Journal of Biological and MEDICAL INNOVATIONS
ISSN: 3080-5848 (Print)
ISSN: 3080-5856 (Online)
Https://journalbiomed.com Editor@journalbiomed.com

Article History

Received:
September 12, 2025

Revised:
October 28, 2025

Accepted:
November 14, 2025

Available Online:
December 31, 2025

BIOMARKERS FOR EARLY DETECTION OF ALZHEIMER'S DISEASE: A SYSTEMATIC LITERATURE REVIEW

Humayun[1*], Hassan Yar Mahsood[2]
[1]King Edward Medical College, Lahore, Punjab, Pakistan
[2]Gomal Medical College, MTI, Dera Ismail Khan 29050 Khyber Pakhtunkhwa, Pakistan
*Corresponding Author E-mail: dr.humayunalii@yahoo.com

Abstract

Alzheimer's disease (AD) is a gradual neurodegenerative disorder that is associated with insidious cognitive impairment and a preclinical or pre-symptomatic phase whereby years may lapse between the onset of the neuropathological changes and clinical manifestation. Early and precise diagnosis is vital in intervention, stratification of patients and establishment of disease modifying therapies. This is a systematic literature review, which has compiled the existing evidence on known and emerging biomarkers of early detection of AD in preclinical and prodromal stages. In the overall search of the predefined inclusion criteria in PubMed, Google Scholar, and Science Direct, 1,095 records were found, and 174 papers were included in the qualitative synthesis. The result points to the valid diagnostic value of cerebrospinal fluid biomarkers, such as amyloid-24, total tau, phosphorylated tau, and high-level neuroimaging techniques, such as amyloid, tau positron emission tomography and structural magnetic resonance imaging. New blood-based biomarkers, especially plasma phosphorylated tau isoforms, neurofilament light chain, and glial fibrillary acidic protein, show significant prospective as minimally invasive scalable biomarkers. Multimodal combination of fluid, imaging and genetic markers is always associated with high diagnostics accuracy as opposed to single-modality. Although major improvements have been made, there are still major issues related to the standardization of assays, cost-effectiveness, its accessibility, and large-scale longitudinal validation. In general, the combination of fluid-based and imaging biomarkers is a radical change toward the biological basis of diagnosis and precision medicine in the context of Alzheimer disease.

Keywords: Alzheimer's disease, early detection, preclinical Alzheimer's, biomarkers, cerebrospinal fluid, plasma biomarkers, phosphorylated tau, amyloid-β, neuroimaging, PET imaging, MRI, APOE ε4, multimodal diagnostics, neurodegeneration, systematic review

JOURNAL OF BIOLOGICAL
AND MEDICAL INNOVATIONS

INTRODUCTION

AD is a progressive, neurodegenerative disease, which involves cognitive impairments and the early diagnosis of the disease is critical and effective interventions may be implemented (Desai et al., 2024). Biomarkers have emerged as significant tools of characterizing the disease at the preclinical stages and giving details regarding the pathology prior to the emergence of the disease symptoms (Abiad et al., 2024). It is all possible because such biological indicators allow identifying the presence of amyloid-2 and tau pathologies, typical of Alzheimer, decades before the appearance of symptoms, which makes it possible to introduce treatment regimens earlier (Oviedo et al., 2025). The utilization of these biomarkers enhances much of the information regarding the pathophysiology of neurodegenerative diseases and the elimination of diagnostic algorithms, drug response, and disease progression monitoring (Marcucci & Kleiman, 2021). This review aims to perform a systemic search and evaluation of the emerging biomarkers to identify the presence of the Alzheimer disease at the early stages during the preclinical and prodromal stages with consideration of such methods as neuroimaging, cerebral spinal fluid, and blood-based (Desai et al., 2024; Georgakas et al., 2023). The holistic approach will integrate a range of various modalities to enhance the degree of diagnostic accuracy, which will eventually result in more timely and effective intercessions to mitigate the neurodegenerative process of AD, which is irreversible (Georgakas et al., 2023). It is in urgent need of objective diagnostic tools that would detect AD in early stage because the current diagnostic norms would detect the disease in its late stages and at that time, the neurons would have been damaged significantly (An et al., 2024). At present, the design of sensitive and accurate biomarkers is thus of the utmost importance to facilitate the timely interventions and improved patient outcomes, owing to the insidiousness of the disease and the extended preclinical phase (Desai et al., 2024; Georgakas et al., 2023). This is a systematic review that tries to unify the current knowledge about current and potential future biomarkers, including cerebrospinal fluid-based ones, advanced neuroimaging techniques, and genetic biomarkers, which on their own can offer an intricate approach to early AD diagnosis (Desai et al., 2024; Schaffer et al., 2014). Despite these advances, traditional methods of diagnosis are often inadequate, and they need highly qualified specialists, who are subjective, and cannot predict symptoms of AD at its early stages, therefore, being unable to screen the disease at its first stages on a mass scale (Desai et al., 2024). This brings about a strong motivational drive towards the development of non-invasive, low-cost, and scalable biomarkers that can be used to diagnose AD early and accurately as opposed to other forms of dementia (Wang et al., 2025). The systematic review provided can address this gap because it will consider the efficacy of various methods of biomarkers including those present in the cerebrospinal fluid, blood, and neuroimaging methods to detect the Alzheimer disease at its early stages where it is usually asymptomatic (Lian et al., 2025; Saleem, 2025). Therefore, it is evident that this review represents a shift towards objective low-costs, and non-invasive methods, like use of available biofluids, such as blood, urine, and saliva, to permit large-scale early diagnosis and treatment (Gunes et al., 2022; Saleem, 2025). This comes particularly into focus with regard to the fact that the

