IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

AYURVEDIC CONCEPTS OF ALZHEIMER'S DISEASE

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Abstract

Alzheimer's disease is considered as a looming public health crisis .
Approximately 10% of all persons over the age of 70 have significant memory loss, and in more than half the cause is AD. It is estimated that the annual total cost of caring for a single AD patient in an advanced stage of the disease is more than $50,000. The family, friends and caregivers of people with AD experience emotional, physical and financial stress as loved one become increasingly forgetful, frustrated, confused and lost during the course of the disease.
Alzheimer's disease is the most common cause of dementia among older people. Dementia is loss of cognitive functioning – thinking, remembering reasoning and behavioural abilities that significantly deteriorates a patient's quality of life.

Introduction

Ageing of the population poses an increased burden on the society. Owing to its relevance, the World health organisation has put forward the theme of **"Ageing well"** as a global priority. WHO states that between the year 2000 and 2050 the proportion of world's population over 60 years will double from about 11% to 22%. The absolute number of people aged 60 years and above is expected to increase from 605 million to 2 billion over the same time period. As people across the world live longer, the soaring levels of chronic illness and diminished well being are poised to become a major global health challenge.

Old age disorders have always been an integral and inseparable part of ***Astanga Ayurveda.*** In fact, the speciality ***Rasayana chikitsa,*** is especially meant to tackle the problems of ageing or ***jarajanya vikaras***. The definition of Ayurveda itself denotes that it is the knowledge of various aspects of life processes, ageing being one of them.

Among the diseases of the old age, Alzheimer's disease (AD) is one of the front runners, that has gained much attention and curiosity in the medical world within the last few decades. It is an age related brain disorder that causes a progressive cognitive impairment and is the main type of dementia. It is the 6th leading cause of death in the United States annually. Before a person with AD dies, he or she lives through years of morbidity as the disease progresses.

Thus, Alzheimer's disease, as a topic of concern, has great relevance in this era and here, as an Ayurvedic Practitioner , it is our duty to contribute the essence of ayurveda for the welfare of the society.

A glimpse into the history :

In 1906, Dr. Alois Alzheimer examined the changes in the brain tissue of a women and found many abnormal clumps and tangled bundles of fibres which are now known as amyloid plaques and neurofibrillary tangles. The patient's symptoms included memory loss, language problems and unpredictable behaviour. Thereafter this disease is named after him.

Incidence and prevalence :

Reports of incidence suggests rates of 1.9 – 2.6 per 1000 for men and 2.1 – 4.1 per 1000 for women aged above 60 years (Bickell & Cooper 1989).This incidence rates are for all causes of dementia. More studies have shown that Alzheimer type dementia (DAT) is more common in women.

Aetiology and risk factors :

There is no proven aetiology for AD. The general inability to convincingly link these phenomenon has resulted in the emergence and propagation of various heavily debated theories that focus the role of one particular element in the pathogenesis of all other abnormalities.

- **Genetic factors:** Alzheimer's disease is known to have a high prevalence in some families and the importance of genetic factors have been confirmed by twin studies (Deary & Whalley 1988). In recent years, genetic research on DAT has focussed on 3 chromosomes 21, 14 and 19.
- **Increasing age:** The relationship between advancing age and disease prevalence is beyond dispute. Among people aged 65, 5% show signs of the disease, while 20% of people aged 85 have symptoms of AD.Every five years after the age of 65, the probability of having the disease doubles.
- **Other factors:** A number of other factors such as Down's syndrome, head injury, viral infection, autoimmune processes, sex, thyroid diseases, use of anti perspirants like Aluminium, long standing alcohol abuse are some of the risk factors to name, but a few.
- **Alzheimer's as Type 3 diabetes – an emerging new outlook** Recent studies propose a common pathophysiology between diabetes and Alzheimer's disease. Researchers discovered that many type 2 diabetics have deposits of a protein called amyloid beta in their pancreas, which is similar to protein deposits found in the brain tissue of Alzheimer's patient. Increasing blood sugar level has also been proposed to increase oxidative stress that could lead to progressive damage to the brain. Nevertheless, this new concept has generated much interest and a hope in that further research in this field would give way to the development of novel therapeutic strategies for treatment of AD.

Pathologic changes:

The pathology of AD is still a highly debated topic. The neuro-degeneration that occurs in AD is consistently associated with a number of characteristic histopathological, molecular and biochemical abnormalities.

