Chapter 4
Introduction to Alzheimer's Disease and Biomarkers

Kanika Gupta
Shri R.K. Patni Girls' College, Kishangarh, India

ABSTRACT

Alzheimer's disease, the leading cause of dementia affecting 50-60% of cases globally, manifests initially with cognitive impairments and progresses with neurodegeneration, brain inflammation, and atrophy. Early diagnosis and treatment rely on identifying biomarkers, which can be invasive or non-invasive, categorized as diagnostic, prognostic, predictive, pharmacodynamic/response, susceptibility/risk, monitoring, and safety biomarkers. They include amyloid Aβ plaques, Brain derived Neurotrophic factor (BDNF), pro-NGF, tau protein (t-protein) neurofibrillary tangles, apolipoprotein, and novel markers in CSF, blood, urine, and lipid profiles. Challenges encompass lumbar puncture, multifactorial progression, early biomarker inexplicability, and pathophysiological understanding gaps.Advancement of Theranostics approach is explained in AD patients. Later in this study, we analyzed these biomarkers using integrative approaches of deep generative models focusing on detecting anomalies in brain structure, biological functions, abnormal metabolite concentrations, and misfolded proteins.

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INTRODUCTION

Alzheimer's disease is the main cause of dementia out of all other diseases which progressively cause neurodegeneration of brain cells known as Alzheimer's dementia.

Globally more than 55 million people are living with all-cause dementia with annual growth of 10 million new cases approximately projected to reach 113 million by 2050 according to a WHO report.('2024 Alzheimer's Disease Facts and Figures', 2024)

The neuropathological implications of AD first occur in the temporal lobe and in neocortical structures of the cerebral cortex which is why the first symptoms tend to be memory, language and thinking problems. The actual brain changes that cause dementia are thought to begin 20 years back before significant symptoms start that microscopically seen as accumulation of beta-amyloid plaque (Aβ42) outside neurons which may damage neurons by interfering with their synaptic signalling.

Inside neurons, tau protein forms neurofibrillary tangles (NFTs) composed of hyper phosphorylated which block the axonal transportation of certain nutrients and other substances important for the normal function and survival of neurons. These proteins serve as hallmarks of AD pathology responsible for death of nerve cells and loss of brain tissue.

AD can occur genetically and sporadically both, in which the common symptoms are amnestic cognitive impairment which typically troubles memory but less commonly other variants could show non-amnestic cognitive impairment which affects language, attention, or problem-solving instead of memory.

AD PROGRESSION

AD occurs in a continuum fashion which progressively begins from asymptomatic brain changes and advancing to severe brain changes that cause dementia.

The progression of AD is broadly divided in three phases namely Preclinical phase, Mild Cognitive impairment (MCI) and Alzheimer's dementia. The last phase i.e. Alzheimer's dementia marked by significant cognitive decline is further divided into three phases on the basis of severity of dementia i.e. Mild, Moderate and Severe dementia.(Malik et al., 2024)

The duration of each of the above phases may vary person to person depending upon genetic factors, age and lifestyle of an individual. The major three phases are further explained on the basis of symptoms progression and underlying biological changes.