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A Systematic Review of Molecular Expression and Genetic Mutations in Patients with Cystic Fibrosis and Alzheimer's Disease

Farzaneh Ahmadi Mirghaed[1], Tina Nabatchi Ahmadi[2], Sannar Sattar Albuzyad[3], Amir Alinejad Khorram[4], Farzad Mahshad[5*]

[1.]Bachelor Student of Cellular and Molecular Biology, Flowerjan Azad University, Flowerjan, Esfahan

[2.]Graduate of General Medicine, Guilan University of Medical Sciences, Guilan, Iran

[3.]MBBS, Radiologist, Tehran University of Medical Sciences, Tehran, Iran

[4.]Urology Department, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[5.]Department of Internal Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Abstract

2019's progress in the development of highly effective modulating therapy has provided unprecedented clinical benefit to more than 90% of cystic fibrosis patients who are genetically eligible for treatment, leading to the identification of the disease-causing CFTR gene and our subsequent understanding of its mechanisms. The main disease in the pathogenesis of cystic fibrosis. In Alzheimer's disease, when the proteins inside the brain do not function properly, they cause disruption in the nerve cells of the brain. These disturbed cells secrete a toxic substance that damages the neurons and prevents the communication between the nerve cells of the brain. The present study was investigated by reviewing more than 79 articles with keywords including: "Molecular expression and genetic mutations", "Cystic fibrosis" and "Alzheimer". The results indicate that along with the progress of Alzheimer's disease, brain cells are disabled and communication between cells is lost. At this time, the cognitive symptoms of the disease begin to worsen. These drugs affect certain chemicals that exchange nerve messages between brain cells. In the case of cystic fibrosis, genetic defects cause dysfunction of a type of regulated chloride channel called CFTR. Dysfunction of this channel causes concentration and adhesion of lung, pancreas, liver, intestine, salivary glands and reproductive system secretions in these patients. Another complication of this disease is the increase in the amount of sodium and chlorine in the body, which causes more sweating. Because one of the main methods of early diagnosis of CF is to evaluate the amount of sweating.

Key words: Cystic Fibrosis, Alzheimer's, Cognitive Symptoms, CFTR, Brain Cells

Introduction

Cystic fibrosis (CF) is a rare and serious disorder that causes severe damage to the respiratory and digestive systems [1-3]. This injury is often caused by the accumulation of thick and sticky mucus in organs with mucous surfaces [4-6]. According to the Cystic Fibrosis Foundation, more than 30,000 people in the United States have cystic fibrosis, and 1,000 more are diagnosed each year. CF is a progressive disease, so it gets worse over time. Regular, daily care can help manage CF [7-9]. But to date, no treatment plan has been established that works for everyone. With a specific treatment plan for each patient, a person can live a full life [10], go to school and work [11]. In order to get CF disease [12], it is enough to transfer one disease gene from the mother and another gene from the father to the patient during the fetal period [13-15].

Disruption of this gene causes disruption and blocking of chlorine channels [16], which are located on the surface of the cells covering the respiratory and digestive tracts [17-19]. The function of these channels is to transfer chlorine and sodium (salt) from inside the lung cells to the secretions in the airways [20]. Following the addition of salt to the secretions, water is also added to these secretions and leads to softening of the secretions [21]. This issue causes the easy discharge of secretions from the lungs of healthy people. While in these patients due to the disorder and blocking of chlorine channels, the pulmonary secretions are very thick [22], sticky and cannot be discharged, which leads to the destruction of the lungs. This problem has also happened in all the channels of the body such as the intestines [23], pancreas and tubes that transport sperm and causes their destruction, that is why CF is a multi-organ disease [24]. The most and most important destruction occurs in the lung, so that finally the complete destruction of the lung has occurred and leads to respiratory failure and death of these patients [25]. Complete lung destruction occurs in developed countries above the age of fifty and in Iran around the age of eight to ten years. The present study was investigated by reviewing more than 79 articles with keywords including: "Molecular expression and genetic mutations", "Cystic fibrosis" and "Alzheimer". The results indicate that along with the progress of Alzheimer's disease, brain cells are disabled and communication between cells is lost [26].

