Alzheimer's Disease: Global Insights from Cause to Care

A Abyad

MD, MPH, MBA, DBA, AGSF , AFCHSE
Consultant, Internal Medicine and Geriatric, Dar Al Shifa Hospital, Kuwait Chairman, Middle-East Academy for Medicine of Aging.
President, Middle East & North Africa Association on Aging & Alzheimer's
Coordinator, Middle-East Primary Care Research Network
Coordinator, Middle-East Network on Aging

Correspondence:
Dr Abdulrazak Abyad
Email: aabyad@cyberia.net.lb

Received: June 2025. Accepted: July 2025; Published:July 20, 2025.
Citation: .Abyad A. Alzheimer's Disease: Global Insights from Cause to Care. World Family Medicine. July-August 2025; 23(5): 69- 76
DOI: 10.5742/MEWFM.2025.805257866

Abstract

Alzheimer's disease (AD) is the most prevalent cause of dementia worldwide, accounting for 60-80% of dementia cases. Characterized by progressive cognitive decline, functional impairment, and neuropsychiatric symptoms, AD places a significant burden on individuals, caregivers, and healthcare systems. Advances in understanding its pathogenesis have centered on amyloid-beta (Aβ) plaques, tau pathology, neuroinflammation, vascular contributions, and genetic predispositions. While no definitive cure exists, emerging therapies targeting amyloid and tau pathways offer cautious optimism. This review integrates global and regional data, discusses evolving diagnostic frameworks, therapeutic progress, physician-specific challenges, vascular risk interactions, and unique considerations in the Middle East context.

Key words: Alzheimer's disease, cause, care,

Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive impairment of memory, cognition, and behavior. Affecting approximately 24 million people globally in 2001, prevalence is projected to exceed 81 million by 2040, making it a profound public health challenge (1,14). The disease's escalating incidence, coupled with the high cost of care and lack of disease-modifying therapies, underscores the urgent need for continued research and improved clinical strategies. This review synthesizes current knowledge from multiple scientific perspectives, integrating epidemiological data, pathogenesis, diagnostic advancements, therapeutic updates, and regional considerations.

Epidemiology

AD prevalence rises exponentially with age, doubling roughly every five years after age 65 (4). The Delphi consensus study estimated worldwide dementia prevalence at 24.3 million in 2001, rising to 81.1 million by 2040 (1,14).

Table 1. Projected Global Prevalence of Dementia (Delphi Consensus Study)

WHO Region	Prevalence in 2000 (millions)	Prevalence in 2020 (millions)	Prevalence in 2040 (millions)
Western Europe (EURO A)	4.9	6.9	9.9
North America (AMRO A)	3.4	5.1	9.2
China and Developing Western Pacific (WPRO B/D)	6.0	11.7	26.1
Latin America (AMRO B/D)	1.8	4.1	9.1
North Africa and Middle East (EMRO B/D)	1.0	1.9	4.7
Sub-Saharan Africa (AFRO D/E)	0.5	0.9	1.6
Total Global	**24.3**	**42.3**	**81.1**

(Adapted from Ferri et al. (7,14))

Alzheimer's Disease in the Middle East

Despite aging populations, robust epidemiological data on AD in the Middle East are lacking. It's believed that prevalence is comparable to Western nations, though cultural stigmas, lack of specialized services, and limited public awareness hinder early diagnosis and care development (4).

Pathogenesis

The pathogenesis of AD is multifactorial, involving abnormal protein accumulation, genetic predispositions, neuroinflammation, and vascular contributions (1,2,14).

Amyloid Cascade Hypothesis

Central to AD research is the amyloid cascade hypothesis, proposing that overproduction or impaired clearance of Aβ peptides—particularly Aβ1-42—leads to plaque formation, synaptic dysfunction, and neuronal death (1,14). Yet, not all individuals with amyloid plaques develop cognitive decline, indicating other mechanisms are also involved (2).

Figure 1. Simplified Amyloid Cascade Hypothesis

APP (Amyloid Precursor Protein)
↓ β- and γ-secretase cleavage
Aβ peptides (Aβ1-40, Aβ1-42)
↓
Oligomer formation → Synaptic toxicity
↓
Plaque formation → Neuronal death

Tau Pathology

Hyperphosphorylated tau proteins aggregate into neurofibrillary tangles, disrupting cellular transport systems and correlating strongly with disease severity (1,14).

Figure 2. Tau Pathology Progression

Normal tau
↓ hyperphosphorylation
Tau oligomers
↓ aggregation
Neurofibrillary tangles
↓
Synaptic dysfunction, cell death

Neuroinflammation

Neuroinflammation mediated by activated microglia and astrocytes contributes to neuronal damage and may represent therapeutic targets (2).

Vascular Contributions

Vascular risk factors such as hypertension, diabetes, obesity, and smoking exacerbate AD pathology. Recent evidence suggests synergistic interactions between vascular pathology and amyloid/tau accumulation (5,18).

