

## Systematic examination of neurological problems such as Guillain-Barré and myasthenia gravis in children and adults involved in infection with the help of radiological and pharmaceutical techniques

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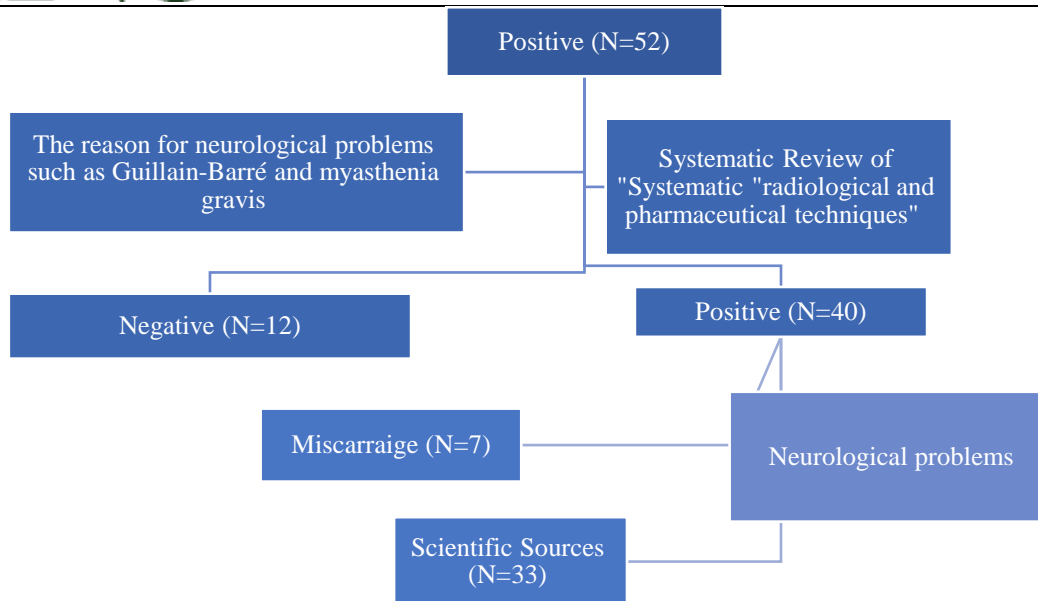
### Abstract

In the present study, a systematic investigation of neurological problems such as Guillain-Barré and myasthenia gravis in children and adults involved in infection with the help of radiological and pharmaceutical techniques has been done. This disease is in the category of autoimmune diseases, which is associated with acute nerve and muscle failure. The results of the present study show that among the first and most obvious signs and symptoms of Guillain-Barre syndrome are the tingling in the legs and the presence of weakness in them. In acute cases, these problems gradually cause paralysis of the whole body. These symptoms can have an upward trend for 2 to 4 weeks. Myasthenia gravis, whose name is composed of two words, myasthenia, which means muscle weakness, and gravis, which means heavy or severe, is an autoimmune disorder in which the body's defense system attacks its own tissues and causes muscle weakness of varying degrees in people. and it is difficult to recognize. The results of the present study indicate that in myasthenia gravis, the immune system produces antibodies that block and destroy many of the neurotransmitter receptor sites called acetylcholine. By reducing the number of available receptor sites, the muscles receive fewer nerve signals, resulting in weakness. Antibodies also block the action of a protein called tyrosine kinase, which is a muscle-specific receptor. This protein plays a role in the formation of the neuromuscular junction. Antibodies that disrupt this protein can lead to myasthenia gravis.

**Key words:** Guillain-Barré, myasthenia gravis, infection, radiology and drug techniques, nerve signal.

### Introduction

Disorders that affect the brain, spinal cord, and nerves are called neurological disorders [1]. The most common symptoms of neurological disorders include all types of pain [2], including headache and back pain. Disruption in the entire nervous system or a part of it can lead to several symptoms [3]. Because the nervous system controls various functions of the body. The proper functioning of muscles, skin sensation, special senses (sight, taste, smell and hearing) and other senses depend on the nervous system [4]. Therefore, neurological symptoms can include muscle weakness or lack of coordination, abnormal sensations in the skin, and impaired vision, taste, smell, and hearing. In addition, neurological disorders can interfere with a person's sleep. Neurological symptoms may be minor, such as tingling in the legs, or dangerous and serious, such as coma due to a stroke [5]. Symptoms can include all types of pain and affect muscle function, sensation, special senses (sight, taste, smell, and hearing), sleep, awareness, and mental function (Figure 1).