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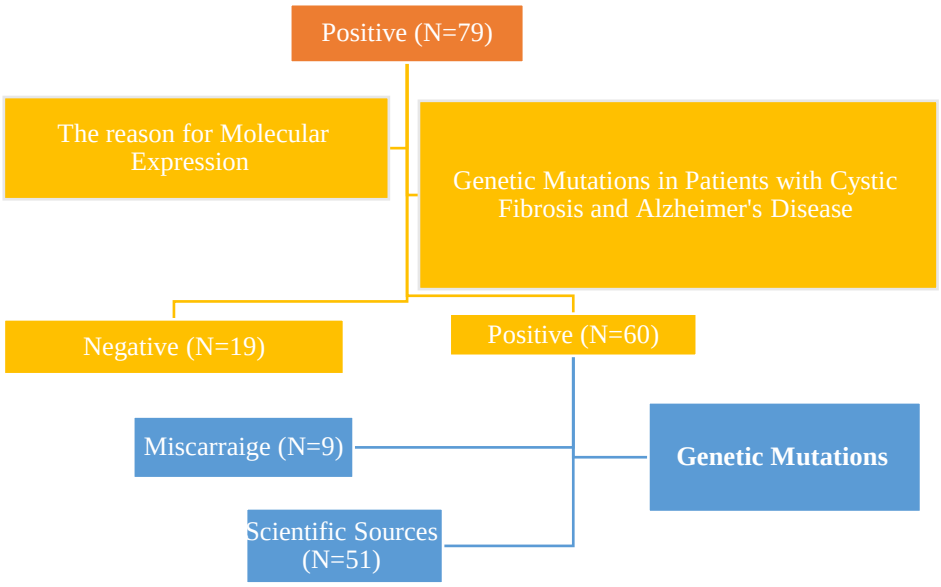

Figure 1. Flow chart of included subjects

Symptoms

CF disease may manifest as intestinal obstruction from the first day of birth [27]. The most common symptom of this disease is chronic phlegm cough that starts from infancy. Weight loss and greasy stools are other symptoms of this disease [28]. These patients sweat a lot, and salt particles are observed on the skin of these patients, and the child is salty when kissing. In simpler words, these patients have a kiss of passion [29]. Also, salt stains appear on the clothes of these patients. Comparison of lung tissue in healthy patients and patients with CF [30]. Lung tissue in a normal person. Lung tissue in a CF patient (full of pus) be hospitalized [31]. Bronchiectasis and dilation of airways in these patients starts from the very beginning of life and if not properly treated, it takes a very progressive course and eventually causes the death of these patients [32].

Epidemiology and prevalence of this disease in Iran

Until several years ago, it was believed among pediatric specialists and sub-specialists that this disease is common in America and European countries [33], and the number of these patients in Iran is so small that their discussion [34], investigation and follow-up are irrelevant. For this reason, this disease has remained far from the eyes of officials and experts in Iran [35], which unfortunately has led to a sharp reduction in the life expectancy of these patients compared to other countries [36]. There are no exact statistics of this disease in Iran, and the incidence and prevalence of this disease in Iran is not exactly known, but considering the high prevalence of consanguineous marriages in Iran (six to 10 times that of Europe and America) [37], it is estimated that the prevalence of this disease in Iran is not only less than other countries, but it may even be more. Currently [38], it is estimated that around six to seven thousand people in the country suffer from this disease. It is possible that due to the ignorance of parents and doctors, a large number of affected patients are still unknown [39]. In the study of Dr. Modaresi and his colleagues in 2012 at the Children's Medical Center, which was conducted on 500 suspected CF patients, about 85 of them (17.5%) were diagnosed with CF [40]. In simpler words, only in the laboratory of the children's medical center among the patients suspected of CF for whom sweat test is performed. The most common organs involved are: Lungs, pancreas, liver, intestines [41].

Breathing problems: The thick, sticky mucus associated with CF often blocks the airways in and out of the lungs. This condition can cause the following symptoms: Wheezing [42], persistent cough with thick mucus and phlegm [43], shortness of breath, especially during exercise, frequent lung infections, nasal congestion, sinus congestion, and sinusitis [44].

Digestive problems: Abnormal mucus can also block the channels that carry enzymes produced by the pancreas to the small intestine [45]. Without these digestive enzymes, the intestine cannot absorb the necessary nutrients from food. This can lead to symptoms including: Greasy and foul-smelling stools [46], constipation, nausea [47], distended abdomen, loss of appetite [48], poor weight gains in childhood, delayed growth in childhood [49].

