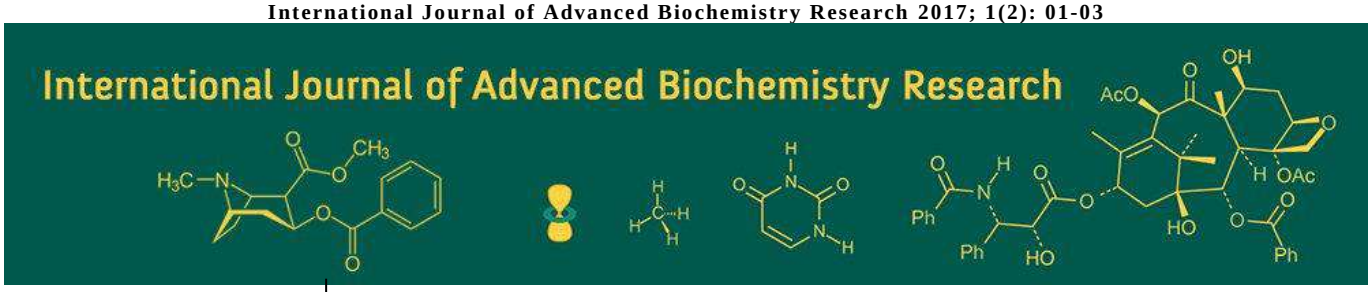

ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2017; 1(2): 01-03
www.biochemjournal.com
Received: 02-05-2017
Accepted: 06-06-2017

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Biochemical signature in Alzheimer's disease

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DOI: https://doi.org/10.33545/26174693.2017.v1.i2a.86

Abstract
Alzheimer's disease (AD) is the most common cause of dementia in the elderly. The lack of a definitive treatment or cure for AD puts a significant financial strain on health care systems.
As part of its clinical profile, AD involves progressive memory loss and deficits in one or more cognitive domains, including aphasia (language disturbance), agnosia (inability to recognize people or objects in the presence of intact sensory function), apraxia (inability to perform motor acts while the motor system is intact), or executive function (organize, sequence actions or form abstraction). They represent a significant decline in earlier levels of functioning in AD patients that can interfere with daily life or work [1].

Keywords: Blood urean nitrogen, creatinine, diabetes, proteins

Introduction
The word "dementia" is derived from Latin the word which implies without mind. As part of its clinical presentation, dementia is a syndrome characterized by deterioration of cognitive ability and other skills, resulting in a gradual decline in daily activities [2]. Even Kraepelin commented on the relationship between dementia and aging in 1896. Alzheimer's disease is one of the terms in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (1994) of the American Psychiatric Association, as well as in the World Health Organization's (WHO) International Classification of Diseases (ICD - 10, 1992). It is important to note that the term dementia refers a number of different subtypes, the most common being Alzheimer's disease.

Risk factors
AD still doesn't have a definitive etiology, but some risk factors for its occurrence have been identified. The most important risk factor for the development of AD is advancing age. There are likely to be additional risk factors, including a familial history of dementia, female gender, head trauma, hypertension, high cholesterol, sedentary lifestyle, obesity, low education, and an allele of apolipoprotein E [3, 4, 5]. Currently cardiovascular disease is proposed as a risk factors and anemia [6]. In addition to the most common sporadic form, AD can appear in early onset familial form suggesting that genetics play an important role in the etiology of the disease [7].

Clinical diagnosis
There are few rules for the clinical conclusion of AD: the National Institute of Neurological and Communicative Disorders and Stroke - Alzheimer's disease and Related Disorders Association Work Group (NINCDS-ADRDA) criteria [8], the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) American Psychiatric Association 1994 and the ICD-10. The NINCDS-ADRDA criteria have been most widely used in research because they are well validated, provide high diagnostic accuracy and allow comparison between studies [9, 10]. The sensitivity in these investigations was higher than the specificity, and patient follow-up increased diagnostic accuracy. Depression, normal pressure hydrocephalus, dementia with Lewy bodies, vascular dementia, and frontotemporal dementias are all disorders that can mimic or overlap with Alzheimer's disease.

Blood and Urine tests

The research facility assessment that is routinely performed incorporates: Erythrocyte sedimentation rate, C-reactive protein (CRP), complete blood count, serum electrolytes (including calcium), glucose, creatinine, liver function tests, thyroid stimulating hormone (TSH), serum vitamin B12 and urine analysis. Optional procedures are serum folate, methylmalonic acid and blood serology for HIV or other viruses, urine collection for heavy metals or toxicology [11].

Biochemical markers

As a result, the quest for a particular biochemical signature is still necessary for the assessment and management of AD. A quick and easy test based on a biochemical marker could also minimize the cost and time it takes to diagnose a patient now. For years, researchers have looked for ante-mortem biochemical markers in different peripheral tissues and cells such as erythrocytes [12], lymphocytes [13], urine [14], hair [15] and skin [16, 17]. However, until now there has been no clarity on biochemical markers for AD that would allow pre-symptomatic detection or definitive pre-morbid diagnosis. Taking into account the wide range of search on analytic markers, a lot of work has been committed in the proposition to unwind the biochemical markers in the extraneuronal tissues.

