International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 6 Issue 3, March-April 2022 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

Guillain Barre Syndrome - A Review

Preethi T, Jayaprakash U, Deborah Rose, K C Arul Prakasam

Department of Pharmacy Practice, Annai JKK Sampoorani Ammal College of Pharmacy, Komarapalayam, Tamil Nadu, India

ABSTRACT

Guillain Barre Syndrome is characterized by the emergence of distal, relatively symmetrical paraesthesia. It occurs when the body's defensive mechanisms mistakenly assault parts of the neurological system. It is classified into subtypes as Acute inflammatory demyelinating polyneuropathy (AIDP),Acute motor axonal neuropathy (AMAN),Acute motor sensory axonal neuropathy (AMSAN),Pharyngeal–cervical brachial variant, and Miller Fisher syndrome.GBS can be caused by a variety of infections such as Campylobacter jejuni infection, cytomegalovirus, Epstein-Barr virus, and Human Immunodeficiency virus. It mainly causes the motor, sensory, and autonomic dysfunction. In the diagnosis of GBS, a lumbar puncture is an important diagnostic tool.Anti-GD1a is linked to the GBS subtype AMAN. Miller-Fisher syndrome is linked to anti-GQ1b.Its treatment includes, Plasma exchange, Immunoglobulin, and corticosteroids. As it is incurable, supportive care and respiratory support is recommended.

KEYWORDS: *Guillain Barre Syndrome, Axonal neuropathy, Demyelination, Paraesthesia*

How to cite this paper: Preethi T | Jayaprakash U | Deborah Rose | K C Arul Prakasam "Guillain Barre Syndrome - A Review" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-6 | Issue-3, April 2022, pp.1420-1426, URL: www.ijtsrd.com/papers/ijtsrd49745.pdf

IJTSRD49745

INTRODUCTION:

Guillain-Barré syndrome or GBS is a demyelinating polyneuropathy that was first identified in 1859. Ascending motor weakness, sensory and autonomic dysfunction are common symptoms, which are often followed by prodromal disease. Campylobacter jejuni, cytomegalovirus (CMV), Mycoplasma pneumoniae, Epstein-Barr virus, and influenza virus have all been found as antecedent infections. GBS has also been linked to vaccination and parturition. GBS is characterized by the emergence of distal, relatively symmetrical paraesthesia. Progressive limb weakening occurs in conjunction with or shortly after sensory difficulties. Patients are usually able to determine a specific day when sensory and motor abnormalities commenced. In half of the patients, pain is a significant factor.(1). GBS occurs when the body's defensive mechanisms mistakenly assault parts of the neurological system. The myelin coating around the nerve may be damaged as a result of an autoimmune reaction. This causes nerve inflammation, which causes a conduction block. Severe cases induce subsequent axonal degeneration, which causes muscle weakness or paralysis, among other symptoms. The hallmark is acute paralysis with loss of tendon reflexes that develops over days or weeks. The most common symptoms are ascending paralysis weakness that starts in the feet and hands and progresses to the trunk. Some subtypes produce changes in sensation or discomfort, as well as autonomic nervous system malfunction. An infection is frequently the cause of the condition. It is the most prevalent cause of paralysis that is not caused by trauma. It has the potential to cause life-threatening complications in some people. (4) This potentially fatal illness is quite uncommon, affecting about one or two people per 100,000 worldwide, with slightly more males affected than females. All age groups are susceptible; the rate of occurrence increases with age, with a slight peak among young people. Although there is no cure for the condition, there are numerous therapies that can help to alleviate symptoms and shorten the length of the illness. (2)