What causes cystic fibrosis? CF occurs as a result of a defect in what is called the "Cystic fibrosis transmembrane conductance regulator" or CFTR gene. This gene controls the movement of water and salt into and out of body cells [50]. A mutation or sudden change in the CFTR gene causes the mucus to become thicker and stickier than normal. This abnormal mucus increases the amount of salt in the sweat and accumulates in various organs of the body, including the intestines, pancreas, liver, lungs [51].

Inheritance with an autosomal recessive pattern: Various defects can affect the CFTR gene. The type of genetic defect is related to the severity of CF. The damaged gene is inherited from parents to children with an autosomal recessive pattern. Although the person carrying the recessive gene is not sick, if he wants to reproduce, he must take necessary genetic care to prevent the disease in the child [52].

How is cystic fibrosis diagnosed? A diagnosis of CF requires clinical symptoms consistent with CF in at least one system and evidence of CFTR dysfunction. This evidence is usually based on abnormal results of the sweat chloride test or the presence of a mutation in the CFTR gene. Clinical signs are not necessary for infants identified through newborn screening [53]. Other diagnostic tests that may be performed include:

Immunoreactive trypsinogen test (IRT): The IRT test is a standard newborn screening test that checks the blood for abnormal levels of a protein called IRT. A high level of IRT may be a sign of CF. However, more tests are needed to confirm the diagnosis [54].

Sweat chloride test: The sweat chloride test is the most common test used to diagnose CF. This test checks the increase of salt level in sweat. This test is performed using a chemical that causes the skin to sweat due to a weak electrical current. Sweat is collected on a pad or paper and then analyzed. CF is diagnosed if the sweat contains higher than normal amounts of salt [55].

Sputum test: Evaluation of the sputum sample is done to check the possibility of pneumonia. Also, the results of sputum sample analysis can be used to determine the effective antibiotic on the infection [56].

X-ray chest X-ray: It is done to check for blockages and various lesions in the airways.

CT scan: CT scan provides detailed images of the body. These images allow the examination of internal structures such as the liver and pancreas. As a result, they facilitate the assessment of the amount of damage to the organs caused by cystic fibrosis [57].

Pulmonary function tests: These tests evaluate the function of the lungs. Disorders detected in these tests can indicate a decrease in lung function due to duct obstruction and reduced respiratory capacity. In addition to cystic fibrosis, these cases may also be caused by other diseases. Therefore, these tests cannot confirm the diagnosis [58].

Medicines needed in the treatment of the disease

Antibiotics: In these patients, infection, especially pneumonia, is seen more than the general population. Also, pneumonia in these patients is more likely to be associated with serious complications [59].

Mucus thinning drugs: These drugs thin the mucus and reduce its stickiness. By stimulating cough, these agents facilitate lung emptying and greatly improve the patient's breathing [60].

Nonsteroidal anti-inflammatory drugs (NSAIDs): These drugs have a limited role as an agent to reduce airway inflammation. The Cystic Fibrosis Foundation recommends the use of high-dose ibuprofen in children 6 to 17 years old with CF who have good lung function. Ibuprofen is not recommended for people with severe lung function abnormalities or people over 18 years old [61].

Bronchodilators: These drugs relax the muscles around the airways. This helps increase airflow. Most of these drugs are used with the help of a nebulizer. CFTR modulators are a class of drugs that can improve the function

of the defective CFTR gene. These drugs represent an important advance in the management of CF [61]. Because they target the function of the mutated CFTR gene. All CF patients should undergo CFTR gene testing to determine if they carry one of the mutations approved for CFTR-modulating drugs [62]. Most of the available data about this drug category are in patients less than 12 years old and in patients with mild or moderate CF lung disease [63].

How can cystic fibrosis be prevented? CF cannot be prevented. However, genetic testing should be done for couples who have CF or have relatives with the disease [64]. Genetic testing can determine a child's risk of developing CF by testing blood or saliva samples from each parent.

What is the long-term outlook for people with cystic fibrosis? The outlook for people with CF has improved dramatically in recent years. This is mainly due to advances in treatment. However, there is no cure for CF [65]. Therefore, lung function decreases steadily over time. The resulting damage to the lungs can cause severe breathing problems and other complications.

Can cystic fibrosis disease be identified during the fetal period with a genetic test? By performing a genetic test during the fetal period, it is possible to determine the presence of the CF gene mutation in the fetus [66]. If both parents are affected by this disorder, genetic testing is performed by placental villus sampling (CVS) at 10 to 14 weeks of pregnancy or amniotic fluid sampling at 16 to 20 weeks of pregnancy. The purpose of this genetic test is to determine whether the fetus has inherited both versions of the cystic fibrosis gene mutation [67].

