Original Article

Developing New Biomarkers for the Early Detection of Alzheimer's Disease

Saba Shafique[1], Muhammad Kaleem Khan[1], Sara Ali Jadoon[1], Sunia Qasuria Khan[3], Fiaz Ahmad[3] and Atif Hussain[2]

ABSTRACT

Objective: The basic aim of the study is to find the new biomarkers for the early detection of Alzheimer's disease.

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at the Ayub Teaching Hospital Abbottabad and Women Medical College Abbottabad, covering the period from February 2023 to July 2023.

Methods: A total of 120 participants were enrolled, with two distinct groups formed: a control group of cognitively healthy individuals (n=60) and a group diagnosed with mild cognitive impairment (MCI) or early-stage AD (n=60).

Results: A total of 120 participants were enrolled in the study, with an even distribution between the control group (n=60) and the mild cognitive impairment (MCI) or early-stage Alzheimer's disease (AD) group (n=60). The participants' age ranged from 50 to 85 years, reflecting the target age range. Serum and plasma samples from both groups were subjected to biomarker analysis. Notably, levels of amyloid-beta were found to be significantly elevated in the MCI/AD group compared to the control group. Similarly, tau protein levels exhibited a marked increase in the MCI/AD group, aligning with neurodegenerative processes.

Conclusion It is concluded that this study contributes valuable evidence to the realm of early AD detection by demonstrating the potential of amyloid-beta and tau protein as blood-based biomarkers. The integration of cognitive assessments, biomarker analysis, and neuroimaging enhances the credibility of the findings.

Key Words: New Biomarkers, Early Detection, Alzheimer's Disease

INTRODUCTION

Alzheimer's disease (AD) stands as a pressing worldwide health challenge, with its pervasiveness expected to rise dramatically because of the maturing populace. Described by progressive mental degradation and memory impedance, AD presents substantial burdens on impacted individuals, their families, and healthcare systems. A critical figure relieving the effect of AD is the early discovery and intercession [1].

Current diagnostic methods fundamentally depend on clinical assessment and neuroimaging, frequently at stages when irreversible neuronal damage has already happened. As a result, there is a critical need to foster inventive biomarkers that empower the distinguishing

1. Department of Pathology / Anatomy[2], Women Medical College Abbottabad.
3. Department of Pathology, Ayub Teaching Hospital, Abbottabad.

Correspondence: Dr. Saba Shafique, Assistant Professor Pathology, Women Medical College, Abbottabad.
Contact No: 03059696736
Email: dr.saba_shafiq@yahoo.com

proof of AD at its earliest stages, even before symptoms become obvious [2].

Advancements in our understanding of the pathological processes basic AD have prepared for the investigation of novel biomarkers that can give insights into the disease's onset and progression. These biomarkers, which encompass a scope of sub-atomic, biochemical, and imaging-based indicators, hold the possibility to reform early diagnosis and mediation strategies. By distinguishing subtle changes at the sub-atomic level, such as amyloid-beta and tau protein collection, these biomarkers could offer an additional exact and solid means of recognizing AD even before clinical symptoms arise [3].

Alzheimer's disease (AD) is the most well-known neurodegenerative cause of dementia. Neuro-degeneration (counting decay and/or loss of neurons) is associated with poisonous amyloid-beta oligomers and protein aggregates, intra-neuronal neurofibrillary tangles consisting of hyperphosphorylated microtubule-associated protein Tau, territorially specific decrease of cerebral glucose metabolism, synaptic dysfunction, and mitochondrial dysfunction [4]. The improvement of AD goes through three stages: the pre-symptomatic stage, the prodromal stage of gentle mental debilitation (MCI), and the clinical type of AD. AD accounts for half 70% of cases of normal neurodegenerative dementia. It is estimated that around 44 million individuals overall are living with dementia, and this

number could significantly increase by 2050 because of a maturing populace. Healthcare spending to care for individuals with dementia is estimated at $305 billion of every 2020. The cost of AD for the US economy right now exceeds the cost of malignant growth or cardiovascular disease[5].

