

# Diagnosis and Treatment of MS in Patients Suffering from Various Degrees of the Disease with a Clinical Approach: The Original Article

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## Abstract

This study Original investigated the diagnosis and treatment of MS in patients (111 Patients) with various degrees of the disease with a clinical approach. MS is an autoimmune disease in which the body's immune system attacks its own tissues. In MS, the malfunctioning immune system destroys myelin. Myelin is a fatty substance that covers and protects the nerve fibers of the brain and spinal cord. When the protective myelin sheath is damaged and nerve fibers are exposed, the speed at which messages are transmitted along the nerve slows or is blocked. The concordance rate for MS in monozygotic identical twins is only 20-35%, indicating that genetic factors have only a moderate effect and transmission is not 100%. The presence of non-Mendelian predisposing factors along with environmental effects plays an important role. For first-degree family members of people with MS, the risk of developing the disorder is seven times greater than in the general population, but the excess family risk for the disease is only 2.5-5%. Research on single nucleotide polymorphisms that play a role in the risk of developing severe disease or developing certain types of MS is ongoing. To date, however, HLA-DRB1 is the only chromosomal locus consistently associated with MS susceptibility. Molecular mimicry has been proposed as an etiological process in MS. The molecular mimicry hypothesis suggests that T cells in peripheral blood may, after being activated to attack a foreign antigen, then mistakenly continue to attack proteins in the brain that have similar epitopes.

**Keywords:** MS, Clinical Approach, Genetic Factors, Autoimmune Disease.

## INTRODUCTION

MS is a potentially devastating disease of the nervous system. MS is known as multiple sclerosis in medical science [1-3]. This disease is considered as an inflammatory and autoimmune disease as well as debilitating. MS targets the brain and spinal cord. This disease leads to their paralysis due to the attack of the body's immune system on the nerves of the brain and spinal cord, which ultimately disrupts the communication between the brain and other organs of the body. In acute cases, it can destroy nerves permanently [4-6]. As mentioned, MS is an autoimmune disease. In autoimmune diseases, the body's immune system mistakenly attacks the body's tissues instead of protecting the body and removing factors such as germs and bacteria. In this disease, the body's white blood cells, which have the role of protecting the body, mistakenly consider myelin, whose role is to protect nerve fibers, as a foreign agent and attack it. These blood cells target one of the organs each time and cause a disturbance in the nerve receptors of the same part [7].

What are the symptoms of MS?

These symptoms are not the same for all people with MS, but the most common symptoms include:

- Tingling or burning sensation in the fingers: One of the most common symptoms of MS is burning, tingling, and numbness in the fingers. This symptom is mostly seen in the toes.
- Dizziness: Any type of dizziness is not a symptom of MS. Dizziness (Figure 1) in these patients causes problems even for straight walking and leads to their imbalance [7-9].