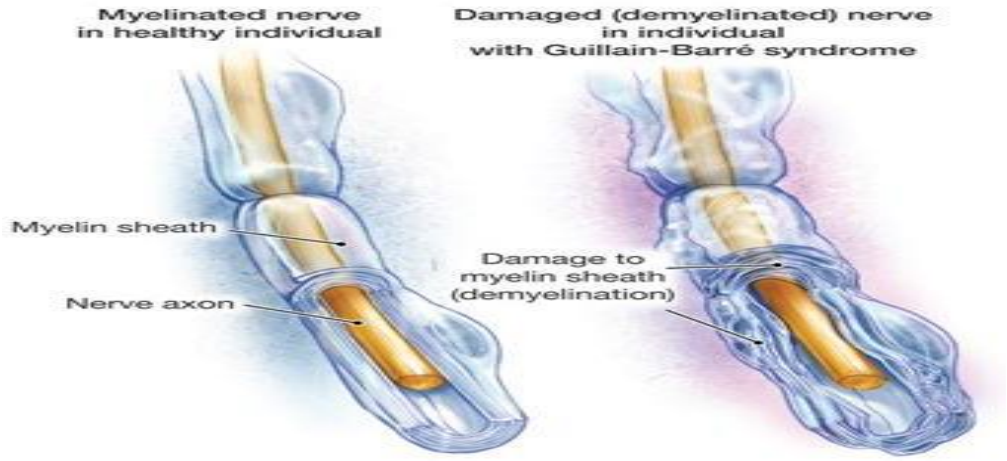

Figure 1: Demyelinatednerve (1)

CLINICOPATHOLOGICAL TYPES:

Guillain–Barre syndrome histologic markers imply a classification based on nerve-conduction studies that includes demyelinating and axonal subtypes-acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy.(3)

GBS subtypes	Main clinical features	NCS findings	Antibodies*
Acute inflammatory demyelinating polyneuropathy (AIDP)	Sensorimotor GBS, often combined with cranial nerve deficits and frequent autonomic dysfunction	Demyelinating polyneuropathy	Various
Acute motor axonal neuropathy (AMAN)	Pure motor GBS; cranial nerves rarely affected	Axonal polyneuropathy, sensory action potential normal	GM1a, GM1b GD1a GalNAc-GD1a
Acute motor sensory axonal neuropathy (AMSAN)	Resembles severe AMAN, but sensory fibres are affected, leading to sensory deficits	Axonal polyneuropathy, sensory action potential reduced or absent	GM1, GD1a
Pharyngeal–cervical brachial variant	Prominent weakness of oropharyngeal, facial, neck and shoulder muscles	Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern	GT1a>GQ1b>>GD1a
Miller Fisher syndrome	Ataxia, ophthalmoplegia, areflexia	Normal in most patients; discrete changes in sensory conduction or H-reflex may be present	GQ1b, GT1a

TABLE: 1 Clinicopathological Types(3)

ETIOLOGY:

GBS can be caused by a variety of infections. Campylobacter jejuni infection, cytomegalovirus, Epstein-Barr virus, and human immunodeficiency virus are all commonly implicated infections (HIV). Immunization (influenza, meningococcal, etc.), Systemic lupus erythematosus, Hodgkin disease, Mycoplasma pneumonia, surgery, trauma, and bone marrow transplantation are all potential triggers. (4)

PATHOPHYSIOLOGY:

Conduction block is the cause of flaccid paralysis and sensory disturbance in GBS patients with demyelinating types. This result, which may be verified electrophysiologically, suggests that the axonal link is still intact. Hence remyelination develops, recovery can occur quickly. Secondary axonal degeneration is common in severe cases of demyelinating GBS. Secondary axonal degeneration is linked to a delayed recovery time and a higher level of residual impairment. When an electrophysiologically detected primary axonal pattern is found, it means

that axons have deteriorated and been severed from their targets, notably the neuromuscular junction, and that they must regenerate in order to recover. The damage is assumed to be confined in motor axonal cases where recovery is quick. (4)

- Acute inflammatory demyelinating polyneuropathy (AIDP) - Macrophages infiltrate myelin sheaths that are still intact and weaken the axons. (5)
- Acute motor axonal neuropathy (AMAN)-Macrophages infiltrate the Ranvier nodes, inserting between the axon and the surrounding Schwann-cell axolemma while leaving the myelin sheath intact. (5)
- Acute motor sensory axonal neuropathy (AMSAN) - The ventral and dorsal roots are involved, similar to AMAN. (5)
- Miller Fisher syndrome - Although there has been few pathological research on MFS, nerve root demyelination has been demonstrated. a significant distinction between MFS and AIDP or acute Anti-GQ1b activation causes motor axonal neuropathy. Anti-GT1a antibodies in MFS that attack oculomotor neuron and bulbar nerves, which are nerves that are supposed to be connected to the brain.GQ1b and GT1a ganglioside levels are relatively high densities (1)

