

An Overview on Dementia: A Major Symptom of Alzheimer's Disease

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Abstract

Dementia is a word for an acquired illness in which two or more cognitive abilities are lost due to a brain disease or injury. The most common form of dementia is Alzheimer's type dementia (DAT). It has been associated to cerebral cortical degenerative anomalies. It's also visible in neurologic diseases that primarily affect subcortical systems such as the basal ganglia and brain stem. The causes are plaques of β -amyloid and tangles of intraneuronal tau protein. Dementia is addressed in this overview. Pathophysiology, epidemiology, and different varieties of dementia; contributing factors to dementia; symptoms, causes, diagnosis, prevention, and care; and new breakthroughs in dementia treatment. It also looks at how patients with mental problems coped during the COVID-19 outbreak. Patients may require more therapies to manage their illness, and some future drugs are now being explored.

Keywords: Dementia, Alzheimer's, Plaques, Cognitive training, β -amyloid

1. Introduction:

Dementia is a term used to describe an acquired illness that results in the loss of two or more cognitive abilities as a result of a brain disease or injury^{1,2}. Dementia is traditionally linked to degenerative illnesses of the cerebral cortex, with AD being the most prominent example. Dementia is also seen in neurologic disorders that involve predominately sub-cortical areas such as the basal ganglia and brain stem^{3,4}. It is mostly connected with the more than one neuropathology, usually Alzheimer disease (AD) with cerebrovascular pathology and Parkinson's diseases¹. Dementia is a clinical diagnosis that requires a new technology to treat the cognitive abilities in the patient that will lead to the decline in cases. In terms of social, physical, and mental health, people with dementia are more reliant and insecure, highlighting the issues that society and health care facilities face⁵. Dementia is a symptom that affects daily functioning and cognition, primarily disrupting the patient's independence. Dementia is better described as a syndrome rather than a single disease because it encompasses a variety of neurodegenerative conditions that can be classified as AD dementia (DAT). Dementia has a variety of origins, including neurological, neuropsychiatric, and medical problems. Alzheimer disease and dementia with Lewy bodies

are the most frequent neurodegenerative dementias in the elderly, but traumatic brain injury and brain tumours are common causes in younger adults². Parkinson's disease symptoms come later in the disease's progression, but it's called dementia with Lewy bodies' symptoms if they appear early on with cognitive impairment and early signs of psychosis. The patient progresses from moderate to severe stages of disease when they exhibit symptoms like risk of aspiration with unsafe swallowing, malnutrition, deep venous thrombosis, infections, and immobility with associated risks for bedsores, eventually becoming incontinent, mute, and bedridden at the end of the phase, demonstrating that these complications are the direct cause of death in the patient with Alzheimer's disease.

2. Pathophysiology:

Dementia of Alzheimer type (DAT) is most common example for the Neurodegenerative disease. The Pathophysiology of Alzheimer disease is mostly based on the Cortical and Sub-cortical areas. Cortical areas include the frontal lobe, parietal lobe, temporal lobe and occipital lobe and sub-cortical areas include diencephalon, pituitary gland, limbic structures and the basal ganglia.