**Figure 1. Flow chart of included subjects**

## You are in Guaris

Myasthenia gravis with the symbol MG in neurology is a type of muscle paralysis caused by immune activity against acetylcholine receptor proteins in the neuromuscular synapse [6-8]. This disease is specific to the end plates of the striated muscles, which affects mostly women. Its maximum prevalence is in the third or fourth decades of life [9-11], but it can be seen in any period of life from childhood to old age. Of course, in elderly people, men and women are equally affected. The symptom of myasthenia gravis is muscle weakness that increases during activity and decreases during rest. Eye control, eyelid movement, facial expression, chewing, speaking, and swallowing are often impaired [12]. Also, the respiratory muscles and the muscles of the lower parts of the body may also be affected. Although myasthenia gravis can affect any voluntary muscle, it most commonly affects the muscles that control the eyes, swallowing, eyelid movement, and facial expression [13]. These symptoms are often not immediately diagnosed as myasthenia gravis, and the diagnosis of this disease may take more than a year. In most cases, the first symptom of the disease is the weakness of the eye muscles, which also causes double vision. In other cases, difficulty in swallowing or speaking disorder may be the first signs of this disease. The degree of intensity and weakness of the muscles involved in myasthenia gravis has major differences between different patients, which ranges from a point or limited to the eye muscles (ocular myasthenia) to a major part of the muscles [1], sometimes including the respiratory muscles, in severe cases. In critical myasthenia gravis, the disease may lead to limb paralysis. In myasthenia gravis, there appears to be an immunological response against one or more proteins of the neuromuscular junction [14]. Therefore, in connective tissue diseases such as rheumatoid arthritis and lupus, this disease occurs more frequently [15].

## Guillain-Barre syndrome diagnosis criteria:

There are two main criteria that must be present to diagnose this syndrome. Contains:

- ❖ **Progressive weakness of the legs and arms:** in the classic form, it starts from the legs and goes up, but sometimes it starts from the arms and is downward. In the early stages of the disease, there may be asymmetric weakness, but in the establishment phase of the disease, it is definitely symmetrical. In case of asymmetry in the establishment phase, the diagnosis should be doubted.
- ❖ **Areflexia:** loss of tendon reflexes is one of the prominent points in the diagnosis of Guillain-Barre syndrome. Exceptionally, reflexes may remain in the early stages of the disease. Reflexes remain in the autonomic pandis form, which is one of the exceptions [16].

There are other clinical manifestations that help in the diagnosis of this syndrome:

- ❖ The progression of the disease is within a few days to 4 weeks. If the symptoms progress after 4 weeks, it is probably not Guillain-Barré.
- ❖ Weakness is almost symmetrical.
- ❖ There are sensory signs and symptoms, but they are not prominent, and what the patient complains about and refers to because of it is motor weakness [17].
- ❖ There is cranial nerve involvement. Up to 50% of cases, fascial involvement may be seen (especially the bilateral form of fascial involvement).
- ❖ Normally, within 2-4 weeks after the establishment of the disease, the recovery period begins. Usually, the disease has an ascending course of 2 weeks, a plateau period of 2-4 weeks, and then a recovery period.
- ❖ Findings of autonomic involvement are common and important. Hypo and hypertension may occur. Tachycardia is also common and fatal bradycardia may occur.
- ❖ The onset of fever at the beginning of the disease is inconsistent with the diagnosis of Guillain-Barré syndrome. Of course, in 75-80% of cases, there is a prodrome with fever. But at the time of the onset of this syndrome, the initial prodrome disease has improved [18].

Other neuropathies such as porphyria, arsenic poisoning, organophosphate poisoning may also cause acute flaccid paralysis. The difference between them and Guillain-Barré syndrome is that in Guillain-Barré syndrome there is a prodromal disease. Also, the proprioceptive disorder that is common and severe in Guillain-Barré is usually not seen in other neuropathies. Guillain-Barré type (it is demyelinating and other neuropathies are usually axonal type. Therefore, their NCS findings are also different) [19].

Botulism can be mentioned among the fatal neuromuscular disorders. In botulism, by inhibiting calcium channels in the presynaptic part of the neuromuscular junction, the resulting toxin inhibits the release of acetylcholine and causes acute flaccid paralysis [20].

Usually, there is a history of consuming canned food in this disease. However, sometimes this record is not obtained. In botulism, autonomic disorders are very common and usually start from the eyes. These patients never experience complete areflexia [21].