What is the sweat test to diagnose this disease? The sweat test is a standard method for diagnosing cystic fibrosis that measures the amount of salt in a person's sweat. The amount of sodium and chloride in the sweat of people with cystic fibrosis is higher [68]. If other symptoms are observed in the person, the sweat test helps the doctor to be certain about the diagnosis of this disease [69].

Feeling salty when kissing a baby is a sign of cystic fibrosis? Feeling salty while kissing a baby is one of the symptoms of cystic fibrosis. Parents are usually the first to notice the symptoms of cystic fibrosis in a baby [70]. The feeling of saltiness while kissing the baby is due to changes in the salt regulating glands in the body. For this reason, the amount of salt in the baby's sweat increases and the baby's skin tastes salty [71].

When should testing for cystic fibrosis (CF) gene mutations be done?

- When screening newborns for cystic fibrosis (CF) [72];
- When an older child or adult has signs and symptoms of cystic fibrosis (CF) or has a positive CF screening test [73[;
- When a person wants to know their carrier status, such as a woman who is pregnant or planning to become pregnant for the first time [74].

Why is testing for cystic fibrosis (CF) gene mutations requested?

- To detect cystic fibrosis (CF) gene mutations [75];
- To screen for or help diagnose CF [76];
- To determine if you are a carrier of the CF genetic mutation;
- To assess the risk of having a baby with CF [77];
- Identification of patients who may respond to CFTR booster therapy [78].

Molecular expression and genetic mutations of Alzheimer's and how to treat it

Alzheimer's in English is a progressive neurological disorder that causes brain cells to die over time and causes problems in the patient's memory, thinking and behavior. Also, this disease is the most common cause of dementia. This disease is progressive, and that is why the symptoms of this disease worsen slowly and over time [79]. The symptoms of Alzheimer's in the initial stages are moderate forgetfulness and in the final stages, it makes the patient unable to communicate with his surroundings and do the things of life. After the diagnosis of Alzheimer's disease [80], the average patient will survive for 4 to 8 years [80], but with the correct treatment and other factors, the patient can survive up to 20 years after the diagnosis of the disease. The main cause of Alzheimer's disease is still not completely discovered, but when the proteins in the brain do not function properly, they cause disruption in the nerve cells of the brain [81]. These disturbed cells secrete a toxic substance that damages the neurons and prevents the communication between the nerve cells of the brain. This damage usually occurs in the memory part of the brain and occurs years before the first symptoms of Alzheimer's appear [82].

Prevalence and prognosis of Alzheimer's disease

Dementia is a condition in which the patient is unable to do daily activities, and Alzheimer's is one of the biggest causes of this condition. About 60 to 80 percent of patients have Alzheimer's dementia. Alzheimer's manifests itself mostly at the age of over 65, but this disease has also been seen in young people between 30 and 60 years old [83], and it is called early-onset Alzheimer's, and it includes about 5% of Alzheimer's patients. In 2013, 6.8 million patients with dementia were registered in the United States (about 2% of the population), of which 5 million were Alzheimer's patients. The number of people with dementia is expected to double by 2050.

At what age does Alzheimer's start?

At what age does Alzheimer's occur? Alzheimer's is one of the diseases that most often occurs in old age and its symptoms are seen in old age. But there are also cases in which men and women show Alzheimer's symptoms at a younger age. For example, people who show Alzheimer's symptoms are usually over 60 years old. In fact, symptoms start to appear from 60 years and above. But there are also cases where people have shown Alzheimer's symptoms at the age of 30 or 40. This is early stage Alzheimer's. The early signs and symptoms of Alzheimer's disease vary from person to person and can have a variety of onsets [84].

What are the signs and symptoms of Alzheimer's?

The most common symptom of Alzheimer's is difficulty remembering new information. Like the body, the brain changes over time, and problems remembering and thinking are part of this aging brain. But serious memory problems, confusion, and mental and behavioral changes can be early signs of Alzheimer's disease and forgetfulness.