- **Macroscopical changes :**

The brain becomes *atrophic*, particularly the cerebral cortex and hippocampus. Brain weight is significantly decreased below normal for the age. The major macroscopic changes can be summarised as: Posterior part of brain atrophy, Ventricular enlargement and Sulcus widening.

- **Microscopical changes :**

The most important microscopic findings are *neuritic " senile " plaques and neurofibrillary tangles (NFT)* in the neocortex. Beta amyloid is the principle constituent of the plaques and is also deposited in cerebral and meningeal blood vessels. These can act as neurotoxin and may cause the death of selectively vulnerable neurons. Amyloid angiopathy is seen in 86% of AD cases.

- **Biochemical changes :**

Biochemically, AD is associated with a decrease in the cerebral cortical levels of several proteins and neurotransmitters ,especially acetylcholine, its synthetic enzyme choline acetyltransferase, and nicotinic cholinergic receptors.

pClinical manifestations – Coping with daily life and Alzheimers

AD is often starts mild and gets progressively worse ,and thus divided into mild, moderate and severe stages. Each stage may last for a few years.

Cognitive Impairement :

- **Memory :-**

It is the first cognitive domain to be affected by the illness.

In the first stage of AD, the memory loss is minimal, usually restricted to recent events. Towards the last stage, patient displays significant global memory loss, where he cannot recall his own identity.

- **Language problems :-**

Word finding difficulty is the main language problem in AD patients. During severe stage , the patient starts communicating in non verbal fashion or remain mute. It may also characterise echolalia or palilalia.

- **Disorientation :-**

The loss of orientation usually progresses from spheres of time, to place and lastly to persons.

- **Impaired problem solving and judgement :-**

The patient's ability to appropriately handle day to day challenges deteriorates.

Behavioural changes :

- **Mood :-**

The most important mood change is depression. Sometimes they will be more aggressive and may show several physical agitations. In some cases the symptoms may increase in the evening or in night time and this is known as **sun downing sign.**

- **Personality changes :-**

The most common change seen is irritability; he/she may become very angry or lose temper without clear provocation. In end stage AD, patients become rigid, mute, and bedridden.

- **Perceptual changes :-**

Patients with AD may experience delusions, hallucinations and paranoia alone or in combination.

The Invisible Victims of Alzheimer's Disease

The responsibility of caring an AD patient, can take an enormous emotional and physical toll, especially when added to the psychological distress of watching a loved one deteriorate. Because of burdens of caregiving, the caregiver of the patient is often referred to as the **hidden or second patient of the disease.**

Disease outcome:

The typical duration of AD is 8-10 years, but the course can range from 1 to 25 years. AD is a progressive disease which ends in death usually by bronchopneumonia, malnutrition, secondary infections or heart disease. **Management:**

In the early stages, memory aids such as notebooks and posted daily reminders can be useful.

Donepezil, Memantine, Rivastigmine are the drugs approved by the FDA for the management of Alzheimer's.

Management consists of largely providing a familiar environment for the patients and providing support for the carers.

Ayurvedic perspective on Alzheimer's disease

To directly relate a modern terminology like Alzheimer's disease within the panorama of Ayurveda is not an easy task. But the principles and ideas to perceive it are well explained by our Acharyas, but in various contexts.

Ayurveda has given equal importance to the conjunction of body, sense organs and the soul in maintenance of *Ayu.*

Tridosas are causes of production, preservation and destruction of the body, thus known as tristhunas.

Alzheimer's disease - Analysing in Ayurvedic principles

Though not explained as a separate disease entity, we may describe AD on Ayurvedic principles, based on its main presenting symptoms. In AD, there is a progressive loss of cognitive functions – thinking, remembering and reasoning along with behavioural abnormalities.

In Ayurvedic parlance, this relates to the concept of ***dhee , dhruti and smrithi bramsha***. *Dhee, Dhruthi* and *Smrithi* are considered as *prajna bheda* by Acharya **Chakrapani**

The perverted *Dhee ,Dhruthi* and *Smrithi* are collectively called as "***Pranjaparadha***" Smrithi

The first cognitive domain affected in AD is the memory or *smrithi vibramsha.* Acharya Charaka states that the ' recollection of the knowledge perceived previously through *drsta* (seen),*sruta* (heard) *and anubhuta* (experienced) is called as smrithi.