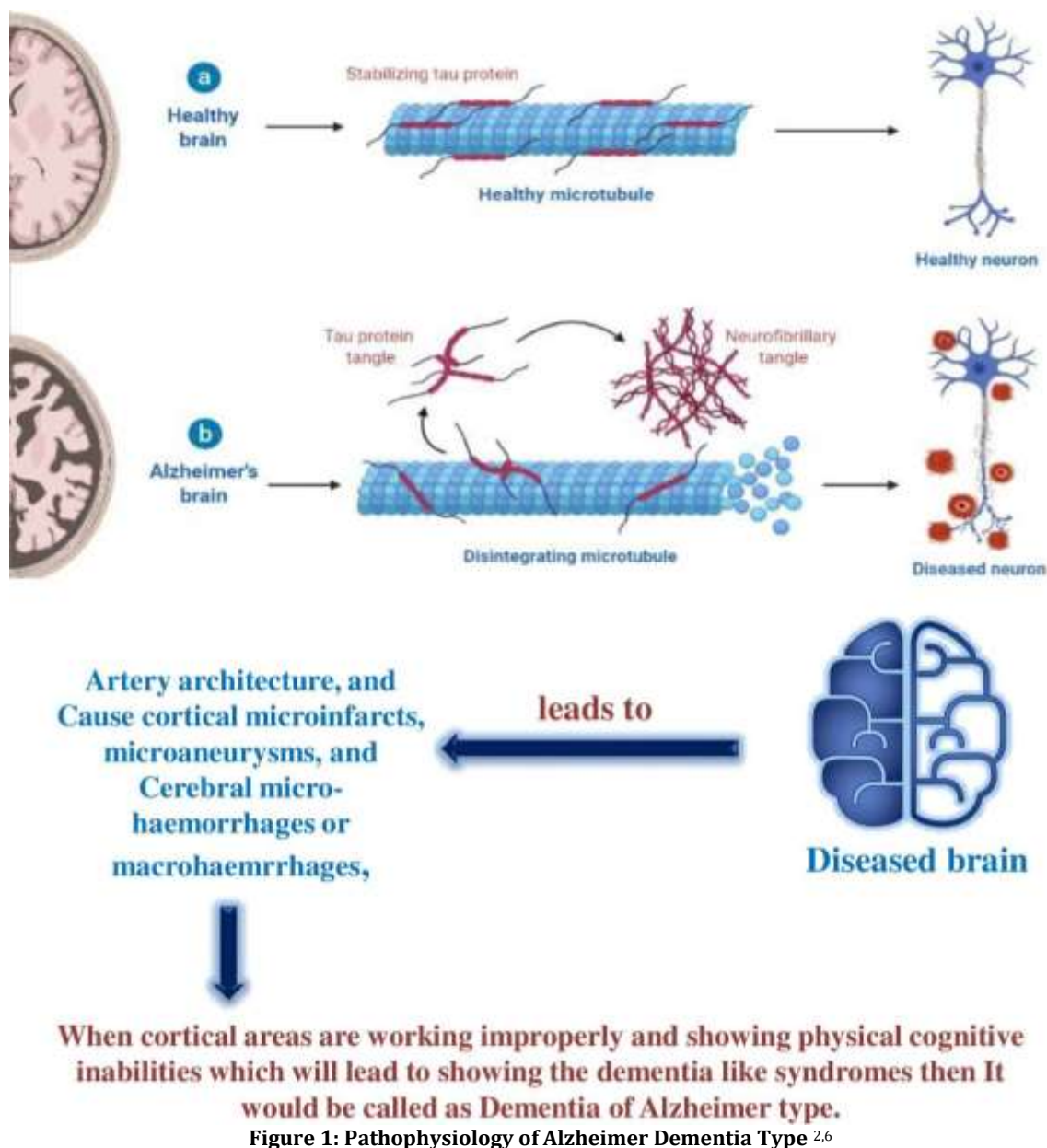


Figure 1: Pathophysiology of Alzheimer Dementia Type ^{2,6}

Both are regarded the same in dementia, but there are some clinical differences. Memory impairment and advancing intellectuality are more severe and fast in DAT than in sub-cortical disorders. Sub-cortical dementias are often devoid of cortical dementia symptoms such as aphasia, agnosia, and apraxia. People with sub-cortical illnesses are described as apathetic (uninterested) and frequently depressed, whereas patients with DAT have little insight and are rarely depressed ^{3,7}. Plaques and tangles are mostly involved in the dementia because plaques are considered as the Neuro-pathological tombstones of amyloid cored, dying, pinched off cholinergic nerve endings that are observed in the outer layer of all cortical lobes except in the occipital, the hippocampus, the amygdala, the hypothalamus and the granular layer of the cerebellum where Tangles are the silver-staining twisted cords that one finds in larger cortical neurons are most active in the younger ones in the elder patients with SDAT (Senile Dementia Alzheimer Type). Acc. to the reports no one yet has been able to report the tangles cells predestined for an early death although this seems likely since the tangles are occurred in the large pyramidal cells of the cortex which are selectively die out in SDAT.

Alzheimer disease (AD) results from the overproduction and impairment of the Beta-amyloid. The Downstream events are tau hyperphosphorylation and neuronal toxicity. Pathological features of AD include;

1. Brain atrophy from regional neuronal and synaptic loss,
2. Extracellular Beta-amyloid deposition in the form of neuritic plaques,
3. Intraneuronal tau protein deposition in the form of intraneuronal neurofibrillary tangles.

Beta-amyloid gets deposited on the cerebral blood vessels. In this, the small amount of amyloid to major amount gets deposited which distort the artery architecture and cause cortical micro-infarcts, micro-aneurysms, and cerebral micro-hemorrhages or macro-hemorrhages (multiple small hemorrhages in the occipital lobes in the patient). Amyloid deposition starts begin 20 years prior for the developing the symptoms that will lead to the dementia Alzheimer type ^{8,9}. The performance of patients with DAT was different as compared to the patients with PD. In patients with DAT, overall mental functioning, memory performance and visuospatial skills were more severely impaired as compared to the patients with PD. There was a significant disturbance on

all language related tasks and evidence of apraxia and depression was also evident. The qualitative and quantitative functions differ in the dementia syndromes which are associated with the Parkinson's disease and DAT³. The similarities do exist in the dementia of PD and DAT and pathological similarities are there which have been noted down and tells about the similar performance of cortical degeneration in Parkinson's disease and Dementia of Alzheimer's Type 7 & performance of subcortical degeneration in the patients with both the disorders¹⁰ (**Figure 1**).

3. Epidemiology:

Like Alzheimer disease, Parkinson's disease, Dementia etc. that lead to the cognitive disabilities in the patient. There are so many cases generated by the Neurodegenerative diseases that states that;

1. Acc. to the researches, it only shows impact on the 65 years older people i.e., AD Dementia will increase from 63 to 137 million in America, from 113 to 170 million in Europe, from 172 to 435 million in Asia^{5,9}.
2. The factors include alcohol consumption, traumatic brain injury (TBI) and Air Pollution are the most risky factors that increase 12% dementia in the patient¹¹.
3. In UK, the changes in the factors suggest that there is 57% increase in the number of the Dementia patients in 2016 and as expected from the researches it estimated that there will be 70% increase in the year 2040 lead to 1.2 million people (**Table 1**)¹¹⁻¹³.
4. In 2013-2014, there were 19,765 people found with dementia in Northern Ireland⁵.
5. Globally, It estimated that every 20 years there is a increase in the patient of the dementia which is based on the shifting population demographic, the aging population⁵.
6. From 2013 to 2050 it is estimated that there will be 115 million patients that will be affected by the Dementia⁵.

