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Original Research Paper

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CLINICAL CHARACTERISTICS OF MOTOR NEURON DISEASE : A SINGLE CENTRE DATA FROM GUJARAT STATE.

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ABSTRACT Motor Neuron Disease (MND) is a heterogenous group of disorders with degeneration of upper and/or lower motor neurons. Limited data is available for clinical characteristics of MND from western India.

Methods: We retrospectively observed all cases of MND, evaluated at our centre. Those with confirmed diagnosis, exclusion of secondary causes and with one year of minimal follow up were included, for the anaysis.

RESULTS: Out of 51 patients of MND, 36 were diagnosed as Amyotropic Lateral Sclerosis (ALS) and 15 patients were having pure Lower Motor Neuron(LMN) type of MND. Male: female ration was 2.8:1 in ALS group , with mean age of 50 years. Out of 10 bulbar onset MND patients, 5 died in the follow-up period. In the LMN subgroup, younger onset monomelic amyotrophy, of upper limb onset (Hirayama) was commonest subtype. No patients with isolated Upper motor Neuron type of MND was found.

SUMMARY: ALS subgroups of patients had younger age of onset in western Indian population, with significant male preponderance. Hirayama disease was commonest LMN type of MND, with onset in 3rd decade and more commonly seen in males.

KEYWORDS : Motor Neuron Disease, Amyotropic Lateral Sclerosis, Hirayama disease, Lower Motor Neuron, Upper Motor Neuron.

INTRODUCTION:

Motor neurone disease(MND) refers to diverse group of conditions, characterised by degeneration of upper and/or lower motor neurons, resulting in progressive disability. It is rare condition with variable incidence rate, clinical spectrum, course and prognosis across the globe.

There are only a few epidemiological and clinical studies of MND patterns from distinct parts of India, with emphasis on difference of age of onset, gender ratio, types of MND and survival pattern.(1,2,3) We studied MND patients retrospectively, presented to our tertiary care centre between 2016-2020. The aim was to describe clinical profile of MND patients, from the state of Gujarat and compare it with data from other parts of India.

MATERIALS AND METHODS:

This observational study was done at VS Hospital(Now SVPIMSR), Ahmedabad, to evaluate clinical profile of motor neurone disease patients, focusing on demographics, clinical characteristics and outcome. We retrospectively reviewed our neurology department records for MND patients, presented to neurology department between Jan 2016 to March 2020.

El Escorial Criteria was used to confirm diagnosis of MND with different levels of accuracy.(4) Those patients who met clinical & electrophysiological criteria of MND were included. Those with inadequate data, secondary causes and follow up of less than 1 year were excluded.Case recorded were scanned and documentation was done in regards to: demographics, age of onset of symptoms, clinical phenotypes, family history, associated medical conditions, electrophysiological parameters, other investigations, follow up (at least up to 1 year) and time of death(if applicable). The follow-up status was acquired via telephonic consultation in some case.

Table 1. Motor neurone disease : subtypes

LMN + UMN involvement

Amyotrophic Lateral Sclerosis (ALS)

- Sporadic
- Familial
- ALS plus syndromes

Pure LMN involvement

- Progressive Muscular Atrophy (SMA)
- Spinal Muscular Atrophy (PMA)
- X- linked Spinobulbar Muscular atrophy (Keneddy's)
- Focal:
- Monomelic (UL) amyotrophy (Hirayama)
- Bibrachial amyotrophy
- Monomelic (LL) amyotrophy
- Madras Motor neuron disease
- Progressive bulbar atrophy

Pure UMN involvement

- Primary lateral Sclerosis

Abbreviations:

LMN:Lower Motor Neuron, UMN:Upper Motor Neuron, UL:Upper limb, LL:Lower limb

RESULTS:

Out of 63 patients screened for suspected MND, 51 patients were included for final analysis, with a definite or probable diagnosis of MND. There were 38 males and 13 females, with a sex ratio of 2.9:1. We classified MND int to three subtypes: Amyotrophic Lateral Sclerosis (ALS) , Pure Lower Motor Neuron (LMN) involvement and Pure Upper Motor Neuron Involvement (UMN) phenotype.(Table 1) In our cohort, ALS was the most common phenotype, with 36 patients. Out of 15 pure LMN patients, Hirayama disease was noted in 9 patients. None of our patient had isolated pure UMN involvement. (Table 2)

In the ALS subgroup, the mean age of onset of symptoms was 50.05 years (range 41-67). There were 17 males and 6 females. All patients presented with weakness and/or wasting, as the first manifestation. Limb onset was commonest (72.2%) and bulbar onset was noted in 27.3%. Upper limb onset was more common than lower limbs (65.3% vs 34.7%) in ALS patients. On physical examination and/or electrophysiological evaluation, all patients had evidence of both- upper motor(weakness, spasticity, brisk DTR, pseudobulbar signs) and lower motor neuron involvement (weakness, wasting, fasciculation, denervation potentials). One patient had positive family history of ALS. Two patients had cognitive

impairment; especially behavioural changes and memory loss. On detailed higher function testing and imaging studies, both were diagnosed as Fronto-temporal dementia.

