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ORIGINAL ARTICLE

PATTERN OF MOTER NEURON DISEASE IN NORTH INDIA-STUDY AT TERIARY CARE CENTER

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ABSTRACT: Pattern of motor neuron disease in India; study at tertiary care Centre study. **AIM:** study of pattern of motor neuron disease. **MATERIAL AND METHODS:** The present study was conducted in Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, and Varanasi. Total 71 Patients of motor neuron disease were included in this study. Cases were selected from patients attending Neurology OPD and IPD. Patients were enrolled from Oct. 2012 to April 2014. **INCLUSION CRITERIA:** All the cases of motor neuron disease. **EXCLUSION CRITERIA:** Patients other than motor neuron disease. **OBSERVATION AND DISCUSSION:** Out of 71 patients 29 were JASSMA, 19 bulber MND, 24 ALS and 2 were of SMA. In JASSMA most of patients were male and adolescent. Disease was started asymmetrically in distal upper limb with thinning of hand, mainly in dominant hand and common symptoms were weakness, thinning, cold paresis, polyminimyoclonus, and brachioradialis sparing. Disease also affect another upper limb and become static after 2.9 years. In bulber onset group disease was very fulminent and rapidly progressive. In ALS group disease was asymmetrically started either from upper and lower limbs. Later on involvement of were taking place with all four limbs with upper and lower motor neuron features. Disease was progressive in all patients. In SMA group disease was very slowly progressive and one patient was of Kennedy disease. **SUMMARY & CONCLUSION:** Pattern of motor neuron disease in our institute showed 40.84% cases of JASSMA, 22.5% cases of Bulbar ALS, 33.8% ALS and 2.8% SMA. 1. Bulber ALS patients had very severe disease and progression were very fast. 2. In JASSMA group disease become static in mean 2.9 years after onset of symptoms. Significant number of JASSMA patients showed abnormality in cervical spine MRI. Significant number of JASSMA patients had onset of symptoms in their dominant hand. Pain and tightness in hand were the first symptoms in JASSMA patients.

KEYWORDS: Diaphragmatic hernia, Congenital diaphragmatic hernia.

INTRODUCTION: MND is a group of incurable progressive neurodegenerative disorders in which degeneration involves upper and lower motor neurons in different body regions, resulting in progressive weakness of bulbar, limbs and respiratory musculature, in different combination.

Classification of MND: The majority of MND cases are classified as sporadic, only 5 to 10% cases are familial.

Hereditary MND:

1. With UMN & LMN involvement.
    a. Familial ALS adult & juvenile onset.
    b. ALS pus syndrome ALS-FTD Wilhelmsen-Lynch Syndrome.

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2. With LMN involvement:
   a. SMA TYPE 1, 2, 3, 4.
   b. SMA variant (AR/AD/X-linked).
   c. Fazio-Londe Syndrome (AR/AD/X-linked).
   d. Kennedy Syndrome (XR).

3. With UMN involvement HSP (AR/AD/X-LINKED).

Sporadic MND: Chronic.

1. With UMN & LMN Involvement (Sporadic ALS and ALS-Variants).
2. With LMN INVOLVEMENT.
   a. Monomelic/Focal/Segmental SMA.
   b. Post-polio syndrome.
   c. Post-irradiation syndrome.
3. With UMN involvement.
   a. Primary latral sclrrosis.
   b. Neurolathyrism.
   c. Konzo.

Acute:

   a. Poliomyelitis.
   b. Herpes zoster.
   c. Coxsackie.

Amyotrophic Lateral Sclerosis (ALS): Is most common variant of motor neuron diseases. In the USA it is commonly known as Lou Gehrig's disease, after the baseball player diagnosed with this disease in 1939. Mainly affects adult male. ALS is sporadic diseases up to 5% cases are familial. ALS is due to loss of neurons at all levels of the motor system-from the cortex to the anterior horn of the spinal cord. Physical signs include both upper motor neuron and lower motor neuron findings. The course of the disorder is inexorably progressive, with 50% of patients dying within 3 years of onset. The clinical features can be considered in relation to neurological regions or levels: bulbar, cervical, and lumbar. A fourth thoracic level is sometimes mentioned.[1]

