

# AN OVERVIEW: GULLAIN BARRE SYNDROME (GBS) CASE STUDIES ON VIRTUE OF SARS-COV-2

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## ABSTRACT:

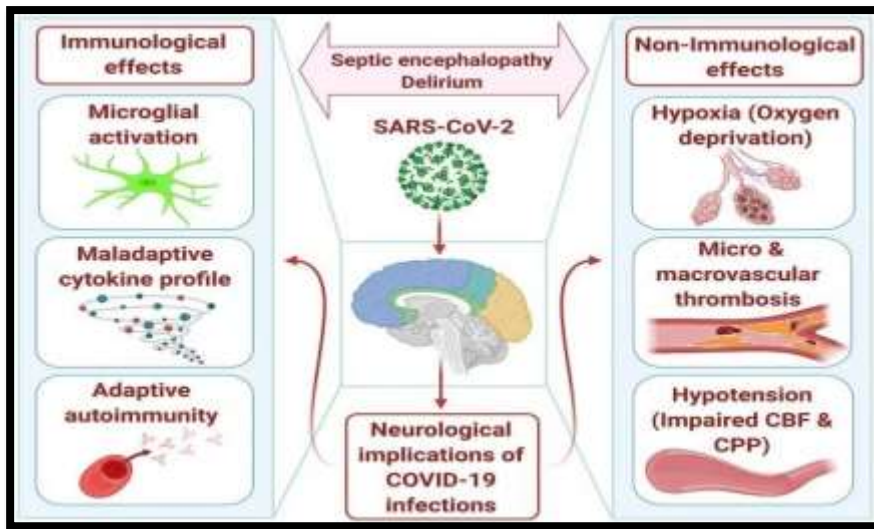
The Covid-19 pandemic continues to spread like wildfire across the globe, and it has disrupted human life, like no other event in recent history. Guillain-Barre (gee-YAH-buh-RAY) syndrome is a rare disorder in which your body's immune system attacks your nerves. Weakness and tingling in your extremities are usually the first symptoms. These sensations can quickly spread, eventually paralyzing your whole body. Among hospitalized patients, 30-80 % exhibit neurological problems. While in most patients, neurological effects are seen concurrently or within few days of the classical Covid-19 symptoms, in some they may predate or develop much later than the initial febrile illness. In this paper we overview a wide spectrum of neurological features have been observed, involving different parts of the neuro-axis, involving the central and peripheral nervous systems that is associated with Guillain Barre Syndrome in SARS-CoV-2 patients.

**KEYWORDS:** Guillain Barre Syndrome (GBS), Neuromuscular Disorders (NMD), SARS-CoV-2.

## INTRODUCTION:

Covid 19 pandemic is a major global health disorder. The first case of covid-19 is occurred in Wuhan, china and quickly spread to other countries. Covid- 19 is an enclosed RNA-virus that can be transmitted through direct exposure to infected animals, human -to- human and environmental contamination.<sup>1</sup>Covid 19 caused by the severe acute respiratory distress syndrome corona virus -2 . SAR CoV-2 is a primarily a respiratory infection as well as associated with various neurological disorder.<sup>2</sup>The neurological manifestation of the covid-19 infection are due to its effects on the CNS, PNS and skeletal muscles.<sup>3</sup>

Guillain- Barre syndrome (GBS) is inflammatory disease related to peripheral nervous system which is more frequently occurred in male than female. The clinical characteristics of GBS are weakness and sensory signs in the legs that progress to arms and cranial muscles.<sup>4</sup> Patients with GBS have increased level of protein and normal cell count in CSF. GBS is caused by aberrant immune response to infection that results in activation of immune system and damage of the nerve roots and peripheral nerves because of structural similarity of this antigen to axon and myelin. Most patients with GBS reach their symptoms peak within 4 weeks. About 18-20% of patients with GBS develops respiratory failure and requires mechanical ventilation.