The most common cause of myopathy in emergency is hypokalemia. Blood potassium should be checked in every patient with acute flaccid paralysis. These patients usually have a history of previous attacks as well as a family history. Sometimes it may be the first attack (first and third decade of life). Usually, after consuming a starchy meal and resting after that, the patient is unable to get up. In myopathies, there is no areflexia despite the obvious weakness [22]. Two points are important.

1- Spectral disorder is not common and severe in Guillain-Barré, but urinary and fecal incontinence is complete in spinal shock [23].

2- The patient with spinal disorder has a distinct sensory level, the upper and lower areas of this level are completely different from each other. This situation does not exist in Guillain-Barré [24].

## Discussion

Research shows that the coronavirus can cause neuromuscular disorders in people who have no previous history. In addition, the virus can cause exacerbation of symptoms in patients with existing disorders and patients undergoing immunotherapy [25].

## Symptoms of myasthenia gravis

Having this condition is associated with signs and symptoms. At the beginning of the disease, the muscles are gradually weakened and aggravated by performing activities during the day. At the beginning of the disease [26], this muscle weakness is usually less at the beginning of the day and becomes worse at night [27]. Weakness and failure of each muscle leads to many hardships and problems.

**1- Weakness of the eye muscles:** In most people with the problem of weakening the eye muscles, the muscles around the eyes are weakened and cause problems such as double vision and drooping eyelids in people. By doing things like watching TV [28], driving, and studying, these muscles become weaker and cause more problems. To reduce the damage caused by these activities, using sunglasses can be a good option [29].

**2- Weakness of the throat muscles and difficulty in swallowing:** With the weakening of the swallowing muscles, there are problems in swallowing food. In this way, a person has difficulty in swallowing food

completely and correctly [30]. That is, by trying to swallow food, some of it remains in the mouth, or instead of food and drinks entering the throat, it enters the nose [31].

**3- Weakness of facial muscles and difficulty in speaking:** Weakening of facial muscles and internal mouth muscles causes problems in speech and speaking [32]. With damage to the muscles of the face and mouth, the ability to speak in a person with the disease is reduced and his speech becomes unintelligible, slow and nasal [33]. Sometimes, due to the weakness of this muscle, it becomes difficult to chew and even close the mouth, and the facial expression always becomes sad and uncomfortable [34].

**4- Weakness of the head and neck muscles:** the weakening of the head and neck muscles sometimes causes the head to droop and the inability to maintain it properly [35]. That is, with the weakening of the neck muscles, the head falls forward or on both sides of the body and the neck cannot hold it on the body.

### **The role of the thymus gland in the occurrence of myasthenia gravis disease**

The thymus gland is located above the chest and plays an important role in the development of the immune system early in life [36]. The cells of this gland are part of the body's immune system. This gland is large in infants and grows until puberty and then shrinks. In adults with myasthenia gravis, the thymus gland is abnormal and contains specific clusters of immune cells that indicate lymphoid hyperplasia [37]. Lymphatic hyperplasia is a disease that is found in the spleen and lymph nodes during the body's immune response. In some people with myasthenia gravis [38], the thymus gland grows or a thymus tumor develops. These tumors are benign, but can become malignant. The link between the thymus gland and myasthenia gravis is still unclear [39], but scientists believe that the thymus gland may give developing immune cells the wrong instructions, causing autoimmune disease and setting the stage for an attack on neuromuscular neurotransmitters [40].

### **Symptoms of myasthenia gravis**

The symptom of myasthenia gravis is muscle weakness that increases during activity and decreases during rest, eye control, eyelid movement, facial expression [41], chewing, speaking and swallowing are often impaired. Also, the respiratory muscles and the muscles of the lower parts of the body may be affected. Although myasthenia gravis can affect any voluntary muscle [42], it most affects the muscles that control the eyes, swallowing, eyelid movement, and facial expression. Symptoms are often not immediately recognized as myasthenia gravis [43]. The diagnosis of this disease may take more than a year. In most cases, the first symptom of the disease is the weakness of the eye muscles, which also causes double vision. In other cases, difficulty in swallowing or speaking disorder may be the first signs of this disease.

### **People at risk of myasthenia gravis**

- ❖ It is mostly seen in women under 40 years and men over 60 years.
- ❖ Neonatal myasthenia gravis is temporary and transient and the symptoms disappear within 2 to 3 months after birth [44].
- ❖ Myasthenia gravis is also common among teenagers. This disease is not hereditary or contagious. Rarely, children show congenital symptoms of this disease.

