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STUDY OF CLINICAL DIAGNOSIS TECHNIQUES ON DEMENTIA AS A RESULT OF ALZHEIMER'S DISEASE

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ABSTRACT

Dementia found in older persons, and the dementia gets due to Alzheimer's Disease. This article focused on clinical diagnosis techniques clinical and neuro-biological sides of Alzheimer's Disease, the study provided short introduction to Alzheimer's Disease and the explain concept of Mild Cognitive Impairment(MCI) and its relation, effects to develop dementia to produce the Alzheimer's Disease in patient with Mild Cognitive Impairment and how to prevent the dementia progress. The article also explained the advances in the using of Biomarkers technique and other techniques for diagnosis and tests of Alzheimer's Disease and the efforts of development its therapies in hospitals and medical centers.

Keywords: Alzheimer's Disease, dementia, biomarkers, neuro-biological.

1. INTRODUCTION:

The first describing for a dementia was by the German psychiatrist and neuro-pathologist Dr. Alois Alzheimer which later became known as Alzheimer (AD). In his article 1907, Alzheimer described the case of woman has age of 51years called Auguste D, suffereing from a disease of peculiar of the cerebal cortex and he presented with language impairment and progressive memory, behavioral symptoms and psychosocial impairment **(Maurer *et al.*, 1997; Alzheimer, 1907)**. Since one hundred years ago, the existence of neuro-fibrillary tangles and plaques as recognized by using autopsy or biopsy techniques still just

definitive methodology to Alzheimer's Disease diagnosing **(McKhann *et al*., 1984)**.

Dementia may be defined as a clinical syndrome which includes progressive degrades of intellectual functions **(Gilman, 2010)**. Several perceptive abilities can be weaken by dementia. Some of behavioral changes and cognitive impairment which occur by dementia will interfere with social activities, personal work and relationships and also effect on the impair person's ability to perform the activities of routine daily like personal care, shopping, cooking, financial management and housekeeping.

The following terms for classifying people with dementia caused by Alzheimer's Disease (1) Probable Alzheimer's Disease dementia, (2) Doable Alzheimer's Disease dementia, and (3) Probable or potential Alzheimer's Disease dementia with proof of the Alzheimer's Disease patho-physiological process.

The primary two are supposed to be used in the most of settings of clinical, and the third one is presently supposed for analysis functions **(McKhann *et al*., 2011)**.

There are various reversible and irreversible reasons of dementia **(Shadlen and Larson, 2010)**. the term of (pseudo-dementias) also refer to reversible dementias and it is rare but potentially treatable and happen secondary to another medical condition involving nutritional deficiencies like vitamin B12.

In many countries especially in the United States, Alzheimer's Disease considers a main problem of public health. Alzheimer's Disease in the United States is the fifth leading cause of death within older adults and about 200$ billion has spent per year on direct care of persons living with dementia, where 5 million American have Alzheimer's Disease (**Thies and Bleiler, 2013)**. There are about 35million have Alzheimer's Disease or another type of dementia in worldwide **(Prince *et al*., 2013)**.

2. Methodology of Study:

In the year of 1984, Related Disorders Association and Alzheimer's Disease determined which the first using the technique of imaging to assess of Alzheimer's Disease various reasons of dementia must be excluding. But, other members within the team expected the potential assessment for the imaging within the diagnosing of Alzheimer's disease directly **(McKhann *et al*., 1984)**. The developing of therapeutic strategy for Alzheimer's Disease, currently, the monitoring and diagnosis of Alzheimer's disease became importance topic in 21century. In the recent study, many methods

and techniques were used for diagnosis the dementia as result of Alzheimer's Disease to determine its progress and to estimate the percentage of the disease. These techniques are:

2.1. Imagining diagnosis Techniques:

This technique used for determine of Alzheimer's disease targeted not to correct Alzheimer's Disease diagnosis but also to identify stages of pre-clinical of Alzheimer's Disease it is not determined by use a clinical test. The last identification targets for the patients identification with the results of neuronic loss shown within imaging researches before decline in performance of cognitive effects and who intervention early may be slowly disease progression **(Norfray and Provenzale, 2004)**.