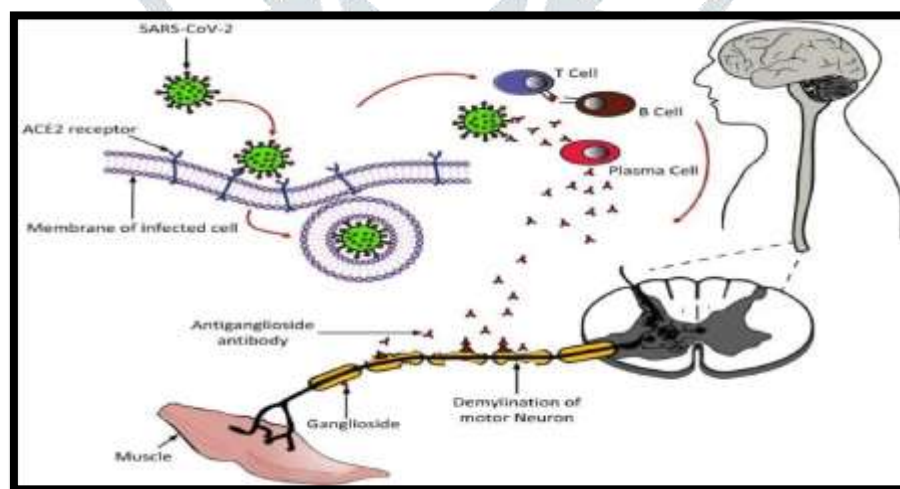


“Fig.1” Mechanism underlying neurological consequences of covid19

## PATHOPHYSIOLOGY OF GULLIAN BARRE SYNDROME:

### Neuromuscular disorder associated with Covid-19:

From February 28 through March 21, 2020, five patients who had GBS after the onset of Covid-19 were examined. During that period, an estimated 1000 to 1200 patients with Covid-19 were admitted. Interval between onset of Covid-19 and GBS symptoms ranged from 5 to 10 days. The first symptoms were lower-limb weakness in 4 patients and facial diplegia followed by ataxia and paresthesia in 1 patient. 3 patients needed mechanical ventilation.<sup>5</sup>On CSF analysis, 2 patients had a normal protein level and all the patients had normal cell count. The electrophysiology findings were generally consistent with an axonal variant in three patients and with a demyelinating process in two patients.

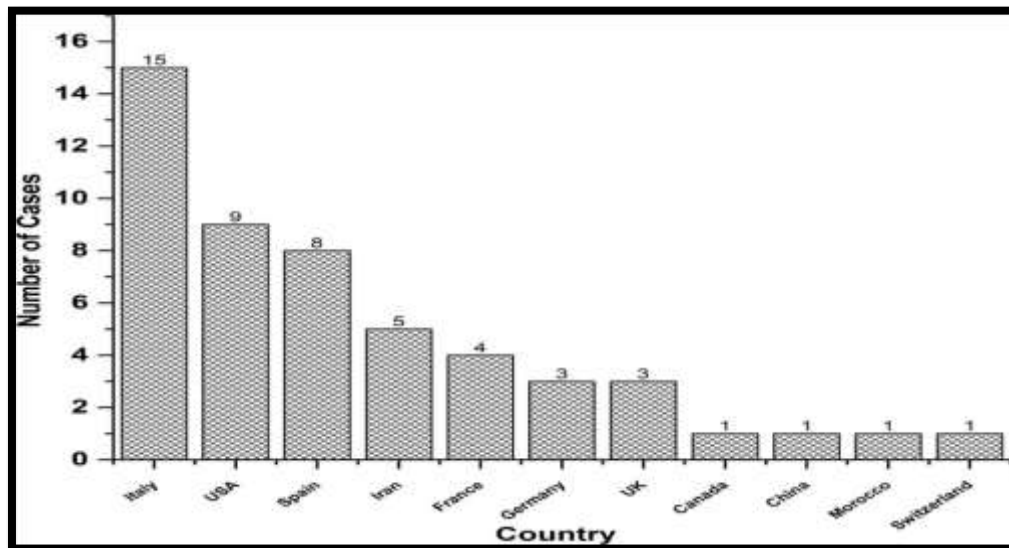


“Fig.2” schematic representation of covid 19 association with GBS

### Links between Guillain-Barré Syndrome and SARS-CoV-2 case study:

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Graph 1. World number of cases associated with Covid 19.