Table 2: Subtypes of dementia

S No.	Contents	Alzheimer's	Vascular	Lewy body	Fronto-temporal
1.	Mechanism	Accumulation of β -amyloid plaques and neurofibrillary tangles in the brain's entorhinal cortex and hippocampus, resulting in neuronal damage and death	Other disorders that interrupt or restrict blood flow to the brain cause neuronal depletion of oxygen levels. As a result of various conditions that disrupt or restrict blood flow to the brain, neuronal depletion of oxygen levels occurs	Dementia caused by abnormal insertion of alpha-synuclein protein into neurons	Occur when nerve cells in the frontal and temporal lobes of the brain are lost
2.	Prevalence	60 to 80 %	10-20 %	10%	5%
3.	Severity	More severe	Less severe than alzheimer's dementia	Mild to moderate	Less but can be seen in younger people
4.	Major parts affected	Neurons and their connections in parts of the brain involved in memory, including the entorhinal cortex and hippocampus	Widespread damage to white matter beneath the cortex	Abnormal deposits of a protein called alpha-synuclein in the brain that can lead to problems with thinking, movement, behavior, and mood	Frontal and temporal lobes
5.	Factors	Hypertension, excessive alcohol consumption, heart disease, diabetes	Diabetes, smoking, Hypercholesterolemia, Hypertension	Mental retardation, Bradykinesia, rapid eye movement (REM), sleep disturbances	Personality changes, behavioral disorders, visuospatial function affected

Table 1: Gender specific age-related prevalence (%) of dementia in the UK (estimates from Dementia UK 2014)⁵

S.No.	Age (Years)	Female	Male	Average
1	60-64	0.9	0.9	0.9
2	65-69	1.8	1.5	1.7
3	70-74	3.0	3.1	3.0
4	75-79	6.6	5.3	6.0
5	80-84	11.7	10.3	11.1
6	85-89	20.2	15.1	18.3
7	90-94	33.0	22.6	29.9
8	95+	44.2	28.8	14.1

7. In Swedish, they have registered the 78,346 patients of Dementia in SveDem (Swedish Dementia Registry) from 2007 to 2017 and in those patients, most common dementia types were Alzheimer Dementia (31%) and mixed Alzheimer Dementia (19%), followed by unspecified Dementia (23%), Vascular Dementia (19%), Lewy Body Dementia (2%), Frontotemporal Dementia (2%), Parkinson's with Dementia (2%) and other (2%)¹⁴.

4. Subtypes of Dementia:

Dementia can be divided into four categories (**Table 2**);

5. Factors involved in Dementia:

Mostly Less education^{15,16}, High blood pressure^{17,18}, obesity¹⁹, hearing loss²⁰, depression^{21,22}, diabetes²³, physical inactivity²⁴, smoking²⁵ and social isolation²⁶ are the major nine potential risk factors of dementia which are associated with 35% of Population Attributable Fraction (PAF)²⁰. Risk factors associated in early life (education), midlife (hypertension, obesity, hearing loss, TBI and alcohol misuse²⁷ and late life (smoking, depression, physical inactivity, social isolation, diabetes, and air pollution) can contribute to increased dementia risk²⁸⁻³⁰ (**Figure 2**).

5.1 Education and Midlife and Late-Life cognitive stimulation:

In today's scenario, the education is very important for the reduction of the Dementia risk and this will have life-long higher educational attainment^{20,24,31,32}. Because of the new abilities, it appears that cognitive ability grows with education, implying that cognitive stimulation is more important in early life. Much of the apparent later effect could be due to people with higher cognitive function seeking out cognitively stimulating activities and education³³. It is difficult to separate out the specific impact of education from the effect of overall cognitive ability^{33,34}, and the specific impact of later-life cognitive activity from lifelong cognitive function and activity^{34,35} (Figure 2).

5.2 Hypertension: It is a serious factor that is associated with increased risk of later-life dementia³⁶. In Framingham, offspring cohort study comprised about the 1440 people where the systolic blood pressure (≥ 140 mm Hg in midlife: mean age 55 yrs.) had connected with the symptom which increased the risk of dementia over an 18 year follow-up period³⁷. A cohort study focuses on the mechanisms by which they reported that midlife hypertension, defined as from age 40 yrs., was associated with decreased volumes and increased white matter hyper-intensity volume but not amyloid deposition³⁸. It noted that blood pressure declines in later-life and this decline is caused by the dementia development^{37,39,40} (Figure 2).

5.3 Diabetes: In 2017 commission, reported that diabetes is one of the risk factors for the dementia and to study the diabetes in the treated and non-treated patient is challenging in the observational studies. When the 14 cohort studies were performed on the 2-3 million people with type-2 diabetes, in a pooled meta-analysis it was observed that diabetes was highly risk factor for any type of dementia⁴¹. According To Sabia et al., 2019, People who are using the medicine metformin to treat dementia, which lowers the prevalence of cognitive impairment, were compared to those who were on another medication or no treatment, according to one meta-analysis of cohort studies of diabetes^{11,42}. Following the completion of the analysis, it has been determined that Type-2 diabetes is a clear risk factor for the development of dementia; however, it is uncertain if diabetic medication reduces this risk. Dementia risk is not reduced by strict diabetes control¹¹ (Figure 2).

5.4 Excessive Alcohol Consumption: Excessive drinking is always associated with the brain changes, cognitive impairment and dementia i.e., known for the centuries⁴³. Increased alcohol use in the body generates a complex association with cognition and dementia, according to thorough cohorts and large-scale record-based research. It will be difficult to comprehend alcohol because it is largely associated with cultural patterns and other socio-cultural and health-related aspects. During a 5-year longitudinal research in France, almost 31 million patients were admitted to hospitals, and it was discovered that patients who used alcohol increased their risk of dementia, and men and women ratios for these risks were determined separately⁴⁴ (Figure 2).