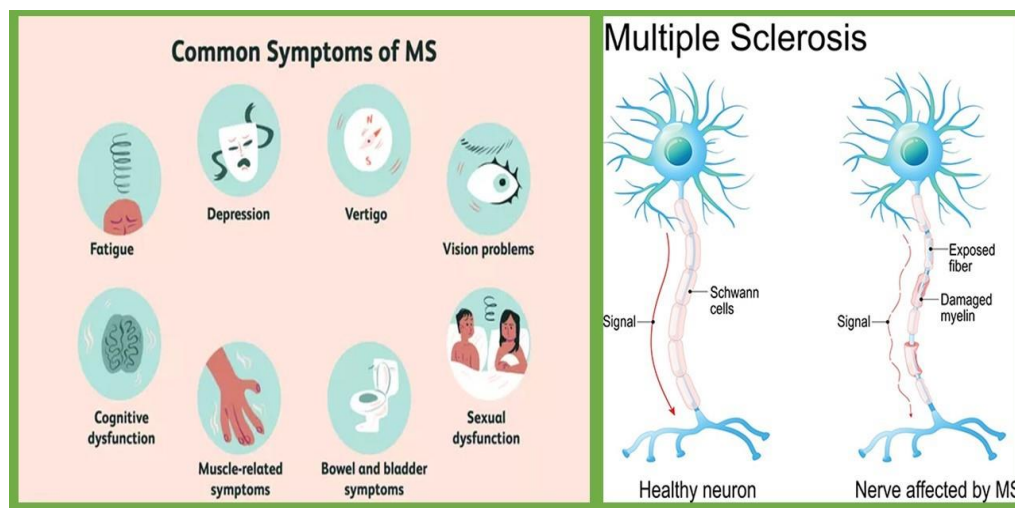


Figure 1. symptoms of MS

- Weakness in memory: Generally, patients with MS do not have sufficient and necessary concentration, and sometimes the person does not have the ability to speak and concentrate at the same time.
- Impaired vision: One of the most common symptoms of this disease is impaired vision, blurred vision, and double vision. The disorder occurs when the white blood cells of a person with MS attack and weaken the optic nerve system [10].
- Constant weakness and fatigue: The next common symptom in this disease is weakness and fatigue in the patient. Fatigue occurs when white blood cells attack and destroy nerves in the spine. Sometimes this fatigue and weakness becomes so much that a person falls into depression.
- Muscle stiffness and spasm: This disease leads to muscle stiffness and involuntary muscle spasm. Generally, this disorder occurs in the legs. Muscle spasm has symptoms such as: Back pain, stiffness and difficulty in bending the knee, joint stiffness and uncontrollable legs and arms [11].
- Disturbance in bowel and bladder control and function: This symptom generally occurs in 80% of affected people. In this case, the person constantly feels the urge to pass stool and urinate frequently. Sometimes it may lead to lack of control of urine or feces.
- Creating sexual disorders: This symptom (Figure 2) is one of the symptoms that occur in the severe stages of this disease. In women, it may lead to vaginal dryness, painful intercourse.

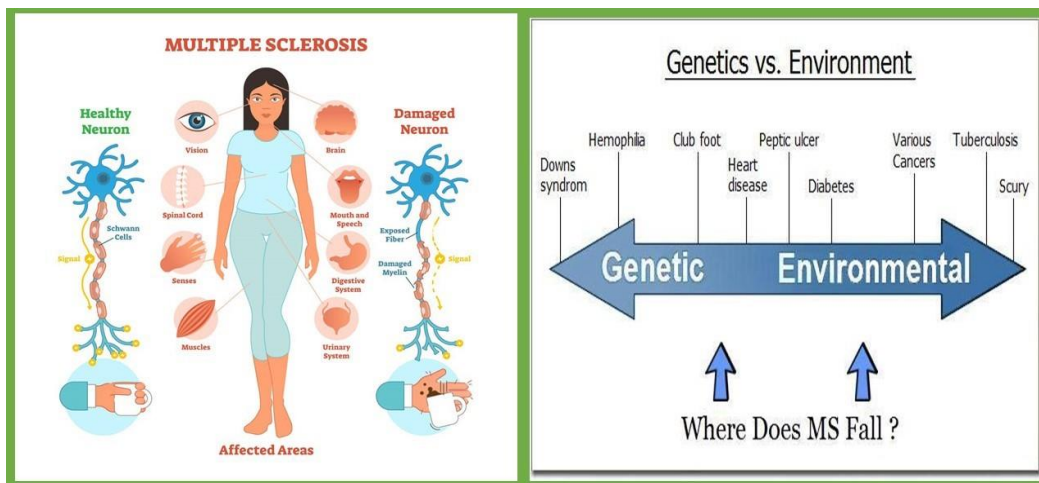


Figure 2. The cause of MS

### Search strategy and selection of articles

Search in Scopus, Google scholar, PubMed databases and by searching with keywords such as "Diagnosis and Treatment of MS in Patients Suffering" and " Various Degrees of the Disease" and "Fracture Problems" and "Special Care Unit" to obtain articles related to the selected keywords [12]. Case report articles, editorials, and articles that were not published or only an introduction of them were available, as well as summaries of congresses and meetings that were in languages other than English, were ignored. Only the original research articles that evaluated the effectiveness of different drugs in the treatment of COVID-19 using standard methods were studied (figure 3).