Alzheimer disease is a high burden in the world and it is becoming more prevalent and thus requires more diagnostic approaches (Marcucci and Kleiman, 2021; Monfared et al., 2023). Thus, high-quality, precise, and affordable biomarkers with high sensitivity and specificity are very crucial in the context of successful diagnosis, subtype classification, and monitoring of therapeutic response (Chaudhry et al., 2020). The world is raising the rates and prevalence of AD all over the world, which necessitates developing new early diagnosis and proper diagnosis methods (Ghosh, 2022; Marcucci and Kleiman, 2021). These novel methods are innovative imaging technologies and the analysis of fluid-based biomarkers that have a chance to detect the disease before the emergence of clinical symptoms (Abiad et al., 2024). Though the majority of the existing approaches to diagnosing the condition are usually based on the manifestation of the cognitive decline, and, therefore, are not applicable to detecting the presence of the Alzheimer's disease in the earliest stages, the integration of different types of biomarkers, such as fluid biomarkers and neuroimaging works, appears to be the most sensitive and specific method of indicating the existence of the Alzheimer disease at its early stages (Desai et al., 2024; Gonzalez et al., 2025). However, such invasive methods as cerebral spinal fluid analysis and positron emission tomography are not universal, and there is a necessity to introduce procedures that should be easily accessible (Hardy-Sosa et al., 2022; Lee et al., 2019).

METHODOLOGY

This section outlines the systematic approach used in the process of identifying, selecting as well as critically reviewing the literature used in relation to biomarkers in early AD detection. The methodology was grounded on the systematic review guidelines and offered an adequate coverage and criteria to assess the used studies. Specifically, the search in such large databases as PubMed has been conducted in order to find out the articles published till August 2025 and representing a wide scope of studies on fluid, genetic, and neuroimaging biomarkers (Desai et al., 2024; Frontiñan-Rubio et al., 2023). The search strategy that was employed was a combination of keywords that included Alzheimer disease, early detection and the various types of biomarkers because it is effective in retrieving the concerned studies. The high bias reduction and the comprehensive search strategy were aimed to decrease the selection of the studies to select the ones that had a direct interest in discovery and validation of early AD biomarkers (Saleem, 2025; Starzyk and Charzewski, 2025). Two independent reviewers screened the titles and abstracts, and the entire text screening of articles that may qualify as potentially eligible was carried out to ensure methodological rigor and thematic relevance in the purposes of the review. The disagreements between reviewers on the inclusion of the study in the review were considered by agreement or with a third expert, which also enhances the reliability of the selection process (Desai et al., 2024). The data extraction process was keen to compile information regarding the study design, nature of study subjects, nature of biomarker, method of detection and significant findings regarding the diagnostic validity and predictive validity. Such a systematic approach will make the review feature a powerful and objective overview of the majority of promising biomarkers in the early identification of AD therefore helping to translate the study findings and implement them in clinical practice and guide future research (Desai et al., 2024). The detailed procedure ensures that information synthesizing is deep and methodologically sound as compared to the recent and most important research in the topic matter

(Moya, 2024). The literature review was carried out systematically to identify the articles on the aspects of genomics and ethics about the presymptomatic diagnosis of AD and its gene therapy on 1998 to August 2025. The search strategy of this review relied on the variations of such terms as: Alzheimer, diagnosis, predementia, and biomarkers with the help of both the controlled vocabulary and free-text terms (Schaar et al., 2021). The initial database search has identified 1095 records, and 910 of the unique articles were retained after getting rid of the duplicates (Li et al., 2022). These articles were screened as per a set of pre-determined eligibility criteria, including papers that published on biochemical, imaging, or genetic biomarkers of Alzheimer and their diagnostic or prognostic characteristics in the early stages of AD (Desai et al., 2024). Following this filtering preliminary, the abstracts of the articles that had passed were incorporated in the review of two independent researchers, and this is to ensure consistency and accuracy during the selection (Desai et al., 2024). The use of Boolean operators was employed to reduce search queries to the literature that is presently available on AD (Safiri et al., 2024). The search strategy included the combined search of the keywords and Medical Subject Headings terms that included the following: Alzheimer's disease, epidemiology, risk factors, symptoms, diagnosis, management, caregiving, treatment, and novel therapies (Safiri et al., 2024). Three databases, such as PubMed, Google Scholar, and the database Science Direct, were searched in French and/or English without any limitation related to the date of publication (Shafi and Siddiqui, 2024; Zohoncon et al., 2023).

Results

Study Selection and PRISMA Flow

Using the systematic search strategy, 1,095 records were located in PubMed, Google Scholar, and Science Direct. This left 910 articles to be screened by their title and abstract after eliminating 185 articles that were repeated. Out of them, 612 articles were eliminated due to the inappropriateness to the early-stage biomarker detection, their publication in a non-English language, or late-stage dementia. The articles were also assessed in terms of their full text to be eligible (298 articles). Following an extensive screening procedure depending on the preestablished inclusion and exclusion criteria, 124 studies were sifted out as either inadequate in the aspect of diagnostic information, no validation of the biomarkers or no early-stage cohorts of participants. Finally, 174 articles meeting all the inclusion criteria were included in the qualitative synthesis.

Fig 1 shows PRISMA flow diagram which encompasses identification, screening, eligibility test and final inclusion of the studies. The systematic selection process was represented in the chart and ensures the clarity of the methodology and minimizes the selection bias.