2.1.1. Anatomic or Structural Imaging

In the year of 1986, and two years later of clinical criteria publication which used for diagnosing Alzheimer's Disease, the technique of Computed tomography scan (CT) that used first of Alzheimer's disease describing that has relation with cortex of the medial temporal lobe atrophy, Computed tomography scan was determined to be 88% correction within Alzheimer's Disease diagnosing (LeMay, 1986). The capability multiplanar of Magnetic Resonance Imaging is suitable for making the Alzheimer's Disease diagnosis; Magnetic Resonance Imaging (MRI) supplies a correct diagnosis of 87%, which is similar to CT **(deLeon *et al.*, 1993)**.

2.1.2. Positron Emission Tomography (PET)

PET is now the best established for clinical diagnosis use in neurodegenerative disorders. The PET technique allows for evaluation of metabolism of glucose by use of FDG. Within Alzheimer's disease, utilization of reduced glucose is in a recognized manner, shown not active in the parietal and temporary lobes; the decreasing in process of metabolism of glucose was pesented to the clinical connect with a reducing within MMSE record and histological connect with neuro-fibrillary tangles and senile plaques density **(Hoffman *et al.*, 2000)**. Glucose Metabolism in the brain produces energy approximately 95% that needed for correct role **(Desgranges *et al.*, 1998)**.

2.1.3. Technique of Single Photon Emission Computed Tomography (SPECT)

The major factors that are using in the brain of Alzheimer's Disease Single Photon Emission Computed Tomography of patients are Tc^{99m} ethylcysteinate dimer (Tc^{99m} ECD) and Tc^{99m} hexamethylpropyleneamine oxime

(^{99m}Tc HMPAO) **(vanDyck *et al*., 1996)**. These factors accurate measurement cerebral blood stream and they are useful for identification the decreased cerebral blood stream within the temporoparietal area in patients of Alzheimer's disease **(Vlasenko *et al*., 1997)**.

2.1.4. Advanced MRI Technique

On pouring, Magnetic Resonance Imaging (MRI) by using dynamic susceptibility contrast-enhanced MRI, to reduce the related cerebral blood quantity has seen in the parietal and temporal areas of patients with Alzheimer's disease, which correlate with the stream of blood cerebral decreasing have shown on SPECT and PET **(Harris *et al*., 1998)**. The sensitive dynamic of MRI sensitivity in Alzheimer's disease diagnosis for moderate and mild of is stated about 90% **(Bozzao et al., 2001)**.

2.1.5. MR Spectroscopy Technique

The technique of MR spectroscopy can observe the changes of metabolism process that connect with structural changes of brain and then may be predicted for playing a role in imaging of Alzheimer's Disease. The plaques existence of senile was connected with neuron losing was exchanged in the reducing in neuron marker N-acetylaspartate,

2.1.6. The evaluation of autopsy-based pathologic

The existence and distribution of amyloid plaques and NFT within the brain used for establishing of diagnosis of Alzheimer's Disease definitive and to limit the disease stage **(Braak *et al*., 2011)**. To decrease Amyloid production the antioxidants can be used like vitamins C, E and A which remove the released radicals by stop bound of carbohydrates to factions of protein, this the principal operation in the production of chains of amyloid **(Pitchumoni and Doraiswamy, 1998)**.

2.1.7. Biomarkers of Mild Cognitive Impairment (MCI)and Alzheimer's Disease

Many biomarker and neuroimaging approaches are used to study MCI and Alzheimer's Disease. In a short term, Alzheimer's Disease biomarker is needful for improvement the good patients selected with clinical tests. In the long term, biomarkers are needed for identifying high-risk level of patients for early therapy, also to monitor disease progress and its response for treatment. This describes some of the broadly used biomarker approaches and the related findings in Mild Cognitive Impairment (MCI) and Alzheimer's Disease.