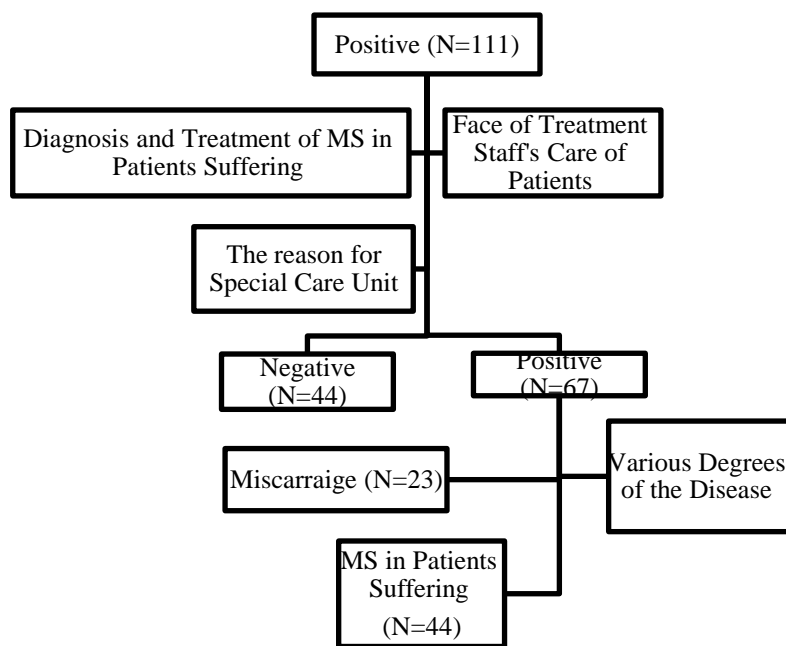


Figure 3. Flow chart of included subjects

## Blood Tests

Blood tests are often an effective way to rule out or confirm other diagnoses. Blood tests can help your doctor rule out other diseases that cause some of the same symptoms as MS. This brings your doctor one step closer to an accurate diagnosis [13]. Because symptoms come and go and there is no test that provides a definitive diagnosis, it can take a long time to diagnose MS. Although the wait can be frustrating, each test will help rule out or confirm other potential causes of your symptoms.

□ MRI test: MRI is painless and non-invasive and can produce accurate images. MRI, performed both with and without color contrast, can identify lesions on the brain and spinal cord. Images can show whether lesions are old or new, or whether they are currently active. In addition to diagnosis, MRI (Figure 4) can help monitor disease progression [14].

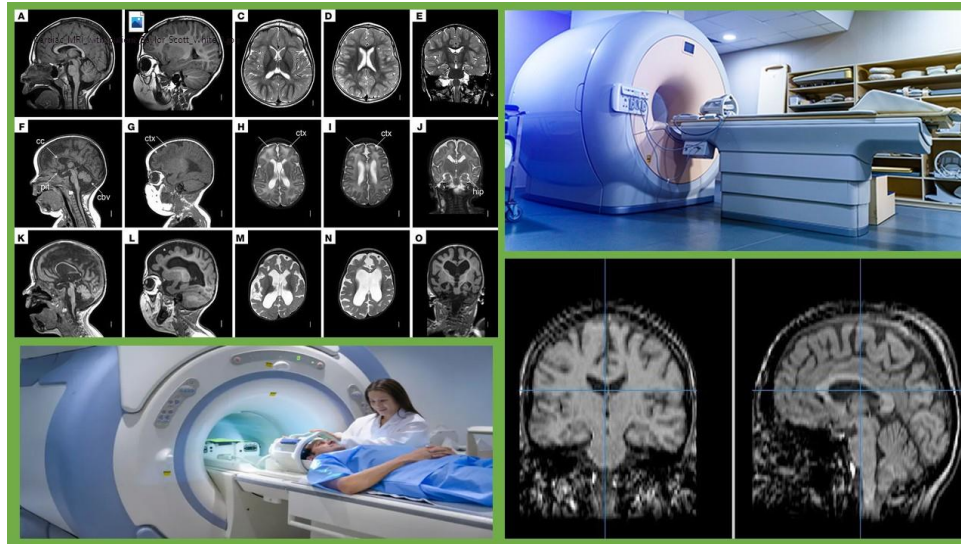


Figure 4. MRI test

□ Cerebrospinal fluid sampling: Although a lumbar puncture cannot rule out or confirm MS, it can help diagnose it. CSF is obtained from a needle inserted between the bones at the bottom of your spine. In people with MS, the spinal fluid sometimes contains high levels of IgG antibodies or proteins called oligoclonal bands, which can also be caused by other diseases. About 5 to 10 percent of people with MS have nothing abnormal in their spinal fluid.

□ Evoked potential tests: This test involves staring at a screen with an alternating checkerboard pattern. This test shows how the electrical activity in the brain responds to external stimulation, such as a sight or sound, and whether there are any disturbances in the pathways of the optic nerve. Are you there or not? There are several types of evoked potential (EP) tests. Visual evoked potential (VEP) tests are the most common [15-17].

□ Eye exam: For many people, vision problems may be the first sign of MS. This can usually manifest as optic neuritis, which is inflammation of the optic nerve, which can cause blurred vision, dull colors, pain in the eyes, blind spots, and contrast sensitivity. Other problems associated with MS include double vision and involuntary eye movements. Anyone presenting with these types of symptoms should see an ophthalmologist, neurologist, or neuro-ophthalmologist to determine whether MS could be the cause.

□ MS Diagnosis Test: Today, many people with MS know that new drugs can reduce their disease progression, but there are still many secrets about the cause of the disorder and no one knows how to prevent or prevent it [18].

About a decade ago, a technology entrepreneur named Art Melore, who was infected with MS in 2000, founded an organization called the accelerated treatment project in Waltam Massachusetts [19]. To help improve these puzzles through further

cooperation between scientists. In one of its efforts, it maintains a repository of thousands of blood samples from patients who visited each of its 10 U.S. clinics. Samples are available to anyone willing to share their data with the project. Scientists have used these samples in more than 70 different studies into the causes of MS and how to diagnose and treat it [20].

