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**Late Onset Multiple Sclerosis Patients Tend to Have Faster Disease Progression.**

**Raed Alroughani<sup>1</sup>, Saeed Akhtar<sup>2</sup>, Samar Ahmed<sup>3</sup>, Jasem Al-Hashel<sup>3</sup>**

**<sup>1</sup>Division of Neurology, Amiri Hospital, Sharq, Kuwait, <sup>2</sup>Department of Community Medicine & Behavioural Sciences, Faculty of Medicine, Kuwait University, Jabriya, Kuwait, <sup>3</sup>Department of Neurology, Ibn Sina Hospital, Kuwait City, Kuwait**

Background: The diagnosis of multiple sclerosis (MS) in older patients presents unique challenges and natural history studies on late onset MS (LOMS; > 40 years) are limited.

Objective: This retrospective cohort study assessed the risk of secondary progression of LOMS and adult-onset MS (AOMS; 18-40 years) patients and examine the prognostic factors associated with time to secondary progression of MS.

Design & Method: Utilizing the national MS registry, we identified AOMS and LOMS cohorts of patients who had relapsing onset MS course. The data on age at onset, gender, presentation at onset, disease duration, prior/ ongoing treatments were obtained. Time to secondary progression was measured as the time to reach sustained EDSS 6. Cox proportional-hazards model was used to evaluate the prognostic significance of studied variables.

Result: For AOMS (n = 804) cohort, the mean ( $\pm$  SD) age at onset was  $27.1 \pm 6.8$  years and mean ( $\pm$  SD) disease duration was  $9.2 \pm 5.2$  years. The corresponding estimates for LOMS (n = 99) cohort were  $45.6 \pm 4.2$  and  $8.0 \pm 5.2$  years. Spinal presentation at onset was significantly more prevalent among LOMS (46.5% vs. 32.3%; p = 0.005). Secondary progressive course was reached in 14.1% and 11.1% of LOMS and AOMS patients respectively. Time (years) to reach secondary progression was significantly (p = 0.001) shorter in LOMS ( $7.1 \pm 3.7$ ) than AOMS ( $12.3 \pm 5.4$ ) patients. The variables significantly associated with time to progressive course were LOMS cohort (adjusted hazard ratio (aHR) = 4.0; 95% CI: 2.1-7.3), female gender (aHR = 1.9; 95% CI: 1.2-2.8), and spinal cord presentation at onset (aHR 1.5; 95% CI: 1.0-2.2).

Conclusion: MS patients with late onset tended to rapidly reach secondary progressive course of the disease. Female gender and spinal symptoms at onset were associated with increased risk of disease progression that warrants aggressive therapeutic approach.