

# بسم الله الرحمن الرحيم





# شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم





# جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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# **Clinical Types of Movement Disorders in Patients with Multiple Sclerosis**

Thesis

*Submitted for Partial Fulfillment of Master Degree in  
Neuropsychiatry*

By

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# List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
<b>25OHD</b>	<b>25-hydroxy vitamin D</b>
<b>ADL</b>	<b>Activities of Daily Living questionnaire</b>
<b>anti-VCA</b>	<b>Anti-viral capsid antigen</b>
<b>APAs</b>	<b>Anticipatory postural adjustments</b>
<b>BBB</b>	<b>Blood-Brain Barrier</b>
<b>BDI</b>	<b>Beck Depression Inventory</b>
<b>BFMDS</b>	<b>Burke-Fahn-Marsden Disability Scale</b>
<b>BFMMS</b>	<b>Burke-Fahn-Marsden Movement Scale</b>
<b>BP</b>	<b>Bodily Pain</b>
<b>CCAS</b>	<b>Cerebellar Cognitive-Affective Syndrome</b>
<b>CIS</b>	<b>Clinically isolated syndrome</b>
<b>CI</b> s	<b>Cognitive impairments</b>
<b>CNPase</b>	<b>Cyclic Nucleotide Phosphodiesterase</b>
<b>CNS</b>	<b>Central nervous system</b>
<b>CoP</b>	<b>Center of pressure</b>
<b>CP</b>	<b>Cerebellar Peduncle</b>
<b>CSF</b>	<b>Cerebrospinal fluid</b>
<b>DBS</b>	<b>Deep Brain Stimulation</b>
<b>DIS</b>	<b>Dissemination In Space</b>
<b>DIT</b>	<b>Dissemination In Time</b>
<b>EAE</b>	<b>Experimental autoimmune encephalomyelitis</b>
<b>EBNA</b>	<b>Epstein-Barr virus (EBV) nuclear antigen</b>
<b>EBV</b>	<b>Epstein-Barr Virus</b>

<b>EDSS</b>	<b>Expanded Disability Status Scale</b>
<b>EMG</b>	<b>Electromyography</b>
<b>ESS</b>	<b>Environmental Status Scale</b>
<b>ET</b>	<b>Essential Tremors</b>
<b>FMRS</b>	<b>Fahn-Marsden dystonia rating scale</b>
<b>FT</b>	<b>Functional Tremors</b>
<b>GH</b>	<b>General Health</b>
<b>GM</b>	<b>Gray Matter</b>
<b>HRQol</b>	<b>Health Related Quality of life</b>
<b>ISS</b>	<b>Incapacity Status Scale</b>
<b>LV</b>	<b>Lesion Volume</b>
<b>MAG</b>	<b>Myelin Associated Glycoprotein</b>
<b>MBP</b>	<b>Myelin basic protein</b>
<b>MCP</b>	<b>Middle Cerebellar Peduncle</b>
<b>MDs</b>	<b>Movement disorders</b>
<b>MH</b>	<b>Mental Health</b>
<b>MHC</b>	<b>Major Histocompatibility Complex</b>
<b>MMPs</b>	<b>Matrix metalloproteinases</b>
<b>MoCA</b>	<b>Montreal Cognitive Assessment</b>
<b>MOG</b>	<b>Myelin oligodendrocyte glycoprotein</b>
<b>MRI</b>	<b>Magnetic resonance imaging</b>
<b>MS</b>	<b>Multiple sclerosis</b>
<b>NAGM</b>	<b>Normally Appearing Grey Matter</b>
<b>NAWM</b>	<b>Normally Appearing White Matter</b>
<b>OCB</b>	<b>Oligoclonal Bands</b>
<b>OPC</b>	<b>Oligodendrocyte Progenitor Cells</b>