Such a test may reduce the time and cost of diagnosing MS. The main tool for diagnosing MS today is magnetic resonance imaging (MRI), which can show inflammation in the brain characteristic of this disorder [21-23]. (Most people believe that multiple sclerosis is an autoimmune disorder the product of an abnormal immune response against the body's own nerves.) But MRIs are expensive. Sometimes a spot that looks like MS on a brain scan is caused by another disease, such as diabetes. The opposite is also true; the normality of MRI does not rule out this disorder. Often the doctor has to repeat the scan and even wait until more symptoms appear, delaying the diagnosis, sometimes for years. Doctors may also do a bone marrow biopsy, in which a sample of the cerebrospinal fluid is taken. and check it for the presence of an immune system protein that should not be present [24].

Electrical tests of nerve function can provide additional clues to the presence of MS. But these tests are not error-free and bone marrow sampling is also invasive. Thomas M. "For an autoimmune disease, there is no specific or accurate test, so you have to try to make a test to make a diagnosis," says Avon, a molecular biologist at Vanderbilt University School of Medicine.

## Types of MS

### Relapsing remitting MS (RRMS)

This type of MS is characterized by periods of active inflammation in the central nervous system, during which old symptoms worsen and new symptoms may appear. Times when symptoms get worse are known as relapses, flares, or exacerbations. With the end of the relapse period, the intensity of the symptoms decreases, but new and permanent symptoms can always remain. The quiet periods (Figure 5) between relapses are called remission [25-27]. Recovery may take months or years before relapse occurs. Relapsing-remitting MS is the most common type of multiple sclerosis. Approximately 80 to 90 percent of people with this disease go through a remission period. Most people with this type of MS eventually develop the secondary progressive type.

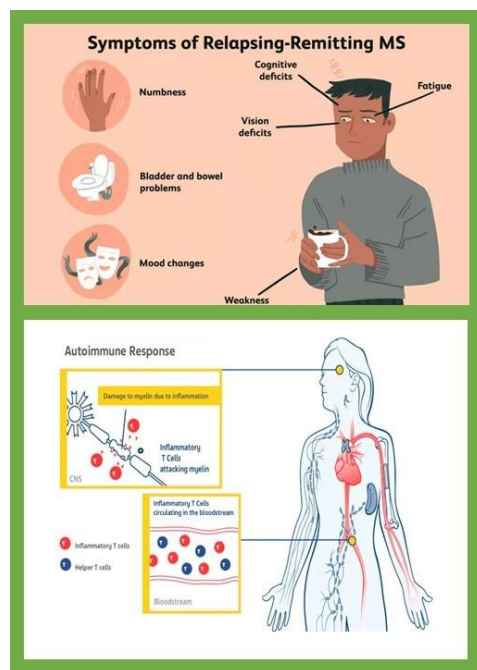


Figure 5. Relapsing remitting MS (RRMS)

## Secondary Progressive MS (SPMS)

This type of MS is generally considered the second phase of relapsing-remitting MS, in which symptoms progress and disability increases. People with secondary progressive MS may still have relapsing periods, although they may fare better than the relapsing-remitting type. Most people who have relapsing-remitting MS eventually develop secondary progressive MS, but each person's experience is different [28].

## Primary Progressive MS (PPMS)

In primary progressive MS, there is no initial relapse that marks the onset of the disease. Instead, MS symptoms appear gradually over time. People with early progressive MS generally don't get better, but they may be able to reduce their symptoms. A small percentage of MS sufferers have the benign type of this disease. According to the National Multiple Sclerosis Society, there is disagreement on how to classify people with benign MS because the progression of the disease varies over a person's lifetime [29].

## Malignant MS

A small number of people with MS develops the malignant type. This type of multiple sclerosis is diagnosed by the rapid formation of lesions in the brain and spine. The malignant type will have severe symptoms, disability and possibly death [30].

## Cause of MS

The cause of MS is unknown, but studies have shown that an external stimulus triggers the immune system to attack cells in the brain and spinal cord. Damage to myelin disrupts the input and output signals of the brain. Some researchers believe that the immune system attacks the body, caused by certain types of viral infections. Others point to low vitamin D levels as the main factor. Smoking also increases the risk of developing MS [31].

## What factors increase the possibility of MS?

Most people with MS have no known risk factors; But in 20% of the patients with this condition, the genetic factor has been involved. The genetic factor means that a family member of the affected person has this disease. Even identical twins have a 20-40% increased risk of developing the disease. Therefore, although having a family history somewhat increases the risk, MS is not considered a genetic or hereditary disease. According to the mayoclinic website, the following factors may increase the risk of developing multiple sclerosis:

- Age: MS can occur at any age, but it is usually more common between the ages of 20 and 40.
- Gender: Women are two to three times more likely to develop MS than men.
- Family history: If a parent or sibling has MS, a person is at a higher risk of developing MS [32].
- Viral infections: Various viral triggers, such as Epstein-Barr's infectious mononucleosis, are associated with MS.
- Race: White people, especially those of Northern European descent, are at greater risk of developing MS.
- Climate: MS is more common in countries with temperate climates, including Canada, the northern United States, New Zealand, southeastern Australia, and Europe.