Genetic factors

About 70% of AD risk is attributable to genetic factors (1,14).

Table 2. Genetic Risk Factors for Alzheimer's Disease

Gene	Function/Effect	Risk Increase
APP	Alters Aβ processing; familial mutations raise Aβ42 levels	Familial AD
PSEN1/2	Components of γ-secretase; affect Aβ42 production	Familial AD
SORL1	Regulates APP trafficking	Familial/Late-onset
APOE ε4	Amyloid clearance, lipid metabolism	4–16x increased risk
CLU	Chaperone for Aβ aggregation	Small risk increase
PICALM	Endocytosis and amyloid trafficking	Small risk increase
TOMM40	Mitochondrial function, linked with APOE	Possible age effect

(Data consolidated from multiple sources (1,14,17).)

APOE ε4 remains the strongest genetic risk factor for sporadic AD, increasing risk up to sixteen-fold in homozygotes (14).

Diagnosis

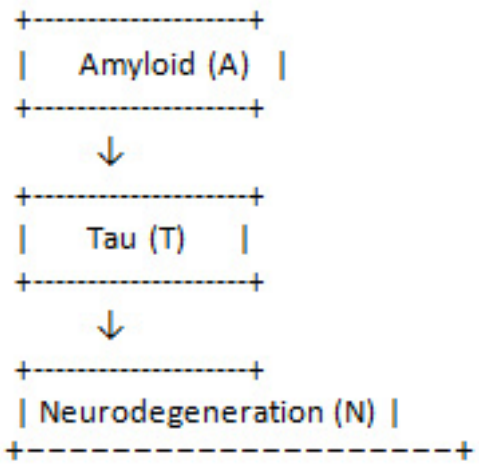
Clinical Diagnosis
Diagnosis relies on comprehensive history, cognitive testing, and functional assessments. Cognitive screening tools include MMSE (10), MoCA, Clock Drawing Test (15), and Test Your Memory (9).

Biomarkers
The 2018 NIA-AA framework defines AD biologically using the AT(N) system (2,13):

Table 3. AT(N) Biomarker Framework for AD

Biomarker Domain	Specific Biomarkers	Clinical Utility
A (Amyloid)	Low CSF Aβ42, Amyloid PET	Diagnosis of amyloid pathology
T (Tau)	CSF phosphorylated tau, Tau PET	Predicts neurodegeneration, symptoms
N (Neurodegeneration)	MRI atrophy, FDG-PET hypometabolism, Blood NfL	Severity, progression tracking

Figure 3. AT(N) Framework Visual Summary



Blood-based biomarkers, such as plasma Aβ42/40 ratios and phosphorylated tau assays, are emerging as accessible diagnostic tools (2).

Assessment Scales in Dementia

Table 4. Selected Assessment Scales in Dementia

Domain	Common Scales	Comments
Cognition	MMSE, MoCA, Mini-Cog (16), TYM (9)	Brief screens for clinical use
Function	ADL, IADL scales	Measure daily functioning
Behavior	Neuropsychiatric Inventory (NPI)	Evaluate neuropsychiatric symptoms
Quality of Life	QOL-AD (patient and proxy)	Increasingly used in trials
Depression	Geriatric Depression Scale (GDS)	Challenges in dementia diagnosis
Carer Burden	Zarit Burden Interview	Measures impact on caregivers

Effective scales must be reliable, valid, brief, and feasible in clinical practice (6,19).

Treatment

Symptomatic Treatments
Cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and memantine offer symptomatic relief but do not halt disease progression (4).

Disease-Modifying Therapies

Table 5. Emerging Anti-Amyloid Therapies

Drug	Trial Highlights	Key Results	Safety Concerns
Aducanumab	EMERGE & ENGAGE trials	EMERGE met endpoint, ENGAGE did not; plaque reduction	High rates of ARIA
Lecanemab	Phase 3 trials	CDR-SB change: -0.45; ~40% achieved amyloid clearance	ARIA ~12%
Donanemab	Phase 2/3 underway	Preliminary iADRS benefit	ARIA incidence higher

(ARIA = Amyloid-Related Imaging Abnormalities) (2,13).

Despite plaque reduction, clinical benefits remain modest, and safety concerns persist (2).

Alzheimer's disease in physicians

Physicians present unique challenges (3):

Table 6. AD in Physicians – Key Challenges and Observations

Issue	Details
Underdiagnosis	High education masks deficits
Stigma	Fear of disclosure delays evaluation
Continued practice possible?	Yes, under supervision for many professionals
Referral programs	State physician health programs help manage risk

Approximately 4,600 US physicians aged ≥70 may have AD, with many able to practice safely under oversight (3).

Alzheimer's disease in the Middle East

Despite rising prevalence, AD awareness and services remain limited (4):

Table 7. AD Challenges and Needs in the Middle East

Challenge	Details
Lack of epidemiological data	No large-scale prevalence studies
Public awareness	Low; symptoms often seen as normal aging
Healthcare provider training	Limited geriatric expertise
Care systems	Heavy reliance on family caregivers
Services	Insufficient support groups and clinics

Recommendations include public education, professional training, and the development of specialized dementia care services (4).