5.5 Smoking: Smokers have higher rate of risk of dementia than non-smokers²⁰, and at a higher risk of premature death before the age at which they might have developed dementia, introducing some bias and uncertainty in the association between smoking and risk of dementia^{45,46}. Stopping smoking at older will reduce the chances of risk of dementia in the people. Among 50,000 men stopping the

smoking at the age older than the 60 years for more than 4 years has subsequently reduced the risk for dementia⁴⁷. Globally, it was estimated that 35% non-smoking adults and 40% of children are exposed to second hand smoke⁴⁸; understandingly the literature of this exposure and dementia risk was scary. Even after controlling for the other confounding factors, one of the study showed that in women of age 55-64 years, second hand smoke exposure was associated with the memory deterioration and the risk increased with the exposure duration⁴⁹ (Figure 2).

5.6 Depression: Depression may be linked to a range of psychological or physiological factors that increase the risk of dementia. The development of a disease is indicated by early symptoms and stages of dementia, and depressive symptoms are a result of dementia onset. Few studies have shown that depression is a risk factor for dementia in the context of diabetes, and none have discriminated between treated and untreated depression. Depression was found to be a risk factor for dementia in a meta-analysis of 32 trials involving 62,598 participants and follow-up ranging from 2 to 17 years⁵⁰. When the period of follow-up was greater, meta-regression analysis revealed a non-significant trend for the link between depression and dementia to be weaker⁵¹. The Australian Longitudinal AD Neuroimaging Initiative studied 755 persons with mild cognitive impairment and a history of depression to see if selective serotonin reuptake inhibitors (SSRIs), such as citalopram, may reduce amyloid plaque development and formation in animal models⁵² (Figure 2).

5.7 Air-Pollutants: Pollutants in the air and particulate matter have been linked to poor health outcomes, including non-communicable diseases^{53,54}. It is the increased levels of dementia risk from air pollutants are still being the mixed effects of them and the impact on animal models are clearly evidences of physiological effects over and above those driven by life-course deprived high nitrogen dioxide (NO₂) concentration, fine ambient particulate matter (PM_{2.5}) from traffic exhaust⁵⁵⁻⁵⁷ and PM_{2.5} from residential wood burning are associate with increase in the cases of dementia. The traffic on the roads also produces NO₂ and PM_{2.5} and it is very hard to separate out the additive effects of different types of pollutants⁵⁵⁻⁵⁷. A systematic review of studies until 2018 including 13 longitudinal studies with 1-15 years follow-up of air pollutants exposure and dementia, found exposure to PM_{2.5}, NO₂ and carbon monoxide were all associated with increased dementia risk⁵⁸. There is lots of burden of dementia and excessive death because of the PM_{2.5} in 10-year US study was particularly high in black or African American individuals and socio-economically disadvantaged communities and related to particulate PM_{2.5} concentrations above the US guidelines⁵⁹ (Figure 2).

5.8 Sleep: Sleep is a factor to affect the dementia, mechanisms is unclear but sleep disturbance has been linked with β -amyloid deposition^{60,61}, reduced the activation of glymphatic clearance pathways⁶², low grade inflammation, increased tau, hypoxia^{60,63} and cardiovascular disease⁶⁴. Sleep disturbance is speculated to increase the inflammation by which it raises β -amyloid deposition, it leads to the AD and further it causes the sleep disturbance⁶⁵. The results of two meta-analyses were similar: the first was a synthesis of longitudinal studies with an average of 9.5 years of follow-up, while the second revealed mixed-quality cross-sectional and prospective cohort studies with various ways of assessing sleep. Sleep disturbances were defined broadly, including the short and long sleep duration, poor sleep quality,

obstructive sleep apnoea, insomnia and circadian rhythm abnormality. All these symptoms were associated with the higher risk of all types of dementia ⁶⁶, and clinically diagnosed AD compared with no sleep disturbances, at the baseline from their analysis, not all the cohort studies excluded those with cognitive impairment or dementia ⁶⁷ (Figure 2).

6 Symptoms:

The symptoms like cognitive decline, behavioral symptoms, functional decline, and cognitive testing remain used for the further clinical diagnosis and staging of patients with Alzheimer Disease (Figure 3).

6.1 Cognitive Decline: Memory impairment is the most prevalent feature of Alzheimer Disease and in non-memory cognitive decline such as executive dysfunction, apathy or personality changes, aphasia (a disorder that damage the part of the brain which produce and process language) is presently seen in many people, in general, memory decline is most popular symptom i.e., language disturbances, it is a symptom of Alzheimer disease which in the mild stages of dementia and progresses throughout other course of the disease. Executive dysfunction is also a major symptom that is shown during the pre-dementia stages and these were similar to all other cognitive domains, it become serious over the disease course (Figure 3).

6.2 Neuropsychiatric symptoms: Dementia patients exhibit a wide range of neuropsychiatric symptoms. Behavioral symptoms are serious over the course of the disease; however, because these are fluctuating symptoms, they are not present at every visit. Excess morbidity has a significant impact on caregiver burden and is the major cause of institutionalization, thus it's crucial to pay attention to these treatable components ⁶⁸. Apathy, anxiety, and irritability are the early neuropsychiatric symptoms of AD, and later, there are two symptoms that become hard for the patient and worsen the disease. Disturbances in appetite, sleep, disinhibition, and disturbances in perception (hallucination) or thought are all symptoms of depression in the later stages of dementia (delusions). There are also more neuropsychiatric symptoms such as anosognosia (loss of vision) and irrelevant conduct, which creates a challenging management dilemma (Figure 3).

