. Md. Anisul Haque, FCPS, MD, PhD, Professor and Chairman of Neurology, BSMMU, Dhaka.

c. Dr. Quazi Deen Mohammad, FCPS, MD, Professor and Head of the Department of Neuromedicine, DMC, Dhaka

**Address of Correspondence :** Dr. Md A Hayee FCPS MD, PhD, Associate Professor and Head of the Department of Neuromedicine, SSMC, Dhaka.

The terminologies used in this study needs clarification

*1. Nomenclature:*

i. Motor neuron diseases (pleural): any disease in which the primary pathology is believed to affect the perikaryon of motor neurons and the manifestations are usually paretic but some conditions are ascribed to neural over activity (cramps, twitching of muscles, spasm or persistent abnormal posture of limbs or trunk).

ii. Pure motor neuropathy: the term is used when it is believed that the primary disorder affects axons of peripheral nerve which is defined by non-clinical criteria, such as electrophysiology, histopathology or other laboratory tests.

iii. Neuronopathy: the term is used to describe the disease of the neurones when, after all tests, it is still not possible to assign the primary pathology either to perikaryon, peripheral nerve or both[16].

*2. Obligatory criteria for motor neuron disease:*

i. Symptoms must include focal weakness of upper motor neuron type i.e. spastic gait or limb clumsiness of corticospinal tract disorder.

ii. There must be signs of lower motor neuron lesion i.e. evidence of focal weakness and wasting of muscles. Focal wasting is needed to differentiate neurogenic atrophy of muscle from generalized wasting or gaunt appearance after weight loss or dietary restriction. Other lower motor neuron lesion signs, not mandatory but helpful, including loss of tendon reflexes and fasciculation. "Diminished tendon reflexes" do not count because "diminished" is difficult to define. "Lost" means that the patellar reflexes are absent with reinforcement and ankle jerks are absent in the kneeling position.

iii. Unequivocal upper motor neuron signs include positive Hoffmann signs with flexor plantar response. Though hypertonicity is a feature of upper motor neuron lesion, yet it is difficult to define objectively on clinical ground and is not under consideration.

*3. Definitions of some clinical syndromes:*

i. Progressive muscular atrophy (PMA): lower motor neuron signs only.

ii. Amyotrophic lateral sclerosis (ALS): lower motor neuron signs and unequivocal upper motor neuron signs.

iii. Amyotrophic lateral sclerosis with probable upper motor neuron signs (ALS-PUMNS): over active tendon reflexes in limbs with weak, wasted and twitching muscles but no clonus or plantar extensor.

iv. Progressive bulbar palsy (PBP): a syndrome in which dysarthria and dysphagia are predominant symptoms and in which there is weakness, wasting and faciculation of tongue. There may or may not be concomitant upper motor neuron signs.

v. Primary lateral sclerosis (PLS): a syndrome characterized by upper motor neuron signs and no lower motor neuron signs. It is uncertain whether PLS is a form of MND[16]. Rarely this syndrome may evolve to full ALS[17].

**Materials and methods:**

Selection of patients: The daily admission register of Medicine Department of Sir Salimullah Medical College and Mitford Hospital, Dhaka and Sher-e-Bangla Medical College Hospital, Barisal were screened continuously for patients who were thought to have disease related to ALS or PMA. The study period was from July 1, 2000 to December 31, 2002. In the present study all patients had lower motor neuron signs. Patients with PLS were excluded. Patients were divided into four groups: ALS, ALS-PUMNS, PMA and PBP.

Exclusion criteria: A total of 260 patients were suspected to have MND according to admission register. They were examined thoroughly to judge whether inclusion criteria were met. Of the 260 patients, so selected, 70 were rejected because they did not meet the clinical diagnostic criteria. These included 40 patients with spastic paraparesis or paraplegia without evidence of lower motor neuron signs and eight patients who met established criteria for the diagnosis of PLS. Eleven patients had disorders unrelated to MND. Charcot-Marie-Tooth disease, lumbosacral plexopathy, post-polio muscle atrophy, progressive supranuclear palsy, benign fasciculation, pseudobulbar palsy related to multiple

strokes were also excluded. In six patients the diagnosis of MND was indeterminate. Five patients with MND who had coexistent sensory motor neuropathy were excluded.

Inclusion criteria: Out of 190 patients who met the criteria, 50 were excluded because they did not have full laboratory studies. Cerebrospinal fluid protein estimation was done in all the remaining 140 patients for the study purpose. Following were the inclusion criteria:

Age between 21 and 80 years of any sex; patients with upper motor neuron lesion signs (hypertonia, hyperreflexia and extensor plantar response); patients with lower motor neuron lesion signs (flaccid paralysis, muscle wasting and fasciculation) and patients with both upper motor neuron lesion signs and lower motor neuron lesion signs.

