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A research on rare disease of amyloidosis in human

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Abstract
Amyloidosis is a rare and serious disease. Amyloidosis occurs when normal proteins in the body become misshapen and clump together. Amyloidosis is causing organ dysfunction and death. Amyloid protein deposits can be found in specific organs, such as the lungs, skin, bladder, or bowel, with systemic amyloidosis being the most common. Although it is not a single type of cancer, it may be associated with some blood cancers such as multiple myeloma, which makes it difficult to study. However, over the past few decades doctors and researchers have begun to understand more about amyloidosis. Research is ongoing to learn more about this disease, which can be fatal. Many different proteins can cause amyloid deposits such as AL amyloidosis, AA amyloidosis, dialysis-related amyloidosis (DRA), familial, or hereditary amyloidosis, age-related (senile). While systemic amyloidosis, and organ-specific amyloidosis, certain types of amyloid deposits have been associated with Alzheimer's disease, the brain is rarely affected by amyloidosis that occurs throughout your body. If amyloidosis can prevent the accumulation of amyloid in the patient's brain, then we can bring amyloidosis under control to a great extent.

Keywords: Amyloidosis, types, etiology, pathology, treatment, amyloid, diagnosis etc

Introduction
Amyloidosis is a rare and serious illness. Amyloidosis occurs when normal proteins in the body become misshapen and clump together. These misshapen proteins are called amyloid deposits or fibrils. Over time, the amyloid deposits build up in organs and tissues in the body. Eventually, this buildup causes symptoms and organ failure because the organs and tissues are not able to work as well as they should [1]. Amyloidosis is leading to organ dysfunction and death [2]. Amyloid protein deposits can be found in specific organs, such as the lung, skin, bladder, or bowel, or they can be systemic. "Systemic" means that the deposits may be found throughout the body. Systemic amyloidosis is the most common [1]. Although it is not a type of cancer, it may be associated with certain blood cancers like multiple myeloma. Because amyloidosis is rare, it has been difficult to study. However, doctors and researchers have begun to understand more about amyloidosis over the past few decades. Research continues to learn more about this illness, which can be life-threatening [1].

Causes
In general, amyloidosis is caused by a buildup of amyloid in your organs. The organs or areas of the body affected depend on the type of amyloidosis that you have.
Some types of amyloidosis are hereditary, while others can be brought on by:
- An individual being on dialysis for a long time
- Certain inflammatory diseases