6.3 Other illnesses in Dementia: Multimorphism is a challenge in dementia, not just because persons with dementia often have other conditions that increase their risk of developing disorders, but also because finding better treatments for dementia patients will be tough. People with dementia sometimes have problems that they don't understand, such as not knowing what to eat or drink, increased falling and infection rates, and they may forget to tell their doctor or family members about their symptoms. They may also struggle to understand the disease because they are unaware of the disease's symptoms ⁶⁹. Professionally, the healthcare system requires an education system that allows them to speak and understand persons with dementia more easily ⁷⁰. Compared to the previous history older population, people with dementia have increased chances for cerebrovascular disease ⁷¹⁻⁷⁴, stroke ⁷⁵, Parkinson's Disease ^{71,73}, diabetes ^{73,75}, skin ulcers, anxiety and depression ^{71,73}, pneumonia, incontinence and electrolyte imbalance ⁷³ (Figure 3).

7 Causes of dementia:

The death rate from dementia is rising every day, but there is little data for end-of-life care.

a) Nutritional Decline

b) Toxic Consumptions

c) Metabolic Causes

d) Vascular Causes

7.1 Nutritional Decline: Dementia can be caused by when patients develop a deficiency of vitamin levels or nutrients. While the thiamine deficiency (Vitamin B1 Deficiency) ⁷⁶ causes the disease known as Wernicke encephalopathy in the earliest phase and if it converts to the Chronic memory disorder then it is known as Korsakoff's Syndrome. Wernicke encephalopathy presents in the neurons deficient in thiamine which undergoes the necrosis. The Korsakoff's syndrome may become apparent after a week when the delirium of Wernicke Encephalopathy subsides with severe anterograde amnesia and less prominent retrograde amnesia ⁷⁷. The treatment for Wernicke encephalopathy is Thiamine through the intravenous route, which must be given before the glucose, as glycolysis itself consumes B1 ⁷⁸. In the study, they have the evidence that Vitamin D deficiency is associated with all types of dementia syndromes ⁷⁹⁻⁸¹.

7.2 Toxic Consumptions: The strong anti-cholinergic properties medications are involved in toxic consumptions like tricyclic anti-depressants, cyclobenzaprine and oxybutynin which cause the dementia. The exposure to the toxic compounds like organophosphate pesticides, pollutants, and heavy metals can cause dementia symptoms that often are non-progressive ⁸² but it also increases the chances for the neurodegenerative dementia for the long time ^{83,84}. Mercury, Manganese, Arsenic and Lead Poisoning having major role to cause the dementia syndrome ^{85,86}.

7.3 Metabolic Causes: Hypothyroidism can play a role as a primary phase which causes the dementia or cognitive deficits ^{87,88}. The symptoms of Hypothyroidism include Apathy, depression, memory and attention problems. The Auto-immune thyroiditis can present with psychomotor slowing, psychosis and lethargy (feeling very tired) ⁸⁹. Metabolic disorders which causes the cognitive impairment such as Chronic Uremia (complications of chronic kidney disease and acute kidney injury), Hepatic Disease of various etiologies, hypercortisolism/Cushing Syndrome (clinical state in which excessive tissue exposure to the cortisol), parathyroid disorders (abnormal levels of calcium in the body) and chronic hemodialysis ("Dialysis Dementia") ⁹⁰⁻⁹².

7.4 Vascular Causes: Vascular Dementia is a vascular cognitive deficiency that causes a decline in daily body functions. Stroke or multiple strokes, Small-vessel Ischemic Disease, also known as Binswanger disease (changes in the small blood vessels in the brain), and rare hereditary diseases such as Cerebral Autosomal Dominant Anterioropathy with Subcortical Infarcts and Cerebral Amyloid Angiopathy are just a few of the causes (protein called amyloid build up the wall of the arteries in the brain) ⁹³. Vascular risk factors include diabetes ⁹⁴, hypertension ^{94,95}, hypercholesterolemia ⁹³ and smoking ⁹⁶ are the major risk factors which causes the cognitive deficits.



Figure 2: Factors involved in dementia



Figure 3: Symptoms of Dementia

8. Diagnosis:

The diagnostic standard for dementia is the Diagnostic and Standard Manual of Mental Disorders, Fifth Edition (DSM-5) ⁹⁷.

8.1 History Examination or Evaluation: There are so many risky factors in which the history focuses on that include the medical conditions, medication complications, existing brain disorder which leads to the another disorders those are linked to it and it includes risky factors (as mentioned in the factors involved in the dementia), vascular disease risk factors (like hypertension, diabetes ^{98,99}) brain disorder (Parkinson's disease, stroke, trauma etc.) and other medication complications like anxiolytics (benzodiazepines) ¹¹, anticholinergics (tricyclic antidepressant, anti-muscarinic) ¹¹, analgesics (codeine containing agents) which causes the cognitive impairment (like sleep aids ¹⁰⁰) ^{11,76,101,102}.

8.2 Impair cognition examination: This examination requires the identification of the cognitive impairment which includes the factors like anxiety, sleeping problems etc. There are some tools that used to detect the disease is the Montreal Cognitive Assessment (MoCA)^{5,103}, Mini-Mental State Exam (MMSE) ¹⁰⁴, Abbreviated Mental Test Score (AMTS), Clock Drawing Test (CDT), Memory Impairment Screen (MIS) & General Practitioner Assessment of Cognition (GPCOG) ¹⁰⁵⁻¹⁰⁸ (**Figure 4**).

8.3 Neurological Examination: Neurologic examination examines objective evidence of neurocognitive disorders such as aphasia, apraxia, and agnosia. Common tests include physical examinations for diagnosing vascular disease and systemic symptoms ¹⁰⁹ that may be associated with abnormal cause's dementia (e.g., Wilson's gold eye color [Kayser-Fleischer rings] disease). Neuroimaging to diagnose cortical and hippocampal atrophy (as seen in AD), or neuropathology that combines possible treatable causes of dementia (e.g., dislocated tumor, or normal pressure of hydrocephalus (which can be blocked) ¹¹⁰, using brain thinking as well MRI or CT scan ¹¹¹⁻¹¹⁸.