Table 1. Characteristics and symptoms of Alzheimer's disease [85]

Symptoms of Alzheimer's disease	Their specifications
Decreased ability to recall new information	Repeated questions or conversations, forgetting appointments or dates, getting lost on a familiar path
Impaired reasoning, performing complex tasks, and judgment	Lack of proper understanding of risks, inability to handle financial affairs, wrong decisions in simple matters
Spatial and visual recognition disorders	Inability to recognize faces and ordinary objects and inability to find things in sight, inability to use simple tools and ordinary tasks such as dressing properly
Speech, reading and writing problems	Inability to remember simple words when speaking Frequent mistakes in speaking, reading and writing
Mood and behavioral changes	Loss of empathy, abnormal mood changes such as agitation, lethargy, and lack of interest in relationships and emotional behaviors, obsessions, or socially unacceptable behaviors.

Early signs and onset of Alzheimer's

Alzheimer's symptoms and early problems of this disease can include the following:

Forgetting recent conversations or events; Placing things in the wrong place, forgetting the names of places and things, difficulty in thinking of the right word to speak, asking repetitive questions, forgetting the names of places and things are some of the early symptoms of mental illness.

Mild Alzheimer's symptoms

Signs and symptoms of mild dementia include the following:

- Memory loss that interferes with daily life;
- Poor judgment leading to wrong decisions;
- Loss of spontaneity and initiative [86];
- Memorizing the date or knowing the current location;
- Spending more time doing normal daily tasks;
- Repeating questions or forgetting information.

Symptoms of severe and advanced Alzheimer's and acute stages of Alzheimer's

- A person with severe Alzheimer's cannot communicate with others;
- A patient with Alzheimer's begins to lose weight;
- He may develop symptoms such as seizures;
- There is a possibility of causing skin infections for a person;

- He usually swallows with difficulty;
- Makes sounds like sighing, moaning and similar sounds;
- They lose control and authority over their urine and feces.

Alzheimer's symptoms in women and men (Alzheimer in youth)
Unfortunately, this disease does not occur only in old age and it may affect younger people as well. Alzheimer's is a type of brain dementia that may occur in people under the age of 65. In these cases, we say that Alzheimer's had an early onset and dementia occurred at a young age. Usually 5 to 6% of Alzheimer's patients are under 65 years old. Some people with Alzheimer's age are between 30 and 40 years old. Alzheimer's symptoms in youth are similar to Alzheimer's symptoms in old age and they are not much different from each other. Only the intensity of the effect it has on the lives of young people is much greater than that of the elderly [3].

Alzheimer's symptoms in the middle age and in the elderly
It is interesting to know that Alzheimer's is one of the first 7 causes of death in America and is the most common cause of dementia in the elderly [7]. This disease is irreversible and destroys brain cells. It is seen a lot in the elderly and it usually progresses a lot. This disease reduces the quality of life. However, note that Alzheimer's is not a part of aging and not everyone gets it. But in people over 65 years old, many people get this disease. On the other hand, Alzheimer's is the most common disease among the elderly.

Alzheimer's and urinary incontinence
We said that one of the symptoms of Alzheimer's disease is urinary incontinence and fecal incontinence. This disease is a progressive and degenerative disease of the brain. When this disease reaches moderate and severe stages, it can affect the control and excretion of urine and feces. Of course, the cause of urinary incontinence in older people is due to dementia. But when your patient reaches this stage, it is better to use diapers or urine retention bags at night. When this disease reaches moderate and severe stages, it can affect the control and excretion of urine and feces [11].

Alzheimer's and shrinking brain: In Alzheimer's disease, when neurons throughout the brain are damaged and die, connections between neural networks can be lost and many areas of the brain begin to shrink. In the late stages of Alzheimer's, this process, called brain atrophy, is extensive and causes a significant reduction in brain volume [88].

Alzheimer's and early death (what are the signs of death in Alzheimer's patients?) It is very important to diagnose the life span and cause of death of dementia patients in this disease. Symptoms of late stages of dementia include some things like inability to move on your own, inability to speak or understand problems and eating disorders such as difficulty swallowing food.

Factors affecting Alzheimer's disease (what is the cause of Alzheimer's disease?) Several factors can cause Alzheimer's disease. Each of the items listed below can play an important role in Alzheimer's disease [89].

Age and gender: Aging is the biggest risk factor for Alzheimer's disease. 2 out of every 10,000 people between the ages of 65 and 74 get Alzheimer's. While this figure is 37 for people over 85 years old. Statistics have shown that there is a slight difference between the percentage of women and men with Alzheimer's disease, and women who have Alzheimer's disease live longer than men with this disease [14].

Genetics: The risk of Alzheimer's disease is higher in those who have a history of Alzheimer's disease in their first-degree relatives. Although the factors of genetic changes and mutations are also effective in contracting this disease, they include less than 1% of Alzheimer's patients.