Symptoms

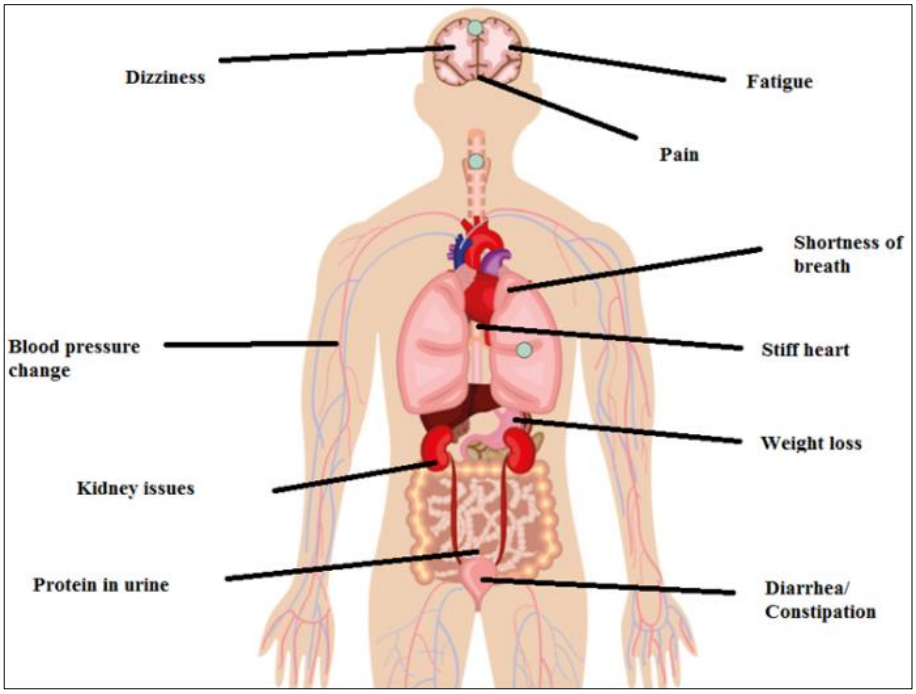

Fig: 1 Symptoms of amyloidsis disorder

In its early stages, amyloidosis might not cause symptoms. When it becomes more severe, the symptoms you have will depend on the type of amyloidosis you have and the organ or organs that are affected.

For example, if your heart is affected, you may experience:

- Shortness of breath
- Fast, slow, or irregular heart rate
- Chest pain
- Low blood pressure, which could cause lightheadedness

If your kidneys are affected, you may experience swelling in your legs due to fluid buildup (edema) or foamy urine from excess protein.

If your liver is affected, you may experience pain and swelling in the upper part of your abdomen.

If your gastrointestinal tract is affected, you may experience:

- Nausea
- Diarrhea
- Constipation
- Appetite loss
- Weight loss
- Feeling of fullness right after eating

If your nerves are affected, you may experience:

- Pain, numbness, and tingling in your hands, feet, and lower legs
- Dizziness when standing up
- Nausea
- Diarrhea
- Inability to feel cold or heat
- General symptoms that can occur include:
- Fatigue
- Weakness
- Bruising around your eyes or on your skin
- Swollen tongue
- Joint pain
- carpal tunnel syndrome, or numbness and tingling in your hands and thumb [3]

Types of Amyloidosis

Many different proteins can lead to amyloid deposits, but only a few have been linked to major health problems. The type of protein and where it collects tells the type of amyloidosis you have. Amyloid deposits may collect throughout your body or in just one area.

The different types of amyloidosis include:

- **AL amyloidosis (immunoglobulin light chain amyloidosis):** This is the most common type and used to be called primary amyloidosis. AL stands for "amyloid light chains," which is the type of protein responsible for the condition. There's no known cause, but it happens when your bone marrow makes abnormal antibodies that can't be broken down. It's linked with a blood cancer called multiple myeloma. It can affect your kidneys, heart, liver, intestines, and nerves.
- **AA amyloidosis:** Previously known as secondary amyloidosis, this condition is the result of another chronic infection or inflammatory disease such as rheumatoid arthritis, Crohn's disease, or ulcerative colitis. It mostly affects your kidneys, but it can also affect your digestive tract, liver, and heart. AA means the amyloid type A protein causes this type.
- **Dialysis-related amyloidosis (DRA):** This is more common in older adults and people who have been on dialysis for more than 5 years. This form of amyloidosis is caused by deposits of beta-2 microglobulin that build up in the blood. Deposits can build up in many different tissues, but it most commonly affects bones, joints, and tendons.
- **Familial, or hereditary, amyloidosis:** This is a rare form passed down through families. It often affects the liver, nerves, heart, and kidneys. Many genetic defects are linked to a higher chance of amyloid disease. For example, an abnormal protein like transthyretin (TTR) is usually the cause.
- **Age-related (senile) systemic amyloidosis:** This is caused by deposits of normal TTR in the heart and other tissues. It happens most commonly in older men.

- **Organ-specific amyloidosis:** This causes deposits of amyloid protein in single organs, including the skin (cutaneous amyloidosis).

Though some types of amyloid deposits have been linked to Alzheimer's disease, the brain is rarely affected by amyloidosis that happens throughout your body.

Risk Factors for Amyloidosis

Men get amyloidosis more often than women. Your risk for amyloidosis goes up as you grow older. Amyloidosis affects 15% of patients with a form of cancer called multiple myeloma.

Amyloidosis may also happen in people with end-stage kidney disease who are on dialysis for a long time (see "Dialysis-related amyloidosis" above).