3. RESULT AND DISCUSSION

Patient of Alzheimer's Disease in general has normal things in physical and neurological examinations **(Camicioli, 2006)**, and the table 3 summarized some of the clinical features to help with differential diagnosis. The structural MRI or non-contrast computed tomography (CT) is helpful to manage normal pressure hydrocephalus, brain tumors and cerebral hematomas. The diagnosing of patho physiologically evidenced dementia of Alzheimer's Disease will be applicable when the patient subjects the cognitive and clinical criteria for dementia of Alzheimer's Disease summarized earlier within a text, therefore; the neuro-pathological test are using vast acceptable criteria , explain the existence of the pathology of Alzheimer's Disease **(Hyman and Trojanowski, 1997)**.

The using of Structural (Anatomic) Imaging in diagnosis of Alzheimer's Disease with the CT has found to produce about 88% accuracy in Alzheimer's Disease diagnosis, and it is similar to the results of **LeMay *et al*., 1986** for CT scan rating in patients with dementia of Alzheimer's.

The technique of Positron Emission Tomography (PET) provided us with good information that FDG and Positron Emission Tomography PET may be not dependably recognize Alzheimer's Disease from another dementia and dementia of Parkinson's disease, due to the decreased glucose metabolism form is alike in both diseases and this results also reported in **Hoffman *et al*., 2000**.

The accurate value of Single-Photon Emission Computed Tomography **(**SPECT) in Alzheimer's Disease diagnosis founded to be about 92% is it more than the provided by criteria of clinic only which is 74% stated in **Read *et al*., 1995**.

The dynamic susceptibility sensitivity MRI Technique in diagnosing mild and moderate Alzheimer's disease is stated to be about 90% and **Bozzao *et al*., 2001** reported the same results in his study.

Spectroscopy MR technique used for increasing the correction of Alzheimer's Disease diagnosis **(Shonk *et al*., 1995)**. As well as to increase coefficient values of apparent diffusion that found in the patients with MCI where MMSE = 25.9 ± 3.1 and probable Alzheimer's disease (MMSE = 17.9 ± 5.7) as shown in figure 4.

The autopsy-based pathological evaluation is the best standard to diagnosis the Alzheimer's Disease. The Amyloid production may be reduced by using the special antioxidants vitamins like A, C, E and which discharge free radicals and by prevent binding of carbohydrates into fragments of

protein, this is a basic process in the production of amyloid chain as **Pitchumoni and Doraiswamy, 1998** stated in their research. Soto, 1998 suggested another method to decrease the formation of amyloid value is for applying for peptides which can prevent the fibrillogenesis of amyloid in laboratory in addition to dissimulate formed fibrils inside the laboratory.

The concept of Mild Cognitive Impairment (MCI) is that symptom identified by memory. MCI is often considered as a gesture to dementia or a transitional state between healthy cognitive aging and dementia **(Sperling *et al*., 2011)**. There are clinical criteria used for the diagnosis of Mild Cognitive Impairment (MCI) by Biomarkers technique and the most of these those that proposed by Petersen and colleagues at the Mayo Clinic **(Petersen, 2014)**, these clinical criteria are presented in table 2.

The clinical outcomes results lead to patient has Mild Cognitive Impairment (MCI) are:

1- Many patients with MCI develop dementia, either because of Alzheimer's Disease or other person's causes.
2- Basic proportion of patient with MCI stay cognitive stable, and some back to
3- normal cognitive status.

There is relationship among (MCI), stages of dementia that cause Alzheimer's Disease and primary clinical in the patient, next figure shows the normal cognitive aging (spotted green line) and Mild Cognitive Impairment (MCI) (spotted black line) and they affected with the two factors, viz time factor (x-axis) represented with years of age and cognitive function (y-axis) as shown in figure 6.