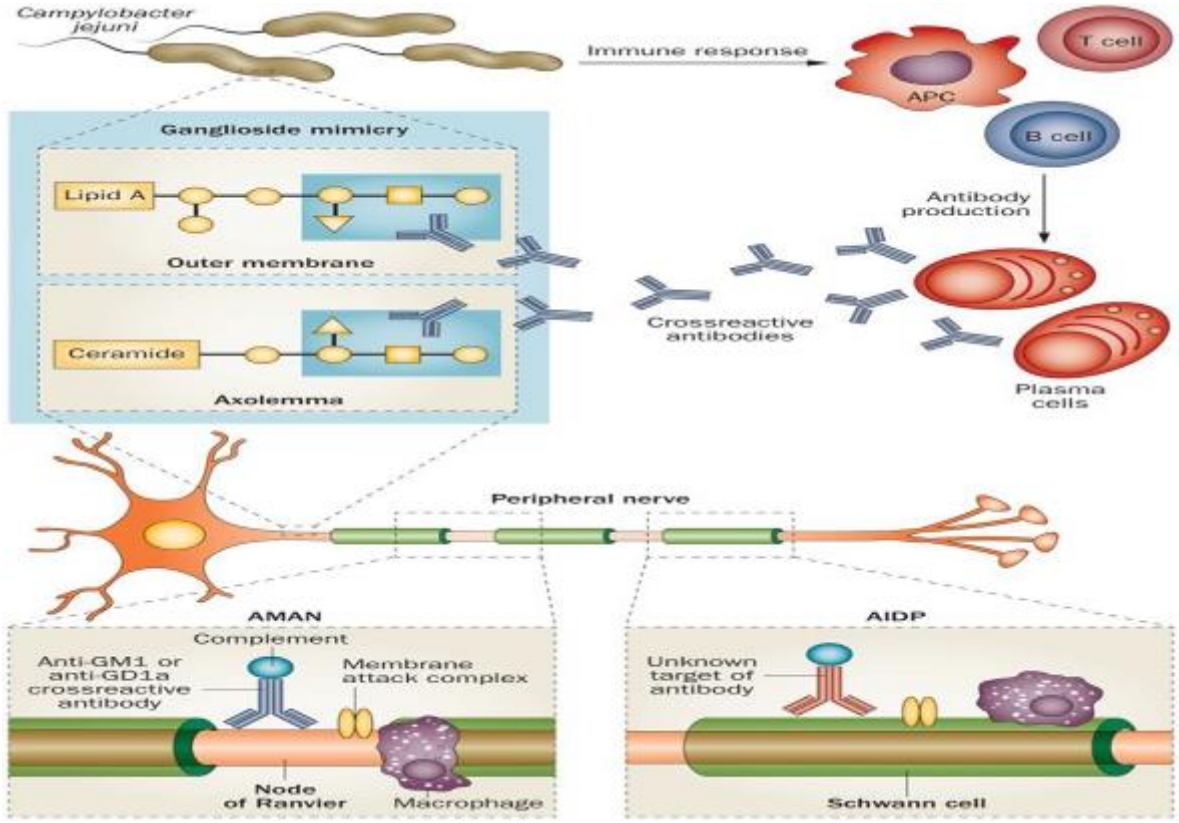

Figure 2: Acute motor axonal neuropathy caused by Campylobacter jejuni(1)

CLINICAL FEATURES:

Motor dysfunction

- Symmetrical limb weakness
- Proximal and distal Neck muscle weakness
- Respiratory muscle weakness
- Cranial nerve palsies: III–VII, IX–XII Areflexia
- Wasting of limb muscles

Sensory dysfunction

- Pain Numbness
- Paraesthesia
- Loss of joint position sense
- Vibration

Autonomic dysfunction

- Sinus tachycardia and bradycardia
- Cardiac arrhythmias
- Hypertension and postural hypotension
- Tonic pupils
- Hyper salivation
- Anhidrosis
- Urinary sphincter disturbances
- Constipation
- Gastric dysmotility
- Venous pooling and face flushing are caused by abnormal vasomotor tone.

