

Overview On Classical And Current Treatment Approach Towards Acute Inflammatory Demyelinating Polyneuropathy (Aidp) (*Guillain-Barre Syndrome*)

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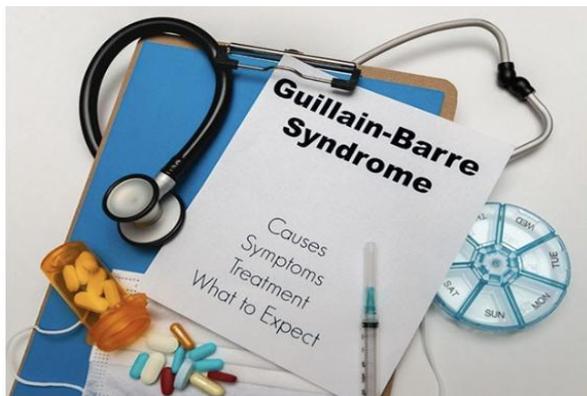
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Abstract: Guillain - Barre syndrome is a autoimmune disease caused when the B cells produce antigens to destroy the pathogen, but the antigens inturn affect the nerves as the pathogens antibody and the nerves proteins resemble each other . The patients of GB syndrome have reported having gastroenteritis (swelling in stomach or intestine - due to pathogen) the symptoms peak in 3-4 weeks and recovery last from months to year. Most of the patients are recovered completely, 15% are left with some neurological disabilities and 5 % of the patients death is seen. GB syndrome can be treated in classical ways using Chinese , Western, Ayurveda, Homeopathy practices and when it comes to current treatment; plasma exchange therapy and immunoglobulin therapy are used . There are investigations stating some COVID-19 patients are showing symptoms of GBS and are more severe than NON-COVID GBS condition.

Keywords: GB Syndrome, C.jejuni, lumbar puncture, nerve conduction, antigangliosides antibodies, plasma exchange therapy , immunoglobulin therapy, COVID GBS, NON-COVID GBS

I. INTRODUCTION (HEADING 1)



GB syndrome is acute paralytic polyneuropathy that is an Acute Inflammatory Demyelinating Polyneuropathy (AIDP) , which is an autoimmune process characterized by progressive reflexes weakness and mild sensory changes. It mainly affect the peripheral nervous system .

It is a weakness caused to the body which starts from feet and symmetrically ascends towards the knee and effects the hand till the elbow. It causes sensory neuropathy that is loss of sensation through out the body ,there is reduced reflex because it is peripheral neuropathy. GB syndrome can be triggered by *Campylobacter jejuni*, *Cytomegalovirus*, *Epstein-BARR virus* etc. The pathophysiology involved in GB syndrome is MOLECULAR MIMICRY i.e. when the infectious agents responsible for infections induces similar activity as that of self proteins which triggers or activates the T and B cells due to foreign antigen. When a pathogen attacks

the B cells produce antibody which attacks the antigen present in the pathogen and degenerates it ,some times the B cells produce excess of antibodies which attack The protein present on myelin sheath of motor nerve or nerve axon which is similar to the antigen Of the pathogen causing neuropathy .(1)

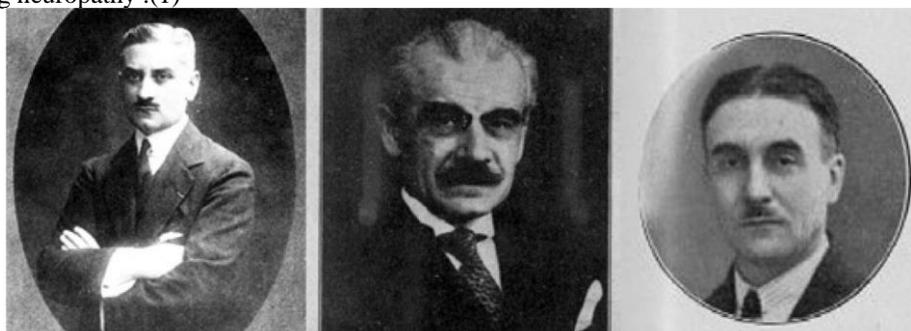


Fig 2. Guillain ,Barre and Strohl defined the GB Syndrome(13)