8.4 Cerebrospinal Fluid testing and Genetic testing: Cerebrospinal fluid (CSF) tests can be performed to find evidence of AD (low amyloid and high levels of tau), another neurodegenerative disease (e.g., high protein 14-3-3 Creutzfeldt-Jakob disease or other causes) ¹¹⁹⁻¹²³. Genetic examination is generally common in the younger patients because this process is generally connected with the families or relatives who have the history of dementia and this examination always shows the rare autosomal dominant forms of dementia in which giving the families a warrant genetic counseling to know more about the disorder in which they need to be examined ^{124,125}.

Tools For Impair Cognition Examination

SERIAL NO.	TOOLS	SENSITIVITY	SPECIFICITY	TIME ADMINISTER	AREAS OF ASSESSMENT
1	Mini-Mental State Examination (MMSE)	0.87	0.82	5-10 min.	Orientation, registration, recall, attention & language
2	Abbreviated Mental Test Score (AMTS)	0.81/0.91	0.85/0.75	5 min.	Orientation, registration, memory, general knowledge
3	Montreal Cognitive Assessment (MoCA)	1	0.87	10-15 min.	Memory, attention & concentration, executive functions, language, visuoconstructioal skills, conceptual thinking, orientation & calculations
4	Clock Drawing Test (CDT)	0.86	0.96	3 min.	clock drawing
5	General Practitioner Assessment of Cognition (GPCOG)	0.82	0.83	6 min.	Recall, Time orientation, clock drawing, information
6	Memory Impairment Screen (MIS)	0.86	0.91	5 min.	Recall

Figure 4: Tools for Impair Cognition Examination: (1) MMSE^{104,126}, (2) AMTS^{127,128}, (3) MoCA^{104,129}, (4) CDT¹³⁰, (5) GPCOG¹³⁰, (6) MIS¹³¹

9. Prevention And Care

To treat this type of disorders we need to be careful about their activities and there are some preventive methods in which a patient can be cured and that are:

9.1 Cognitive Training in people with Dementia: A Cochrane found in the 33 trials of cognitive training, around 2000 participants' mild to moderate dementia and sometimes it is more severe at the risk of bias¹³². The people with in trials are compared with the treated patient to know the cognition changes in the body whether they improved or not. The cognitive abilities includes the fluency and improvement in the body and these changes will not show the direct evidence to suggest that cognitive training was better than cognitive stimulation therapy.

9.2 Exercise and Physical activity: Dementia and Physical Activity RCT¹³³, rated moderate to high aerobic intensity and strength training did not delay mental retardation in humans and moderate to severe dementia firmness. US Reduces Disability in Psychological Study¹³⁴, we have implemented multicomponent interventions at home which includes exercise education, training to increase fun events, and how to solve activator-behavior-sequence problem in 6 weeks by case managers. There are 255 people living in the community with adult dementia for more than 60 years with their family caregiver and able follow 140 (54 · 9%). The research found increased physical activity; days of taking 30 minutes or more exercise before and again after comparing the intervention.

9.3 Hospitalization: Hospitalization for people with dementia is associated with adverse, unintended consequences, including stress, declining performance and understanding, and high economic costs¹³⁵⁻¹³⁷. People with dementia feeling long and regular intake again repatriation; the cost of health care for four people moderate dementia is almost double that people without dementia¹³⁸⁻¹⁴⁰. Early detection of physical illness in people with dementia, especially pain, falls, diabetes, incontinence, and sensory impairment, are significant¹⁴¹⁻¹⁴³.

9.4 Prevent Abuse, reduce in dementia: Abuse may go unnoticed if families or professional staff feel that there is no better management options are therefore not properly recognized and reported¹⁴⁴. The good evidence is sure to make the interventions which increase the knowledge about the abuse behavior which help to maintain and detect the disorder and reporting the abusive behavior is an major step to stop it^{145,146}. Management of the most serious cases of abuse, which includes financial abuse, physical violence, and occasional murder, involves criminal justice systems. In California, medical professionals had a crime was indicted and sentenced under anti-adult abuse laws for the illegal chemical prevention of patients.

9.5 Family Support: For dementia patients, the families have difficulties to handle them because when the dementia progressively increases the mental illness also increases that made difficult for them to take complex decisions in the daily life, so, at that time families are major support for them to take the decisions. A person with mild dementia, decisions about daily life, social care, and treatment can usually be done by a person with dementia, usually with family support. As dementia progresses, the person with it dementia loses the ability to do more complex decisions and the caregiver becomes a substitute decision maker,

changing partner relationships and reversing the role of parents and children¹⁴⁷⁻¹⁴⁹.

9.6 Prevent Post-Stroke dementia: Stroke and dementia are related to each other which increase the risk and stroke increases the chances of dementia in which principally 90% stroke and 35% of dementia have been estimated to be preventable. According to the study, strokes doubles the chances of developing dementia and stroke is more common disease than the dementia. Previously psychological testing (<7 days) by the Montreal Cognitive Assessment predicts longevity cognitive outcome, functional outcome, and death after stroke and should be the case part of the treatment method¹⁵⁰.