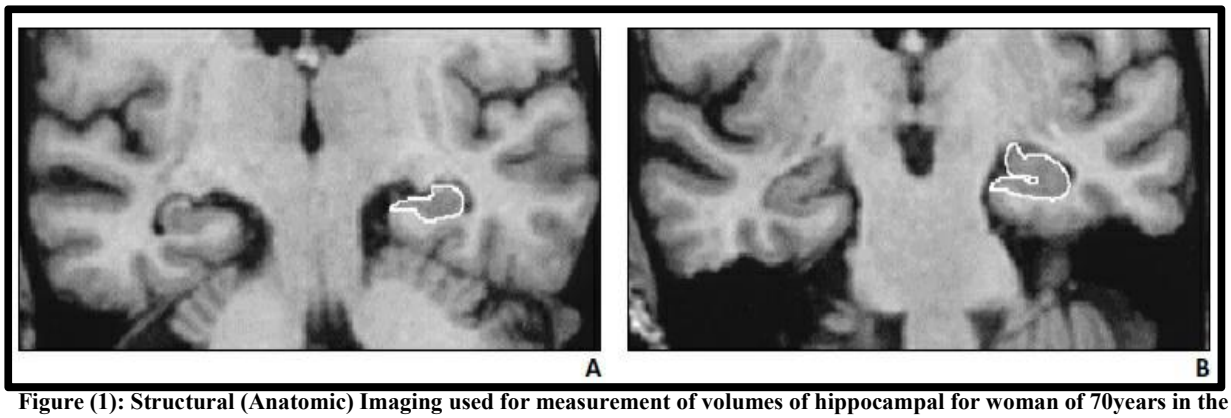

Figure (1): Structural (Anatomic) Imaging used for measurement of volumes of hippocampal for woman of 70years in the time of primary MCI diagnosis. (A) Image shows volume of relatively normal in hippocampus body. (B) Image at area which more anterior than that shown in image (A).

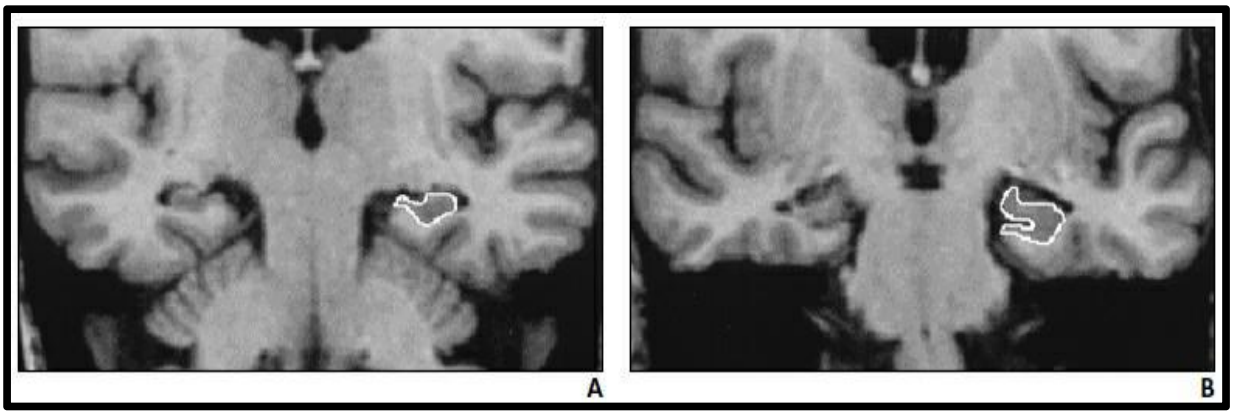

Figure (2): volumes of hippocampal Measurement for woman of 70years in the time of primary MCI diagnosis. (A) Image shows relatively reduced volume in hippocampus body. (B) image at area which more anterior than that shown in image (A).

Table (1): table shows the clinical features which distinguish the Alzheimer' Disease from other dementias.