- Vitamin D: Vitamin D deficiency and lack of sunlight are associated with the risk of developing MS [33].
- Autoimmune diseases: If you have other autoimmune disorders such as thyroid disorders, severe anemia, psoriasis, type 1 diabetes or inflammatory bowel disease, the risk of developing MS is somewhat higher.
- Smoking: Smokers are more susceptible to this disease than non-smokers [34].

## MS diagnosis

The diagnosis of MS is usually based on individual symptoms and the results of various medical tests that may include:

- Neurological evaluation of motion and physical coordination (Figure 6), vision, balance and mental function.
- Blood test to reject other conditions.
- Magnetic resonance imaging (MRI) for the diagnosis of conventional MS brain lesions.
- Testing of spinal cord fluid (LP) to obtain a spinal cord fluid.

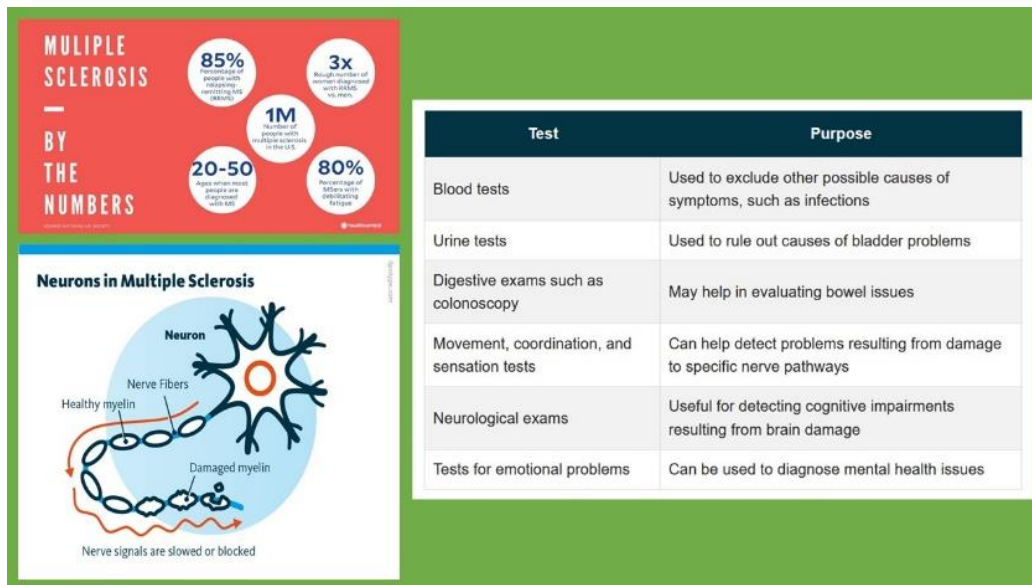


Figure 6. MS diagnosis

Early diagnosis of MS is very important because it reduces the progression of the disease. However, no specific tests can definitely diagnose the disease. In addition, the symptoms of MS and their severity are very different in different people [35].

The role and effect of physiotherapy: Physiotherapy is very necessary in these patients. And it is useful on several levels and plays an important role in delaying the negative symptoms of the disease. Exercises are selected according to the patient's strengths and weaknesses [36].

The best dose (intensity, frequency and duration) of treatment is determined based on the patient's condition. Exercises are considered a safe and effective tool in rehabilitation and are also beneficial for improving mood and quality of life. The use of

therapeutic corticosteroids and inactivity due to fatigue and weakness may lead to osteoporosis and pathological fractures. Weight bearing exercises are therefore beneficial. A resistance training program is recommended to maintain bone and muscle mass [37]. Physiotherapy exercises reduce aerobic capacity disorders, lower limb muscle strength, fatigue and depression. Functional limitations such as impaired walking and balance are reduced.

**Hydrotherapy (hydrotherapy):** Water training programs (called hydrotherapy) have a positive effect on people with multiple sclerosis. This enhances public health, improves energy and mental health, and helps social interaction if physical disabilities. Due to the decrease in the effect of gravity, water exercises allow patients with even severe lower extremity to do stall and movement exercises. A systematic and meta -analysis study recommends a combination of water therapy with normal physical therapy for MS patients [38-40].

**Aerobic exercise:** Aerobic exercise has a positive effect on fatigue. Low to moderate aerobic exercises can improve aerobic fitness and reduce fatigue in MS patients who are mild or moderate.