Smrithi is predominantly , ***Udana*** and ***Prana vayu dharma.***

Smrithi utpathi

Indriya and Indriyartha sannikarsha ⟹ *Manas* ⟹ *Athma* ⟹ *Budhi* ⇩ *Anubhava* ⟸ *Smrithi*

Any hindrance to any one of this factor, leads to an improper cognition

Smrithi bramsha

According to Ayurveda, when mind gets clouded by ***Rajas and Tamas***, smrithibramsa results, that may further lead to *dhee and dhrithi bramsha.*

Dhee and Dhruthi bramsa :

Dhee is the ***nischayatmaka jnana*** and dhrithi is the ***niyamatmaka jnana***, that gets deranged during the subsequent stages of the Alzheimer's.

Even though, dhee, dhruti and smrithi bramsa are main faculties of manas, the main *mano karma* like ***indriya abhigraha*** (cognition of objects) and *mano dharmas* like ***chinta, vichara, uha, dhyeya and sankalpa*** does not primarily derange in AD. They get afflicted only when the samprapthi progresses. Dhee, dhruti and smrithi are divisions of prajna or budhi.Thus it may be assumed that it is the faculty budhi that is primarily deranged here, which is mainly under the control of Prana and Udana vayu.

Concept of Organic brain disorders in Ayurveda

In Alzheimer's, there occurs a decreased mental function, not due to a psychiatric illness, but due to a medical or physical disease, so it is an **organic brain disorder,** due to **neuro degeneration**.

Thus, in Ayurvedic parlance, while working on the concept of Alzheimer's disease, it cannot be regarded as a kevala manasika vikara, by rajas and tamas avarana to manas, but primarily a sareerika vikara, where the **tridosas** and their karmas have to be considered.

In Ayurveda too, the abode of all disease in world are considered both sareera and manas.

The main presenting symptoms of AD, ***smrithi ksaya, indriya bala hani,moha, sanjna nasa*** etc ,though mainly described under the theme of *manasika vikaras* like unmada, apasmara etc, are also described under the context of :

- ***Vata vrdhi laksana:*** *Sanjna nidra nasa, bala indriya upaghata, majja sosha, moha,dainya,bhaya,sokha, pralapa* (Vagbata, A.Sang.soo.)
- ***Vata prakruthi:*** *Chala dhruthi,smruthi,budhi chesta* (A.H.saa)

- ***Prana avrutha vyana:***

  - The maintenance of ***Indriya patava*** is the main function of Vata. (Vagbata)

Thus, the concepts like organic brain disorders are not new to Ayurvedic classics. So, it may be stated that Alzheimer's disease cannot be considered as pure *manasika vyadhi*, rather here, it is primarily a derangement to *tridosas* and subsequent *mala sanchaya* due to *dhatwagni vaigunya* in body, that plays a pivotal role in samprapthi.

Though an exactly similar Ayurvedic terminology cannot be given to AD, the tridosa theory can act as the tool, in its better understanding.

The Role of Tridosa in Dhee, Dhriti and Smrithi vibramsa :

- **Role of Vatha :**

Vayu is the most important factor to be considered in the oldage, mainly due to its natural predominance during that stage of life. Acharya Charaka in soothrasthana 12th adhyaya, states the importance of vayu as :

- *Initiates a movements (**pravartaka chestaanam)***
- *Leads and controls the " manas " (**niyanta praneta cha manasah)***
- *Prompts speech (**pravartako vaachah)***
- *Causes structural formation of all bodily dhatus (**sarva shareera dhatu vyuhakara)***
- *Source of exhilaration and courage (**harsha utsaaha yor yoni)***
- *Maintains life span (**aayusho anuvrthi prathyaya bhuta)***

AD is predominantly a progressive neurodegenerative disorder of the oldage. Acharya Susruta mentions the period between 40 – 70 as ***parihani kala.*** Acharya Charaka, considered the age above 60 years as ***jeerna***. He advocates that during this period of life, dhatus, sense organs, strength, energy,virility, prowess, acquisition, retention, speech and memory gradually degenerate due to predominance of vayu.

While analysing the modern pathology, atrophic changes of brain is one of the key macroscopic changes. This all relates to the relevance of ***vata*** in these disease stages. In *Bhaisajaya Ratnavali,* there is mentioning of ***"Mastishka apachaya"*** that holds some similarity with the above concept.