Bulbar-onset patients present with slurring of speech, difficulty in swallowing or both. Bulbar involvement can be lower motor neuron (Bulbar palsy), upper motor neuron (Pseudobulbar palsy), or both. Cervical-onset amyotrophic lateral sclerosis presents with upper-limb symptoms, either bilateral or unilateral. Proximal weakness can present as difficulty with tasks associated with shoulder abduction and distal weakness can manifest with impairment of activities requiring pincer grip. The arm can be strikingly wasted with profuse fasciculation and brisk reflexes. Lumbar onset implies degeneration of the anterior-horn cells of the lumbar region and is associated with lower motor neuron symptoms and signs in the legs, such as a tendency to trip or difficulty on stairs. In its typical form with evidence of both spinal and cortical involvement, the diagnosis is usually clear. The combination of asymmetrical weakness and wasting in the limbs associated with clinical evidence of corticospinal tract damage typically comes on insidiously over months and accounts for about 85% of all cases of MND Pure Lower Motor Neuron Syndromes - Around 10% of patients of MND present as pure lower motor

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neuron involvement. It is more slowly progressive than full blown ALS. Regional variants where involvement remains confined to the lower or upper limbs are described.[2,3] It is important to appreciate that there is a group of inherited conditions called spinal muscular atrophies in which a pure lower motor neuron pattern of weakness develops in early life and progresses very slowly.[4,5] Specific genetic tests are available for X-linked bulbospinal neuronopathy (Kennedy's disease), which causes a slowly progressive lower motor neurone syndrome, sensory neuropathy, and partial androgen insensitivity leading to gynaecomastia and the recessive form of proximal spinal muscular atrophy which can occasionally come on in adult life.[4] A slowly progressive pure lower motor neuron syndrome in one limb may be due to an immune mediated condition called multifocal motor neuropathy with conduction block.[5]

Pure Upper Motor Neuron Syndromes: A small percentage of patients never develop any lower motor neuron signs or at least not until very late in their illness. The term primary lateral sclerosis has been used to describe this condition which is generally considered to be etiologically related to ALS.[6,7] The principal distinguishing features of primary lateral sclerosis are the symmetrical progression of a spastic tetraparesis with pseudobulbar palsy.

Juvenile Asymmetric Segmental spino-muscular Atrophy (JASSMA) of Distal Upper Extremity also called: Juvenile muscular atrophy of distal upper extremity (Hirayama disease) is a cervical myelopathy. Predominantly affecting male adolescent presented with insidious onset and slow progression of muscle weakness and muscular atrophy of the distal upper limb, including thenar, hypothenar, interossei muscles, and wrist flexors and extensors, with sparing of brachioradialis muscles. The border of muscular atrophy runs obliquely over the volar and dorsal surfaces of the forearm, called oblique amyotrophy.[7] The phenomenon of cold paresis is widely observed in the patients, characterized by exacerbating of finger weakness on exposure to cold environment.[8,9] Resting fasciculation is not observed, but contraction fasciculation is well documented.[10,11,12,)]

MATERIAL & METHODS: The present study was conducted in Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, and Varanasi. Total 71 Patients of motor neuron disease were included in this study. Cases were selected from patients attending Neurology OPD and IPD. Patients were enrolled from Oct. 2012 to April 2014.

Inclusion Criteria: All the cases of motor neuron disease.

Exclusion Criteria: Patients other than motor neuron disease.

Valid informed consent were taken from all patients. All patients were subjected to a detailed clinical history, physical and neurological, electrophysiological and neuro radiological examination, as per the standard protocol prepared by us. The past history of any illness, history of chronic illness, personal history, history of addiction, drugs/toxin exposure, occupational, dietary habits and family history is to be taken in detail. The patients were undergo routine blood counts, blood sugar estimation, liver function test, renal function test, test for collagen vascular diseases, HIV ELISA, screening for malignancy, EMG, MRI scan of Brain and cervical spine were done in all patients.

Electrophysiological examination including nerve conduction study and electromyography was done in Neurology lab over Medlac synergy EMG machine.