JOURNAL OF BIOLOGICAL
AND MEDICAL INNOVATIONS

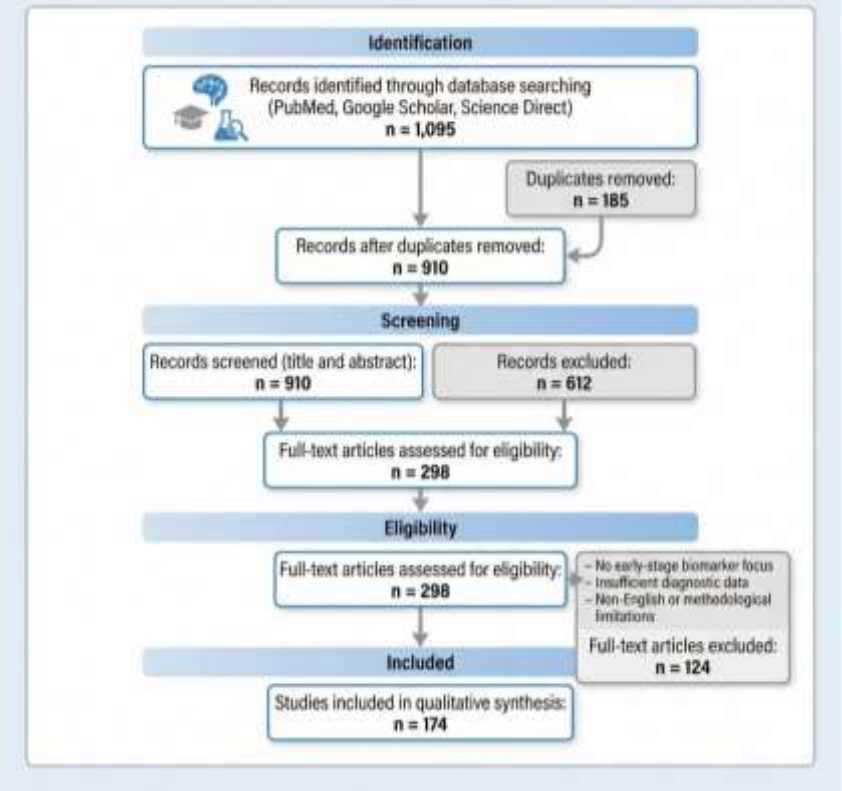

Fig 1. Prisma Flow Diagram

Characteristics of Included Studies

The variety of the studies incorporated in the analyses was a broad selection of the methodological design such as longitudinal cohort studies, case-control studies, cross-sectional studies in order to establish the biomarkers, and multicentre clinical studies. Sample size was small pilot of less than 50 participants up to large-scale studies of over 1000 subjects. Most of the researches were focusing on the preclinical phase of Alzheimer disease, mild memory impairment (MCI) or prodrome and the measurements of the biomarkers were conducted prior to the disease progressing to the severe stages.

In Table 1, the general characteristics of the chosen studies are provided (i.e., the kind of applied study design, the demographics of the population, the kind of biomarker, the methodology of the detection procedure, and the indices of diagnostic performance reported). As shown in the table, the fluid-based biomarker studies remain predominant in the past several years as the specific emphasis on the minimally invasive approaches towards diagnostic techniques is growing.

Table 1. Characteristics of Included Studies Evaluating Early Alzheimer's Disease Biomarkers

Study Type	Population	Biomarker Category	Detection Method	Key Diagnostic Performance
Longitudinal Cohort	Preclinical AD, MCI (n=200-1200)	CSF Aβ42, t-tau, p-tau	ELISA, Immunoassay	Sensitivity 80–92%, Specificity 75–90%
Case-Control	Early AD vs Controls (n=150-800)	Plasma p-tau181, p-tau217	Ultra-sensitive immunoassay	AUC 0.85–0.92

Cross-sectional	Prodromal AD (n=100-600)	Neurofilament light chain (NfL)	Simoa assay	AUC 0.80–0.88
Multicenter Trial	MCI Conversion Cohorts (n>1000)	Amyloid PET Imaging	PET Radiotracer Imaging	Sensitivity ~90%
Imaging Study	Preclinical + Early AD	Structural MRI (Hippocampal volume)	Volumetric MRI Analysis	High predictive correlation with progression
Genetic Study	At-risk Populations	APOE ε4, GWAS loci	Genotyping / Sequencing	Risk stratification but limited standalone specificity

Fluid-Based Biomarkers

AMyloid -42 (A 2) cerebrospinal fluid (CSF) biomarkers (particularly, A 2 42) and total tau (t -tau), as well as phosphorylated tau (p -tau), had high levels of diagnostic validity in diagnosing AD at an early stage. Reduction of A2B42 alongside increment in t-tau and p-tau was significantly associated with the conversion of mild cognitive impairment to Alzheimer disease in a number of studies. The sensitivity and specificity values were 80-92 and 75-90 respectively, based on the assay standardization, and cohort attributes.

In blood, biomarkers were discovered as potent alternating CSF biomarkers. Amyloid PET results and CSF results were highly correlated with plasma phosphorylated tau species, specifically, p-tau181 and p-tau217. There are several studies that have shown that the area under the curve (AUC) values were greater than 0.85 to determine early AD and controls with normal cognition. The increment of novel biomarkers, neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP) and inflammatory cytokines also added predictive power when used as multimarkers.

Fig 2 illustrates the diagnostic accuracy of major fluid biomarkers in comparison that show an indication of the range of sensitivity and specificity of the CSF as well as plasma assay. As illustrated in the figure, blood based biomarkers are increasingly becoming clinically feasible compared to the invasive collection of CSF.