10 Curative approaches for dementia:

Both non-pharmacologic and pharmacologic methods are used to treat the dementia patients as explained below¹:

10.1 Non-Pharmacological Management/ Treatment: It is a management which uses the socially interaction with the patients to help them to build the confidence and supervise the situations. As mentioned in the **Table 3**;

10.2 Pharmacological Evaluation: Types of treatment are used as mentioned below (**Table 4**);

10.2.1 Acetylcholine-Estrase Inhibitors : Treatment with ACE inhibitors used to manage the mild-to-moderate dementia in the patients and these are classified into three drugs which recognized by the FDA and marketed in US i.e., Galantamine, Rivastigamine ,Donepezil^{55,63,151-158} (**Table 4**). The drug **Memantine** is also used as approved by the FDA^{9,76,156,159,160} (**Table 4**). **Medications for Behavioral Changes:** Symptoms of depression are treated with **serotonin reuptake inhibitors (SSRIs)** selected due to low propensity to create anticholinergics effects. **New "Atypical" antipsychotic drugs (Quetiapine, risperidone, olanzapine)** they are often used in low doses. Normal and atypical antipsychotic agents, however, carry a Black box warning label for associated with an increase in cardiovascular disease and death and cerebrovascular adverse events in the elderly with psychosis related to dementia¹⁵³⁻¹⁵⁵.

10.2.2 Future Management for Dementia: The majority of current therapeutic trials are focusing on therapies that directly influence the pathologic cascade pathway in Alzheimer's disease. Because of the development of neuroinflammation in a subset of lessons, one that works immunization testing in people was disturbed. There was something extraordinary about the elimination of amyloid from the cortex in many of the study's deceased participants, implying that amyloid deposits can be eliminated. Active vaccinations (i.e., injections) and diseases caused by the development of "β- amyloid and tau and polymerization" are the focus of current research^{161,162}.

Table 3: NON-PHARMACOLOGICAL TREATMENT

Name	Therapy and Uses
Psychological Therapy	Psychological training and activities such as learning and playing games that involve the mind (e.g., chess, bridge) can help maintain comprehension and performance, as shown in random tests ^{163,164}
Relaxation therapy	Frustration and stress resulting from challenging activities should be avoided. Music or art therapy, and more methods of experience, can help maintain understanding or improve the quality of life ¹⁶⁵ .
Social	Because old childhood memories are kept for a long time, reminiscent, inclusive treatments psychotherapy uses personal history of news and early human life events, may improve mental well-being ¹⁶⁶ .
Exercise	Exercise, both aerobic (e.g., walking, swimming) and non-aerobic / conditioning (e.g., weights), improves cardiovascular health with the benefits of blood pressure and stroke risk, as well as randomized trials suggest that these interventions may have a positive psychological impact as well physical activity. However, not all randomized trials have shown the benefits of exercise cognition ^{167,168}
Biological clock	Security, including the patient's mental, physical and financial well-being, should be monitored by a caregiver, with regard to home safety, such as the risk of kitchen fires that may be associated with it burns of the patient. Behavioral problems, such as physical abuse, are a major cause of the emergency room visits and facility facilities, and are associated with adverse patient outcomes (e.g., psychological and medical complications) and families). The intervention of a caregiver may to prevent the admission of patients to facilities. For example, a family can learn to recognize fear, frustration, and anger (e.g., screaming, screaming), and dealing with symptoms of anger (e.g., re-directing patients' attention to something they enjoy), which may prevent negative ones results ¹⁶⁹ .
Diet	A random the clinical trial found that combined diet, exercise, mental training, and vascular risk intervention interventions improve understanding in people at risk for dementia ¹⁷⁰
Socio-Economic activity	Outdoor safety home includes work, where the caregiver may facilitate the patient to reduce or to suspend work, for example when handling equipment or making decisions about a company finances. Also, driving may need to be adjusted, which includes driving restrictions neighborhood and daytime driving to avoid getting lost. Although no single test is associated for better driving safety, driving ability should be re-tested periodically and discontinued recommended based on the severity of dementia, accident prevention and injury ¹⁷¹ .

Table 4: Pharmacological treatment for Dementia

	Acetylcholine-Esterase Inhibitors			Glutamate Receptor Modulators	Combination Drugs
	Galantamine	Rivastigmine	Donepezil	Memantine	Memantine and Donepezil
Stage Modification	Mild-to-Moderate	Mild-to-Moderate	All types of Dementia	Moderate-to-Severe	Moderate-to-Severe
Brand Name	Razadyne, Reminyl	Exelon, Exelon Patch	Aricept, Aricept RDT	Namenda, Namenda XR	Namzaric
Dosage Modifications	<p>Extended Release Capsule:</p> <p>Starting dose: 8mg once daily for 4 weeks;</p> <p>If tolerated it will be increase to 16mg once daily for ≥4 weeks; if immediately needed, dose increase to the 24mg once daily.</p> <p>Immediate Release Tablets or Oral Solution:</p> <p>Starting Dose: 4mg twice daily for 4 weeks;</p> <p>If tolerated it will be increased to 8mg twice daily for ≥4 weeks; if immediately needed, dose increased to 12mg twice daily.</p>	<p>Capsule:</p> <p>Starting dose: 1.5mgdaily twice for 2 weeks;</p> <p>If tolerated it will be increased to 3mg twice daily for 2 weeks; then 4.5mg twice daily for 2 weeks; then 6mg twice daily for a 2 weeks.</p> <p>Transdermal Patch:</p> <p>Starting Dose: 4.6mg/24 hours patch once daily for a 4 weeks;</p> <p>If tolerated it will be increased to 9.5mg/24hours for ≥4 weeks;</p> <p>If immediately needed, dose increased to 13.3mg/24hours.</p>	<p>Tablet or Oral disintegrating tablets:</p> <p>Starting Dose: 5mg once daily for 6 weeks;</p> <p>If tolerated it will be increase to 10mg; if immediately needed, dose increase to the23mg once daily.</p>	<p>Extended Release Capsule:</p> <p>Starting dose: 7mg once daily for 1 week;</p> <p>If tolerated it will be increase to 14mg once daily, then 21mg once daily, then 28mg once daily for 1 week as recommended interval.</p> <p>Immediate Release Tablet or Oral Solution: Starting dose : 5mg once daily for 1 week;</p> <p>If tolerated it will increase to 5mg twice daily for 1 week; then 5mg in am and 10mg in pm; then 10mg twice daily for a 1 week as recommended interval.</p>	<p>Capsule:</p> <p>Target dose: 28mg Memantine extended-release with 10mg Donepezil once daily in the evening.</p> <p>In severe renal impairment:</p> <p>Maximum dose: 14mg Memantine extended-release with 10mg Donepezil once daily.</p>