Diagnosed

Your doctor will ask you about your symptoms and whether anyone in your family has cardiac amyloidosis or other heart conditions. They'll give you a physical exam, too.

The doctor may do several tests to diagnose or rule out cardiac amyloidosis, like:

- Blood and urine tests
- Imaging tests to see inside your body, like ultrasound, echocardiogram, electrocardiogram, MRI, or CT scan
- Biopsy
- Genetic testing, if cardiac amyloidosis runs in your family

Treatment

- Supportive care
- Type-specific treatment

Currently, there are specific treatments for most forms of amyloidosis, although some therapies are investigational. For all forms of systemic amyloidosis, supportive care measures can help relieve symptoms and improve quality of life.

Renal

Patients with nephrotic syndrome and edema should be treated with salt and fluid restriction, and loop diuretics; because of the ongoing protein loss, protein intake should not be restricted. Kidney transplantation is an option when the underlying disease process is controlled, and can provide long-term survival comparable to that in other renal diseases.

Cardiac

Patients with cardiomyopathy should be treated with salt and fluid restriction and loop diuretics. Other drugs for heart failure, including digoxin, angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, and beta-blockers, are poorly tolerated and contraindicated. Heart transplantation has been successful in carefully selected patients with AL or ATTR amyloidosis and severe cardiac involvement. To prevent recurrence in the transplanted heart, patients with AL amyloidosis must be given aggressive chemotherapy directed at the clonal plasma cell disorder, and patients with symptomatic ATTR amyloid polyneuropathy or cardiomyopathy should be considered for anti-TTR therapies.

Gastrointestinal

Patients with diarrhea may benefit from loperamide. Those with early satiety and gastric retention may benefit from metoclopramide.

Nervous system

In patients with peripheral neuropathy, gabapentin, pregabalin, or duloxetine may relieve pain.

Orthostatic hypotension

Often improves with high doses of midodrine; this drug can cause urinary retention in older males, but the drug complication of supine hypertension is rarely a problem in this population. Support stockings can also help, and fludrocortisone can be used in patients without peripheral edema, anasarca, or heart failure. [4]

AL amyloidosis

Prompt initiation of anti-plasma cell therapy is essential to preserve organ function and prolong life. Most drugs used for multiple myeloma have been used in AL amyloidosis; choice of drug, dose, and schedule often must be modified when organ function is impaired. Chemotherapy using an alkylating agent (Eg, melphalan, cyclophosphamide) combined with corticosteroids was the first regimen to show any benefit. High-dose IV melphalan, combined with autologous stem cell transplantation can be highly effective in selected patients [5].

Proteasome inhibitors (Eg, bortezomib) and immunomodulators (Eg, lenalidomide) also can be effective. Combination and sequential regimens are being investigated. Localized AL can be treated with low-dose external beam radiation therapy because plasma cells are highly radiosensitive.

- ATTR amyloidosis
- For ATTR amyloidosis:
- Liver transplantation
- Tetramer-stabilizing drugs
- Gene silencing drugs

Liver transplantation

Which replaces the primary site of synthesis of the mutant protein with a new organ producing normal TTR—can be effective in certain TTR mutations if done at disease onset (early neuropathy and no heart involvement). Transplantation later in the course of the disease often leads to progressive amyloid cardiomyopathy and neuropathy due to the misfolding and deposition of wild-type TTR protein onto pre-existing amyloid deposits. Several drugs have been shown to stabilize TTR tetramers circulating in the plasma, inhibiting TTR misfolding and fibril formation and effectively slowing neurologic disease progression while preserving quality of life. These TTR stabilizers include diflunisal, a widely available generic anti-inflammatory drug, and tafamidis [6, 7].TTR gene silencing using anti-sense RNA or RNA interference to block translation of TTR mRNA efficiently reduces serum levels of TTR, improves neurologic outcomes in about 50% of patients, and appears capable of repairing injured nerves in some patients [8, 9]. Two gene silencing drugs, patisiran and inotersen, are available.

