

## Diagnostic and Prognostic Biomarkers of Cognitive Impairment in Geriatric Population

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### ABSTRACT

Aged population pose a major burden on public health sector due to huge number of associated comorbidities in older adults. Geriatric population comprises of individuals with chronological age between 65 years to 74 years of age accounting for 10 % of total population in Pakistan. Aging process is observed at molecular, cellular and organ level in body. Although life expectancy is improved in last few decades but there is a major challenge of functional decline reducing quality of life. Neurodegenerative disorders are associated with physical decline as well as cognitive decline in individuals. For brain health, multiple diagnostic tools are used to access the progression of dementia, Alzheimer's disease and cognitive impairment. These include CAMCOG, Adiponectin assay, p-tua 181 Elisa kit and telephone interview for cognitive status *etc.* Through proper diagnosis, health care professionals can improve brain function in older adults.

**Keywords:** Geriatric population, brain health, Alzheimer's disease, dementia, neuro-degenerative disorders, CAMCOG, p-tau biomarker, cognitive impairment

### Introduction

Biological aging is an inevitable process affecting individuals at cellular and organ levels due to reduced regenerative potential of organs in old age [1]. Geriatric population encompasses individuals ranging from 79 years up to 84 years of age which is approximately 4.35% of Pakistan population. Aging results in physical and cognitive decline over the course of time [2]. Neurodegenerative and Neurodevelopmental diseases affecting individuals are characterised by conditions like cognitive impairment, repetitive actions, restricted or antisocial behavior and other medical problems. The geriatric population is more vulnerable to these neurological disorders. The prevalence of cognitive dementia is about 14% of the population above 70 years of age, 16% have Mild cognitive impairment while two third of the population with dementia also suffers from Alzheimer's disease. Accelerated aging is a more rapid process than expected leading to appearance of earlier signs of aging than normal. The markers involved during this process are telomere length, oxidative stress markers and Horvath's epigenetic clock resulting in neuropsychiatric disorders. These include anxiety, posttraumatic stress disorder and depression [1]. Mental health problems lead to many challenges for the patient, their families and to the medical health care services, so early diagnosis of cognitive impairment can provide an opportunity for appropriate treatment and psychosocial support to patient worldwide. Early diagnosis by the clinicians is a key step toward improving the mental health of the geriatric population.

### Age-associated Memory Impairment

In later years of life, the cognitive impairment led to memory loss. Memory loss can be characterized into sensory memory, short term memory and remote memory. It poses a great burden on caregivers as the sensory loss reduce palatability of food items, thus decreasing food intake. The short-term memory loss is involved in processing speed decline and intelligence of an individual. For this purpose, a 24-hour caregiver is usually required by the elderly. In the modern era, nursing homes are being developed by the governmental public health sector to facilitate the geriatric population. These not only provide meal assistance but also provide a platform where isolated environment can be avoided. Alzheimer's disease is an advanced form of dementia affecting the central nervous system of body. Patients are in constant need of one caregiver as they might lose their sense of direction and environment. Clinically the neural loss can be identified by PET scans, amyloid beta and tua biomarkers identification [3].

### Functional Neurological Disorder (FND)

Functional neurological disorder (FND) is a disability associated with neurology and psychiatry. With age, neurological degeneration has led to multiple diseases involving Alzheimer's disease, dementia, depression and anxiety. Geriatric psychiatric disorders are among one of the risk factors in non-communicable diseases contributing in global burden of disease. The major cause behind this is isolation due

to societal norms faced by elderly in later years of life. This poses a burden on mental health of an individual as assessed through neuropsychiatric assessment methods including FND-movt and FND-par. The psychiatric stressors also play a key role in physical disability, thus, reducing capacity of activities of daily life (ADL) in geriatric population [4].

### Screening Tools for Early Diagnosis

Screening is defined as a systematic process to identify individuals at risk. It can be done through a simple test based on a single score at a single point of time. This helps to screen out individuals requiring proper diagnostic assessment by health care professionals. It must be kept in mind that it does not provide any information regarding the course of a patient's mental health. Progressive ailments including dementia or Alzheimer depends on cognitive decline over time assessed through information recorded via taking history of patient. Some distinguished screening instruments for early cognitive impairment diagnosis are listed below [5]:

Instrument	Operative time (min)	Test subject
Ascertain dementia 8	3	Informant
Kokmen Short Test of Mental Status	5	Patient
MiniCog	3	Patient
Memory impairment screen	4	Patient
St Louis University of Mental Status examination (SLUMS)	7	Patient
Rapid cognitive screen	3	Patient
Telephone Interview for Cognitive Status	7-10	Patient
Mini-Mental Status Exam (MMSE)	7-10	Patient
Addenbrooks Cognitive Exam	15	Patient

### Diagnosis of Alzheimer's Disease

To isolate biomarkers for diagnosis of Alzheimer's disease, following body fluids are used:

1. Blood
2. Cerebrospinal fluid (CSF)
3. Others (saliva, tears, urine)

**Types of Biomarkers**

Biomarkers are of two types either invasive or non-invasive:

**Non-Invasive Biomarkers for AD Diagnosis**

Noninvasive neuroimaging techniques have improved the diagnosis process of Alzheimer disease in the last decade. These techniques allow the diagnosis of AD both in asymptomatic phase as well as symptomatic phase. Volumetric approaches of high resolution are along with diagnostic tools in order to study the changes in brain structure and protein accumulation in brain in early phase.