II. HISTORY:

GB syndrome was identified in 1859, when a patient named Jean Baptist Octave Landry was diagnosed with “acute ascending paralysis “. In his medical report the mentioned condition was named after his name “Landry ascending paralysis”-this name was given to describe sub-acute ascending peripheral , sensory and motor dysfunction. The symptoms and the condition were described , but its cause and progression of the disease were not found till mid nineteenth century and early twentieth century by

neurologist. The focus was on curing the symptoms and differentiating the symptoms from other disease. However, in 1916 Guillain ,Barre and Strohl published a paper that defined the disease for the next upcoming years . Initially it was known as Landry- Guillain - Barre - Strohl syndrome and later it as Guillain - barre syndrome (GBS).(2)

III. EPIDEMIOLOGY:

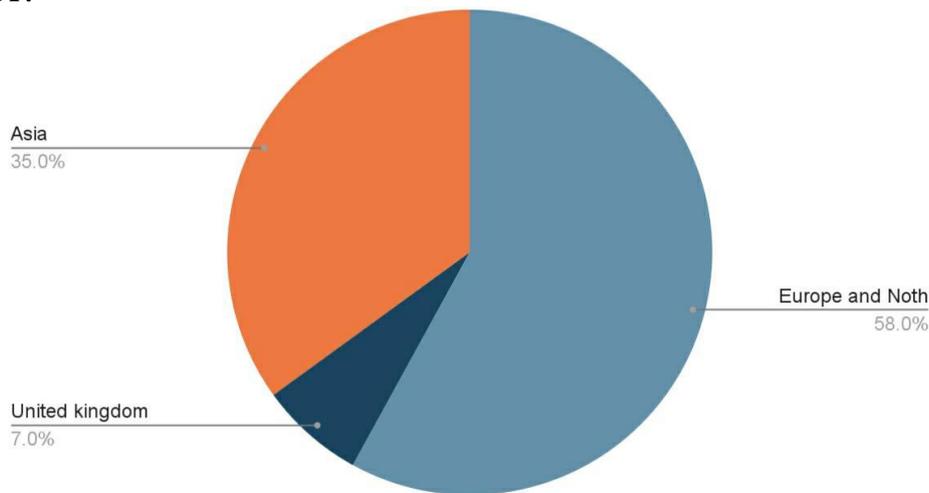


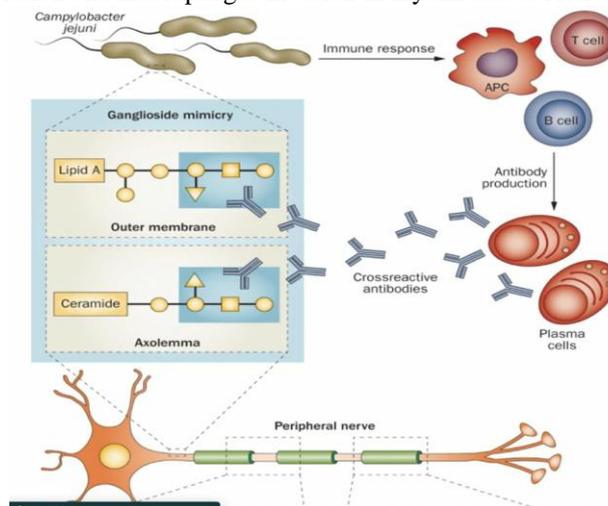
Fig 3. Percentage of people having GBS in Asia, UK, Europe and North America

