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Clinical evaluation of motor neuron disease in Erbil Governorate: A cross-sectional study

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Abstract

Background & Objectives: Melasma is an acquired hyperpigmented patches dispersed symmetrically on body parts that are exposed to sun, mostly on face of female patients. The precise etiology is obscure, but it has numerous hazards such as; ultra violet exposure, genetic factors, hormonal imbalances like thyroid hormone abnormalities. In this study we aimed to evaluate serum thyroid hormones levels in melasma patients.

Methods: A complete of 51 female patients with melasma were enrolled during this study over a period of six months. The cases were clinically diagnosed and examined by Wood's light, then sent for thyroid hormone levels assessment and the finding were reported.

Results: In the current study 51 females with melasma. Their ages ranged between (19-46) years, with (59.9%) between (28-38) years. The duration of melasma was from 6 months to 9 years. Thirty-eight of them were married and had pregnancy. Thyroid stimulating hormone levels were high in 22 of them (43.1%), 20 out of 22 cases that was had high levels of thyroid stimulating hormone had dermal type of melasma by Wood's lamp examination and their p-value was significant (0.001).

Conclusion: We found significantly high levels of thyroid stimulating hormone in cases of melasma mainly among those of dermal type.

Key words: Dermal type, Melasma, Thyroid hormones.

Introduction

Motor neuron disease (MND), is a group of neurodegenerative diseases, characterized by loss of upper and lower motor neurons in the central nervous system. The cause of MND remains unknown, but is postulated to combined environmental and genetic factors.[1-3]Although incidence and prevalence of MND is very low, but because of high mortality and morbidity, and progression of our understanding about pathophysiology of disease, it has special clinical and research interest.[1,4]The worldwide prevalence of MND is 4.5 (4.1-5.0) per 100000 people, and the incidence is 0.78 (0.71-0.86) per 100000 persons per year.[1] There is a significant geographic heterogeneity, with highest incidence in Australasia, North America and western Europe, and lowest incidence is in Sub-Saharan Africa and Central Asia.[1,4,5] During recent decades there was significant increase in incidence of MND cases, which could be explained by aging of population and more facilities for identification of cases.[1,6]Geographic variability of MND, suggests presence of environmental or demographic risk factors.[6]Despite more than 50% of population of world is in Asia, there is limited epidemiological studies of MND in this continent.[5] Although there is no a prevalence study about MND in Iraq, but according to a systematic analysis for the Global Burden of Disease Study, there was 782 cases reported in 2016, with 3.6% increase in age-standardized rate through study period (1990-2016).[1]According to

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the mode of presentation and prominent symptoms and signs of patients, MND can be subclassified into amyotrophic lateral sclerosis (ALS), progressive bulbar palsy (PBP), pseudobulbar palsy (PsBP), progressive muscular atrophy (PMA), primary lateral sclerosis (PLS). Amyotrophic lateral sclerosis is by far the most common pattern and accounting about 70-80 percent of all cases.[4,7] It is the only MND pattern that has evident link with genetic etiology, accounting about 5-10 percent of cases of ALS.[8,9] In the most typical forms of disease, the onset is perceived by the patient as weakness in a distal part of one limb, noted first as an unexplained tripping from slight foot-drop, or by impairment of tasks that require fine finger movements, stiffness of the fingers, and slight weakness or wasting of the muscles of hands.[10]Most studies show that MND is a disease of elderly peoples, with peak incidence at 7th-8th decades, and it's rare before age 50 years,[1,6,11-13]while other studies showed that mean age of onset is earlier in Asia;[1,5] in china mean age of onset was 52 years,[14-16] and in India it was 46 years.[17]The specific objectives of this study were to find age of presentation of MND, chief complaint and presenting symptoms of disease, time from presentation to diagnosis, assess different patterns and male to female ratio of the disease.