Vascular Risk Factors and AD Progression

Vascular risk factors significantly influence AD progression (5,18).

Figure 4. Impact of Vascular Risk Factors on Cognitive Decline in AD

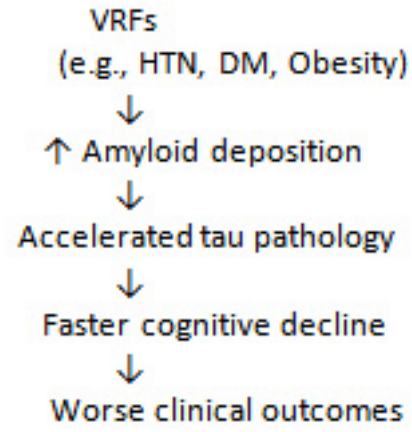


Table 8. Cognitive Decline Associated with VRFs in AD

Group	MMSE Decline	CDR-SB Increase	Significance
No VRFs	Slow	Minimal	Reference group
1-2 VRFs	Moderate	Moderate	Significant difference
≥3 VRFs	Rapid	Marked increase	Highly significant
APOE ε4 + ≥3 VRFs	Most rapid	Greatest decline	Significant synergy

Managing vascular health is crucial in mitigating cognitive decline in AD patients (5).

Future Directiions

Research priorities include:

- Precision medicine using genetic, biomarker, and lifestyle data.
- Development of blood-based biomarkers.
- Therapeutics targeting tau pathology and neuroinflammation.
- Regionally tailored strategies for under-represented populations (1,2,4).

Conclusion

Alzheimer's disease remains a formidable challenge globally. Advances in pathogenesis, diagnostics, and emerging therapeutics offer hope but require continued investment and region-specific strategies. Addressing modifiable risk factors, improving early diagnosis, and developing disease-modifying treatments are critical next steps in the fight against AD (1,14).

References

1. Ballard C, Gauthier S, Corbett A, Brayne C, Aarsland D, Jones E. Alzheimer's disease. Lancet. 2011;377(9770):1019–31.
2. Clinical Debates in AD: Differences in Nomenclature. Alzh Outline.pdf.
3. Devi G. Alzheimer's Disease in Physicians — Assessing Professional Competence and Tempering Stigma. N Engl J Med. 2018 Mar 22;378(12):1073–5.
4. Abyad AR. Alzheimer's disease in the Middle East. alzheime-In the Middle East.doc.
5. Lee WJ, Liao YC, Wang YF, Lin YS, Wang SJ, Fuh JL. Summative Effects of Vascular Risk Factors on the Progression of Alzheimer Disease. J Am Geriatr Soc. 2020;68(1):129–36.
6. Sheehan B. Assessment scales in dementia. Ther Adv Neurol Disord. 2012;5(6):349–58.
7. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. Lancet. 2005 Dec 17;366(9503):2112–7.
8. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. J Am Geriatr Soc. 2003 Oct;51(10):1451–4.
9. Brown J, Pengas G, Dawson K, Brown LA, Clatworthy P. Self administered cognitive screening test (TYM) for detection of Alzheimer's disease: cross sectional study. BMJ. 2009 Jun 9;338:b2030.
10. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing. 1972 Nov;1(4):233–8.
11. Antonelli Incalzi R, et al. A prospective study of the Abbreviated Mental Test in an elderly population. Age Ageing. 2003;32(3):303–8.
12. Alzheimer's Disease Assessment Scales and cognitive subscales. Ass Scales in Dementia.pdf.
13. National Institute on Aging, Alzheimer's Association. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzh Outline.pdf.
14. Alzheimer's Disease International. World Alzheimer Report. A-Review.docx and Alzheimer.docx.
15. Brodaty H, Moore CM. The clock drawing test for dementia of the Alzheimer type: A comparison of three scoring methods in a memory disorders clinic. Int J Geriatr Psychiatry. 1997;12(6):619–27.
16. Borson S, et al. Mini-Cog as a screening tool. J Am Geriatr Soc. 2003;51(10):1451–4.
17. Brooke P, Bullock R. Validation of a 6 item cognitive impairment test with a view to primary care usage. Int J Geriatr Psychiatry. 1999;14(11):936–40.
18. Hancock P, Larner AJ. Test Your Memory (TYM) cognitive screening test: psychometric properties and validation. Int J Geriatr Psychiatry. 2011;26(3):284–92.
19. National Institute for Health and Care Excellence (NICE). Dementia: supporting people with dementia and their carers in health and social care. NICE guidelines [CG42]. 2006 Nov.
20. National Institute on Aging. Alzheimer's Disease Neuroimaging Initiative (ADNI). alzheime-In the Middle East.doc.