Table 2: Clinical characteristic of MND patients

	ALS (36 patients)	Hirayama (9 patients)	Bibrachial amyotrophy (3 patients)	Keneddy's syndrome (2 patients)	PMA (1 patient)
Age of onset	50.05 years	24.77 years	55.4 years	43. 2 years	59 years
Male:Female	26:10	7:2	2:1	2:0	1:0
Involvement					
UMN+LMN	+	-	-	-	-
LMN	-	+	+	+	+
UMN					
Onset					
UL	17	9	3	0	0
LL	9	0	0	0	1
Bulbar	10	0	0	2	0
Death	12	0	0	0	0
Limb Onset	7/23				
Bulbar onset	5/10				

Abbreviations: ALS : Amyotrophic Lateral Sclerosis, PMA: Progressive Muscular Atrophy, UMN: Upper Motor Neuron, LMN: Lower Motor Neuron, UL: Upper limb, LL: Lower limb

All Hirayama patients presented with unilateral focal weakness of hand and forearm muscles. Seven out of nine patients were male and mean age of onset was 24.8 years (range 18-29). No UMN features were noted. Of other pure LMN type of MND patients, three patients had bi-brachial involvement and one patient fulfilled criteria for Progressive muscular atrophy (PMA). Two patients were suspected to have Kennedy's syndrome; based on clinical, electrophysiological and other endocrinal features. One patient was confirmed with genetic testing.

We included all patients with a minimum of 1 year follow up data (range 12- 34 months). There were 12 death, out of which 5 patients had bulbar onset MND.

DISCUSSION

We present clinical data of Motor neurone disease patients from a single centre of Gujarat state. Studies on clinical characteristics and follow up of MND patients from western India are very limited. Large case series and studies from north, east and south India showed differences in clinical patterns of Indian patients, when compared to Asian or western data. (1,2,3)

Asian epidemiological studies are finite, with prevalence rate ranging from 1.9 to 9.9 per 100000. A Population survey from southIndia showed prevalence of around 4 per 100000 population. (1) Western literature on MND noted uniform incidence rate of ALS at 2.16 per 100000 person years. (5)

Amyotrophic Lateral Sclerosis (ALS)

ALS is a disorder of motor neurons, resulting in rapidly progressive weakness and poor prognosis. It affects elderly patients and shows signs of both upper and lower motor neuron dysfunction(UMN+LMN) in at least 3 regions (out of bulbar, cervical , thoracic or lumbosacral).

In the present cohort, male to female ratio was 2.83:1, which is comparable to other Indian, Asian and caucasian studies. (6,7) Higher male prevalence may be related to referral bias; due to hospital based data rather then population survey. The mean age of onset is 50.05 years. Nalini A. et al also showed similar result (age of onset 46.2 years), which is in contrast to western ALS population (55 to 65 years of age). (8,9) Researchers have contributed it to be association with large proportion of younger population in India; i.e; 76% were below 40 years of age in one study. (10) Other Asian studies also have documented difference of age on onset of ALS patients, ranging from 52 years in China and 61 years in Japan. (11)

Weakness and wasting were the most common presenting symptoms, for limb onset ALS patients. Bulbar-onset patients complained of difficulty in speaking, more often than difficulty in swallowing , during the first visit. In the ALS group, limb onset was commoner than bulbar onset, which is similar to other Indian and western data.

Largely ALS is a sporadic disease; but positive family history was noted in <5% of Asian ALS patients. We could not do any genetic testing in our single familial ALS patient due to financial constraints. (12) Two patients had fronto-temporal type of dementia in our cohort. Cognitive and behavioural changes associated with ALS were documented from USA in as high as 50% of the patients in one study. (13) Common toxic or genetic factor has been considered. It may also have significant effect on patient care, decision making and survival.

We did not calculate mean survival in this cohort, because of small sample size and short follow up time. But, 5 out of 10 bulbar onset ALS patients died during the interim period; in contrast to 5 out of 26 patients with limb-onset. Evidence from Asian and Indian ALS studies have shown longer survival, especially with limb onset and age of onset less than 50 years.(1,2,14)

Monomelic Amyotrophy

After the first description by Hirayama et al in 1959, juvenile onset amyotrophy of unilateral focal upper limb have been described from number of Asian studies. It represented in 17.6% of patients of MND, as compared to 11.3% described by Nalinidevi et al. (2) The mean age of onset was in the third decade, with a greater male predominance. 4 out of 9 patients had evidence of denervation on electrophysiological testing in non-symptomatic limb also. Long term survival rates are very positive, in longitudinal studies by Gouri-Devi et al.(15)

Other LMN syndromes

Kennedy's syndrome is a X linked recessive disorder with very slow progressive course, limb-girdle weakness, facial fasciculations, bulbar involvement, gynecomastia and other endocrinal abnormalities.Our both patients were in their forties, with diabetes, absent SNAPs of both Sural nerves, on conduction testing. Genetic testing for abnormal CAG repeats (androgen receptor gene on X chromosome) is confirmatory test.

Progressive Muscular Atrophy (PMA) is also a pure LMN type of disease, which occurs in 5th or 6th decade, and affects distal part of limbs. Bibrachial involvement of C5-6-7 roots were also noted in three patients. These both disorders are diagnosis of exclusion and various infectious, inflammatory and immune mediated processes affecting roots or nerves need to be rule out. None of the our cohort patients had madras motor neurone type or monomelic lower limb amyotrophy.

To summarise, Motor Neuron Disease is an uncommon, heterogenous group of disorders. A single centre MND patients data from Gujarat state showed similar patterns, described from various other parts of India. ALS is the most common subtype, with age on onset around 50 years and male predominance. Bulbar onset MND in our cohort had earlier deaths as compared to limb onset. Hirayama disease is the second most common subtype with 3rd decade onset and localised involvement of unilateral forearm and hands. More

similar studies will help us to define geographical variations of clinical profile, which can be translated in patient care and management approaches.

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