Table 1. Neurologic Conditions associated with SARS-CoV-2 infection

Disease entity	Presentation	Supportive Neurodiagnostic testing	Pathogenesis
<b>Encephalopathy</b>	Altered mental status	MRI: non-specific EEG: abnormal (slow) CSF: nl cells and Pro CSF SARS-CoV-2 RT-PCR: NEG	Multiple organ failure Hypoxemia Systemic Inflammation Endothelialitis
<b>Encephalitis</b>	Altered mental status and CNS dysfunction	MRI: non-specific (? WM changes) EEG: abnormal (slow, +focal) CSF: pleocytosis & elev. Pro CSF SARS-CoV-2 RT-PCR: NEG CNS Inflammation	CNS Inflammation
<b>Viral Encephalitis</b>	Altered mental status and CNS dysfunction	MRI :new abnormality EEG: abnormal (slow, +focal) CSF: Pleocytosis and elev. Pro CSF SARS-CoV-2 RT-PCR: POS Brain Tissue: POS (Ag or RNA)	Brain parenchymal Neuro-invasion

<b>Viral Meningitis</b>	Headache, nuchal rigidity	MRI: meningeal enhancement, CSF: pleocytosis & elev. Pro CSF SARS-CoV-2 RT PCR: POS	Subarachnoid invasion
<b>Stroke</b>	Focal motor or sensory deficit	MRI: ischemia or bleed, abnormal coagulation factors increased inflammatory markers	Coagulopathy
<b>Anosmia/Ageusia</b>	Olfactory or taste dysfunction	Abnormal smell/taste tests	Peripheral vs Central neuroinvasion
<b>ADEM</b>	Head ache, acute neurologic symptoms	MRI: hyperintense FLAIR lesions with variable enhancement	Post-infectious
<b>Guillain-Barre Syndrome</b>	Flaccid muscle weakness	CSF: increased protein, nl WBC CSF SARSCoV-2 RT-PCR: NEG EMG/NCS: abnormal	Post-infectious
<b>Muscle injury</b>	Myalgia	CPK elevated	Myopathy or Myositis

All the patients were treated with IVIG; 2 received a second course of IVIG and 1 started plasma exchange. At 4 weeks after treatment, 2 patients remained in ICU and were receiving mechanical ventilation, 2 were undergoing physical therapy and one was able to walk independently. On the basis of this observational series, it is not possible to determine whether severe deficits and axonal involvement are typical features of Covid 19-associated GBS. We could not determine the effect of reduced vital capacity due to neuromuscular failure from GBS. GBS with Covid-19 should be distinguished from critical illness neuropathy and myopathy, which tend to appear later in the course.<sup>8</sup>

### A recent case of Covid-19 related GBS:

- 65 yr old male suffering from Hypertension, Ischemic Heart Disease, Post PTCA, visited our cardiologist with complaints of fatigue, lethargy and difficulty in walking for 2-3 days. No history of fever, cough or dyspnea.<sup>9</sup>
- Lab results showed bicytopenia, Xray chest showed bilateral . infiltrates, Covid RT-PCR positive. Admitted for observation in Covid ICU in view of comorbidities and raised inflammatory markers.
- Neurology call sought for by intensivist 4 days later, as the patient continued to complain of numbness and sense of weakness in legs.

### Is COVID-19-related Guillain-Barré syndrome different?

Differences in the presentation of Typical GBS, Dengue, Zika virus and COVID SARS related GBS.<sup>10</sup> Most patients with COVID-19-related GBS were elderly. Where demyelinating neuropathy is more common with typical GBS and GBS related to dengue and Zika virus, majority of COVID-19-related GBS patients had AMAN and AMSAN. More than half of patients showed poor outcome in the form of long ICU stay, residual paresis and dysphagia.

Till now, about 20 cases of GBS associated with COVID-19 infection have been reported encompassing several of its clinical variants, such as AIDP, AMAN/AMSAN, Miller Fisher syndrome, polyneuritis cranialis, and



facial diplegia.<sup>11</sup> Almost 50% of these cases required MV and 10% of them died, suggesting that GBS associated with COVID-19 is more severe than GBS related to other etiologies, although excellent recovery after therapy is reported.<sup>12</sup> According to that it may be possible that the neuromuscular dysventilation caused by GBS adds to the COVID-19-related respiratory dysfunction, resulting in a more severe clinical presentation.<sup>13</sup>