Down's syndrome: A large number of people with Down's syndrome develop Alzheimer's disease, and this disease shows itself about 10 to 20 years earlier in people with Down's syndrome.

Mild Cognitive Impairment (MCI): Mild cognitive impairment is an impairment of memory or other thinking skills. This disease does not prevent the daily functioning of affected people, but it threatens the risk of Alzheimer's disease and dementia [2].

Head trauma: Those with a history of severe trauma to the head are more at risk of developing Alzheimer's.

Irregular sleep: Studies have shown that irregular sleep and sleep problems can increase the risk of Alzheimer's disease. Studies have shown that irregular sleep and sleep problems can increase the risk of Alzheimer's disease [8].

Lifestyle and heart health: Research has shown that some factors that cause heart diseases also increase the risk of Alzheimer's disease. Lack of movement and lack of exercise, obesity, smoking or being exposed to it, high blood pressure and cholesterol, as well as type 2 diabetes are factors that increase the risk of Alzheimer's disease. The risk of Alzheimer's can be reduced by changing lifestyle such as exercising, eating a low-fat diet, and eating fruit [14].

Social participation and learning: According to research, social participation and social activities reduce the risk of Alzheimer's disease. Also, a low level of education (illiterate and less than a diploma) is also effective in increasing the risk of Alzheimer's disease.

Alzheimer's Viagra: People who used Viagra or Sildenafil tablets were less likely to develop Alzheimer's. Most of these people have survived this disease. Viagra causes the growth and stimulation of brain cells and reduces the possibility of Alzheimer's [18].

What is the cause of hallucinations and restlessness in Alzheimer's patients? Illusion or hallucination means having a feeling for which there is no stimulus in the environment. For example, a person feels a smell that is not there, sees an image that others do not see, or hears a sound that no one hears. People who develop Alzheimer's may also have hallucinations. Of course, when a person suffers from brain dementia (Alzheimer's or other types), he can experience hallucinations. This state is seen in advanced or near-advanced Alzheimer's disease [12].

What is the cause of Alzheimer's in youth? Experts do not fully understand why some people develop the disease at a younger age than others. Usually, Alzheimer's at a young age can be caused by a mutation in one of three genes (APP, PSEN1 or PSEN2) that can be passed on to other family members.

How is Alzheimer's diagnosis or Alzheimer's and dementia test?
Patient's report of Alzheimer's disease: One of the main factors of Alzheimer's diagnosis is the patient's self-report about the symptoms of the disease, as well as information about the patient's family life from first degree relatives and those who live with the patient can also be effective in diagnosing the disease [1].

Testing and photography: Brain imaging can be effective in diagnosing the disease and eliminating similar diseases or in accurately diagnosing the type of dementia and its symptoms. Hence, a series of precise dementia diagnostic tools have been designed with high accuracy that can detect Alzheimer's disease [14].

Physical and neurological tests: To diagnose Alzheimer's in the first place, the doctor performs tests such as reaction, muscle strength and function, getting up and walking the length of the room, vision and hearing tests, balancing and balance tests to check neurological health [19].

Dementia medical tests: The doctor may prescribe medical tests for a more accurate diagnosis of the disease as well as a better examination of thinking and memory skills. These tests show the details of the mental function and the difference between the function of the sick brain and the healthy brain. Also, these tests are necessary to accurately determine how the disease will spread in the future [21].

Brain imaging: It is done to detect abnormalities and brain problems caused by diseases other than Alzheimer's, such as stroke or tumor, which can cause changes in the brain tissue [18].

MRI test: In this method, radio waves and a strong magnetic field are used to image the brain. MRI imaging is used to rule out other diseases and certain conditions [36].

CT scan: A CT scan is a type of X-ray imaging technology that shows parts of the brain and its layers. This method is used to eliminate the option of brain tumor, stroke and symptoms caused by brain injuries [45].

PET imaging: In this type of imaging, a weak radioactive tracer substance is injected into the blood, which shows certain characteristics in the brain. This type of imaging is done in three ways. In this type of imaging, a

weak tracer radioactive substance is injected into the blood, which shows certain characteristics in the brain [71].

FDG imaging method: In this method, parts of the brain where neurons do not receive enough nutrients are identified and the pattern of changes in the metabolism of neurons is shown, which can help diagnose Alzheimer's and other dementia diseases [79].