Oxidative stress markers

Developing information from trial models and human cerebrum studies propose that oxidative stress assumes a significant part in neurodegeneration in AD [18]. There is expanding proof that Aβ not only can prompt oxidative stress but additionally its generation is also expanded as a result of oxidative stress [19]. So, the markers of oxidative stress such as reactive oxygen species (ROS) levels and the DNA oxidation product 8- hydroxy guanosine (8-OHdG) can be measured in lymphocytes, superoxide dismutase (SOD), glutathione peroxidase (GPx), in red blood cells and glutathione redox system (reduced glutathione (GSH), oxidized glutathione (GSSG)) can estimated in the plasma from probable/possible AD patients along with age matched non demented healthy subjects.

Platelet APP isoform ratio

Amyloid precursor protein (APP) handling irregularities are accept to be an early change in AD. Since platelets show concentrations of APP isoforms equivalent to those found in brain, they address a significant peripheral source of APP to study the APP metabolic changes in AD [20]. To unwind the pathogenic mechanism of AD, current article focuses on the identification of platelet APP isoform ratio in AD compared to age matched non demented healthy subjects.

Plasma Aβ1-42 levels

Beta amyloid (Aβ) can typically be identified in plasma but the levels are 100-fold lower than in CSF. The source of Aβ in plasma is unknown. Past researches have shown that Aβ infused into the ventricular CSF of rodent is quickly cleared into blood, probably by sub ependymal vessels and the choroid plexuses [21]. Other researches have recommended peripheral sources, like platelets, for Aβ in plasma [22]. The importance of Aβ levels in plasma with regards to the Aβ accumulation in brain is unclear. Current article centres on the detection of Aβ1-42 levels in plasma as a biochemical marker of AD.

Red blood cells Aβ1-42

Aβ is transported in both direction across the blood brain barrier [23], bringing about a powerful balance between brain Aβ and circulatory Aβ. Red Blood cells especially in AD subjects are consequently presented to calculable degrees of Aβ in spite of low degrees of Aβ answered to be related with RBC's [24]. Moreover ongoing literature uncovers that RBC's tight spot Aβ fibrils *in vitro* [25]. The interplay of Aβ fibrils with RBC and the role of RBC in the expulsion of Aβ fibrils from the circulation has been studied in a murine model [26]. In light of these researches, the current review centers around the red cell connection with Aβ and the helpfulness of RBC headed Aβ for the determination of AD, the progression of sickness and for observing drug response in clinical preliminaries.

Conclusion

The ongoing theory managed with focusing on biochemical markers in the peripheral venous blood and their connection to AD as it is still unclear that the fundamental changes are specific for AD and to what extent changes in blood composition reflect pathological changes found in the brain. The objectives of this article is to concentrate on the value of foundational oxidative stress, platelets APP proportion, plasma and RBC Aβ1-42 levels in the finding of AD. The review material included blood tests from clinically analyzed probable/possible AD cases and from age matched healthy controls.

In summary, the current review up to now confirms that there is increase in systemic oxidative stress during the disease cycle. The increase in the degrees of ROS and 8-OHdG in lymphocytes, coupled with increase in erythrocyte antioxidant enzymatic activities of SOD and GPx and the affected plasma glutathione redox system, (low reduced glutathione (GSH), high oxidised glutathione (GSSG) levels and the low GSH/GSSG molar ratio) support the diagnosis of AD. The combination of these biochemical markers may be useful in choosing AD patients for treatment preliminaries and in the assessment of the development of the disease.

From the aftereffects of our discoveries the accompanying ends can be made, although more researches are required on a large sample with pre-symptomatic subjects or patients with other sorts of dementia, to decide the symptomatic presentation of biochemical markers to recognize early Alzheimer disease, the current review recommend that these biochemical markers have a clinical possible assistance to resolve this diagnostic challenge.

References

1. Brown RC, Lockwood AH, Sonawane BR. Neurodegenerative diseases:an overview of environmental risk factors. Environ Health Perspect. 2005;113(9):12.
2. Lishman, WA. The Psychological Consequences of Cerebral Disorder. Organic Psychiatry. (2nd edition) Oxford Blackwell scientific publication, 1987.
3. Kivipelto M, Helkala EL, Laakso MP, Hänninen T, Hallikainen M, Alhainen K, *et al*. Midlife vascular risk factors and Alzheimer's disease in later life: longitudinal, population based study. BMJ. 2001;322(7300):1447-51.
4. Huang W, Qiu C, von Strauss E, Winblad B, Fratiglioni L. APOE genotype, family history of dementia, and