Materials and methods

This is a cross-sectional study of 25 patients with MND was conducted from April 2019 to June 2021, in the neurology department, academic medical center in Rizgary Teaching Hospital, Erbil/Iraq. All patients underwent a thorough history taking and clinical examination. History was taken directly from patients; those who were unable to communicate, history was obtained from close relatives.Electrophysiological study, blood tests (complete blood count, erythrocyte sedimentation rate, renal function test, liver function test, serum electrolytes, thyroid function test), as well as cranial and spinal magnetic resonance imaging were performed for all patients. Toxicology screening was already done for a patient who visited another neurologist in other center before attending our neurology department. All patients informed about the study and signed the written informed consent. The confidentiality of the personal information of the patients was protected throughout the study period.Any patient with history of progressive weakness, and/or speech and swallowing difficulty were assessed for features of upper motor neuron signs (spasticity, hyperreflexia, and pathologic reflexes), and lower motor neuron signs (atrophy, fasciculation and hyporeflexia). Electrophysiological study was performed, by one electrophysiologist in Hawler teaching hospital, for those who had above-mentioned clinical features; patients with electrophysiological features of active denervation (fibrillation potentials and positive sharp waves), along with chronic denervation in multiple myotomes[18], were included in the study. In brief, patients diagnosed with MND, according to the revised El Escorial criteria[19].Patients with an alternative clinical diagnosis, those who have had inconclusive/inconsistent electrophysiological study, or an imaging finding diagnostic of other diseases were excluded from the study (eg, those with sensory impairment, incontinence, or significant cognitive impairment, abnormal sensory potentials in nerve conductive study, and feature of radiculomyelopathy on imaging).The data have been analyzed by the Statistical Package for Social Sciences (SPSS, version 25). Categorical variables have been presented in the form of frequencies and percentages. Means and standard deviations have been used to summarize the numerical variables. Fisher's exact test

was used instead of the Chi Square test when the expected frequencies were less than five for more than 20% of the cells of the tables. A p-value of ≤ 0.05 was considered as statistically significant. This study was approved by the ethical committee of Kurdistan Board of Medical Specialties.

Results

Twenty-five patients with MND were included in the study.Their mean age was 52.2 years (± SD of 10.0 years) while the median age was 52 years. The age range was 34-69 years. The age distribution is presented in table (1), which shows that 60% of the patients were male.

Table (1): Patients gender and their age distribution at the time of clinical evaluation.

	No.	(%)
Age (years)		
< 45	5	(20.0)
45-54	8	(32.0)
55-64	8	(32.0)
≥ 65	4	(16.0)
Mean (±SD)	52.2	(±10.0)
Gender		
Male	15	(60.0)
Female	10	(40.0)
Total	25	(100.0)

During clinical evaluation, around one-third of the patients (32%) presented with quadriparesis, 16% presented with lower limb weakness, and another 16% with dysarthria and dysphagia, as presented in Figure (1).

Figure (1): Main complaint(s) of patients with MND at the time of clinical assessment.

The majority (40%) had an onset of the disease between the ages of 45-54 years, while in 28% of them, the disease started before the age of 45 years figure (2). Mean age at onset was 50.7 (± SD of 10.2 years), with a median of 51.5 years.

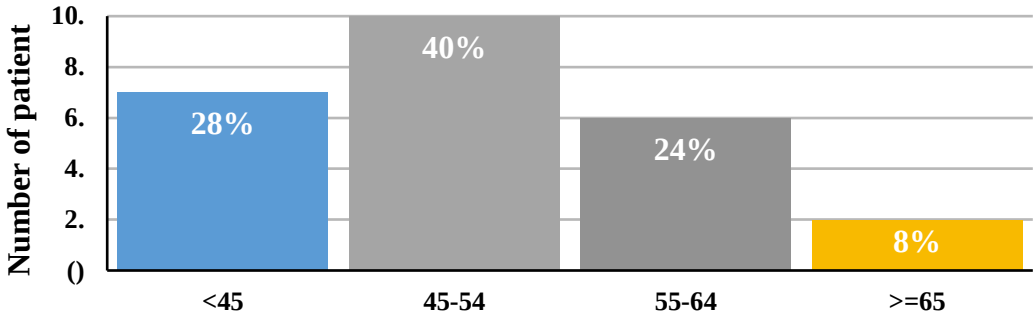

Figure (2): Frequencies and percentages of MND patients in each age group at onset of the disease.