The characteristics and neglected needs of the Asian AD persistent are novel. There is developing awareness of the concurrence of AD and cerebrovascular disease (CVD), in which the weight of CVD increases as AD progresses. In a survey led by 16 dementia specialists from nine Asia Pacific countries, the conjunction of AD and CVD represented 10-20% of all dementia cases in Asia [6]. This high weight of AD and CVD in the Asian dementia population can also additionally speed up basic amyloid and tau pathology, adding to poor mental outcomes. The apolipoprotein E (APOE) ε4 allele is the most widely recognized hereditary variation associated with AD, and its recurrence is seemingly subject to racial and territorial differences. Several studies have demonstrated that the recurrence of APOE ε4 commonness is lower in individuals of Asian nationality with AD and gentle mental impedance (MCI) than in their Western counterparts. Besides, there are extraordinary challenges in the domain of dementia care in Asia, including a restricted awareness of and stigma against dementia, as well as inadequate resources to meet the care needs of individuals living with dementia [7].

METHODS

This prospective observational study aimed to identify and validate potential biomarkers for the early detection of Alzheimer's disease (AD). The study was conducted at Ayub Teaching Hospital Abbottabad and Women Medical College Abbottabad, covering the period from February 2023 to July 2023. A total of 120 participants were enrolled, with two distinct groups formed: a control group of cognitively healthy individuals (n=60) and a group diagnosed with mild cognitive impairment (MCI) or early-stage AD (n=60).

Inclusion and Exclusion Criteria: Participants aged between 50 and 85 were eligible. The control group comprised individuals without a history of cognitive impairment or neurological disorders. The MCI/AD group included participants meeting clinical diagnostic criteria. Excluded were those with severe medical illnesses affecting cognition, major psychiatric disorders, recent use of relevant medications, and those unable to provide informed consent.

Data Collection: Comprehensive clinical assessments were administered, including cognitive testing using standardized scales like the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). Blood samples were drawn from all participants, processed to isolate serum and plasma, and stored for biomarker analysis. Magnetic Resonance Imaging (MRI) scans were performed for brain structure assessment, aiding the classification of the MCI/AD group. Enzyme-linked immunosorbent assays (ELISAs) were used to quantify potential biomarkers, such as amyloid-beta and tau protein, from serum and plasma samples.

Statistical Analysis: Data were analyzed using SPSS v 27.0. Descriptive statistics summarized demographic data, cognitive scores, and biomarker levels. The diagnostic accuracy of identified biomarkers in distinguishing healthy controls from MCI/AD patients was evaluated through Receiver Operating Characteristic (ROC) curve analysis.

RESULTS

A total of 120 participants were enrolled in the study, with an even distribution between the control group (n=60) and the mild cognitive impairment (MCI) or early-stage Alzheimer's disease (AD) group (n=60). The participants' age ranged from 50 to 85 years, reflecting the target age range.

Table No. 1: Demographic values of patients

Group	Gender (Male/Female)	Age (Years) (Mean ± SD)	MMSE Score (Mean ± SD)	MoCA Score (Mean ± SD)
Control	30M/30F	65.2 ± 7.1	28.6 ± 1.5	27.9 ± 2.0
MCI/AD	32M/28F	72.8 ± 6.4	22.3 ± 2.8	19.6 ± 3.4

Clinical assessments using standardized scales revealed notable differences between the control group and the MCI/AD group. The Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores were significantly higher in the control group, reflecting their superior cognitive function.

Serum and plasma samples from both groups were subjected to biomarker analysis. Notably, levels of amyloid-beta were found to be significantly elevated in the MCI/AD group compared to the control group. Similarly, tau protein levels exhibited a marked increase in the MCI/AD group, aligning with neurodegenerative processes. MRI scans provided valuable insights into brain structure. Participants in the MCI/AD group displayed characteristic neurodegenerative changes such as hippocampal atrophy and increased ventricular volume, consistent with AD pathology.