Maximum Dose	Oral capsules ER: 8mg, 16mg, 24mg Oral Tablets: 4mg, 8mg, 12mg Oral Solution: 4mg/1mL	Topical Film ER and Transdermal Film ER: 4.6mg, 9.5mg, 13.3mg/24hours Patch Oral Capsules: 1.5mg, 3mg, 4.5mg, 6mg	23 mg as available on brand-name tablet only	Oral Solution: 5mL, 10mg Oral Tablets: 5mg, 10mg Oral Capsules ER: 7mg, 14mg, 21mg, 24mg	Oral Capsule ER: 7-10mg, 14-10mg, 21-10mg, 28-10mg
Pharmacokinetics	CYP450 does not involved but metabolized by CYP3A4 and CYP2D6	CYP 450 minimally involved in the Rivastigmine metabolism	Metabolized by the CYP3A4 and CYP2D6	CYP 450 does not play any significant role in the metabolism of the drug	See the left side boxes of Donepezil and Memantine
Contraindications/Precautions	C/I in Hepatic disease, Renal failure, Renal impairment, Peptic Ulcer disease, COPD, Cardiac arrhythmias, seizure disorder, Parkinson's Disease, Pregnancy, Children, Infants	C/I in Carbamate hypersensitivity, Abrupt discontinuation, peptic ulcer disease, GI disease, Diarrhea, Hepatic disease, Renal impairment, renal failure, Asthma, COPD, Bradycardia, cardiac arrhythmias, Hypotension, Bladder obstruction, head trauma, Seizure disorder, Pregnancy, tobacco smoking, Children, Infants	C/I in Abrupt discontinuation, Apheresis, AV block, Celiac disease, Fever, Heart Failure, Human Immunodeficiency Virus (HIV) infection, Hyperparathyroidism, Hypocalcemia, Hypokalemia, Hypomagnesemia, Hypotension, Hypothermia, Hypothyroidism, long QT syndrome, Myocardial Infarction, Pheochromocytoma, QT prolongation, Rheumatoid arthritis, sick sinus syndrome, Sickle Cell disease, Sleep deprivation, Stroke, Systemic Lupus Erythematosus (SLE), peptic ulcer disease, Asthma, GI disease, Hepatic disease, COPD, Pulmonary disease, Seizure disorder, Pregnancy, Children, Infants	C/I in Hypersensitive people, Renal failure, Renal impairment, Renal Tubular Acidosis (RTA), Urinary Tract Infections (UTI), Hepatic disease, Geriatric, Pregnancy, Children, Infants	Contraindications of Donepezil and Memantine can be considered
Advantages	Used for the symptomatic treatment of mild-to-moderate Alzheimer's Disease; may provide cognition benefit in mixed vascular dementia and Alzheimer's Disease.	Oral and Transdermal Formulations are used for the mild-to-moderate dementia due to AD or Parkinson's Disease; Transdermal Patch used in severe AD and Dementia with Lewy Bodies	Among the drugs listed, this be available too long, and a doctor acquaintance, still widely used; available as normal drug and covered by many lives insurance plans.	Used to treat the moderate-to-severe AD both as monotherapy and in combination with Donepezil	Used to treat the moderate-to-severe, in combination with Donepezil or Memantine separately for the better results
References	9,76	9,76	9,76	9,76	9,156

11 Dementia and COVID-19:

During COVID-19 pandemic, the mentally ill people have suffered a lot because of their needs, works, having problems with lifestyles etc. Suffering and death are related disease (COVID-19) is exacerbated by an increase of ¹⁷² years with pre-existing conditions such as hypertension as well diabetes, ¹⁷³ so many people with dementia are present some accident. People with dementia may find it difficult to stick to it measures to reduce transmission of the virus, as possible not understanding or remembering the changes needed to behavior, such as physical isolation and hygiene, leading to an increased risk to them and their caregivers ¹⁷⁴. Thus, people with dementia are at greater risk in COVID-19 because of their age, high flexibility, and difficulty in maintaining physical

distance ^{172,173,175}. A social guide to dementia the COVID-19 epidemic highlighted important things and actions and was given guidance and resources among the six stages of dementia: Good prevention, good diagnosis, good management, good support, Good Life and Good Death. The English Department of Health and Community Disruption Care Program Board (DHSC) next released a review of research on dementia during COVID-19 epidemic (full data available on article and the source is ¹⁷⁶.

12 Conclusion:

Dementia defined as an acquired syndrome that leads to the loss of two or more cognitive abilities caused by brain disease or injury. Mainly the cause of dementia can be detected by various methods those are history examination, physical

examination, laboratory testing and brain imaging (MRI). Dementia can be treated by the pharmacological and non-pharmacological methods in which their efficacy of treatment remains limited. But during COVID-19 pandemic, the people mostly have faced this problem in which the treatment lacks at some time so in future, its need to promote and generate more therapies to treat the dementia that helps the people to manage their mental illness.

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