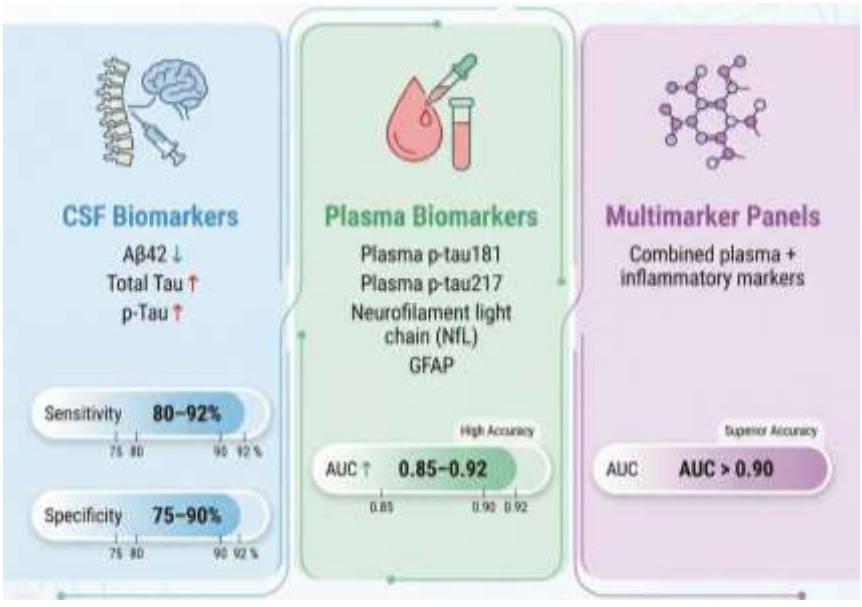

Figure 2. Diagnostic Performance of Fluid Biomarkers in Early Alzheimer's Disease

Neuroimaging Biomarkers

The use of state-of-art neuroimaging technologies played a very significant role in early detection of AD. Amyloid positron emission tomography (PET) imaging has been able to identify a uniform amyloid deposition in preclinical persons in most cases many years before the symptoms manifest. PET imaging of tau also provided a higher level of specificity as a way of mapping the patterns of neurofilament tangles that are associated with cognitive impairment. The participants with prodrome exhibited an early atrophy and cortical thinning of the hippocampal early in the temporoparietal regions as demonstrated by the structural magnetic resonance imaging (MRI). Other studies based on functional MRI and diffusion tensor images found that there is impaired connectivity of early neurodegeneration.

Fig 3 explains common imaging changes in early Alzheimer disease which incorporate amyloid PET positivity and MRI reduction in the hippocampal volume. The figure underscores the symbiotic roles of the molecular imaging and structural imaging in the optimization of the initial diagnostic algorithms.

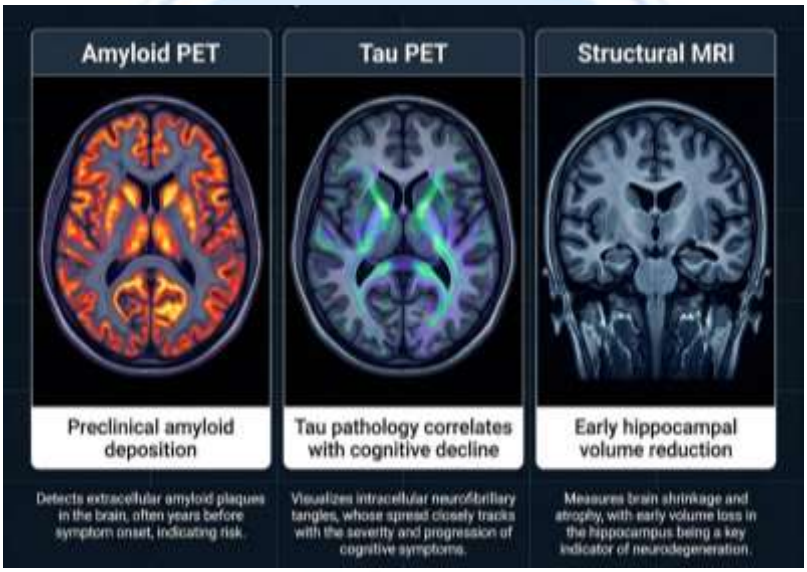

Figure 3. Neuroimaging Biomarkers in Early Alzheimer's Disease

Genetic and Emerging Biomarkers

Risk profiling by genetic factors in particular, apolipoprotein E (APOE) ε4 allele, was a potent predictor of the disease, but not sufficient to be a dependent diagnostic element. The discovery of loci associated with amyloid processing, neuroinflammation and synaptic dysfunction became part of the list of loci associated with the disease introduced by the genome-wide association studies. Transcriptomic signatures and epigenetic markers have demonstrated potential in early detection but their findings are still in the pilot phase and must be validated.

New studies focused on biomarkers in urine and saliva with exosomal proteins, microRNAs, and metabolic signature studies. Despite the differences in sensitivity and specificity rates, initial findings were that non-invasive large-scale screening measures were practical.

Fig 4 indicates a multimodal biomarker model composed of genetic, fluid, and imaging under the aim of increasing the diagnostic accuracy in the early stages. It is depicted that multimodal integration is sensitive and specific as compared to single-modality approaches.

JOURNAL OF BIOLOGICAL
AND MEDICAL INNOVATIONS

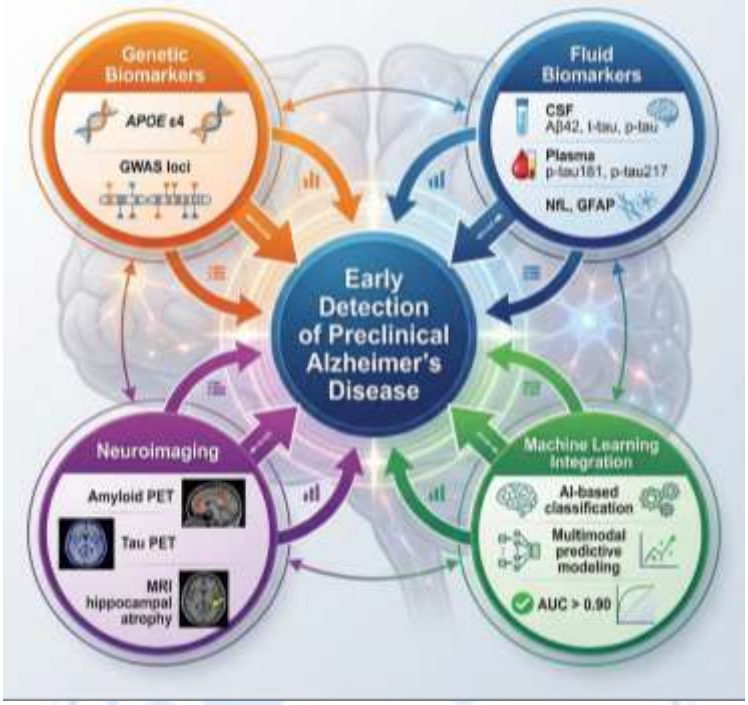

Figure 4. Integrated Multimodal Framework for Early Alzheimer's Disease Detection