Others

- Papilledema (6)

INVESTIGATIONS:

SERUM BIOCHEMISTRY

Urea and electrolytes are normally normal, although there may be signs of SIADH (syndrome of abnormal

ADH secretion) or renal failure. In 33 percent of individuals, ALT and gamma GT levels may be elevated. Creatine kinase levels may be elevated. (1)

INFLAMMATORY MARKERS

The rate of erythrocyte sedimentation is frequently increased, and C-reactive protein is occasionally high. (1)

ANTI-GANGLIOSIDE ANTIBODIES

Anti-GM1 antibodies are seen in 25% of patients and are linked to a worse prognosis. Anti-GD1a is linked to the GBS subtype AMAN. Miller-Fisher syndrome is linked to anti-GQ1b. (1)

LUMBAR PUNCTURE

Protein level in the cerebrospinal fluid is increased. In the diagnosis of GBS, a lumbar puncture is an important diagnostic tool. The WBC count in the CSF fluid is generally normal, and the protein level is raised, while the protein level may be normal at first, then rise to a peak in 4 to 6 weeks. (5)

NERVE CONDUCTION VELOCITY AND ELECTROMYOGRAM

They're usually referred to as EMG/NCV studies because they're done in conjunction with electromyogram. The speed at which signals travel along nerves is measured by NCV. The electromyogram (EMG) measures muscle activity and can show loss of reflexes, which is a disease symptom of delaying nerve responses. Reduced motor nerve conduction velocities or block, longer distal latencies, and an aberrant F response are all common electro-diagnostic findings. (5)

RESPIRATORY FUNCTION TEST

Reduced vital capacity, as well as maximal inspiratory and expiratory pressures, may be seen. Arterial blood gases may suggest that respiratory failure is developing. (1)

DIFFERENTIAL DIAGNOSIS

Neurological

- Myasthenia gravis
- Eaton-Lambert (myasthenic) syndrome
- Multiple sclerosis
- Transverse myelitis

Metabolic

- Hypokalaemic periodic paralysis
- Hypermagnesaemia
- Hypophosphataemia
- Acute intermittent porphyria

Infective

- Post diphtheria neuropathy
- Polio
- Botulism
- Tick paralysis

Drugs / toxins

- Heavy metal poisoning (e.g. lead)
- Toxic biological substances (including snake and scorpion toxins)
- Drugs (including stavudine, nitrofurantoin and aminoglycosides)

Others

- Acute polymyositis
- Critical illness myopathy(1)

TREATMENT:

The mainstay of treatment of Guillain Barré syndrome remains good intensive care, with respiratory support.(10)

PLASMA EXCHANGE

Brettle et al. were the first to report on the better outcome of a patient with Guillain-Barré syndrome after plasma exchange in 1978. 99 Large multicentre trials were then used to prove the efficacy of plasma exchange. Plasma exchange started within the first two weeks of the disease, which cut down on hospital stays, mechanical ventilation time, and time to ambulation. (7)Neurotoxic antibodies, complement factors, and other humoral mediators of inflammation are hypothesized to be removed through plasma exchange. Plasma exchange is effective when administered within the first four weeks after the onset of weakness in patients who are unable to walk alone (GBS Disability Scale score 3), but the most significant impact is shown when treatment begins within the first two weeks. Typically, a plasma exchange regimen consists of five sessions spread out over two weeks and requiring approximately five plasma volumes. Two plasma exchange sessions, on the other hand, resulted in a faster commencement of motor recovery in mildly afflicted individuals (still able to walk). (8) Plasma exchange is a procedure that includes withdrawing 3–6 litres of plasma over many hours and replacing it with albumin or, in some situations, fresh frozen plasma, at specialized centres. It's critical to keep track of your blood pressure, pulse, and fluid intake and output during plasma exchange. (9)

SIDE EFFECTS:

- Hypotension,
- Septicaemia,
- Hypocalcaemia, and
- Irregular coagulation (7)