Critical charastristics	Alzheimer's Disease	dementia Vascular	dementia of Parkinson's	lewy bodies dementia	dementia of Frontotemporal
Patient profile	More than 65years	More than 40 years Vascular risk factors	More than 65years	75years	50 to70 years 50% dominant autosomal
Background history	Deterioration and Onset of Gradual	Acute onset, stepwise deterioration	Deterioration and Onset of Gradual	Deterioration and Onset of Gradual	Onset of Gradual and Deterioration
Primary symptoms	Memory Losing	Executive dysfunction	Visual hallucinations	Visual hallucinations Fluctuating attention	Memory intact Disinhibition, apathy or aphasia
findings of Physical	No motor impairment (until late stage)	Pyramidal (upper motor neuron) signs	Parkinsonism (precedes dementia by 1 year)	Parkinsonism (presents within 1 year of dementia	Usually none (rarely associated with motor neuron disease)

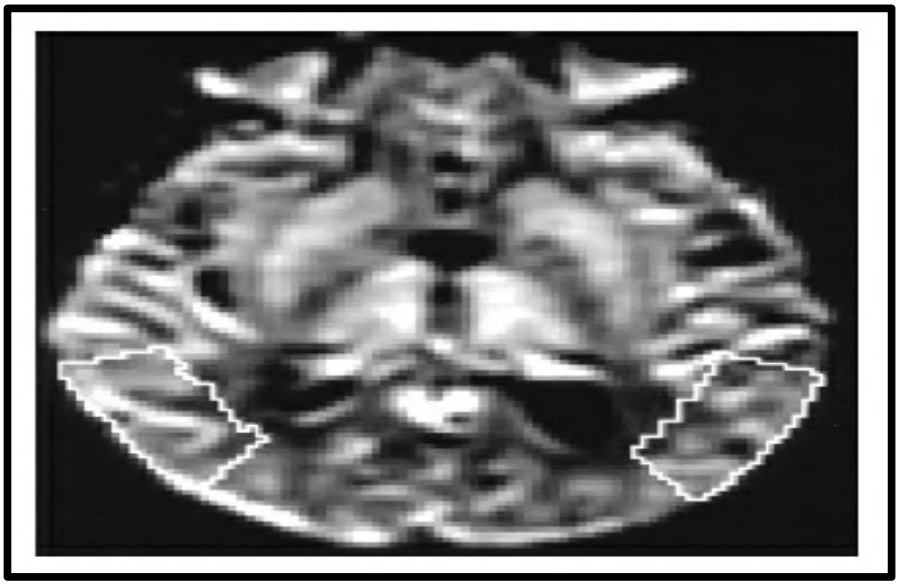

Figure (3): images of volume of role potential of cerebral blood for spporting in Alzheimer's disease diagnosis. Image has shown in woman of 83year who may be affected with Alzheimer's disease.