To sum up, Myasthenia gravis is considered an autoimmune disease [45]. That is, the immune system becomes excessive in its function and by secreting antibodies against nerve-to-muscle receptors, it creates a disturbance in the transmission of messages from nerves to muscles. This disease is one of the groups of neuromuscular junction diseases [46]. In myasthenia gravis disease, there is a problem in the connection between the nerve terminal and the muscle. In order for the muscle to be stimulated and do something, a message from the nerves must reach it. Nerve endings release chemical substances and these substances cause the command in the muscle or in other words, the contraction of the muscle [47]. In this disease, for unknown reasons, the body's immune system secretes antibodies that affect only the nerve-to-muscle receptors and destroy them [48]. The scientists of the University of Medical Sciences in Iran studied 91 children diagnosed with Guillain-Barre syndrome (under 15 years old) in terms of respiratory failure. 13 patients (14.4%) needed mechanical ventilation. Clinical, electrodiagnostic and laboratory characteristics of patients in the respiratory failure group were compared with the group without respiratory failure [49]. Progression to respiratory failure was more common in younger children ( $p < 0.001$ ), children with cranial nerve involvement ( $p < 0.034$ ) and absence of upper limb tendon reflexes ( $p = 0.04$ ). Lack of production of motor unit action potentials with ( $p < 0.009$ ) and spontaneous potentials ( $p < 0.0001$ ) and a drop of more than 80% in the range of motor waves in the investigation of nerve conduction with ( $p < 0.0001$ ), a significant relationship they had respiratory failure [50].

### **Causes of myasthenia gravis**

As mentioned, this disease occurs due to a disorder in the body's immune system and weakens the voluntary muscles [50].

### There are different causes of this disease

**1- Antibody and nerve receptors:** neurotransmitters exist in the part of nerve cell receptors in the body. In suffering from this disease [51], some parts of the nerve cell receptor are blocked or destroyed. So, the connection between muscle and nerve is lost [52]. In this disease, antibodies are produced that destroy or block acetylcholine, which is a nerve receptor in the nerve-muscle junction [53]. As a result, as a result of this destruction [54], the coordination between the members is lost and the ability to move in them faces a problem [55].

**2- Thymus Gland:** Part of the body's immune system is formed by the thymus gland. The thymus gland is located in the upper part under the breastbone [56]. Based on research, the thymus gland stimulates or produces antibodies that block acetylcholine (neuronal receptor) [57]. This gland is large at the beginning of the baby's birth and its size decreases with age, but in adults with myasthenia gravis [58], the size of the thymus gland is large [59].

**3- Other causes of myasthenia gravis disease:** This disease is a disease that does not have the power to spread to other people [60]. Likewise, the probability of contracting it through heredity is very small, but in case of transmission of the disease from the pregnant mother to the child, if the baby is treated immediately after birth, it is usually treated until the age of two months and no trace of the disease remains in them [61].

### Factors that aggravate the disease

At the time of contracting this disease, some factors such as fatigue, contracting some diseases and also medicines, not having enough rest and being active during the day [62], pregnancy, surgeries, imbalanced blood pressure and other such factors cause exacerbation and the disease worsens [63].

### How to diagnose myasthenia gravis

Diagnosing myasthenia gravis disease is difficult especially in people who have just started the disease and have few symptoms [64], but in general, there are different ways and methods to identify and diagnose this disease [65].

**1- Examination by a doctor:** In this method, the doctor checks the patient and all his symptoms related to this disease. In this way, all the muscles of the eye, face and muscle disorders are examined [66].

**2- Prescribing a blood test:** by performing a blood test, blood changes and the level of antibodies in the blood, which are usually very high in infected people, as well as other features related to the disease are examined in the blood test [67].

### Prevention of myasthenia gravis

Just as the cause of this disease is not known, the ways to prevent it and try not to get it are still not known. This disease is not a common disease and its incidence is very low [68].

### Treatment of myasthenia gravis

Myasthenia gravis has the ability to be controlled and treated well, and it can be controlled to a great extent by performing methods and reduce the symptoms [69].

**1- Drug treatment:** using drugs that control the disease and increase the amount of acetylcholine in the blood, which strengthens the connection from the nerve to the muscle [70], strengthens the muscles and prevents them from being destroyed [71].