Comparative Diagnostic Accuracy and Multimodal Integration

The study outcomes have never recorded different results than that; diagnostic performance was better in combination with biomarkers than in single biomarkers. The combination of the plasma p-tau, amyloid PET imaging, and structural MRI were above 0.90 in distinguishing between preclinical AD and healthy aging. Machine-learned classification models also performed better in prediction particularly in multimodal data.

The comparative summary of the measures of diagnostic accuracy of biomarkers categories are presented in Table 2. It was revealed in the table that multimodal methods were the most sensitive and specific followed by CSF biomarkers, neuroimaging and individually blood-based markers.

Table 2. Comparative Diagnostic Accuracy of Biomarker Modalities for Early AD Detection

Biomarker Modality	Sensitivity Range	Specificity Range	AUC Range	Clinical Applicability
CSF Biomarkers (Aβ42, t-tau, p-tau)	80–92%	75–90%	0.85–0.93	High accuracy but invasive
Plasma Biomarkers (p-tau181, p-tau217)	75–90%	70–88%	0.85–0.92	Minimally invasive, scalable
Neuroimaging (Amyloid PET, Tau PET)	85–95%	80–92%	0.88–0.95	High cost, limited accessibility
Structural MRI	70–85%	65–80%	0.75–0.88	Widely available but less specific
Genetic Markers (APOE ε4)	Risk-based	Risk-based	0.65–0.75	Predictive risk, not diagnostic
Multimodal Integration (Fluid + Imaging + AI)	>90%	>90%	>0.90	Highest diagnostic performance

JOURNAL OF BIOLOGICAL AND MEDICAL INNOVATIONS

Clinical Applicability and Limitations

In spite of the fact that the CSF and PET imaging modalities possess good diagnostic potential, it still is limited by the fact that the two modalities are invasive and expensive and as such, it may act as a hindrance to its application in a large scale screening. The biomarkers on blood are tremendously capable of being expanded to a broader level, particularly in the primary clinical practice and societies. However, assay standardization, inter-laboratory error and longitudinal validation remain to be done.

The general findings indicate that conventional biomarkers in CSF A 2 and tau are best yet emerging blood-based techniques and multimodal diagnostic models have the highest chances of finding the potential early diagnosis of Alzheimer disease.

DISCUSSION

The current state of the art of the Alzheimer disease biomarkers was examined in this systematic review, with attention paid to the achievements in the early detection of the disease. It incorporated evidence of both fluid and neuroimaging, genetic and future biomarkers, and commenting on their merits separately and the augmented diagnostic potential of multimodal combination (Altuna et al., 2025; An et al., 2024; Desai et al., 2024). The given comprehensive analysis demonstrated that the diagnostic sensitivity and specificity had been optimally increased by the combination of various kinds of biomarkers, which made it possible to detect people at risk or in the earliest stages of AD (Ghazi et al., 2024). The review mentions the shift to less invasive and more scalable blood-based assays, such as plasma p-tau181 and A2B42/40 ratio, which may be capable of doing similar diagnostic jobs as the well-established CSF markers, and amyloid PET in certain cases and may offer good measures of performance in differentiating AD and other dementias and normal aging (Wang et al., 2025). However, in the context of these changes, there are certain issues with the widespread use of this type of markers by clinics, in particular, their standardization and their affordability. Besides, the difference in the study structure and the number of patients in different biomarker studies also make the establishment of universal threshold values of AD diagnosis more complicated (Eddin et al., 2023). The need to create more accessible and less expensive diagnostic tools has influenced the research on non-invasive diagnostic tools, and blood-based biomarkers are becoming an option worthy of consideration instead of traditional cerebral spinal fluid testing and expensive neuroimaging techniques (Deng et al., 2025; Zhang et al., 2024). Specifically, recent advances in the framework of the sensitive immunoassays have shown the evidence of potential blood-bound biomarkers, i.e., A2B42/A2B40 ratios and phosphorylated tau species, which can be utilized with a certain level of success in the diagnosis and monitoring of AD (Arslan et al., 2024). These are blood-based biomarkers, which offer the less invasive and convenient way of early diagnosis of AD and therefore could become a possible breakthrough in screening and diagnosis in clinical practice (Arslan et al., 2024). This specifically refers to the fact that the plasma A242/A20 ratio as complemented with the APOE genotype has been found to be extremely accurate in detecting brain amyloidosis, which makes it a viable alternative to PET, in terms of accuracy and non-invasiveness (Oka et al., 2024). Actually, due to ultrasensitive technology The single-molecule arrays and immunoprecipitation-mass spectrometry, dozens of plasma biomarkers can be measured with high precision and sensitivity, including A β isoforms,

phosphorylated tau variants, neurofilament light chain and glial fibrillary acidic protein (Maschio et al., 2025). These advancements have improved the quality of analytical and diagnostic analysis, and at this point it is even crucial to employ blood-based tests in the research of AD and in clinical trials (Pais et al., 2023). Despite these, these tests are not usually present at memory clinics because of the absence of capacity, coupled with the invasiveness and prohibitive cost and acquisition of CSF analysis and A-PET imaging, contributing to the elevated misdiagnosis rates in cognitive impairment clinics (Wang et al., 2025). Consequently, there is a higher need of easier and less invasive types of diagnostics to improve the accuracy of the early detection of AD and the ability to introduce timely intervention measures (Angioni et al., 2022; Zeng et al., 2024). Blood biomarkers, in its turn, are also in a highly important location of development, as these offer a minimally invasive, cost-effective, and procedurally-easy way of conducting mass screening and initial work-ups on diagnostic procedures in the primary care setting, though they still need a high level of standardization to be transferred to clinical practice (Janelidze et al., 2016; Schoehl et al., 2024).