In most of the patients, the symptomatology started in one limb and had involved the contralateral limb after of a period; eighteen patients (72%) had limb onset, seven patients (28%) had bulbar onset of disease.At the time of assessment, duration of the disease was < 12 months in 32% of the patients, 12-23 months in 36%, and ≥ 24 months in 32% of the cases. The time from presentation to diagnosis was ≤ 12 months in 80% of the patients, and the mean was 10.8 (± SD of 7.2 months). The pattern of the gait was normal in 40% of the patients, 20% had foot drop, and another 20% were not able to walk due to severity of weakness. More than one-third (36%) of the patients had spastic dysarthria, and 36% were of normal speech. Wasting and fasciculation of the tongue was present in 68% of the patients, wasting of the extremities was present in 76% of the patients, while fasciculation of extremity was present in 68% of the patients. Abdominal reflexes were impaired in 60% of the patients. Regarding the motor weakness scale, grades of weakest muscles are presented in Table (2).

Table (2): Main physical signs of patients seen during clinical examination.

	No.	(%)
Tongue examination		
Normal	8	(32.0)
Wasting and or fasciculation	17	(68.0)
Wasting of extremity		
Present	19	(76.0)
Absent	6	(24.0)
Fasciculation of extremity		
Present	17	(68.0)
Absent	8	(32.0)
Motor weakness scale		
0.00	2	(8.0)
1.00	1	(4.0)
2.00	4	(16.0)
3.00	3	(12.0)
4.00	14	(56.0)
5.00	1	(4.0)
Total	25	(100.0)

*By Fisher's exact test.

Amyotrophic lateral sclerosis was the commonest pattern of presentation (72%) followed by progressive bulbar palsy (16%). No statistically significant associations (p > 0.999) were found between the age of onset of the disease and disease pattern Table(3).

Table (3): Association of pattern of MND with age of onset of the disease.

	Age of onset (years)						
	< 45		≥ 45		Total		
Pattern of MND	No.	(%)	No.	(%)	No.	(%)	P*
Amyotrophic lateral sclerosis	6	(85.7)	12	(66.7)	18	(72.0)	
Progressive bulbar Palsy	1	(14.3)	3	(16.7)	4	(16.0)	
Pseudo bulbar palsy	0	(0.0)	1	(5.6)	1	(4.0)	
Progressive muscular atrophy	0	(0.0)	1	(5.6)	1	(4.0)	
Primary lateral sclerosis	0	(0.0)	1	(5.6)	1	(4.0)	> 0.999
Total	7	(100.0)	18	(100.0)	25	(100.0)	

*By Fisher's exact test.

It is evident in table 4 that there was no statistically significant association between gender and pattern of MND (p = 0.860).

Table (4): Frequencies and percentages of different patterns of MND in each gender.

	Gender						
	Male		Female		Total		
Pattern of MND	No.	%	No.	%	No.	%	P*
Amyotrophic lateral sclerosis	11	(73.3)	7	(70.0)	18	(72.0)	
Progressive bulbar Palsy	2	(13.3)	2	(20.0)	4	(16.0)	
Pseudo bulbar palsy	1	(6.6)	0	(0.0)	1	(4.0)	
Progressive muscular atrophy	0	(0.0)	1	(10.0)	1	(4.0)	
Primary lateral sclerosis	1	(6.7)	0	(0.0)	1	(4.0)	0.860
Total	15	(100.0)	10	(100.0)	25	(100.0)	

*By Fisher's exact test.

No significant association was detected between gender and the age of onset of the disease (p > 0.999) as presented in Table(5).

Table (5): Relation between gender distribution and age of onset of disease.

	Age of onset (years)						
	< 45		≥ 45		Total		
Gender	No.	(%)	No.	(%)	No.	(%)	P*
Male	4	(57.1)	11	(61.1)	15	(60.0)	
Female	3	42.9)	7	(38.9)	10	(40.0)	> 0.999
Total	7	(100.0)	18	(100.0)	25	(100.0)	

*By Fisher's exact test.