**Balance exercises:** Specific balance exercises can improve balance in these patients. Poor postural control increases the risk of falling. Decreased walking speed, decreased step length, speed and joint movement are observed in most walking studies in MS.

**Neurorehabilitation:** Motion imagery is increasingly used in neurorehabilitation to facilitate motor function. Motion pictures and rhythmic auditory (Figure 7) stimulation can be used for rehabilitation in walking in MS patients [41].

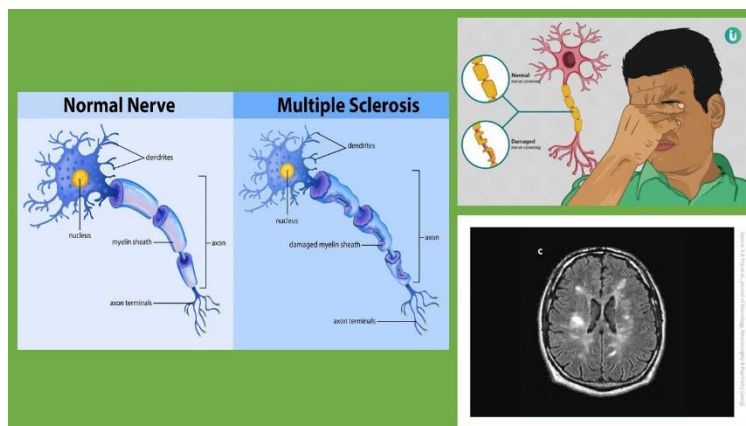


Figure 7. Neurorehabilitation

## Discuss

The results suggest that doctors can analyze blood for repeats of these genes to determine whether a person has MS (Figure 8 & 9). Avon's work so far shows that the test detects true cases of MS more than 90 percent of the time and is similarly successful in ruling out the disease [42-44]. "We can compare MS patients with controls and patients with other neurological disorders and easily separate them," says Avon. "A blood test for MS is now commercially available." A test called gMS®Dx was developed by a company called Glycominds based in Simi Valley, California. This test looks for antibodies (immune system proteins) directed at a sugar molecule called GAGA4 glucose antigen. Such antibodies are often present at high levels in MS

patients. A positive result—that is, a high concentration of these antibodies—can help make the diagnosis in patients with MS-like symptoms for whom brain scans are insufficient [45].

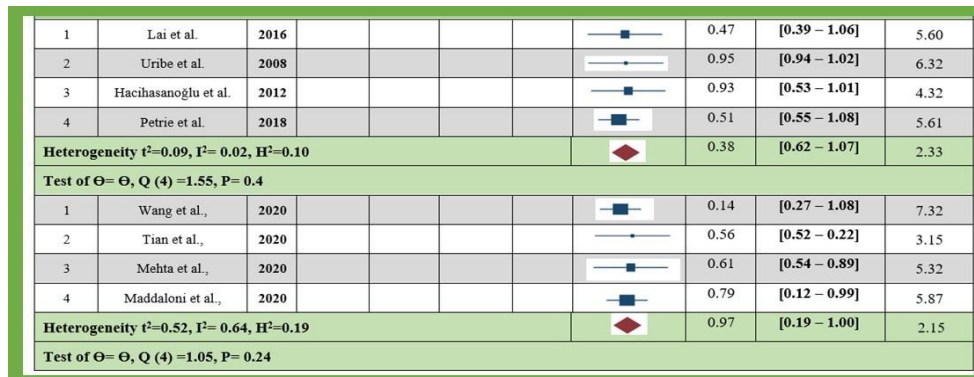


Figure 8. Forest plot showed Diagnosis and Treatment of MS in Patients Suffering

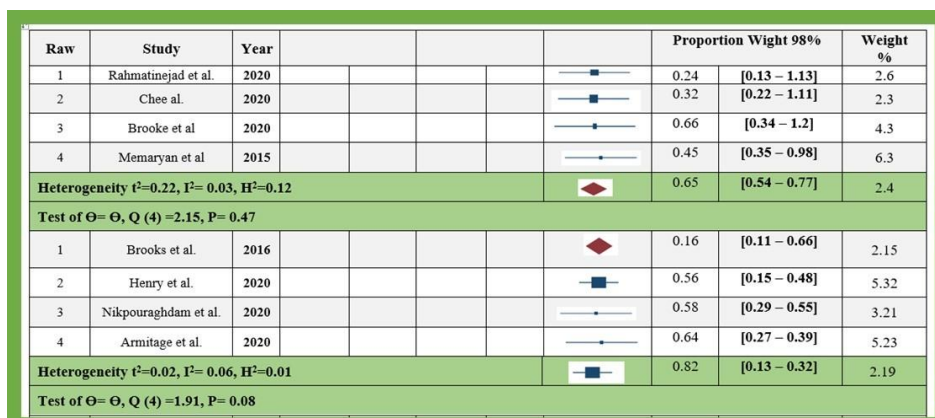


Figure 9. Forest plot showed Various Degrees of the Disease with a Clinical Approach

### Nutritional recommendations for MS

Diet has been shown not to affect the nature of the disease, but it can help with some of your challenges. For example, if you are tired, a diet high in fat and simple carbohydrates will not help. A better diet improves your overall health. Not only will you feel better in the short term, but you'll have a foundation for a healthy future [46-48].