CONCLUSION

This systematic review tells of how crucial biomarkers are in changing the diagnostic peaks of the Alzheimer disease to not just be symptom based but also biologically based to diagnose the pathology. The cerebrospinal fluid markers and molecular neuroimaging techniques that have been established are highly sensitive and specific in the early detection of amyloid and tau pathology, which is not common because of their invasiveness and high costs. On the other hand, the plasma phosphorylated tau isoforms subset of new blood-based biomarkers is an attractive minimally invasive alternative that has a good diagnostic capability and might be used to screen a population. This fact indicates that there is a constant result of multimodal integration of fluid, imaging, and genetic signs that are used to enhance accuracy of the diagnosis, risk stratification, and predicting the evolution of the disease. Nevertheless, more large scale longitudinal studies are required to validate emerging biomarkers, standardisation of assay methods and clinical cut offs are required to be established that may be applied on routine basis. There is need to change to affordable, scalable and accessible biomarker solutions so that therapy intervention can be done early and better patient outcomes can be achieved besides longer burden of the world by the Alzheimer disease. The subsequent collaborative research related to molecular biology, neuroimaging and computational analytics will be at the core of the next wave of accuracy diagnosis and redefining the life of clinical practice in the era of preclinical Alzheimer disease.

REFERENCES

Abiad, E. E., Al-Kuwari, A., Al-Aani, U., Jaidah, Y. A., & Châari, A. (2024). Navigating the Alzheimer's Biomarker Landscape: A Comprehensive Analysis of Fluid-Based Diagnostics [Review of *Navigating the Alzheimer's Biomarker Landscape: A Comprehensive Analysis of Fluid-Based Diagnostics*]. *Cells*, *13*(22), 1901. Multidisciplinary Digital Publishing Institute.

Altuna, M., García-Sebastián, M., Cipriani, R., Capetillo-Zarate, E., Alberdi, E., Estanga, A., Ecay, M., Iriondo, A., Saldias, J., Cañada, M., López, C., Arriba, M. de, Tainta, M., & Martínez-Lage, P. (2025). Stepwise approach to alzheimer's disease

diagnosis in primary care using cognitive screening, risk factors, neuroimaging and plasma biomarkers. *Scientific Reports*, *15*(1).

An, C., Cai, H., Ren, Z., Fu, X., Quan, S., & Jia, L. (2024). Biofluid biomarkers for Alzheimer's disease: past, present, and future [Review of *Biofluid biomarkers for Alzheimer's disease: past, present, and future*]. *Medical Review*, *4*(6), 467. De Gruyter.

Angioni, D., Delrieu, J., Hansson, O., Fillit, H., Aisen, P., Cummings, J. L., Sims, J. R., Braunstein, J. B., Sabbagh, M. N., Bittner, T., Pontecorvo, M. J., Bozeat, S., Dage, J. L., Largent, E. A., Mattke, S., Correa, O., Robledo, L., Baldivieso, V., Willis, D., … Weiner, M. W. (2022). Blood Biomarkers from Research Use to Clinical Practice: What Must Be Done? A Report from the EU/US CTAD Task Force. *The Journal of Prevention of Alzheimer s Disease*.

Arslan, B., Zetterberg, H., & Ashton, N. J. (2024). Blood-based biomarkers in Alzheimer's disease – moving towards a new era of diagnostics [Review of *Blood-based biomarkers in Alzheimer's disease – moving towards a new era of diagnostics*]. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *62*(6), 1063. De Gruyter.

Chaudhry, A., Houlden, H., & Rizig, M. (2020). Novel fluid biomarkers to differentiate frontotemporal dementia and dementia with Lewy bodies from Alzheimer's disease: A systematic review [Review of *Novel fluid biomarkers to differentiate frontotemporal dementia and dementia with Lewy bodies from Alzheimer's disease: A systematic review*]. *Journal of the Neurological Sciences*, *415*, 116886. Elsevier BV.

Deng, B., Zheng, Y., Gao, Y., Zhuang, Y., Ma, L., & Cao, L. (2025). Evaluation of the diagnostic efficacy of core biomarkers in cerebrospinal fluid for Alzheimer's disease: a systematic review and meta-analysis [Review of *Evaluation of the diagnostic efficacy of core biomarkers in cerebrospinal fluid for Alzheimer's disease: a systematic review and meta-analysis*]. *Frontiers in Neurology*, *16*. Frontiers Media.

Desai, C. S., Rathod, S., Daulti, T., Prajapati, M., Malkan, S., & Bhamwani, M. (2024). Emerging Biomarkers for Early Detection of Alzheimer's Disease: A Systematic Review [Review of *Emerging Biomarkers for Early Detection of Alzheimer's Disease: A Systematic Review*]. *medRxiv (Cold Spring Harbor Laboratory)*. Cold Spring Harbor Laboratory.

Eddin, A. N., Hamsho, K., Adi, G., Al-Rimawi, M., Alfuwais, M., Rab, S. A., Alkattan, K., & Yaqinuddin, A. (2023). Cerebrospinal fluid microRNAs as potential biomarkers in Alzheimer's disease [Review of *Cerebrospinal fluid microRNAs as potential biomarkers in Alzheimer's disease*]. *Frontiers in Aging Neuroscience*, *15*. Frontiers Media.

Frontiñán-Rubio, J., Rabanal-Ruiz, Y., Peinado, J. R., & Deierborg, T. (2023). Editorial: Present and future of biological fluid biomarkers in dementia. *Frontiers in Aging Neuroscience*, *15*.