Discussion

In contrast to other studies that shows MND is rare before age 50[1,6] years, this case series shows that our patients with MND has peak age of onset at 45-54 years (10 patients, 40%), followed by those below 45 years (7 patients, 28%). Most studies show that its peak age of onset is late fifties and early sixties[4,20,21], and others show at 70-80 years with a sharp decline after that.[11,12,22,23] On the contrary we had few patients who present after 60 years. This observation in our patients could be related to less likelihood of elderly people to be seen by a neurologist, some patients might have been reluctant to see a doctor or, probably, lack of referral from other colleagues of various specialties. Although environmental factors may have a role, many studies were done searching for such factors, but they are insufficient for attribution to MND. In our patients, mean age at onset of the disease was 50.7 years, comparable to studies done in china, that was about 52 years[14-16]. We have seen that MND is more common in men, with male to female ratio of 3:2, in agreement with many other studies.[3,4,23-25] Some studies found different effect of age for males and females on disease incidence and prevalence,[6,24,25] but we couldn't find such associations between age and gender differences.During clinical evaluation, quadriparesis was the main complaint of our patients followed by lower limbs weakness and dysarthria and dysphagia. In most of the patients, the symptomatology started in one limb (72%), typically from distal part of the limb, and had involved the contralateral limb after a period. Less commonly it started from bulbar muscles (28%), in which, most of these patients were diagnosed as progressive bulbar palsy during our assessment; in no one of them disease started from trunk. This finding is similar to other studies that show approximately two-third of patients have limb-onset, and one-third have bulbar-onset of disease.[26]In the majority of patients there was some degree of pyramidal weakness in extremities (even if they did not complaint about), with grade 4 as the most commonly observed power. Wasting and fasciculation of extremities was common findings, especially in those who had limb-onset, in contrast tongue wasting and fasciculation were more commonly seen in bulbar-onset of disease.One of patients who was a sixty-six years old male presented as brachial amyotrophic diplegia (flail arm), which is a variant of MND. It is rare and has better prognosis compared to classical ALS, but there is limited case series about the

understanding of this variant.[27,28]This case in our study presented with limited disability involving arms only with slow progression over three years. Most of patients in our study had speech abnormality, with spastic dysarthria as commonest one. Most gait problem in those who could walk was foot drop, followed by spastic gait. It was directly related to grade of weakness and tone of lower limbs musculature. It was very common to see frontal release signs (primitive reflexes) in our patients, most prominent ones were palmomental reflex and glabellar tap.Our patients were compatible with revised El-Escorial criteria for diagnosis of ALS. Majority of patients (80%) were diagnosed during first year. Mean delay in diagnosis was 10.8 months, comparable with other studies.[29,30] Four patients were diagnosed as soon as 2-3 months after onset of disease, and fewer diagnosed after 2 years. Probably the cause of this delay in diagnosed in such cases were slow progression of disease (especially in a young patient with minor symptoms in one limb), and reluctance of some patients to see a doctor (more commonly seen in elderly, due to attributing of symptoms to aging process or concomitant disease like osteoarthritis, early in the course of disease). Those who had prominent bulbar palsy was diagnosed earlier, likely due to rapid progression of disease and more functional disability.Although our sample was too small to have clear vision on different patterns of MND in our locality, but still it was in accordance with others in percentage of MND patterns. Seventy-two percent of our cases were ALS, 20% were PBP and PsBP combined together, and 4% for each of PLS and PMA; these are very close to other studies.[23,31] While studies suggest that PBP is more common in elderly women,[32] and PMA is commoner in elderly men.[13] we didn't find statistically significant associations between any pattern of MND with age or gender.Although it is known that 5-10% of ALS are familial, and in Asia it is seen to be less than 5%,[5,14,17] the current study did not record any familial case.Main limitation of our study was its small sample size, we need further multi center epidemiology studies, with larger sample size, for better understanding of MND in our locality.

Conclusion

MND targets a younger age group than expected in Erbil Governorate. However, the overall clinical picture, patterns of the disease, and time from onset to diagnosis is somewhat consistent with other international studies.

Conflicts of interest

There were no conflicts of interest.

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