**2- Surgery:** When the cause of the disease is the tumor gland, it is treated by removing this gland completely or removing the tumor part of the gland [72].

**3- Plasma exchange:** The plasma in the blood contains a large number of antibodies [73]. Antibodies in the blood are separated by performing plasma milling and the blood plasma without antibodies is returned to the body. In this method, the disease in the person is temporarily treated [74].

**Is myasthenia gravis dangerous?** Gravis disease can be controlled and tried not to progress, but if the disease progresses and is not treated, it can be life-threatening [75].

**What people are susceptible to gravis?** The possibility of contracting this disease is possible in all people and in all age groups, but it has been seen more in women under 40 years and men over 50 years [76].

**Can myasthenia gravis be treated?** This disease cannot be cured definitively, but it can be prevented by taking measures [77].

**Table 1. Forest Plot Investigating the Relationship between Neurological and Cardiovascular Diseases in Young People and Children with Infection and Blood Pressure**

Raw	Study	Year		Proportion	Wight 98%	Weight %
1	Abolmaali et al.	2022		0.64	[0.11 – 1.72]	3.02
2	Ahmad et al.	2022		0.52	[0.42 – 2.11]	4.00
3	Bauer et al	2022		0.96	[0.44 – 1.02]	6.32
4	Burakgazi et al	2022		0.65	[0.25 – 0.98]	5.12
<b>Heterogeneity <math>t^2=0.00</math>, <math>I^2= 0.00</math>, <math>H^2=0.9</math></b>				0.55	[0.34 – 0.58]	
<b>Test of <math>\Theta= \Theta</math>, <math>Q (4) =3.45</math>, <math>P= 0.77</math></b>						
1	Cegolon et al.	2022		0.56	[0.11 – 0.66]	1.55
2	Farina et al.	2022		0.66	[0.15 – 0.48]	4.33
3	Finsterer et al.	2022		0.48	[0.19 – 0.55]	6.77
4	Fragoso-Saavedra et al.	2022		0.64	[0.17 – 0.29]	3.03
<b>Heterogeneity <math>t^2=0.05</math>, <math>I^2= 0.07</math>, <math>H^2=0.78</math></b>				0.82	[0.03 – 0.32]	
<b>Test of <math>\Theta= \Theta</math>, <math>Q (4) =3.01</math>, <math>P= 0.11</math></b>						
1	Ginikopoulou et al.	2022		0.97	[0.39 – 1.06]	3.11
2	Hanson et al.	2022		0.95	[0.54 – 1.02]	6.05
3	Jacob et al.	2022		0.43	[0.63 – 1.01]	4.06
4	Lee et al.	2022		0.51	[0.25 – 1.08]	7.03
<b>Heterogeneity <math>t^2=0.12</math>, <math>I^2= 0.01</math>, <math>H^2=0.99</math></b>				0.68	[0.22 – 1.07]	
<b>Test of <math>\Theta= \Theta</math>, <math>Q (4) =1.45</math>, <math>P= 0.14</math></b>						
1	Lupica et al.	2022		0.84	[0.27 – 1.08]	6.08
2	Marcec et al.	2022		0.76	[0.52 – 0.22]	5.82
3	McAlpine et al.	2022		0.11	[0.54 – 0.89]	5.85
4	Pimentel et al.	2022		0.39	[0.12 – 0.99]	6.09
<b>Heterogeneity <math>t^2=0.21</math>, <math>I^2= 0.04</math>, <math>H^2=0.39</math></b>				0.77	[0.19 – 1.00]	
<b>Test of <math>\Theta= \Theta</math>, <math>Q (4) =3.35</math>, <math>P= 0.34</math></b>						

## Conclusion

The results of this study show that Guillain-Barré syndrome (GBS) is caused in a number of cases by autoantibodies that are created through microbial molecular mimicry. Also, there is a large discrepancy between the tissue distribution of ganglioside antigen and the disease phenotype. Results have also shown that, based on



serological reactions with single ganglioside or glycolipid species, some GBS-associated autoantibodies may only bind to ganglioside complexes (GSC). The results of our study showed that it may be difficult to diagnose myasthenia gravis. Because it can be difficult to distinguish between normal changes and neurological disorders caused by it. Ceramic test is a diagnostic test that compares sensitivity to Tensilon test. The cold test is an option for patients with heart disease or asthma that may have contraindications for delphinium use. In this test, an ice pack is kept on the patient's eyes for one minute. Drooping eyelid should be temporarily removed in a patient with myasthenia gravis.

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