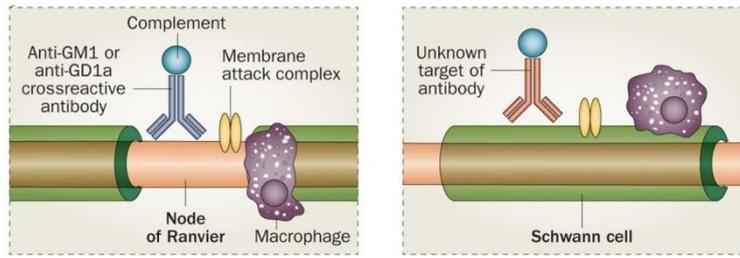
GB syndrome is a rare disease with an occurrence of 0.81-1.89 percentage in one lakh people. It commonly occurs in men compared to women, GB syndrome occurs less frequently in children that is 0.34-1.34 percent in one lakh compared to adults . The occurrence of GB syndrome increase with age .The proportion of patients with GB syndrome have AIDP(acute inflammatory demyelinating polyneuropathy) and AMAN(acute motor axonal neuropathy) are more around the world. The percentage of people having GB syndrome having AIDP is 60-80% in Europe and North America , and the percentage of people having GB syndrome having AMAN ranges 6-7% in united kingdom and Spain to 30-60% in Asia. The geographical diversity is possibly one of the main cause for this disease . Due to variation in geographical location there is variation in genetics and infection that triggers GB syndrome. World wide there is 1.3 percent cases per one lakh people. GB Syndrome was common in the 5th decade in western countries, but in India it occurs more commonly at a younger age .(3.1-3.3)

IV. PATHOGENESIS:

GB syndrome is post infectious disorder, where respiratory and Gastrointestinal tract symptoms were observed and in some patients with GB syndrome have a specific type of infection of *C.jejuni*. *C.jejuni* is one of the least causing agent. There were several other pathogens that were responsible for GB syndrome namely:- *Cytomegalo virus*, *Haemophilus influenzae*, *Epsteil-barr virus*, *Mycoplasma pneumonia*. Antibodies that cross react with various gangliosides have be seen in patients with GB syndrome. The infection due to *C.jejuni* produces antibodies which reacts with gangliosides, cross reactive antibodies are produced in some individuals. There are only some *C.jejuni* strains that contain lipo-oligosaccharide that is similar to carbohydrate component of gangliosides of human peripheral nerves. The specific *C.jejuni* variant i.e. THr51 is the reason for GBS. *C.jejuni* is responsible for activating immune and autoimmune reactions which leads to dysfunction of nerves and produces symptoms of GB syndrome.

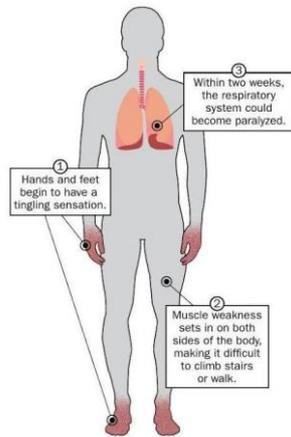
The produced antibodies that cross react with gangliosides is transported by lipo-oligosaccharide (GM1 and GD1) which is present on the outer membrane of *C.jejuni*. The antigens which are Attacked in acute motor axonal neuropathy are located in node of Ranvier. Nodal Axolemma is binded by anti-GM1 and anti-GD1a antibodies, which leads to activation and production of MAC(Membrane attacking complex) on the outer surface of Schwann cells, due to this there is a damage Leading to detachment of paranodal myelin and failure in nerve conduction. Periaxonal spaces is Invaded by macrophages from nodes by removing injured axons. The antigens Targeted in acute inflammatory demyelinating polyneuropathy are located on myelin sheath. The Formation of MAC leads to vesicular degeneration and macrophages invasion in myelin due to Activation by antibodies. (3.1-3.1)





V. SYMPTOMS:

- GB syndrome starts with tingling and weakness starting from feet and leg and spread to upper body and arms. Untreated GB syndrome having muscle weakness can turn into paralysis .
- Unsteady walking or inability to walk or climb stairs.
- Double vision or inability to move the eyes.
- There is a rapid heart beat .
- There is difficulty in breathing .
- There is low or high blood pressure.
- Difficulty in bowel function and bladder control.
- Severe pain that may feel achy, shooting or cramp
- Difficulty with facial movements including speaking ,chewing or swallowing .(4).



