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SALIVARY BIOMARKERS FOR ALZHEIMER'S DISEASE

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ABSTRACT:

Alzheimer's disease (AD) is a neurodegenerative disease and is the leading cause of progressive dementia. It is estimated that 46.8 million people suffer from dementia worldwide, with the highest prevalence found in the older age groups (+65 years). By 2030, it is estimated that the prevalence will increase to approximately 74.7 million people, partly due to the increasing numbers of elderly people in the world. Cognitive deficits in AD progress with the duration of the disease caused by accelerating neurodegenerative processes. Formation of specific AD pathology, amyloid plaques between neurons and the accumulation of intracellular neurofibrillary tangles composed of tau, begin decades prior to the clinical expression of AD, and it is therefore essential to find a biomarker for early preclinical diagnosis and treatment monitoring.

Most studies of AD biomarkers published to date have used are:

1. **Cerebrospinal Fluid samples:** obtained by lumbar puncture, (an invasive procedure) for the Ab42 deposits are mainly found in the brain.

2. **Blood samples:** (less invasive than CSF sample) for the plasma t-tau levels, plasma C-reactive protein (CRP) levels and serum levels of cholinesterase.
3. **Saliva:** (non-invasive biomarkers) for AD diagnosis as T-tau, P-tau, amyloid-b and alpha-synuclein, lactoferrin proteins are all detectable in saliva and have potential diagnostic utility.

Current Evidence of Salivary Biomarkers for Alzheimer's Disease:

1. **Amyloid-b:** The accumulation of Ab plaques, the foremost hallmark of AD, begins 15–20 years prior to the clinical onset of cognitive and functional decline. Studies have shown that salivary **Ab42** is detectable and increased in AD, with **Ab40** remaining unchanged.
2. **Tau:** An aggregated and phosphorylated form of tau protein is the major constituent of neurofibrillary tangles (NFT) in AD. Studies have proven the presence of tau in saliva. **T-tau** showed no change & **P-tau** showed increased levels.
3. **Alpha-synuclein:** The presynaptic neuronal protein **alpha-synuclein (α-syn)** is the most abundant protein & major component in the Ab plaques in patients with AD. There has been no investigation of salivary α-syn in AD but studies have shown increased levels in Parkinson's disease.
4. **Lactoferrin:** An antimicrobial peptide with Ab binding properties which targets bacteria and is abundantly present in human saliva. Studies have shown decreased levels in AD.
5. **Acetylcholinesterase:** Acetylcholinesterase inhibitors are the primary drug prescribed in AD, which increases acetylcholine (AChE). Studies have shown decreases in the activity of AChE in saliva of these patients.

There has been considerable advancement in the detection of AD-related salivary biomarkers, as these biomarker's sampling and analysis is easy to perform, inexpensive and non-invasive.

Keywords: Alzheimer's disease; Salivary Biomarkers, Amyloid-b; T-Tau, P-tau, Alpha-synuclein, Lactoferrin, Acetylcholinesterase

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