Alzheimer disease risk: a 6-year follow-up study. Arch Neurol. 2004;61(12):1930-4.
5. Kivipelto M, Ngandu T, Fratiglioni L, Viitanen M, Kåreholt I, Winblad B, *et al*. Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. Arch Neurol. 2005;62(10):1556-60.
6. Atti AR, Palmer K, Volpato S, Zuliani G, Winblad B, Fratiglioni L. Anaemia increases the risk of dementia in cognitively intact elderly. *Neurobiol Aging*. 2006;27(2):278-84.
7. Tanzi RE. A genetic dichotomy model for the inheritance of Alzheimer's disease and common age-related disorders. J Clin Invest. 1999;104(9):1175-9.
8. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology. 1984;34(7):939-44.
9. Blacker D, Albert MS, Bassett SS, Go RC, Harrell LE, Folstein MF. Reliability and validity of NINCDS-ADRDA criteria for Alzheimer's disease. The National Institute of Mental Health Genetics Initiative. Arch Neurol. 1994;51(12):1198-204.
10. Gearing M, Mirra SS, Hedreen JC, Sumi SM, Hansen LA, Heyman A. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part X. Neuropathology confirmation of the clinical diagnosis of Alzheimer's disease. Neurology. 1995;45(3):461-6.
11. Olafsdottir M, Marcusson J. Diagnosis of dementia at the primary care level. Acta Neurol Scand Suppl. 1996;165:58-62.
12. Bosman GJ, Bartholomeus IG, de Man AJ, van Kalmthout PJ, de Grip WJ. Erythrocyte membrane characteristics indicate abnormal cellular aging in patients with Alzheimer's disease. *Neurobiol Aging*. 1991;12(1):13-8.
13. Pirttila T, Mattinen S, Frey H. The decrease of CD8-positive lymphocytes in Alzheimer's disease. J Neurol Sci. 1992;107(2):160-5.
14. Ghanbari H, Ghanbari K, Beheshti I, Munzar M, Vasauskas A, Averback P. Biochemical assay for AD7C-NTP in urine as an Alzheimer's disease marker. J Clin Lab Anal. 1998;12(5):285-8.
15. De Berker D, Jones R, Mann J, Harwood G. Hair abnormalities in Alzheimer's disease. Lancet. 1997;350(9070):34.
16. Soininen H, Syrjänen S, Heinonen O, Neittaanmäki H, Miettinen R, Paljärvi L, *et al*. Amyloid beta-protein deposition in skin of patients with dementia. Lancet. 1992;339(8787):245.
17. Heinonen O, Soininen H, Syrjänen S, Neittaanmäki H, Paljärvi L, Kosunen O, *et al*. beta-Amyloid protein immunoreactivity in skin is not a reliable marker of Alzheimer's disease. An autopsy-controlled study. Arch Neurol. 1994;51(8):799-804.
18. Markesbery WR, Carney JM. Oxidative alterations in Alzheimer's disease. Brain Pathol. 1999;9(1):133-46.
19. Chauhan V, Chauhan A. Oxidative stress in Alzheimer's disease. Pathophysiology. 2006;13(3):195-208.
20. Liu HC, Wang HC, Ko SY, Wang PN, Chi CW, Hong CJ, *et al*. Correlation between platelet amyloid precursor protein isoform ratio and cognition in Alzheimer's disease. J Alzheimers Dis. 2007;11(1):77-84.
21. Ghersi-Egea JF, Gorevic PD, Ghiso J, Frangione B, Patlak CS, Fenstermacher JD. Fate of cerebrospinal fluid-borne amyloid beta-peptide: rapid clearance into blood and appreciable accumulation by cerebral arteries. J Neurochem. 1996;67(2):880-3.
22. Chen M, Inestrosa NC, Ross GS, Fernandez HL. Platelets are the primary source of amyloid beta-peptide in human blood. Biochem Biophys Res Commun. 1995;213(1):96-103.
23. DeMattos RB, Bales KR, Cummins DJ, Paul SM, Holtzman DM. Brain to plasma amyloid-beta efflux: a measure of brain amyloid burden in a mouse model of Alzheimer's disease. Science. 2002;295(5563):2264-7.
24. Kuo YM, Kokjohn TA, Kalback W, Luehrs D, Galasko DR, Chevallier N, *et al*. Amyloid-beta peptides interact with plasma proteins and erythrocytes: implications for their quantitation in plasma. Biochem Biophys Res Commun. 2000;268(3):750-6.
25. Jayakumar R, Kusiak JW, Chrest FJ, Demehin AA, Murali J, Wersto RP, *et al*. Red cell perturbations by amyloid beta-protein. Biochem Biophys Acta. 2003;1622(1):20-8.
26. Ravi LB, Poosala S, Ahn D, Chrest FJ, Spangler EL, Jayakumar R, *et al*. Red cell interactions with amyloid-beta(1-40) fibrils in a murine model. Neurobiol Dis. 2005;19(1-2):28-37.