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The Revised EL Escorial Criteria:

Diagnosis of ALS Requires:

Presence of:

1. Evidence of lower motor neuron degeneration (LMN) by clinical electrophysiological and neuropathological examination.
2. Evidence of upper motor neuron degeneration (UMN) by clinical electrophysiological and neuropathological examination and,
3. Progressive spread of symptoms or signs with in a region or to other regions as determined by history and examination.

The Absence of:

1. Electrophysiological and pathological evidence of other disease processes that might explain the signs of LMN and or/UMN degeneration and,
2. Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs.

OBSERVATIONS:

First symptom code	Diagnosis							
	JASSMA		Bulber MND		ALS		SMA	
	No.	%	No.	%	No.	%	No.	%
Change in voice	0	0.0	11	69.8	1	4.2	0	0.0
Difficulty in holding object rt. Hand	9	31.0	0	0.0	8	33.3	0	0.0
Difficulty in holding object lt. hand	3	10.3	0	0.0	4	16.7	0	0.0
Difficulty in lifting object lt. UL	0	0.0	0	0.0	2	8.3	0	0.0
Difficulty in lifting object Rt. UL	0	0.0	2	12.5	3	12.5	2	100
Difficulty in swallowing	0	0.0	1	6.2	1	4.2	0	0.0
difficulty in walking both LL	0	0.0	2	12.5	3	12.5	0	0.0
Pain in lt. UL	2	6.9	0	0.0	0	0.0	0	0.0
Pain in Rt. UL	9	31.0	0	0.0	0	0.0	0	0.0
SLLEPAGE OF SLEEPER	0	0.0	0	0.0	1	4.2	0	0.0
Thinning of rt. Hand	1	3.4	0	0.0	1	4.2	0	0.0
Tightness of lt. hand.	1	3.4	0	0.0	0	0.0	0	0.0
Tightness of rt. hand.	4	13.8	0	0.0	0	0.0	0	0.0
Total	**29**	**100**	**16**	**100**	**24**	**100**	**2**	**100**

Table 1: First symptom code Vs Diagnosis

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Symptoms	JASSMA (N=29)		Bulber MND (N=16)		ALS (N=24)		SMA (N=2)	
	No.	%	No.	%	No.	%	No.	%
Weakness	28	96.6	15	93.8	23	95.8	2	100
Thinning	29	100	15	93.8	22	91.7	2	100
Hand wasting	29	100	15	93.8	23	95.8	2	100
Forearm wasting	26	89.7	15	93.8	23	100	2	100
Brachioradialis sparing	23	79.3	0	0.0	0	0.0	0	0.0
Proximal myotomal	0	0.0	5	31.2	16	66.7	2	100
Forearm weakness	26	89.7	14	87.5	19	79.2	1	50.0
Minipolymyoclonus	22	75.9	0	0.0	0	0.0	0	0.0
Cold paresis	25	86.2	0	0.0	0	0.0	0	0.0
Fasciculation	23	79.3	16	100	24	100	2	100
Change in voice	0	0.0	16	100	2	8.3	0	0.0
Difficulty in swallowing	0	0.0	16	100	3	12.5	0	0.0
Nasal regurgitation	0	0.0	16	100	2	8.3	0	0.0
Gynaecomastia	0	0.0	0	0.0	0	0.0	1	50
Sensory symptom	0	0.0	0	0.0	0	0.0	1	50
Family history	4	13.8	0	0.0	1	4.2	0	0.0
Higher mental function	0	0.0	1	6.2	0	0.0	0	0.0
Cranial nerve involvement	0	0.0	16	100	4	16	0	0.0
Rt UL bulk	28	96.6	8	50	20	83.3	2	100
Rt UL tone	13	44.8	3	18.8	1	4.2	2	100
RtUL power	28	96.6	12	75	18	75	2	100.
Lt UL bulk	14	48.3	0	0.0	4	16.7	2	100
Lt UL power	15	51.7	5	31.2	3	12.5	1	50
MRI Brain	0	0.0	7	43.8	17	70.8	2	0.0
MRI Cervical Spine	19	65.5	5	31.2	9	37.5	1	50
Disease Progression	16	55.2	16	100	24	100	2	100