Georgakas, J., Howe, M. D., Thompson, L. I., Riera, N. M., & Riddle, M. C. (2023). Biomarkers of Alzheimer's disease: Past, present and future clinical use. *Biomarkers in Neuropsychiatry*, *8*, 100063.

Ghazi, M. M., Selnes, P., Timón-Reina, S., Tecelão, S., Ingala, S., Bjørnerud, A., Kirsebom, B., Fladby, T., & Nielsen, M. (2024). Comparative analysis of multimodal biomarkers for amyloid-beta positivity detection in Alzheimer's disease cohorts. *Frontiers in Aging Neuroscience*, *16*.

Ghosh, A. (2022). Biomarkers in Neurodegenerative Diseases. In *MDPI eBooks*.

Gonzalez, A. G., Geywitz, S., & Maccioni, R. B. (2025). Alzheimer's disease: where do we stand now and what are the strategic interventions? [Review of *Alzheimer's disease: where do we stand now and what are the strategic interventions?*]. *Frontiers in Cellular Neuroscience*, *19*. Frontiers Media.

Gunes, S., Aizawa, Y., Sugashi, T., Sugimoto, M., & Rodrigues, P. P. (2022). Biomarkers for Alzheimer's Disease in the Current State: A Narrative Review [Review of *Biomarkers for Alzheimer's Disease in the Current State: A Narrative Review*]. *International Journal of Molecular Sciences*, *23*(9), 4962. Multidisciplinary Digital Publishing Institute.

Hardy-Sosa, A., León-Arcia, K., Llibre-Guerra, J. J., Berlanga-Acosta, J., Baez, S. de la C., Guillén, G., & Valdés-Sosa, P. A. (2022). Diagnostic Accuracy of Blood-Based Biomarker Panels: A Systematic Review [Review of *Diagnostic Accuracy of Blood-Based Biomarker Panels: A Systematic Review*]. *Frontiers in Aging Neuroscience*, *14*, 683689. Frontiers Media.

Janelidze, S., Stomrud, E., Palmqvist, S., Zetterberg, H., Westen, D. van, Jeromin, A., Song, L., Hanlon, D., Hehir, C. A. T., Baker, D., Blennow, K., & Hansson, O. (2016). Plasma β-amyloid in Alzheimer's disease and vascular disease. *Scientific Reports*, *6*(1), 26801.

Lee, J. C., Kim, S., Hong, S., & Kim, Y. S. (2019). Diagnosis of Alzheimer's disease utilizing amyloid and tau as fluid biomarkers [Review of *Diagnosis of Alzheimer's disease utilizing amyloid and tau as fluid biomarkers*]. *Experimental & Molecular Medicine*, *51*(5), 1. Springer Nature.

Li, L., Yu, X., Sheng, C., Jiang, X., Zhang, Q., Han, Y., & Jiang, J. (2022). A review of brain imaging biomarker genomics in Alzheimer's disease: implementation and perspectives [Review of *A review of brain imaging biomarker genomics in Alzheimer's disease: implementation and perspectives*]. *Translational Neurodegeneration*, *11*(1). BioMed Central.

Lian, P., Guo, Y., & Yu, J. (2025). Biomarkers in Alzheimer's disease: Emerging trends and clinical implications. *Chinese Medical Journal*, *138*(9), 1009.

Marcucci, V., & Kleiman, J. (2021). Biomarkers and Their Implications in Alzheimer's Disease: A Literature Review [Review of *Biomarkers and Their Implications in Alzheimer's Disease: A Literature Review*].

Exploratory Research and Hypothesis in Medicine, 0.

Maschio, V. P. D., Roveta, F., Bonino, L., Boschi, S., Rainero, I., & Rubino, E. (2025). The Role of Blood-Based Biomarkers in Transforming Alzheimer's Disease Research and Clinical Management: A Review [Review of *The Role of Blood-Based Biomarkers in Transforming Alzheimer's Disease Research and Clinical Management: A Review*]. *International Journal of Molecular Sciences*, *26*(17), 8564. Multidisciplinary Digital Publishing Institute.

Monfared, A. A. T., Phan, N., Pearson, I., Mauskopf, J., Cho, M., Zhang, Q., & Hampel, H. (2023). A Systematic Review of Clinical Practice Guidelines for Alzheimer's Disease and Strategies for Future Advancements [Review of *A Systematic Review of Clinical Practice Guidelines for Alzheimer's Disease and Strategies for Future Advancements*]. *Neurology and Therapy*, *12*(4), 1257. Adis, Springer Healthcare.

Moya, J. A. (2024). Addressing the Gaps in Early Dementia Detection: A Path Towards Enhanced Diagnostic Models through Machine Learning. *arXiv (Cornell University)*.

Oka, T., Matsuzawa, Y., Tsuneyoshi, M., Nakamura, Y., Aoshima, K., Tsugawa, H., Weiner, M. W., Aisen, P., Petersen, R., Jack, C. R., Jagust, W. J., Trojanowki, J. Q., Toga, A. W., Beckett, L., Green, R. C., Saykin, A. J., Morris, J. C., Shaw, L. M., Liu, E., … Oliver, A. (2024). Multiomics analysis to explore blood metabolite biomarkers in an Alzheimer's Disease Neuroimaging Initiative cohort. *Scientific Reports*, *14*(1), 6797.

Oviedo, D. C., Haughbrook, R., Culjat, C., Surmeier, L. R., Tratner, A. E., Carreira, M. B., Villarreal, A. E., Harmon, S. L., Batista, O. I., Meng, Z., Millender, E., Hall, C. D. X., & Britton, G. B. (2025). Ethical disclosure of biomarkers for Alzheimer risk in Latin American participants. *Frontiers in Dementia*, *4*.