Your diet should include the following:

- All kinds of vegetables and fruits;
- Lean protein sources, such as skinless fish and chicken;
- Whole grains and other sources of fiber;
- Nuts;
- Beans;
- Low-fat dairy products;

- Suitable water and other liquids.

### Prevent MS

There is still no comprehensive guide to prevent MS. Because this disorder is still unknown. Especially since we don't know the cause of it, and as a result, we can't give a definite opinion on how to prevent it [49].

But some research in this field has shown the positive effects of the following:

- Vitamin D;
- Fasting;
- Coffee.

This disease usually progresses faster in men than in women. It may also progress more quickly in people who are diagnosed after age 40 and in people who have a high rate of relapse. About half of people with MS will develop MS within 15 years of being diagnosed with a cane or other they use auxiliary methods [50]. At 20 years after diagnosis, about 60% are still moving and less than 15% need to take care of their basic needs. Your quality of life depends on your symptoms and how you are treated. This rarely fatal but unpredictable disease can change without warning. Most people with MS do not develop severe disability and live full lives. Multiple Sclerosis (MS) is a progressive autoimmune disorder. This means that the immune system, which is responsible for keeping the body healthy, mistakenly attacks parts of the body that are essential for maintaining health. In this situation, the protective coverings of nerve cells are damaged and this damage leads to brain and spinal cord dysfunction. The symptoms of MS are unpredictable and vary in severity. Some patients experience chronic fatigue and numbness, but severe cases of MS lead to paralysis, blindness, and reduced brain function.

The myelin sheath normally protects the nerve fibers of the brain, spinal cord and optic nerve. The underlying nerve fibers can also be damaged or destroyed in this attack. As the attack progresses, the myelin sheath becomes inflamed and gradually destroyed, leaving areas of scar tissue (sclerosis). Inflammation of the myelin sheath disrupts electrical impulses between the brain and other parts of the body. Multiple sclerosis refers to multiple areas of scar tissue, often called lesions, that develop along damaged nerve fibers and are visible on an MRI scan. The word sclerosis means pathological hardening of the tissue. Lesions from MS, resulting in disruption of nerve impulses throughout the body, cause most of the symptoms associated with multiple sclerosis [51-53].

Table 1. Comparison of MS symptoms in women and men

More common experiences for women with MS	More common experiences for men with MS
MS is diagnosed more in women than in men. Vitamin D deficiency may be a reason for the higher incidence in women.	Men appear to be more nervous or loss of nerve function than women.
Secondary progressive MS and relapsing-remitting MS are more common in women than in men.	Approximately equal number of men and women with primary progressive MS is diagnosed.
Women have more MS lesions or scar tissue.	Men tend to have more cognitive problems later in life, although they sometimes do better on tasks that require attention and concentration.

Pregnancy is usually associated with a temporary reduction in the risk of recurrence, but some treatments may not be recommended during pregnancy.	
Menopause reduces gender-related differences in subsequent MS diagnoses.	

The effect of different drugs

### Beta interferons

One of the most common drugs used by neurologists to treat MS are beta interferons. Beta interferon drugs reduce the severity and frequency of MS complications, including those that a patient may experience while treating MS with interferons [54-56]. There are flu-like conditions such as pain, fatigue, fever and chills, which of course usually disappear after a few months, but the drugs slightly increase the possibility of infection, and this is because of this position that drugs reduce the number of white blood cells to prevent the attack on the myelin sheath and control the disease.

These drugs include (Betaferon in the treatment of MS)

- Onex (interferon beta - one E);
- Betaseron (interferon beta - one B);
- Extavia (interferon beta - one B);
- Pelegridy (perginterferon beta-one A);
- Rabif (interferon beta - one E) [1].

### Glatiramer (Copaxone or Glatopa)

This drug prevents your immune system from attacking myelin and protects your nerves.

### Triflunomide

A drug in the treatment of MS, which is in the form of a tablet or pill and you take it once a day, when a neurologist encounters patients who use this drug, its common side effects are diarrhea, liver tests. Abnormal, nausea and hair loss, and due to the fact that liver problems can cause many problems in a person's life and can also cause problems such as birth defects, the neurologist regularly prescribes liver tests to know the condition of your liver [57-59]. It is forbidden to take this medicine during pregnancy, and if you plan to get pregnant, you should definitely talk to your doctor before taking this medicine, because this medicine will remain in your body for a long time.