Table 2: Symptoms Vs Diagnosis

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Jerks	JASSMA (N=29) Reduced		Brisk		Bulbar MN (N= 16) Reduced		Brisk		ALS (N=24) Reduced		Brisk		SMA (N= 2) Reduced		Brisk	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Rt Biceps jerk	19	65.5	0	0.0	O	0.0	16	100	0	0.0	24	100	2	100	0	0.0
Rt Triceps Jerk	7	24.1	0	0.0	0	0.0	16	100	0	0.0	24	100	2	100	0	0.0
Rt Brachioradialis Jerk	19	65.5	0	0.0	0	0.0	15	93.8	0	0.0	23	95.8	2	100	0	0.0
Lt Biceps Jerk	10	34.5	0	0.0	0	0.0	14	87.5	0	0.0	24	100	2	100	0	0.0
Lt Triceps Jerk	4	13.8	0	0.0	0	0.0	15	93.8	0	0.0	24	100	2	100	0	0.0
Lt Brachioradialis Jerk	7	24.1	0	0.0	0	0.0	16	100	0	0.0	24	100	2	100	0	0.0
Rt Knee Jerk	0	0.0	0	0.0	0	0.0	16	100	0	0.0	24	100	2	100	0	0.0
Rt Ankle jerk	0	0.0	0	0.0	0	0.0	15	93.4	0	0.0	24	100	2	100	0	0.0
Lt Knee Jerk	0	0.0	0	0.0	0	0.0	16	100	0	0.0	24	100	2	100	0	0.0
Lt Ankle Jerk	0	0.0	0	0.0	0	0.0	16	100	0	0.0	24	100	2	100	0	0.0

Table 3

DISCUSSION: In JASSMA group the onset of disease was in second decade in 28 patients. One patient had later onset of disease. And mean age of patients were 24.07±10.145 years in our study. Symptoms were started asymmetrically in all patients.

From India it has been described from northern[13,14,15] as well as southern[16] parts of the country. In our study out of 29 patients 28 patients were male.

In our study all patients had asymmetric onset of disease later on involves other upper limb. As the disease progress thinning of hand mainly thenar and hypothener eminence and forearm developed with sparing of brachioradialis muscle. The disease typically has an insidious onset, slow progression and often a self-limiting course. The weakness and atrophy are confined to hand and forearm muscles. There is relative sparing of brachioradialis muscle that gives rise to characteristic oblique amyotrophy.[17,18,19]

22 patients had history of non-rhythmic coarse tremors in hands called Minipolymyoclonus. Coarse non-rhythmic tremors are common in fingers. Autonomic disturbances such as alteration in skin temperature, excessive sweating in hands and worsening of symptoms in cold environment, are often observed.[20,21,22] 25 patients in our study had history of worsening of symptoms in cold. 23 patients in our study had history of fasciculations which was restricted over upper limbs only. In one study 27% had fasciculations.[18,23,24] In our study the most common first symptom was difficulty in holding object and pain in limbs followed by tightness in dominant limbs. In other studies weakness

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and thinning were most common symptoms. The course of disease becomes static after 2.5 to 3yrs of onset of symptoms. The initial progressive course of non-progressive juvenile-onset SMA is followed by a spontaneous arrest after few years of onset.[25,26,27,28]

Recent studies suggest structural abnormalities in the cervical region in patients with JASSMA. Hashimoto et al. (1976)[19] reported straight neck due to lack of cervical vertebral Iordosis on plain radiographs. Localized atrophy of the lower cervical cord was observed on CT myelography.[20] On MRI, increased posterior epidural space has been demonstrated during neck flexion.[29,30] We performed cervical MRI in 16 patients of JASSMA and compared the findings with 5 normal and 5 disease-negative controls to look for any specific feature of JASSMA.

In our study JASSMA were lower motor neuron disease. No bulbar symptoms Tone were normal or slightly reduced. Deep tendon reflex were reduced. The weakness is progressive over 2-4 years, followed by a slow decline or total arrest. Gourie Devi and Nalini showed that within a few years of progression disease process appears to arrest and patients followed up more than 20 years never go on to develop progression to other areas of motor system.