### **Risk Factors of Neuromuscular Disorders in SARS-CoV-2 patients:**

The risk of a severe course of SARS-CoV-2 infection is increased in all but the mildest forms of NMDs.<sup>14</sup>

Following are the factors that conferring high risk of developing severe COVID-19 complications:

- Muscular weakness of the chest and/or diaphragm, resulting in reduced FVC.
- Use of non-invasive or invasive ventilation devices.
- Presence of tracheostomy.
- Presence of dysphagia and oropharyngeal weakness (reduced airway clearance).
- Risk of rhabdomyolysis with fever, fasting or infection.
- Concomitant diabetes, obesity, severe cerebrovascular or heart diseases.<sup>15</sup>

### **TREATMENT AND MANAGEMENT OF GBS IN SARS-COV-2 PATIENTS:**

Many neuromuscular patients could be considered at high risk of complications from COVID-19 infection such as those with:

- Presence of respiratory failure or cardiac involvement,
- Long-term treatment with corticosteroids and/or immunosuppressive treatments
- Pulmonary fibrosis, or severe thoracic deformities/severe contractures preventing ventral decubitus
- Comorbidities that may be associated with certain neuromuscular diseases (e.g., diabetes, obesity, & hypertension)<sup>16</sup>

#### ➤ **Bio-therapies:**

As for biotherapies (e.g., rituximab and equivalents), it is justified to maintain them if they are effective and well tolerated to avoid the potential occurrence of a relapse, in conjunction with strict application of public health recommendations. For the initiation of a biomedication, decisions will have to be made on a case-by-case basis. It may be advisable to delay initiation of B-cell depleting therapies, until the peak of the outbreak is over in their region.<sup>17</sup>

#### ➤ **Use of intravenous Immunoglobulins:**

The treatment of dysimmune neuropathies (e.g. CIDP, MMN-CB)

most often involves the iterative administrations of either intravenous or subcutaneous immunoglobulins, performed in the hospital or at home, the benefit of which has been widely demonstrated. Interruption of this

therapy may result in the exacerbation of the symptoms of neuropathy. Switching to oral corticosteroids is not recommended during SARS-CoV 2 infection and may worsen the disease in dysimmune motor neuropathies.

### ➤ **IVIG for treatment of Covid-19 disease:**

May provide immunomodulatory effect in hyper-inflammation state. Proposed mechanisms whereby IVIG exerts anti-inflammatory action include saturation of Fcγ receptor binding, anti-idiotypic binding to anti-viral antibodies, and binding of proinflammatory cytokines.<sup>18</sup> Limitations: Absent or variable specific neutralizing antibody titer(s) against novel pathogen(s), Inconclusive data.

### ➤ **Oxygen therapy and ventilator support:**

NMD patients should be closely monitored and early ventilatory support should be considered in NMD patients who develop interstitial pneumonia, as hypoxemia might quickly lead to clinical deterioration. Hypercapnia is not a classic feature of SARS-CoV-2 pneumonia, and its appearance might signal the onset of respiratory muscle weakness. NIV carries the risk of widespread diffusion of exhaled air and airborne viral transmission, although recent reports show that newer systems with good interface fitting might reduce this risk.<sup>19,20</sup>

### **CONCLUSION:**

Non-urgent appointments should be postponed or, if appropriate, replaced by telemedicine. Acts such as electroneuromyography and muscle and nerve biopsies must be reserved for diagnostic emergencies such as in the case of vasculitis, Guillain-Barre' syndrome, myasthenia gravis, oncomyositis. Hospitalization should be reserved for emergencies, the conduct of treatments that cannot be postponed.

### **ABBREVIATION:**

CNS-Central Nervous System

PNS-Peripheral Nervous System

CSF-Cerebrospinal fluids

NMD-Neuro Muscular Disorder

CIDP-Chronic Inflammatory Demyelinating Polyradiculoneuropathy

MMN-CB-Multifocal Motor Neuropathy with Conduction Block

IVIG-Intravenous Immune Globulin

CPK-Creatine Phosphokinase

FVC-Forced Vital Capacity

EMG-Electromyography

PTCA-Percutaneous Transluminal Coronary Angioplasty

AMAN-Acute Motor Axonal Neuropathy

AMSAN-Acute Motor and Sensory Axonal Neuropathy

NIV-Non Invasive Ventilation

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