VI. DIAGNOSIS AND SCREENING OF GBS:

The diagnosis of GBS is quite difficult because the symptoms caused by this disease are similar to other diseases. The following methods are carried out to diagnose the disease:-

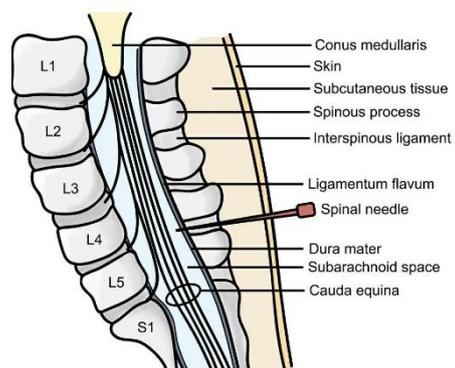
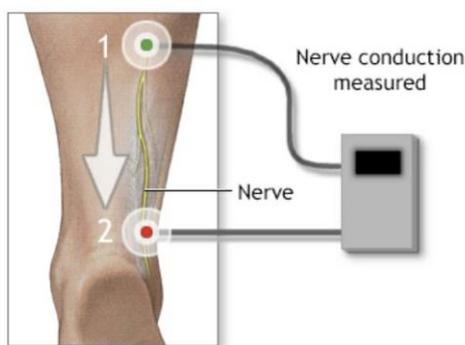
Lumbar puncture:- in this process the needle is inserted in the lower region of spine i.e. the lumbar region and the cerebrospinal fluid was collected and analyzed. According to analysis if the Protein level in the fluid is elevated than the normal range one can suspect GBS. Also the differential diagnoses should be considered, such as leptomenigeal malignancy, lymphoma, HIV polyneuropathy and poliomyelitis for further confirmation.

Nerve conduction studies:- It is a clinical diagnosis which helps in differentiating demyelinating and axonal types of GBS. In this procedure, the electric currents are subjected to the electrodes placed onto the skin and checked for the time duration of transmission of the signals. For the GBS suspected patients, if the signals are not traveling appropriately they are considered to be diagnosed with GBS. This impaired transmission of signals are due to antiganglioside antibodies.

Antiganglioside antibodies test: This test involves the presence or absence of antiganglioside antibodies. The person with GBS shows positive to the presence of these antibodies. This is how they are diagnosed with GBS. With the recent investigations MRI and nerve ultrasound are found to be potential diagnosis tool. (5.1-5.3).

Fig: 6 Nerve conduction studies.(11.2)

Fig 7: Lumbar Puncture(11)



VII. CLASSICAL TREATMENT OF GB SYNDROME :

Integrated medicines of Chinese and western classical system is used for treatment of GBS.

It was found that traditional **Chinese medicine** provided better improvement of the disease by improving the motor nerve conduction functions. It has shown several uses in demyelinating, autoimmune neuronal disorders etc. They also observed improvement in facial paralysis, decrease in numbness in peripheral nerves. The method they followed were acupuncture treatments which helped the recovery if their muscular functions to a greater extent. With further advancements the acupuncture was made electrical for easy treatment.

The **western treatments**, the patients were asked to bed rest and the patients limbs were placed in appropriate functional position. It was observed there were improvement in heart, gastro and lung functions. Incase there abnormalities were observed they were symptomatic treatments was carried out.

In **homeopathy system** of medicines, the altering of immune system was observed which improved the reduced muscle tone.