### Fingolimod

Taking this pill is also one of the ways to treat MS, fingolimod is a prescribed pill by a neurologist to be taken once a day. If you have not had chicken pox, you must be vaccinated against chicken pox during treatment with this medicine. Common side

effects that neurologists encounter when seeing their patients are headache, diarrhea, back pain, cough, and abnormal liver tests. Use this medicine, the brain doctor (neurologist) closely monitors your condition and stays by your side. Research has shown that the drug is associated with a multifocal and progressive disease called leukoencephalopathy (PML), which is a brain infection [60].

Dimethyl fumarate (Tecfidera) is one of the other drugs used to treat MS

A pill to control the symptoms of MS twice a day, this drug can reduce the patient's immune cells, so the neurologist regularly monitors the patient's blood test to monitor the patient's blood test to monitor the patient's blood test have control over the immunity of his body. The most common side effects of this drug are the face of the facial redness, also called flushing, and then stomach aches, diarrhea and nausea are other complications that may hurt the patient [61]. According to research, an active component of this substance (similar to Tecfidera) can be associated with four -channel leukoencephalopathy (PML). Other MS treatment is that it should be in the form of intravenous injection in the hospital and under the supervision of a specialist. Brain and nerves are done, but you go to the hospital every few months and you do not need to use these MS treatments regularly.

The effect of Natalizumab (Tysabri) and Acrizumab

Among other choices in the treatment of MS, if other drugs fail to respond, the effects of natalizumab (Tysabri) and acrizumab are. The drug natalizumab (Tysabri) prevents immune cells from being received by nerve cells in the brain and spinal cord (in fact, they isolate the place that can lead to nerve damage) and ecrizumab is a drug that is absorbed by central B cells. And it prevents immune cells from attacking your body. These drugs are also related to PML, and for this reason, you should be regularly monitored by a neurologist to review your condition with blood tests [41].

Alemtuzumab (Lamictal) and mitoxantrone (Novantrone) are the last lines in the treatment of MS.

Chemotherapy drugs are used in the treatment of cancer. These drugs are used to treat MS when the MS patient does not respond to other mediators. With the help of these drugs, the body's immune system is limited and can no longer attack nerve cells become Neutron is part of the FDA's black box drugs because it can lead to heart damage and leukemia [23].

Get help from a neurologist to control the condition and treat MS.

If you are using other medicines to treat MS and you get few side effects from them. These side effects disappear after some time and there is no need to treat them, anyway, MS is considered a relatively difficult disease that requires the patient to be treated and under the control of a neurologist, and the neurologist is required to monitor and observe your patient continuously. If the progress of this disease is slowed down by MS treatment drugs or stopped in some cases, the patient can continue his normal life and instead of these boring and boring questions for himself, for example, MS is a fatal disease or am I have MS and life has become difficult for me. Think about the fact that you are living your life by controlling the symptoms of MS, and at the same time neurologists and scientists are constantly searching for a cure for this disease, considering that they have very good hopes in their recent results, they will help you live a better life and maybe soon they will get a definitive cure for MS [31].

Complications of the disease and the effect of physiotherapy in the treatment of MS.

Pain patients with MS often experience pain directly from the disease, secondary to medication or other symptoms. Physiotherapy helps relieve pain through exercise, stretching, massage, posture training, or hydrotherapy [7].

Vision problems, such as blurred or double vision, often occur in patients with MS. A physical therapist can teach how to be safe at home and provide strategies to improve balance and coordination in low-light settings. In patients who do not have the

ability to move much, using a wavy mattress along with proper transfer techniques and daily inspections of the skin can help to maintain its integrity and prevent the formation of pressure ulcers.

## Conclusion

MS is an autoimmune disease in which the body's immune system thinks that myelin is a foreign and attacking cell and attacks them and begins to destroy these cells, for this reason, MS treatment focuses on suppression of immune cells is concentrated and medicine control this system to a great extent. If the patient has relapsing-remitting MS disease, which is also called RRMS, it means that the environmental conditions are among the factors for him. And the neurologist may first use drugs that control the symptoms of MS to treat the patient's MS; These drugs slow down the course of your disease and prevent early attacks. In fact, MS disease occurs when your immune system (the immune system is the system that fights against microbes in your body) attacks the myelin sheath and your nerves and causes the destruction of this shell. Thus, to treat MS, it is necessary to weaken the immune system to stop attacking the myelin sheath. That's exactly what symptom control medications do. By counteracting your immune system, these drugs can weaken it for repeated attacks. Medicines that control MS symptoms are used as subcutaneous injections or intramuscular injections. Sometimes this injection may make your skin itchy, red, or inflamed.

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