

Blood Biomarkers and Neuroimaging in Alzheimer’s Disease: Convergence, Discordance, and Clinical Meaning

Henry Demian Oyoyo^{1,2}, Precious Kehinde Fadele³, Dimeji Olawuyi^{1,2}, Victor Oluwafemi Femi-Lawal^{1,2}, Jonas Ibekwe^{1,2}, Chukwuebuka Asogwa^{1,2}, Ajibola Ajibola Moshood^{1,2}, Timileyin Victoria Olanrewaju^{1,2}, Olajire Ajegbemika^{1,2}, Marvellous Adelaja^{1,2}, Olumide Noah⁵, Chukwuma Igwe^{1,2}, Samuel Omojola^{1,2}, Blessed Olaomo^{1,2}, Mayowa Ojo Owolabi^{6,7}, Rufus Akinyemi^{6,7}

¹ Department of Medicine and Surgery, University of Ibadan, Ibadan, Nigeria | ² College Research and Innovation Hub (CRIH), Ibadan, Nigeria | ³ Department of Medicine and Surgery, University of Nigeria, Enugu, Nigeria | ⁴ Department of Physiotherapy, University of Ibadan, Ibadan, Nigeria | ⁵ Department of Medicine and Surgery, University of Lagos, Lagos, Nigeria | ⁶ Department of Medicine and Surgery, College of Medicine, University of Ibadan, Ibadan, Nigeria | ⁷ Center for Genomics and Precision Medicine, Ibadan, Nigeria

INTRODUCTION

Alzheimer’s disease (AD) is characterized biologically by amyloid-β deposition, tau pathology, and neurodegeneration within the recognized framework, occurring years before cognitive symptoms emerge.

- Standard Benchmarks:** Cerebrospinal fluid (CSF) and PET neuroimaging biomarkers serve as diagnostic gold standards. However, their high cost and invasive nature hinder global application.
- Blood Alternatives:** Highly-scalable blood-based biomarkers (BBBs) are rapidly emerging for fast mass-screening protocols.
- Clinical Need:** This review systematically analyzes biological convergence patterns and the clinical meaning of discordant blood-to-imaging patient profiles.

METHODS

We conducted a narrative review of clinical studies published between **2010 and 2026** evaluating plasma biomarkers in close relation to imaging benchmarks:

- Fluid Assays Evaluated:** Plasma Amyloid-β (), phosphorylated tau (and), Neurofilament Light Chain (), and Glial Fibrillary Acidic Protein ().
- Imaging Anchors:** Amyloid PET scans, Tau PET scans, and structural brain Magnetic Resonance Imaging (MRI).
- AT(N) Interpretation:** All diagnostic markers were mapped to evaluate diagnostic accuracy metrics (AUC), temporal progression dynamics, biological convergence levels, and sources of profile discordance.

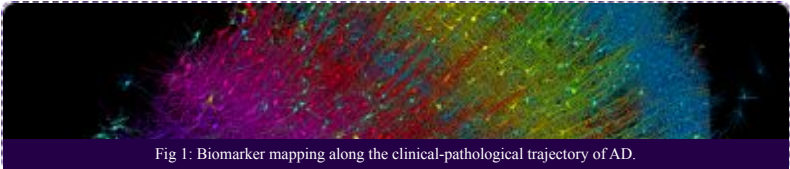
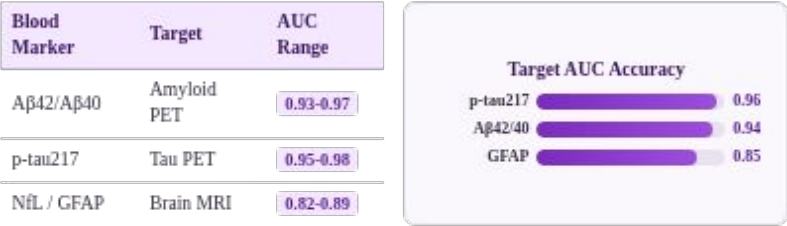


Fig 1: Biomarker mapping along the clinical-pathological trajectory of AD.

RESULTS & DATA ANALYSIS

A. Diagnostic Concordance

Plasma biomarkers display robust clinical correlation with respective PET and MRI markers during progressive phases of disease:



B. Biological Profile Discordance

Discordant results occur primarily during preclinical stages, reflecting biological progression differences rather than assay error:

- Temporal Offsets:** Soluble plasma p-tau changes precede fibrillar tau aggregation visual on PET scans by several years.
- Physiological Interferences:** Confounded by assay methods, APOE-ε4 carrier genetics, systemic clearance (renal function), or overall body composition.

KEY TAKEAWAY

A staged diagnostics model utilizing cost-effective blood biomarkers as a primary frontline triage, followed by highly-targeted neuroimaging confirmation, substantially reduces global screening costs, increases precision, and maximizes clinical trial selection efficiency.

CONCLUSIONS

Blood-based and neuroimaging biomarkers capture complementary dimensions of Alzheimer’s disease biology. A staged diagnostic strategy, using blood biomarkers for large-scale screening and triage, followed by targeted neuroimaging for confirmation and staging can improve diagnostic accuracy, prognostication, trial efficiency, and global accessibility. Interpreting convergence and discordance within biological and clinical context is essential for precision implementation in research and practice.



Fig 2: High-throughput biobanking facilities supporting blood-biomarker validation assays.