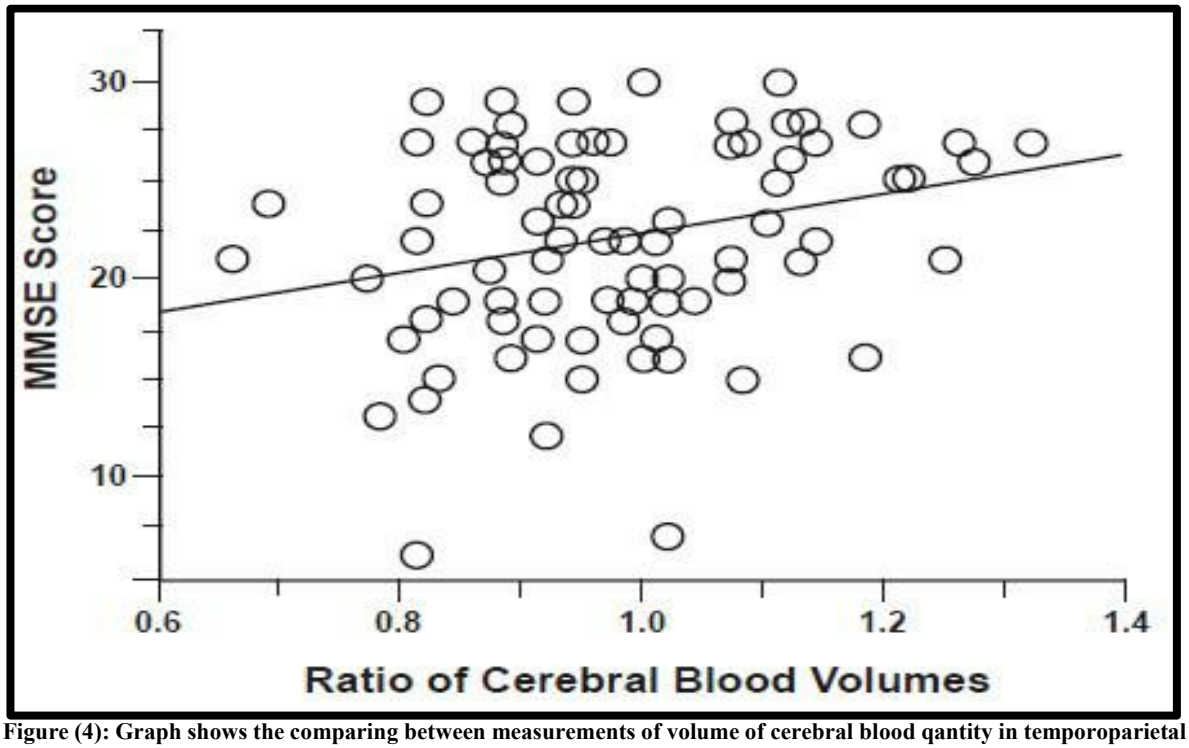

Figure (4): Graph shows the comparing between measurements of volume of cerebral blood qantity in temporoparietal areas and measurements of cerebral blood quantity in cerebellar cortex.

Table (2): Clinical criteria of Mild Cognitive Impairment (MCI)

Sr. No.	Clinical criteria of MCI
1	Preferably supporter by an informant, self cognitive complaint
2	other cognitive impairments and/or Objective memory that: a) irregular for the personal's age and education, b) Explain a good from past levels of functions
3	Simple ability for achievement many activities of everyday living
4	No presence of dementia