<b>PET</b>	<b>Positron emission tomography</b>
<b>PF</b>	<b>Physical Functioning</b>
<b>PKD</b>	<b>Paroxysmal kinesigenic dyskinesia</b>
<b>PLP</b>	<b>Proteolipid protein</b>
<b>PPMS</b>	<b>Primary Progressive MS</b>
<b>QoL</b>	<b>Quality of life</b>
<b>RE</b>	<b>Role Limitation due to Emotional Problem</b>
<b>RIS</b>	<b>Radiologically isolated syndrome</b>
<b>RLS</b>	<b>Restless leg syndrome</b>
<b>RRMS</b>	<b>Relapsing remitting MS</b>
<b>RP</b>	<b>Role Limitation due to Physical problem</b>
<b>SARA</b>	<b>Scale for the Assessment and Rating of Ataxia</b>
<b>SCP</b>	<b>Superior Cerebellar Peduncle</b>
<b>SDMT</b>	<b>Symbol Digit Modalities Test</b>
<b>SF</b>	<b>Social Functioning</b>
<b>SF-36</b>	<b>Short Form 36 Questionnaire</b>
<b>SPMS</b>	<b>Secondary progressive MS</b>
<b>Th1</b>	<b>T- helper type 1</b>
<b>TSPO</b>	<b>Translocator protein</b>
<b>UPDRS</b>	<b>Unified Parkinson's Disease Rating Scale</b>
<b>VCAM-1</b>	<b>Vascular cell adhesion molecule-1</b>
<b>VLA-4</b>	<b>Very late antigen-4</b>
<b>VT</b>	<b>Vitality</b>
<b>WM</b>	<b>White matter</b>

## Abstract

**Background:** Little is known about the true prevalence and clinical characteristics of movement disorders in early multiple sclerosis (MS), associated clinical disability and their effect on QOL. We conducted a cross sectional study to fill this knowledge gap.

**Objectives:** to study the prevalence of movement disorders in early stages of multiple sclerosis, presence of other clinical disability and their effect on QOL.

**Patients and method:** This is a cross sectional observational study. The patients group included 250 patients with RRMS whom were recruited consecutively from the MS units of Ain Shams and Nasr institute hospitals. Each eligible patient was interviewed and examined for presence of MDs, Patients were divided into 2 groups, group A without MDs and group B showing MDs. General and neurological examination including Expanded Disability Status Scale (EDSS) score at time of interview for both groups. Magnetic resonance imaging (MRI) of brain and cervical spinal cord obtained at the time of interview with documentation of MS plaques involvement for both groups. RRMS patients with MDs (group B) are subjected to different assessment for depression by Beck Depression Inventory (BDI), cognitive assessment by Montreal Cognitive Assessment (MOCA) scale, disability and quality of life (QOL) by the Short Form 36 Health Survey Questionnaire.



**Results:** This study included 250 RRMS. onset of their movement disorders was  $2.69 \pm 2.34$  years from MS diagnosis with mean EDSS  $3.515 \pm 1.04$ . Cerebellar signs are present in 97% of total number of MDs and 26% of total sample, regarding tremors, 36 patients in this study showed tremors representing 53.7% of movement disorders patients, 14.4% of total sample of RRMS patients. This study showed presence of 5 cases of restless leg syndrome 7.5% of total number of MDs. Four cases of dystonia are present in this study representing 6% of MDs patients. Patients with MDs showed presence of depressive symptoms and cognitive affection with negative impact on QOL. Tremors severity is not correlated with either cognition or depression scores where ataxia is correlated with depression score only. MRI assessment of patients with MDs showed higher lesion load and involvement of infratentorial structures especially cerebellum and its connections and brain stem.

**Conclusion:** Movement disorders are common to occur in patients with MS than previously known especially ataxia and tremors early in the course of the disease. Presence of MDs is related to high lesion load and strategic location of these lesions. Special assessment of MDs as independent cause of disability with concomitant depression and CI especially early in the disease course should be taken in consideration due to their negative impact on QOL.

**Key words:** Movement Disorders, Multiple Sclerosis, Tremors, Ataxia.

# INTRODUCTION

**M**ultiple sclerosis (MS) is a chronic inflammatory disease of the brain and spinal cord that is a common cause of serious physical disability in young adults (*Dendrou et al., 2015*). MS patients have various clinical presentations depending on the involved area of the central nervous system (CNS). The definite etiology of MS is still not known but most probably it is multifactorial (*Guzel et al., 2015*).

There is a debate whether inflammation initiates neurodegeneration or neurodegeneration occurs independently of inflammation (*Losy, 2013*). The course of MS is highly varied and unpredictable. In most patients, the disease is characterized initially by episodes of reversible neurological deficits, which is often followed by progressive neurological deterioration over time (*Olek, 2011*).

The pathological findings in MS include inflammation, demyelination (degeneration), remyelination, axonal loss and glial scar formation (failure of repair) (*Bruck, 2005*). The main character of the inflammatory phase is associated with the destruction of the blood-brain barrier and local expression of pro-inflammatory cytokines and chemokines (*Gumus et al., 2015*).