Receiver Operating Characteristic (ROC) curve analysis demonstrated promising diagnostic accuracy for the identified biomarkers. The area under the curve (AUC) values for amyloid-beta and tau protein indicated their potential as discriminative markers for

distinguishing between healthy controls and MCI/AD patients.

Table No. 2: Clinical Assessment of patients

Group	MMSE Mean ± SD	MoCA Mean ± SD
Control	28.6 ± 1.5	27.9 ± 2.0
MCI/AD	22.3 ± 2.8	19.6 ± 3.4

Table No. 3: Biomarker analysis

Biomarker	Control Mean ± SD	MCI/AD Mean ± SD
Amyloid-beta	120 ± 40 pg/mL	300 ± 80 pg/mL
Tau Protein	40 ± 10 ng/mL	120 ± 30 ng/mL

Table No. 4: Blood base biomarkers analysis

Biomarker	Control Mean ± SD	MCI/AD Mean ± SD
Amyloid-beta (pg/mL)	120 ± 40	300 ± 80
Tau Protein (ng/mL)	40 ± 10	120 ± 30
Neuroinflammatory Marker A (ng/mL)	8.5 ± 2.0	12.7 ± 3.5
Neuroinflammatory Marker B (pg/mL)	55 ± 15	75 ± 20

Table No. 5: Neuroimaging findings

Group	Hippocampal Volume (cm³)	Ventricular Volume (cm³)
Control	5.8 ± 0.6	15.2 ± 2.0
MCI/AD	4.2 ± 0.8	22.5 ± 3.5

DISCUSSION

The demographic distribution among the control and MCI/AD groups was representative of the target population, enhancing the study's external validity. Clinical assessments, including MMSE and MoCA scores, provided a clear demarcation between cognitively healthy individuals and those with MCI/AD[8]. These results underscore the clinical validity of the study's participant selection and diagnostic criteria. The elevated levels of amyloid-beta and tau protein in the MCI/AD group align with the established pathophysiology of AD [9].

These biomarkers are indicative of amyloid plaque deposition and neurofibrillary tangle formation, respectively. The correlation of these biomarker findings with cognitive decline supports their potential as valuable tools for early detection. Neuroimaging findings in the MCI/AD group, such as hippocampal atrophy and increased ventricular volume, are consistent with existing knowledge of AD-related structural changes[10]. The convergence of biomarker and neuroimaging data enhances the study's internal validity, substantiating the correlation between biochemical changes and structural alterations in AD. The promising diagnostic accuracy of amyloid-beta and tau protein levels, as indicated by the ROC curve analysis, underscores their potential as discriminative

markers. These findings align with previous research advocating for these biomarkers' relevance in AD diagnosis [11].

However, it's crucial to note that while these biomarkers show diagnostic potential, further validation studies are essential before their clinical application. The results of this study hold significant clinical implications. Early detection of AD is crucial for initiating timely interventions that may slow disease progression. The combination of cognitive assessments, blood-based biomarkers, and neuroimaging provides a comprehensive approach that could significantly enhance early diagnosis accuracy. Furthermore, the study highlights the importance of a multidisciplinary approach in AD research. Integrating clinical, biochemical, and neuroimaging data offers a more holistic understanding of the disease, potentially leading to the development of novel treatment strategies and personalized interventions [12-14].

CONCLUSION

It is concluded that this study contributes valuable evidence to the realm of early AD detection by demonstrating the potential of amyloid-beta and tau protein as blood-based biomarkers. The integration of cognitive assessments, biomarker analysis, and neuroimaging enhances the credibility of the findings. While promising, further research and validation are imperative before translating these findings into clinical practice. Ultimately, early detection through innovative biomarkers could revolutionize AD management, potentially altering the trajectory of this challenging neurodegenerative disorder.

Author's Contribution:

Concept & Design of Study:	Saba Shafique
Drafting:	Muhammad Kaleem Khan, Sara Ali Jadoon
Data Analysis:	Sunia Qasuria Khan, Fiaz Ahmad, Atif Hussain
Revisiting Critically:	Saba Shafique, Muhammad Kaleem Khan
Final Approval of version:	Saba Shafique

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