**Results:**

Clinical syndromes: Out of 140 patients who met inclusion criteria, there were 89 men with mean age (±SD) 54.9 (±12.32) years with age ranging from 25 to 82 years. There were 51 women with mean age (±SD) 53.4 (±14.52) in years with age ranging from 15 to 85 years. Sixty seven patients had ALS, 58 had ALM-PUMNS, 11 had PMA and four had PBP. Eleven (12.36%) of the 89 male patients and eight (15.68%) of the 51 female had symptoms before of age 39 years. Fasciculation was the major symptom which was clinically evident in 126 (90%) of the 140 patients. The remaining 14 patients without clinical fasciculation were of PMA six, ALS four and ALS-PUMNS four.

Cerebrospinal fluid protein content: Out of 140 patients, CSF protein value was greater than 50 mg/dl in 35 (25%). In seven (5%), the CSF protein value was greater than 75mg/dl. Rest 98 (70%) had CSF protein less than 50 mg/dl (ranging from 15 to 50mg/dl).

**Table – I**

*Distribution of patients according to sex (n=140).*

| | Number | % | Mean age (years) |
|---|---|---|---|
| Male | 89 | 63.57 | 54.90 |
| Female | 51 | 36.43 | 53.40 |
| Male : Female | 1.74:1 | | |

**Table – II**

*Distribution of MND patients according to clinical types (n=140).*

| Clinical types | Number | % |
|---|---|---|
| ALS | 67 | 47.85 |
| ALS-PUMNS | 58 | 41.42 |
| PMA | 11 | 7.85 |
| PBP | 04 | 2.88 |

**Table – III**

*Presentation of the patients before 35 years.*

| Symptoms before 35 | Number | % |
|---|---|---|
| Male | 11 | 12.36 |
| Female | 08 | 15.68 |

**Table – IV**

*Distribution of the patients according to CSF protein value (n=140)*

| CSF protein value | Number | % |
|---|---|---|
| <50mg/dl | 98 | 70 |
| 50 to 74mg/dl | 35 | 25 |
| >75mg/dl | 07 | 05 |

**Discussion:**

This study was carried out to know the CSF protein level of Bangladeshi MND patients. The study subjects were taken from the medicine department of Sir Salimullah Medical College and Mitford Hospital, Dhaka and Sher-e-Bangla Medical College Hospital, Barisal. During the study period, 140 patients who fulfilled the diagnostic criteria of MND were evaluated.

This study revealed that majority of the patients were between 36 to 60 years. This finding correlates with the finding of a study in Bangladesh[18] but does not correlates with the European studies[6,7]. However, the finding is also similar to an Indian study by K Sood in 1990[19].

The male female ratio of the study subjects was 1.74:1 which is similar to different studies[9,10,20].

This study revealed that the mean age (with SD) of the male was 54.9 (±12.32) years and that of female was 53.4 (±14.52) years. This finding correlates with that of an Indian[19] and a Mexican study[21]. Motor

neuron disease patients were divided into ALS, ALS-PUMNS, PMA, and PBP. It was found that patients having ALS was 47.85%, ALS-PUMNS was 41.42%, PMA was 7.85% and PBP was 2.88%. This is similar to the finding of an American study[22]. It also correlates with that of Indian studies[19,23] but differs from other studies[24,25]. This dissimilarity is probably due to geographical variation, which could also be supported by similarity with the Indian study[19].

The study subjects of this series presented before 35 years in 14% and the rest 86% presented after that age. This picture corroborates with that of Younger's[22] and Ashraf's studies[18].

Seventy percent patients of this study had CSF protein value less than 50 mg/dl, 25% had between 50 to 74 mg/dl and the rest 5% had above 75mg/dl. This finding is similar to that of study in Columbia where they showed that CSF protein content was greater than 50mg/dl in 25% cases and 5% patients had CSF protein more than 75gm/dl[22]. Finding of current study is also similar to the finding of a very old study by Guiloff in 1953[26]. In another study of living MND patients, CSF value over 75gm/dl occurred in 5% of the patients[27] which is similar to this finding but does not corroborate with other studies[28].

In conclusion it may be said that CSF protein of MND patients usually do not rise but 30% of patients may show raised CSF protein. Sometimes the value may be more than 100mg/dl. This finding is similar to the other studies but the age of the patients are younger in Bangladesh which is similar to that in many Indian studies.

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