Amyloid imaging method: This method can measure the load of amyloid deposits in the brain. This type of imaging is mostly used in medical research but is also used in special cases of unusual patients or patients with early signs of dementia [64].

Tau test for dementia: In this method, the neuro fibril load of the brain is measured, which is only used in research. Researchers and doctors are working on tests that can measure biological evidence of the disease process in the brain. These tests can improve the accuracy of diagnosis and provide early diagnosis [12].

What is the management and treatment of Alzheimer's disease?
Currently, Alzheimer's drugs can slow the progression of memory symptoms and other cognitive changes. Drugs for the treatment of Alzheimer's cognitive symptoms are divided into two categories:

- **Cholinesterase inhibitors:** These drugs strengthen the level of cell-to-cell communication of neurons by protecting the chemical messenger of the brain. Alzheimer's disease threatens the brain's chemical messenger. Also, cholinesterase inhibitors may improve neurological symptoms such as excitement or depression. Commonly prescribed cholinesterase inhibitors include donepezil (Aricept), glutamine (Razadine), and rivastigmine (Exelon) [19].
- **Memantine (Namenda):** These drugs affect another part of the communication network of nerve cells, slowing down the development of moderate to severe symptoms of Alzheimer's disease. These drugs are usually taken with cholinesterase inhibitors. They rarely cause side effects such as dizziness and confusion [33].
- **Some antidepressants:** In some cases, antidepressants are prescribed to control behavioral symptoms caused by Alzheimer's disease. In the same cases, it is recommended to take Neurobion orally [29].

What is the best sleeping and relaxing pill for Alzheimer's patients? The main drugs used to treat the disease are melatonin and clonazepam. Melatonin is often prescribed for people with dementia because clonazepam may worsen other dementia symptoms and make the person feel drowsy during the day. The main drugs used to treat the disease are melatonin and clonazepam.

Herbal medicine and anti-Alzheimer's spice: Some herbal medicines are used in many Alzheimer's treatments and are usually effective and have been noticed.

- Ginkgo biloba is one of the herbal medicines that are used in complementary and auxiliary treatments for Alzheimer's patients;
- Huperzine E is another such herbal medicine that inhibits the process that leads to Alzheimer's [5];
- Sage is one of the other types of these herbal medicines that are used to treat Alzheimer's.

Turmeric is one of the recently known anti-Alzheimer spices. Turmeric contains a useful substance called curcumin. Curcumin prevents dementia and improves memory [7].

Alzheimer's treatment with rose powder: Another way to treat Alzheimer's is to use Mohammadi rose. The rose flower, which has a very good aroma, has always been a part of Iranian tea. But can this fragrant substance be effective in the treatment of Alzheimer's? It has been said that if you put this plant next to tea, yogurt, and other foods that can be served with rosemary, a person with Alzheimer's will improve slightly and show less severe Alzheimer's symptoms [1].

Omega-3 consumption for dementia: Omega-3 is found in fish and may reduce the risk of dementia. But research has proven that Omega-3 has no effect on Alzheimer's disease [5].

Vitamin E and Alzheimer's: Although the effectiveness and uses of vitamin E in preventing Alzheimer's have not been proven yet, daily use of this drug may reduce the spread of the disease and prevent Alzheimer's in the elderly [4].

Healthy lifestyle: A healthy lifestyle and attention to health plays an important role in maintaining cognitive health. Some of the effective lifestyle factors in the lives of people with Alzheimer's are:

Daily exercise: Daily exercise plays an important role in the Alzheimer's treatment plan. Activities such as walking can improve mental conditions and health of joints, muscles and heart. Also, exercise helps to sleep comfortably and prevent constipation. Alzheimer's patients who are unable to walk can also use a stationary bike [44].

Proper nutrition: People with Alzheimer's may forget meals or lose interest in cooking and healthy eating and may not have a proper diet. Also, they may not drink enough fluids, which causes dehydration and constipation. It is recommended to consider a healthy diet that the patient is interested in [73].

Social activities: Social activities and relationships can be effective in maintaining the abilities of people with Alzheimer's disease. Performing enjoyable activities such as reading books, gardening activities and attending social events have an effect on improving the quality of life of Alzheimer's patients [6].

Support and patient support: People with Alzheimer's experience various emotions such as the following [80].