Some of the techniques are:

- Magnetic Resonance Imaging
- Positron emission tomography (metabolic activity)
- Amyloid imaging
- Flortetapir
- Flortetaben

Recently omics technologies have made the analysis of wide range of AD possible for both familial and occasional cases and facilitate the use of body fluids such as blood, urine, tears etc [6].

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• Inexpensive</li> <li>• Reproducible</li> <li>• Fast and convenient</li> <li>• Easy to implement in large population</li> <li>• Self-collected by patients e.g urine, saliva and tears</li> <li>• No prior training of clinicians required</li> </ul>	<ul style="list-style-type: none"> <li>• Less accurate</li> <li>• Less consistent results</li> <li>• Low concentration of biomarkers after crossing blood-brain barrier</li> <li>• Lack of validated studies</li> </ul>

**Invasive Biomarkers for AD Diagnosis**

In Neuromelanin rich brainstem structure locus coeruleus (LC), during asymptomatic stage of AD there is an increase of Tau NTFs. These levels are increased during the progression phase of AD following the neural loss which is associated with cognitive dysfunction in hippocampus and cortex due to reduced noradrenaline levels.

**Cerebrospinal Fluid**

An ideal fluid biomarker should be reliable, reproducible and noninvasive in terms of collection, but CSF does not meet the criteria which limit its use but because of the close relationship between the fluid and the brain, that provides information about the changes during the pre-clinical stages of AD. Increased total Tau and phosphor Tau in CSF and decreased Abeta-42 are specific biomarkers of Alzheimer’s disease [7].

**Blood Phosphorylated Tau-181 Biomarker for AD**

The ultrasensitive blood immunoassay of p-tau 181 is considered the most effective tool to diagnose Alzheimer’s disease. This analysis can be used for cognitively unimpaired older adults, individuals diagnosed with mild cognitive impairment (MCI), Alzheimer’s disease, and fronto-temporal dementia. It is observed that there is a gradual increase in plasma p-tau181 along the AD progression, depicting lowest levels in amyloid  $\beta$ -negative young adults and cognitively unimpaired elderly and high concentrations in the amyloid  $\beta$ -positive cognitively unimpaired elderly and MCI groups [8].

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• High accuracy</li> <li>• High concentration of biomarker</li> <li>• Ability to test large no of candidate</li> <li>• Pathophysiological biomarker</li> </ul>	<ul style="list-style-type: none"> <li>• Invasive</li> <li>• Clinicians require prior training</li> <li>• Less accepted by the patient e.g., CSF collection</li> </ul>

**Adiponectin as Biomarker for Cognitive Impairment**

For assessment of functional capacity of brain, adiponectin and adipocytokines plays a key role in memory and cognition analysis. The test results show reduced levels of Adiponectin is reduced in blood of

patients with mild cognitive impairment, Alzheimer’s disease and primary cognitive disorder.

**Adiponectin Assay**

According to a study carried out in older people using a test CAMCOG i.e., a neurocognitive test that assesses 8 different domains of cognition. The assay kit used during the experiment is Quantikine Human Total Adiponectin immunoassay ELISA kit. The serum level of adiponectin is reduced in geriatric population with major depressive disorder MDD.

**Diagnosis of Delirium**

A neuropsychiatric condition characterized by inattention and global cognitive impairment. There are multiple causes including medical illness, complication and drug intoxication and because of that delirium is often underdiagnosed. Clinical diagnosis of delirium is based on the presence or absence of certain characteristics in the body. Few of those are listed below in A-D criteria:

- Disturbance of consciousness
- Change in cognition or perceptual disturbance
- Disturbance fluctuates from a short period to a day
- History and physical examination [9]

**Tools for Evaluation**

A standard tool for evaluation is the CAM confusion assessment method. The CAM algorithm relies on the presence of acute symptoms, inattention, and fluctuating course of cognitive decline in older population. The sensitivity of algorithm is 94-100% [7].

**Conclusion**

Cognitive impairment in geriatric population raises many challenges for health care professionals and caregivers. To tackle these issues, appropriate diagnosis and management is required. Multiple diagnostic tools for better treatment are used in the modern era according to their requirement. Additionally, emphasis on psychological support, education and skills to improve quality of life must be introduced in nursing homes. Public health can play a vital role in the rehabilitation process of elderly in later years of their life.

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