Nerve conduction study shows pure motor neuropathy in 18 out of 29 patients. Electromyography (EMG) was neurogenic in all JASSMA patients.

In bulbar MND group mean age of patients were 52.88±13.002 with male preponderance. All the patients were from poor socioeconomic status. And short history of symptoms were present. 11 out of 16 patients had change in voice as a first symptom. Followed by difficulty in swallowing and nasal regurgitation. 15 out of 16 patients had weakness in limbs followed by thinning of limbs both proximal as well as distal. 8(50%) patients had rt. Upper limb thinning followed by involvement of other limbs. All patients had history of generalized fasciculations and brisk reflexes.[31,32,33]

ALS is a fatal neurodegenerative disorder that selectively affects neurons of the voluntary motor system.[34] It begins rather heterogeneously among patients, with initial symptoms of muscle weakness and paralysis that are limited to one limb or one muscle group. The disease then rapidly progresses and causes widespread paralysis and spasticity throughout the whole body. In most cases death occurs within 1–5 years after onset.

Pathologically, ALS is characterized by extensive loss of lower motor neurons in the spinal cord and brain stem, atrophy of ventral roots, degeneration of upper motor neurons in the motor cortex and corticospinal tract, somatic and axonal inclusions of aberrant neurofilament proteins, and reactive astrocytosis.[35] In our study 23 patients had weakness in limbs mainly from upper limbs 22 patients had thinning of limbs followed by thinning of forearm. Only three patients had bulbar symptoms in ALS group. Most of ALS patients had reduced bulk of limbs followed by weakness and involves all four limbs.

In our study most of patients had history of fasciculations initially localized to one limb followed by generalized fasciculations. All reflexes were brisk with positive jaw jerk.

In our study nerve conduction study shows pure motor neuropathy and EMG were neurogenic. In MRI brain 17 patients shows abnormal MRI brain rest 7 patients shows normal MRI brain. Disease was progressive in all ALS cases.[36,37]

In our study we found 2 cases of spinal muscular atrophy (SMA). one patient was adult onset SMA (Type 4) and other was Kennedy`s disease both patients were male.

Mean age of presentation were 53.50±14.849 years. SMA type 4 mildest form of SMA, patients do not manifest symptoms until adulthood, with a mean age of onset in the 30s. Both patients were

farmer and presented as difficulty in lifting object. Followed by difficulty in walking and later on involved all four limbs.

Patients usually report trouble in getting up from the floor, rising from a chair or crouch going up stairs. Many patients develop fasciculations in limb muscles, leading to a mistaken diagnosis of amyotrophic lateral sclerosis. Type 4 patients usually remain ambulatory. Both patients had thinning and weakness of limbs with reduced power and decreased deep tendon reflexes. Both were had negative family history.[38,39,40]

In our study Kennedy`s disease patient had facial tremors, gynacomestia proximal and distal muscle weakness but patient was able to walk without support. Seefeld et al. in 1995[24] probably reported the first two cases of Kennedy´s disease in Brazil and, after that, in 1998 Kaimen-Maciel et al.[25] reported a family with 3 cases and one carrier.

Our patient had lower motor neuron features with thinning and reduced deep tendon reflexes. In the early 1890s, the Austrian clinician Guido Werdnig and the German physician Johann Hoffman were the first to describe the severe form of SMA, at the University of Graz, Austria, and in Heidelberg, Germany, respectively.

SUMMARY& CONCLUSION:

1. Pattern of motor neuron disease in our institute showed 40.84% cases of JASSMA, 22.5% cases of Bulbar ALS, 33.8% ALS and 2.8% SMA.
2. Bulber ALS patients had very severe disease and progression were very fast.
3. In JASSMA group disease become static in mean 2.9 years after onset of symptoms. Significant number of JASSMA patients showed abnormality in cervical spine MRI. Significant number of JASSMA patients had onset of symptoms in their dominant hand. Pain and tightness in hand were the first symptoms in JASSMA patients.
4. Two JASSMA patients had positive family history in our study.
5. In Bulbar MND group disease was of short duration and fulminat in course.
6. No statistical significant difference was found in level of As, Hg, Pb in CSF between cases and control.

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