- **Atharva veda** states that ***vata*** is located in the upper portion of **"mastishka"**
- **Prana vata*:*** Located in *moordha, preserves the function of buddhi, indriya, hrdaya and manas*. (Vagbhata, AH.soo20)
- **Udana vata*:*** Plays some of the psychological functions in association with prana : maintains *dhee, dhruthi, smruthi, manobodhana and vakpravruthi* (AH soo)
- **Vyana vata *:*** Located in *hrdaya* , it act as executor of direction of *budhi,* regarding voluntary movements (gati) through *chestavaha srotas.* (A.Sang.soo20)

- **The Role of Pitta :**
  - Susruta states one of the function of pitta as ***" medhakrt "*** (Su.soo15)
  - Vaghbata advocates pitta as the cause of *budhi, medha, ojakrt, dhairyam etc.*
  - **Sadhaka pitta*:*** Located in hrdaya, attends to functions of *budhi, medha, abhimana and utsaha.* (A.Sang.soo.20)
  - **Alochaka pitta*:*** Bhela recognised 2 divisions of alochaka pitta as ***Chakshurvaiseshika :*** functions with atma mana sannikarsha to perceive knowledge.
    Budhivaiseshika : Located in srngataka, it enables *dhyana* (concentration) , *pratyahara* (response), and *yojana* (planning)

- **The Role of Kapha :**
  - ***Shiras*** is a seat of kapha.
  - **Chakrapani** explains its function as resisting degeneration (*sthiratwam)* and decay *(ashaithilyam).*
  - The main entities *utsaha, jnana-ajnana, budhi, moha* etc.depends on it.
  - ***Tarpaka kapha:*** Located in *shiras,* it nourishes and soothes the sense organs. Dalhana states that ***sneha in mastaka majja*** is nourished by tarpaka kapha

The Role of Ama and Dhatwagni vaigunya :

AD is identified as a protein misfolding disease, due to accumulation of abnormally folded amyloid beta protein and tau protein in the brains of the patients. They act as neurotoxins , thus contributing to cerebral atrophy.

The concept of ***ama*** or improper ***mala sanchaya*** occurring as a result of *dhatwagni vaishamya* can be used to relate this.

The localisation of *ama* during its circulation through body is an important factor in the causation of disease.

This localisation is again dependent on healthy or diseased state of ***srothases.***

Acharya Dalhana has quoted in a context as mastishka is similar to majja dhatu. "

Therefore it can be thought that it is the ***dhatwagni vaigunya*** especially of the majja dhatu that is being deranged here, resulting in ama.

The theory of correlating AD as a metabolic disorder like type 3 diabetes, can also be substantiated with this principle of dhatwagni vaigunya.

Nidana :

- **Ahara:** Ajeerna,vishama,virudha ahara, dusta anna, vyapanna madya paneeya leading to sarvadosa prakopanam should be considered.(A.H.Ni.1/19) Researches show that, common staples in American diet such as processed cheese, processed meat, beer, white foods like pasta, cakes, white sugar, high fat dietary products etc. lead to inflammation, build up of plaques in brain and as a result, cause impaired cognitive function.
- **Vihara:** Reduced physical activity might precede the onset of clinical AD. In observational studies, subjects who are physically active often demonstrates less cognitive decline, than people who are inactive.
- Head trauma **(abhigata),** long standing alcohol abuse, Al toxicity **(visha)** are some of well known risk factors.
- **Beeja dushti –** Alzheimer's can well be correlated as a ***Kulaja vikara*** as per our classics.AD is known to have a high prevalence in some families, inherited in autosomal dominant model.
- **Prajnaparadha:** The dhee, dhrithi and smrithi bramsa creates a perverted functioning of budhi and it further leads to sarvadosa prakopanam.
- **Kala:** It is the unavoidable factor for disease manifestation. Kala parinama in the form of ageing cannot be controlled. AD normally occurs in the old age.
- **An unexplainable cause –** "**Daiva" :** There are still some mysterious cause for incidence of AD, that have not been explained even in modern science. The cause of sporadic occurrence of AD, early onset before old age etc still remains unexplained. These can be correlated as ***Daiva or Karmaja vyadhi***

Samprapthi : The above said nidanas, along with factors like '*beejadusti'* (dhatu leena ama) and a triggering cause such as '*daiva',* afflicting a person who is already in stage of *swabhavika dhatu ksaya and ojohani (vardhakya),* causes a vata pradhana tridosa kopa. The vitiated dosa circulate all over the body, first localises in shiras and later in manas. Further, it causes a dhatwagni vaigunya in the body, with a more potential affliction of majjadhatu due to its *sthana visesha(shiras).* Along with the subsequent *Srotho vaigunya,* this again progresses the samprapthi, forming a *mala sanchaya or ama* due to an improper *dhatu parinama* . Owing to this, there occurs a progressive dhatu ksaya and ojo hani in the person.

