

Clinical and Cognitive Divergence in Early- vs. Late-Onset Alzheimer's Disease: A Large-Scale Analysis from an LMIC Cohort

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BACKGROUND



Early-onset Alzheimer's disease (EOAD) frequently presents with clinical phenotypes distinct from late-onset AD (LOAD). While LOAD is well-characterized, EOAD often faces diagnostic delays and differing progression rates.

OBJECTIVE



To compare cognitive performance, clinical severity, illness duration, and vascular risk factor (VRF) distribution between EOAD and LOAD in a large clinical cohort from a Low- and Middle-Income Country (LMIC).

METHODS



Study Design

Cross-sectional comparative study



Participants

Patients with Alzheimer's disease (N = 746)
• EOAD (onset <65 years): n = 196
• LOAD (onset ≥65 years): n = 550



Assessments

• Global cognition: Addenbrooke's Cognitive Examination-III (ACE III)
• Disease severity: Clinical Dementia Rating (CDR)
• Illness duration (months)
• Vascular Risk Factors (VRFs)



Statistical Analysis

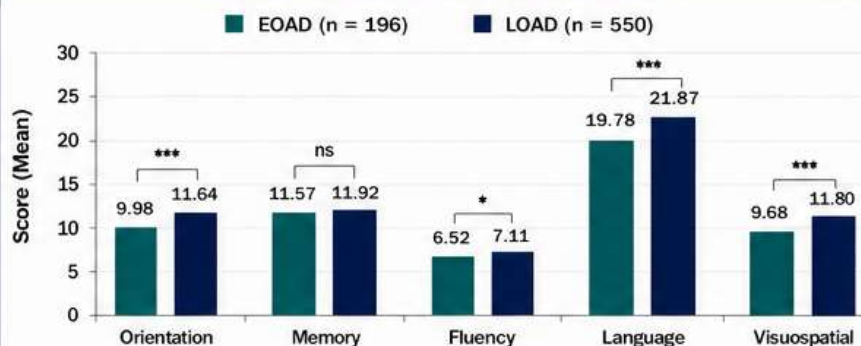
Independent samples t-tests for continuous variables (cognition, education, duration) and Chi-square tests for associations between

1. COGNITIVE PERFORMANCE AND CLINICAL CHARACTERISTICS

Measure	EOAD (n = 196) Mean (SD)	LOAD (n = 550) Mean (SD)	Mean Difference (EOAD – LOAD)	p-value
ACE III Total Score (ACER)	54.99 (23.12)	63.60 (17.77)	-8.61	< .001***
CDR (Global Score)	1.156 (0.665)	1.051 (0.556)	0.105	0.032*
Illness Duration (months)	37.56 (28.94)	27.99 (22.07)	9.56	< .001***
Education (years)	12.96 (3.97)	12.99 (4.38)	-0.03	0.864

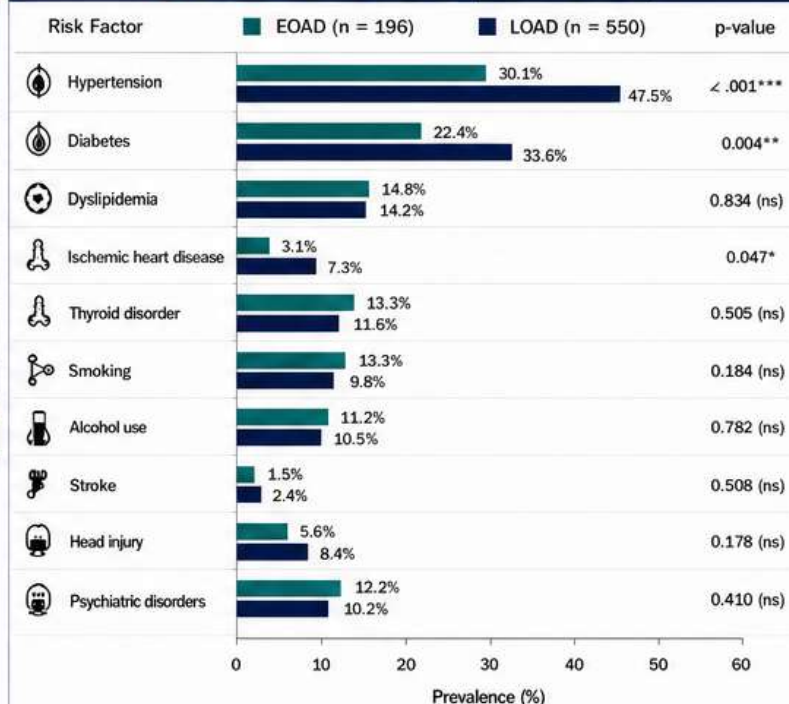
* p < .05, ** p < .01, *** p < .001

2. ACE III DOMAIN SCORES (MEAN ± SD)



ns = not significant (p ≥ .05); * p < .05; *** p < .001

3. VASCULAR RISK FACTORS (PREVALENCE %)



* p < .05, ** p < .01, *** p < .001, ns = not significant

CONCLUSIONS



- EOAD patients exhibit significantly more impaired global cognition due to multidomain deficits compared to LOAD.
- EOAD is associated with greater clinical severity and longer illness duration, likely reflecting diagnostic delays or a more protracted disease course.
- Vascular risk factors are more prevalent in LOAD; however, EOAD carries its own substantial burden and should not be overlooked.

CLINICAL IMPLICATIONS



Improve awareness and early detection of EOAD to reduce diagnostic delays.



Provide specialized cognitive rehabilitation and long-term support for EOAD patients.



Balance vascular risk reduction strategies for LOAD in public health programs.



Tailor interventions based on age at onset and clinical phenotype.

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