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Challenges to Establish Definite Diagnosis of Alzheimer's Disease

Indrapal Singh

Department of Geriatric Mental Health, Chhatrapati Shahuji Maharaj Medical University, India

We are living in a time of significant scientific advancements allowing us to live longer. However, with longer lifespan, there is increased likelihood of age-related disorders such as Alzheimer's disease (AD). The people living with AD and other dementia worldwide are growing very fast and the figures are expected to increase from 35.6 million in 2010 to 115.4 million by 2050 (Alzmer report). Research is probably more important now than in the past in the field of AD considering enormous burden on nation and individual families. However, there are great challenges associated with research because of difficulty establishing definite diagnosis of AD.

Current standard diagnostic criteria (DSM IV TR and ICD-10) can be helpful of making either probable or possible diagnosis of AD even with the help of neuropsychological testing. Moreover, these criteria do not focus on preclinical stage of AD or mild cognitive impairment (MCI), when although there is no significant impairment of activities of daily living (ADL) but patho-physiological changes are well evident. The only mean of definite diagnosis of AD is brain biopsy which is not feasible in living subjects. At early stages of AD, when the memory impairment is subtle or episodic, the diagnosis is very difficult to make even by the experienced physicians. Difficulty in communication might be another reason for difficulty in cognitive assessment of a patient secondary to either hearing impairment or any language dysfunction. Cognitive deterioration of the patient make them unreliable informant and diagnosis becomes a challenge where other collateral source of information is not available. In addition, many medical or psychological disorder like depression or delirium or drugs like benzodiazepines might affect the cognition and make it further complicated to diagnose AD and its severity. Consequently, the patients with AD might be diagnosed wrongly as other dementia or cognitive impairment on initial assessment and vice versa. Many of these problems might contribute to diverse and inconsistent research-findings related to AD.

Refinement of diagnostic criteria of AD and appropriate biomarkers are the potential solution to meet diagnostic challenges. Recently, after 27 years, new criteria and guidelines for the diagnosis of AD have been published by three expert workgroups- the Alzheimer's Association and the National Institute on Aging (NIA) of the National Institutes of Health (NIH). The guidelines for AD also include pre-symptomatic and mildly symptomatic but pre-dementia phase of AD, along with dementia caused by Alzheimer's. [2-4] Biomarkers have also been given the importance in the diagnosis of AD in new guidelines. The biochemical biomarkers such as amyloid β peptide 42 (Aβ42), tau protein, and hyperphosphorylated tau protein (p-tau) in cerebrospinal fluid (CSF) are being used for AD diagnosis in various researches and found to be reliable and valid with sensitivity and specificity levels between 80% and 90% for detecting AD versus normal elderly [5,6]. These biomarkers are also important to diagnose AD in preclinical stage when potential disease-modifying therapeutic strategies under research likely to be most effective. However, to obtain CSF for biomarkers through lumber puncture (LP) is an invasive procedure which requires certain degree of skill. In addition, LP is not as acceptable and popular as drawing blood samples to both the patients as well as researchers/clinicians. Currently, the Blood-based biomarkers are under research for AD diagnosis and these markers would be very advantageous due to the ease of sample collection, acceptability among patients and cost effectiveness.

Further research and development of biomarkers for AD like blood glucose of diabetes mellitus might prove to be the answer for the current problem of establishing a relatively definite and early diagnosis of AD both for research and clinical management of the patients with AD.

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***Corresponding author:** Indrapal Singh, Assistant Professor, Department of Geriatric Mental Health, Chhatrapati Shahuji Maharaj Medical University, India, E-mail: dripsingh@rediffmail.com

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