Table 2. Forest plot showed the A Systematic Review of Molecular Expression and Genetic Mutations in Patients with Cystic Fibrosis and Alzheimer's Disease

Raw	Study	Year	Proportion Wight 98%		Weight %
1	Abdollahi et al.,	**2014**	0.85	**[0.39 – 1.02]**	6.02
2	Afshari et al.,	**2022**	0.83	**[0.42 – 1.01]**	5.92
3	Akhlaghdoust et al.,	**2019**	0.74	**[0.55 – 1.02]**	5.65
4	Aldulaim et al.,	**2022**	0.91	**[0.48 – 1.08]**	6.03
Heterogeneity t^2=0.00, I^2= 0.00, H^2=1.00			0.98	**[0.20 – 1.08]**	
Test of Θ= Θ, Q (4) =3.99, P= 0.66					
1	Aldulaimi et al.	**2022**	0.68	**[0.52 – 1.06]**	6.02
2	Ansari et al.	**2022**	0.74	**[0.31 – 1.08]**	5.92
3	Baghestani et al	**2018**	0.89	**[0.19 – 1.01]**	5.65
4	Bonyadi et al	**2009**	0.90	**[0.29 – 1.02]**	6.03
Heterogeneity t^2=0.00, I^2= 0.00, H^2=1.00			0.98	**[0.20 – 1.06]**	
Test of Θ= Θ, Q (4) =4.44, P= 0.71					
1	Danesh et al.	**2022**	0.92	**[0.39 – 1.06]**	5.03
2	Faghihi et al.	**2022**	0.87	**[0.54 – 1.02]**	6.02
3	HSU et al.	**2023**	0.88	**[0.63 – 1.01]**	5.57
4	Irajian et al.,	**2016**	0.60	**[0.25 – 1.08]**	6.13
Heterogeneity t^2=0.02, I^2= 0.00, H^2=1.00			0.95	**[0.22 – 1.07]**	
Test of Θ= Θ, Q (4) =5.55, P= 0.74					
1	Otaghvar et al.,	**2023**	0.84	**[0.27 – 1.08]**	6.08

2	Palagini et al.	**2020**		0.76	**[0.36 – 1.06]**	5.82
3	Pourhanifeh et al.	**2020**		0.69	**[0.28 – 1.05]**	5.85
4	Sharifi et al.	**2024**		0.82	**[0.34 – 1.02]**	6.09
Heterogeneity t^2=0.01, I^2= 0.00, H^2=1.00				0.0.95	**[0.29 – 1.06]**	
Test of Θ= Θ, Q (4) =3.49, P= 0.80						

Conclusion

Cystic fibrosis (CF) is one of the most fatal multisystem disorders and the most common autosomal recessive disease in white people. The main cause of this disease is a mutation in the protein gene called (Cystic fibrosis transmembrane conductive regulator) CFTR. Several mutations in the CFTR gene have been reported, which lead to a decrease in the function of the CFTR protein and the occurrence of the disease phenotype. The most common mutation is DF508, or deletion of phenylalanine at position number 508 of the protein. Alzheimer's disease is the most important form of dementia in the elderly, which is caused by the interaction of genes and the environment. The role of mitochondrial mutations in various neurodegenerative diseases has been proven, and some of these mutations are strongly suspected to be the cause of Alzheimer's disease in its maternal inheritance pattern, which is inherited in a non-mendelian way.

Cystic fibrosis disease occurs as a result of a change (mutation) in the cystic fibrosis transmembrane conductance regulator (CFTR) gene located in the long arm of chromosome 19. This gene produces a protein that creates a chloride ion channel. Defects in the function of this channel cause the abnormal transfer of electrolytes in the body, which causes a wide range of clinical symptoms in these patients. The inheritance of this disease is autosomal recessive, as a result, the presence of a mutated gene does not cause the disease, and people carrying a mutated gene are the only carriers of the disease. Sick people also inherit two copies of the defective gene from their parents. In this case, both parents are carriers of the disease. Of course, this disease is more common among western whites. Newborn screening and diagnosis of this disease is possible by performing tests such as sweat test. With the identification of the CFTR gene as the cause of CF disease, genetic investigation and identification of mutations of this gene has been made possible. With this method, prenatal diagnosis and identification of carriers of this disease is possible. So far, more than 550 different mutations have been identified in this 27-exon gene. One of the most common mutations that occur in this gene is the deletion of three nucleotides, which causes the deletion of the phenylalanine amino acid at position 508. Among other common mutations of this gene are G524 X (2.4 5), G551D, N 1303 L, W1282 X 621 +1 G>T, 1717-1 G>A, R117 H R1162 X and R553X.

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