ATTRwt amyloidosis

Tetramer-stabilizing drugs

TTR stabilization using tafamidis, in patients with ATTR amyloid cardiomyopathy has been shown to decrease all-cause mortality and cardiovascular-related hospitalizations [7]. Unlike hereditary ATTR amyloidosis, liver transplantation is not effective for patients with ATTRwt because the amyloidogenic protein is a structurally normal TTR.

AA amyloidosis

For AA amyloidosis caused by familial Mediterranean fever, colchicine 0.6 mg orally once or twice a day is effective. For other AA types, treatment is directed at the underlying infection, inflammatory disease, or cancer.

Colchicine or anti-IL1, anti-IL6, or anti-TNF drugs may be used to interrupt the cytokine signaling, diminishing the inflammatory process driving hepatic production of serum amyloid A (SAA).

Other treatments to help with symptoms include:

- Diuretic medicine to remove extra water from your body
- Thickeners to add to fluids to prevent choking if you have trouble swallowing
- Compression stockings to relieve swelling in your legs or feet
- Changes to what you eat, especially if you have gastrointestinal amyloidosis [10]

Material and Method

We conducted this research paper by observing the different types of reviews, as well as conducting and evaluating literature review papers.

Result and Discussion

In our research, we found that amyloidosis is a rare and serious disease. Amyloidosis occurs when normal proteins in the body become misshapen and clump together. Amyloidosis is causing organ dysfunction and death. Amyloid protein deposits can be found in specific organs, such as the lungs, skin, bladder, or bowel, with systemic amyloidosis being the most common. Although it is not a single type of cancer, it may be associated with some blood cancers such as multiple myeloma, which makes it difficult to study. However, over the past few decades doctors and researchers have begun to understand more about amyloidosis. Research is ongoing to learn more about this disease, which can be fatal. Amyloidosis is caused by a buildup of amyloid in your organs. Many different proteins can cause amyloid deposits such as AL amyloidosis, AA amyloidosis, dialysis-related amyloidosis (DRA), familial, or hereditary amyloidosis, age-related (senile). While systemic amyloidosis, and organ-specific amyloidosis, certain types of amyloid deposits have been associated with Alzheimer's disease, the brain is rarely affected by amyloidosis that occurs throughout your body. If amyloidosis can prevent the accumulation of amyloid in the patient's brain, then we can bring amyloidosis under control to a great extent.

Conclusion

In our research, we concluded that amyloidosis is a rare and serious disease. Amyloidosis can be a life-threatening disease in the future, especially when it affects the heart and kidneys. Amyloidosis occurs when normal proteins in the body become misshapen and clump together. Amyloidosis is causing organ dysfunction and death. Amyloid protein deposits can be found in specific organs, such as the lungs, skin, bladder, or bowel, with systemic amyloidosis being the most common. Amyloidosis is caused by a buildup of amyloid in your organs. Many different proteins can cause amyloid deposits such as AL amyloidosis, AA amyloidosis, dialysis-related amyloidosis (DRA), familial, or hereditary amyloidosis, age-related (senile). While systemic amyloidosis, and organ-specific amyloidosis, certain types of amyloid deposits have been associated with Alzheimer's disease, the brain is rarely affected by amyloidosis occurring throughout your body. If amyloidosis can prevent the accumulation of amyloid in the patient's brain, we can bring amyloidosis largely under control. Early diagnosis and treatment are important and can help improve survival.

Future aspect

Amyloidosis can be a life-threatening disease in the future, especially when it affects the heart and kidneys. Amyloidosis can be fatal, especially if it affects your heart or kidneys. Early diagnosis and treatment are important and can help improve survival. Researchers are constantly researching this and searching for the diagnosis of this disease as soon as possible so that in future the problem caused by this disease can be treated as soon as possible. Why do some types of amyloid make people sick and how can the formation of amyloid be prevented. Studies are ongoing to find new treatments.

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Ethical Approval

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Conflicts of Interest

All authors are declaring that they have no conflicts of interest.

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