During this disease course, the sareerika dosas especially praana , *udana* are vitiated due to adhistana visesha. Their primary function is to maintain the karmas of *dhee, dhruti, smrithi, indriyas, manas etc.* So due to their vaigunya, they afflict primarily the manovaha srothas, owing to which secondarily the patients presents with symptoms with smrithi, dhee, dhruthi bramsa in which rajas and tamo avarana

may also play a role later on,leading to further progression of samprapthi. The main samprapthi ghatakas can be summarised as follows:

- Dosa : Shareeka dosa **: Vata** – Prana, Udana , Vyana.
  Pitta - Sadhaka , Alochaka
  Kapha – Tarpaka
- Doosya : Saptha dhatu especially majja, Ojas.
- Srothas : All srothas particularly manovaha srothas
- Sthana samsraya : Shiras, Manas
- Roga marga : Madhyama
- Saadhyasadhyata : Asadhya (yapya)

Manovaha srotho pareeksha: Due to manas being a sthana visesha, adopting the definition of Unmada by Vagbata : ***mano, budhi, sanjna, jnana, smrithi , bhakti, seela, chesta, achara vibrama*** can be considered as a stage wise progression of Alzheimer's disease.
Towards the end , an Alzheimer's patient loses all spheres of orientation and memory, not able to recall even his own identity.

Chikitsa :

As it is a *marmasrita vyadhi*,it is an asadhya vikara. The main aim of treatment should be to prevent further degeneration and to improve the patient's general well- being.

Considering it as a dhatuksayaja vikara especially of oldage, ***Brumhana chikitsa*** has much relevance. The *vata upakrama* can be ideally adopted here.

Chikitsa cannot be generalised, it depends on the ***avastha visesha*** of roga and rogi. Chikitsa can be divided into two types: sodhana and samana
Sodhana : Due to reduced rogi bala , sodhana cannot be adopted widely in this case.

- **Snehana** can be administered as vicharana or a sadya snehana. Later, a sweda and mrdu virechana can be adopted.
- For shira sodhana, **nasya** can be performed. It should be performed with great caution as patient may not be always cooperative. In vatika vikaras, brumhana nasya is to be adopted. It can be done as prathimarsa nasya.
- **Vasthi** is regarded as ***chikitsaardha***.Vagbatta specially indicated it in *marmopagataja and sarvangavayavaja vikara.* Adopting yogavasthi, karmavasthi and kalavasthi would be ideal.

Samana :

Dhatu ksaya hara, agnideepana and medha vardhana drugs should be given more priority.
Shirodhara, Takradhara, Thalapothichil, sarvangadhara,abhyanga can be widely performed.According to some ayurvedic practitioners, **shirovasti** is not regarded as an ideal choice in management of dementia, as per their experience.
Saraswataristam, Smriti sagara rasa, Unmada gajankusa rasa etc are widely used.

Rasayana :

Alzheimer's is a neurodegenerative disease especially of old age. The role of rasayana dravya in *dhatu kshyaja and dhatwagni vaigunyakara vikara* is indispensible. *Medhya and Vayasthapana guna dravyas* may be of immense potential in this case, Acharya Vagbata has specially indicated Rasayana dravyas in *deerghayu, smrithi, medha, arogya* and maintenance of *taruna vayas.*
Alzheimers disease is an emerging medical challenge.Annually about 5.3 million individual suffer from this disease, that is regarded as untreatable. AD is regarded as a dhatu ksayaja vikara and asadhya vyadhi as per Ayurvedic parlance. The management mainly aims to increase the Quality of life of the affected individual and their family. Ayurvedic management mainly Rasayana chikitsa can play a pivotal role here.

Research references:

- **Curcumin:** exerts anti-inflammatory and anti-amyloid properties. Clinical trials are underway examining the effects of curcumin as a treatment of AD.
- **Yoga:** Memory span and attention measured before and after yoga showed significant improvement in dementia as per recent research.
- **A study on medhya rasayana drugs with special reference to its action in AD, showed improved orientation and constructional praxis**
- **Guloochi:** The hydroalcoholic extract of Tinospora cordifolia shows effective action on neurodegeneration and an improved memory retention activity, ($p < 0.01$) **[scopemed.org]**
- **Mandookaparni :** Centella asiatica extract selectively decreased beta amyloid levels in hippocampus of Alzheimer's disease animal model. **[pubmed.gov]**
- **Shankhupushpi:** Supplementation of Convolvulus pluricaulis attenuates scopolamine induced increased tau and amyloid precursor protein expression in rat brain showing its neuroprotective effects **[pubmed.gov]**