In **Ayurveda**, GBS symptoms resembled a condition called sarvanga vatavyadhi in which speech abnormalities, pining sensations, motor function abnormalities and sever pain were the symptoms which were treated with panchakarma practices. The recent findings of case study involving a 46 year old man was completely paralyzed and he was not able to walk, stand, sit or talk properly. After consulting several practitioners and hospitals which showed no effective result to his problem he resorted to Ayurvedic treatment. After several investigations by nerve conduction studies and electromyelogram, he was diagnosed with GBS. Before admitting in hospital, he had fever which did not subside with local medications. After sometime gradually there was weakness in lower limbs which progressed to upper limbs (mamsanahasrotovikrti). The muscle tone and reflex was reduced, abnormal speech(astanidhpariksa) were developed in that individual. The Ayurvedic treatment involved application of candanabalakaditailam downwards for 10 minutes, an ayurvedic paste applied in circular movements, sesame oil enema was given alternating days which leads to improvement in clinical condition. Clinically Ayurveda showed the beneficial results by recovering the motor functions completely within few months to years. Ayurveda treatment can be considered as a alternative treatment at a cheap price compared to expensive IVIG therapy.(6.1-6.3).

VIII. TREATMENT:

There is no treatment or cure for GB syndrome but there are certain clinical therapies which can reduce the risk of the disease and also reduce the recovery time of GB patients. Among the several methods of treating the disease, initially the patients with GBS is admitted in ICU.

At present there are 2 treatments which are used to block the damage of nerves immune related disorder, namely; plasma exchange / plasmapheresis and immunoglobulin therapy.

These therapies are started with in two weeks of symptoms observed in GBS patients for effective Treatment.

Plasma exchange therapy:- This therapy is best used for the disease whose etiology or the cause is autoimmune. It is a procedure in which the infected plasma of GBS patients exchanged with the healthy plasma. In this, the blood is withdrawn from the GBS patient and separated into its components i.e. RBC, WBC, platelets and Plasma. The plasma is removed and exchanged while the blood cells are put back through blood infusion using replacement fluid. The analysis was done based on calculation of apheresis, exchange volume etc. This leads to reduction in the severity of the disease.

Immunoglobulin therapy:- This is the commonly used treatment to patients with GBS. GBS produces harmful antibodies due to infection. Therefore in this therapy the healthy antibodies from donated healthy blood is injected directly into the veins of patient which blocks the proliferation of harmful infected antibodies responsible for causing GB syndrome. By this therapy it was observed that attack by immune system on nervous system was reduced, also there was reduction in recovery time.

Another therapy includes medication of steroids (anti-inflammatory steroids) i.e. corticosteroid which reduces the risk of GBS by reducing inflammation in nerves. Although not all steroids are used for treatment.(7.1-7.3).

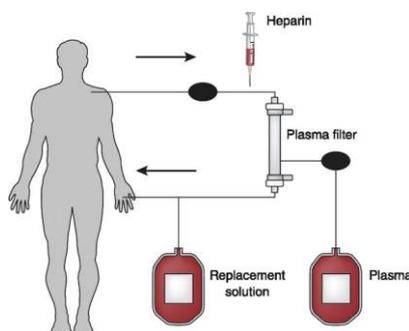


Fig 8: Plasma exchange therapy (15).

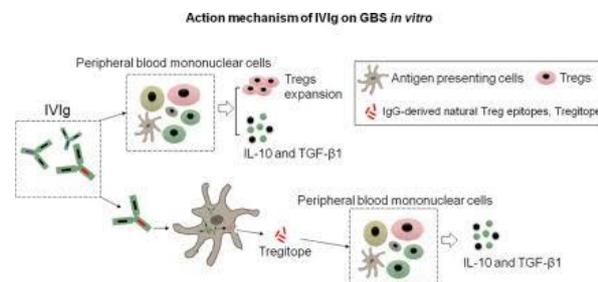


Fig 9: Intravenous immunoglobulin therapy

IX. PROS AND CONS OF CURRENT TREATMENT OF GBS

Immunoglobulin therapy which includes the injecting the immunoglobulin through intravenous have found to have several consequences. Few among them are; allergies, slight fever, pain in muscles and joints, headaches just after injecting, tight feeling in chest etc. It was also found in later stages That the standard does of IVIG i.e.2g/kg was not sufficient enough to produce effective results in GBS patients, as it lead to continual deterioration in number of GBS patients over a period of time After improvement in the initial stage. It shows irregularities related treatment where the force of muscle improves when IVIG was given at repeated dose.