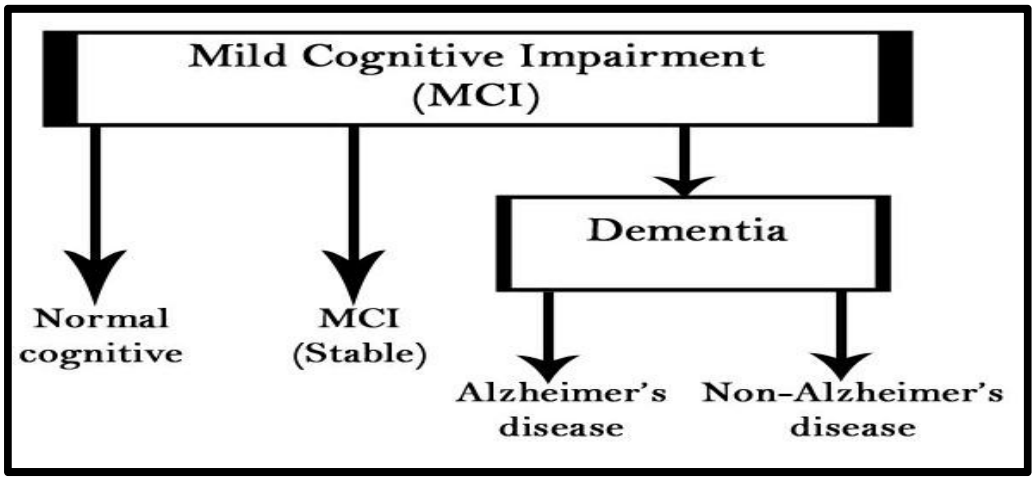

Figure (5): Clinical outcomes results of patients with MCI

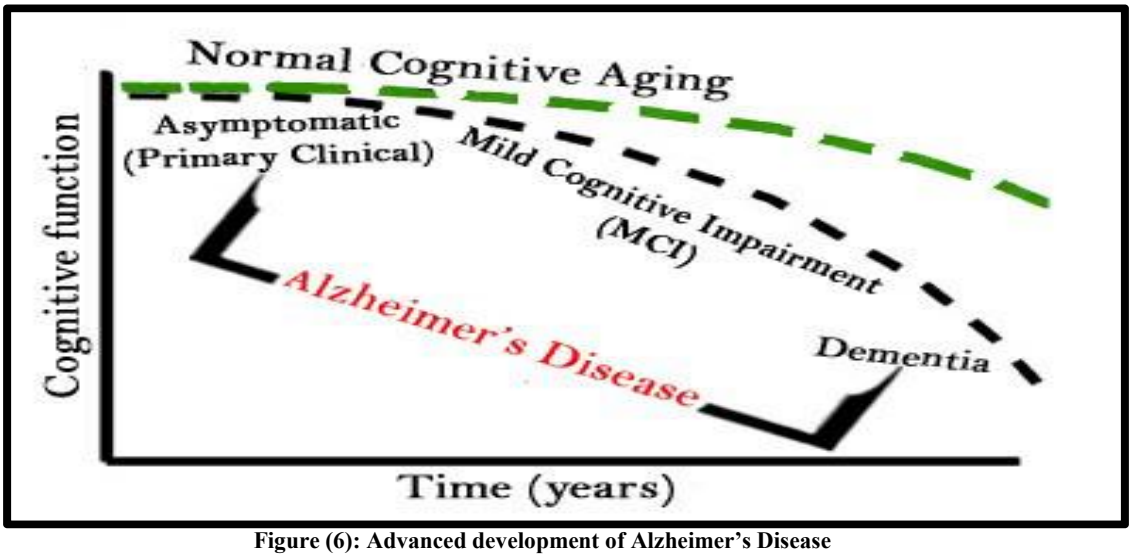

Figure (6): Advanced development of Alzheimer's Disease

4.0 CONCLUSION

The neuropathologist and psychiatrist Dr. Alois Alzheimer is explained the first time Alzheimer's Disease, many efforts, studies and progress has made to understand the biological and clinical aspects of this disease. There are large substantial has been done for characterizing pre-dementia levels and stage of Alzheimer's Disease, like (MCI), and options developing of diagnosis and therapy available to manage Alzheimer's Disease. The ability to find treatment for Alzheimer's Disease in the end not only depends on having view point of cellular processes and molecular which going oblique and also having optimal and standard biomarkers for making diagnosis and at same time therapeutic intervening in at-risk individuals.

The term of Alzheimer's Disease Neuroimaging Initiative (ADNI) statnig in 2004 **(Weiner *et al*., 2012)**, and The ADNI and similar large-scale initiatives are probably to speedily advance our information on dementia and Alzheimer's Disease and can catalyze improvement of considerably more practical therapies for Alzheimer's Disease than exist nowadays. There are some important issues the reader must be know them and that issues will be resolved in the future to move toward a 'treatment' for Alzheimer's Disease in our current century 21^{st} .

These issues summarized in next points:

1- What the harms and advantages related to change the therapeutic strategy from (1) one which includes treating individuals with public dementia of Alzheimer's Disease to (2) one wherever the individuals treat with MCI, and in the end to (3) one wherever the people treat that will be

well however see an Alzheimer's Disease like imaging biomarker pattern or biochemical are moving nearer to treat laboratory abnormal research outcomes as against the patient.

2- The optimum biomarkers combination for (1) early Alzheimer's Disease determination, and (2) progress and response of disease observation to therapy?

3- The optimum strategy of therapy for (1) inhibits of Alzheimer's Disease; (2) therapy of Alzheimer's Disease, and (3) discontinuous against familial Alzheimer's Disease this means targets of therapy, function of medicines against style of life adjustment, the standard time for entering).

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