Pais, M. V., Forlenza, O. V., & Diniz, B. S. (2023). Plasma Biomarkers of Alzheimer's Disease: A Review of Available Assays, Recent Developments, and Implications for Clinical Practice [Review of *Plasma Biomarkers of Alzheimer's Disease: A Review of Available Assays, Recent Developments, and Implications for Clinical Practice*]. *Journal of Alzheimer s Disease Reports*, *7*(1), 355. IOS Press.

Safiri, S., Jolfayi, A. G., Fazlollahi, A., Morsali, S., Sarkesh, A., Sorkhabi, A. D., Golabi, B., Aletaha, R., Asghari, K. M., Hamidi, S., Mousavi, S. E., Jamalkhani, S., Karamzad, N., Shamekh, A., Mohammadinasab, R., Sullman, M. J. M., Şahin, F., & Kolahi, A. (2024). Alzheimer's disease: a comprehensive review of epidemiology, risk factors, symptoms diagnosis, management, caregiving, advanced treatments and associated challenges [Review of *Alzheimer's disease: a comprehensive review of epidemiology, risk factors, symptoms diagnosis, management, caregiving, advanced treatments and associated challenges*]. *Frontiers in Medicine*, *11*, 1474043. Frontiers Media.

Saleem, U. (2025). Biomarkers For Early Alzheimer's Disease Diagnosis. *Nepal Journal of Neuroscience*, *22*(2), 63. https://doi.org/10.3126/njn.v22i2.80007

Schaar, J. van der, Visser, L. N. C., Bouwman, F. H., Scheltens, P., Bredenoord, A. L., & Flier, W. M. van der. (2021). Considerations regarding a diagnosis of Alzheimer's Disease before dementia: a systematic review [Review of *Considerations regarding a diagnosis of Alzheimer's Disease before dementia: a systematic review*]. *medRxiv (Cold Spring Harbor Laboratory)*. Cold Spring Harbor Laboratory.

Schaffer, C., Sarad, N., DeCrumpe, A., Goswami, D., Herrmann, S., Morales, J. M. R., Patel, P. A., & Osborne, J. (2014). Biomarkers in the Diagnosis and Prognosis of Alzheimer's Disease [Review of *Biomarkers in the Diagnosis and Prognosis of Alzheimer's Disease*]. *SLAS TECHNOLOGY*, *20*(5), 589. Elsevier BV.

Schöll, M., Verberk, I. M. W., Campo, M. del, Delaby, C., Therriault, J., Chong, J. R., Palmqvist, S., & Alcolea, D. (2024). Challenges in the practical implementation of blood biomarkers for Alzheimer's disease [Review of *Challenges in the practical implementation of blood biomarkers for Alzheimer's disease*]. *The Lancet Healthy Longevity*, *5*(10), 100630. Elsevier BV.

Shafi, V., & Siddiqui, I. (2024). Alzheimer's Disease Investigated via Gene-Environment Interactions, Biochemical Pathways, Cellular Processes, and Disease Phenotype Variability. *Research Square (Research Square)*.

Starzyk, A., & Charzewski, P. (2025). The Science of Memory Loss: Insights into Alzheimer's Disease. *Quality in Sport*, *38*, 57948.

Wang, R., Peng, S., Zhu, J., Xu, Y., Wang, M., Zhang, L., Qiu, Y., Hou, D., Wang, Q., & Liu, R. (2025). Innovations in Alzheimer's disease diagnostic technologies: clinical prospects of novel biomarkers, multimodal integration, and non-invasive detection. *Frontiers in Neurology*, *16*.

Wang, S., Liu, D., Li, H., Jia, X., Zhou, H., Yu, W., Li, T., Pan, L., Chen, B., Wang, Y., Zhan, N., Song, Y., & Yan, K. (2025). Assessing diagnostic performance of plasma biomarkers in Alzheimer's disease versus cognitively unimpaired individuals: P-tau217 emerges as the optimal marker in Chinese cohorts. *Frontiers in Aging Neuroscience*, *17*.

Zeng, X., Chen, Y., Sehrawat, A., Lee, J., Lafferty, T. K., Kofler, J., Berman, S., Sweet, R. A., Tudorascu, D., Klunk, W. E., Ikonomović, M. D., Pfister, A., Zetterberg, H., Snitz, B. E., Cohen, A. D., Villemagne, V. L., Pascoal, T. A., Kamboh, M. L., Lopez, O. I., … Karikari, T. K. (2024). Alzheimer blood biomarkers: practical guidelines for study design, sample collection, processing, biobanking, measurement and result reporting [Review of *Alzheimer blood biomarkers: practical guidelines for study design, sample collection, processing, biobanking, measurement and result reporting*]. *Molecular Neurodegeneration*, *19*(1), 40. BioMed Central. https://doi.org/10.1186/s13024-024-00711-1

Zhang, Y., Bi, K., Zhou, L., Wang, J., Huang, L., Sun, Y., Peng, G., & Wu, W. (2024).

JOURNAL OF BIOLOGICAL
AND MEDICAL INNOVATIONS

Advances in Blood Biomarkers for Alzheimer's Disease: Ultra-Sensitive Detection Technologies and Impact on Clinical Diagnosis [Review of *Advances in Blood Biomarkers for Alzheimer's Disease: Ultra-Sensitive Detection Technologies and Impact on Clinical Diagnosis*]. *Degenerative Neurological and Neuromuscular Disease*, 85. Dove Medical Press.

Zohoncon, T. M., Sawadogo, J., Ouattara, A. K., Zouré, A. A., Ouedraogo, M. N. L., Ouédraogo, P., Djigma, F. W., Nadembega, C., Kaboré, R., Ouermi, D., Obiri-Yeboah, D., & Simporé, J. (2023). Presymptomatic Diagnosis and Gene Therapy for Alzheimer's Disease: Genomic, Therapeutic, and Ethical Aspects—A Systematic Review. *Advances in Alzheimer s Disease*, *12*(4), 55.