It also showed the IgG level variation in serum where a low increase in IgG level in serum after standard dose lead to slow recovery and worsened the prognosis. However it showed better activity in severe GBS patients and not for mildly affected patients. This treatment is contradicting for patients with improper renal functions, IgA antibodies etc.

Plasma exchange which work by replacing the affected antibodies with effective antibodies may lead to development of newly induced infections, lead to hypertension, irregular heart rate either low or high, more chances of relapse of syndrome after a year in some cases was known and probability in loss of muscle functions for a week. Contradicting action shown with coagulopathy, thrombocytopenia and instable hemodynamic. However there were more advantages observed with this treatment like increase in walking ability with aid, motor recovery time was shorter. Both the treatments were quite expensive for any average income individual. (8.1-8.4).

X. LONG TERM OUT LOOK FOR THOSE WITH GB SYNDROME:

The full recovery in the GB syndrome patients is seen in most of the patients but recovery may be Little slow and tedious it can take few weeks to few years. In few patients, after few years the Symptoms were observed again.

The long term problems associated with GBS may be: weakness in legs face and hands is observed, unable to walk without the aid, pinning sensation, tingling sensation or pain and numbness, imbalanced and uncoordinated *movements*, fatigue etc.

For the lookout of those with GBS for long term can be associated with supportive help from,

A **Counselor**:- GB syndrome patients not just face physical difficulties but also have emotional painful times. Some individuals needs psychological counselling to help them from Emotional difficulties

A **Physiotherapist**:- who helps in muscular movements.

A **Speech therapist**:- who renders help with swallowing and communication associated problems.(9)

XI. IMPACT OF COVID-19 ON GUILLAIN – BARRE SYNDROME (GBS):

GBS being an acute acquired auto-immune disorder of peripheral nerves usually occurs after an infection. Although the mechanism of GBS production in COVID patients is not yet investigated, it's assumed that COVID-19 stimulates inflammatory cells which further produces inflammatory cytokines. The over all process is immune mediated which there by mimics auto immune disorder and leads to neurological complications. The viral antigens mimics the neural antigens that leads to infections. Studies have shown that there was an increase in GBS patients post COVID-19 pandemic. As per the studies, the GBS diagnosed during the pandemic including NON-COVID-GBS patients and COVID-GBS patients had higher number of disability when compared to admission before pandemic. This neurological syndrome may occur at both post infection and para infection. COVID-GBS is predominantly demyelinating and considered to be more severe than NON-COVID-GBS.(10.1-10.3)

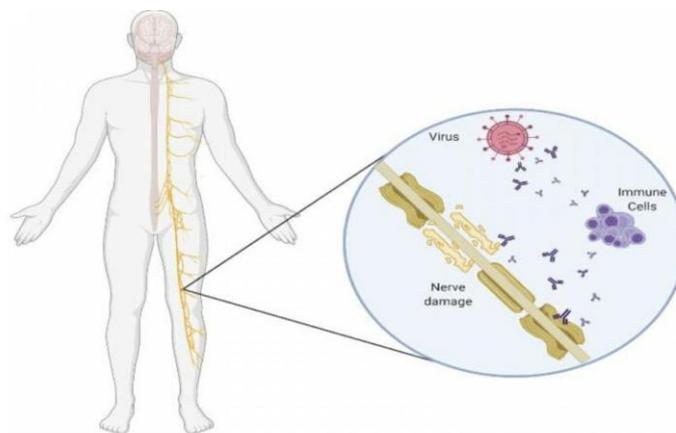


Fig 10: Viral antigens mimics the neural antigens leading to infection.(14)

XII. REFERENCE

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