INTRAVENOUS IMMUNOGLOBULIN

Several immunologically mediated illnesses are treated with intravenous immunoglobulin. It is thought to work through a variety of mechanisms, including anti-idiotypic autoantibody suppression. (7) Immunoglobulins are a plasma-derived medication

that was first used to treat individuals with antibody deficiency as a replacement therapy. (15) Intravenous immunoglobulin therapy provides patients with large doses of antibodies derived from plasma from a range of donors. Individuals with Guillain-Barré syndrome may benefit from intravenous immunoglobulin because it prevents antibodies from harming nerve insulation or nerves. (11)

MECHANISM OF ACTION

IVIg influences B and T lymphocyte activation and effector functions, neutralizes pathogenic autoantibodies, impairs antigen present, and has a significant anti-inflammatory effect that's intermediated byrelations with the complement system, cytokines, and endothelial cells. (12)T-cell proliferation and cytokine production are suppressed by intravenous immunoglobulin after mitogenic and allogenic stimulation in vitro. The mechanisms causing the inhibitory action are unknown, however they may involve various pathways. (13)

DOSE: IVIg 400mg/kg/day for 5 days at a time (14)

CONTRAINDICATIONS:

- Selective IgA deficiency
- Anaphylaxis following previous intravenous immunoglobulin infusion
- Severe congestive cardiac failure
- Insufficiency of kidney (7)

SIDE EFFECTS:

COMMON:

- Flushing,
- Headache,
- Malaise,
- Fever,
- Chills,
- Fatigue
- Lethargy

RARE:

- Renal impairment,
- Thrombosis,
- Arrhythmia,
- Aseptic meningitis,
- Haemolyticanaemia, and
- Transfusion-related acute lung injury(16)

CORTICOSTEROIDS

A pilot trial found that a five-day combination of intravenous methylprednisolone (0.5 g/d) and intravenous immunoglobulin (0.4 g/kg bodyweight/d) was more effective than intravenous immunoglobulin alone. (6) The use of steroids in the treatment of acute GBS has been studied in six trials. (17)

MECHANISM OF ACTION:

Corticosteroids are thought to diminish inflammation, hence reducing nerve damage in inflammatory neuropathy. In a rat model of GBS, experimental autoimmune neuritis, corticosteroids have been proven to speed healing, but only when given in high dosages. (18)

DOSE: Methylprednisolone -0.5 g/day (6)

SIDE EFFECTS:

- Glaucoma,
- Depression,
- Hypertension
- Myopathy
- Osteonecrosis
- Ecchymosis,
- Mild hirsutism,
- Perioral dermatitis(19)

CONTRAINDICATION:

Systemic

- Systemic fungal infections
- Intrathecal administration
- Cerebral malaria
- Live attenuated virus vaccination
- Idiopathic thrombocytopenic purpura

Topical

- Dermatological: Bacterial, viral, or fungal infection
- Ophthalmic: Acute untreated purulent ocular infections, fungal or mycobacterial ocular infections, viral conjunctivitis, or keratitis (19)

SUPPORTIVE CARE:

The need of bowel and bladder care, sufficient nutrition, monitoring for respiratory failure and giving ventilator assistance, if necessary, heart monitoring, and physiotherapy cannot be overstated. (4) Dysautonomia Management: Acute dysautonomia is a leading cause of mortality in GBS patients. In the majority of GBS patients, cardiac and hemodynamic disturbances appear as hypertension, postural hypotension, and tachycardia. (20,21) Antihypertensives with short half-lives should be investigated (Labetalol, Esmolol, or nitroprusside infusions). Furthermore, medicines used to treat dysautonomia may exacerbate the condition (glycopyrrolate for increased secretions, neostigmine for ileus, and b blockers for tachycardia). (22)

Deep vein thrombosis Prevention: If you've been confined to your bed for a long period. To avoid deep vein thrombosis, all patients should be administered subcutaneous fractionated or unfractionated heparin

and support stockings until they are able to walk freely. If you expect to be bedridden for an extended amount of time and have previously had a tracheostomy, start taking warfarin or coumadin as an oral anticoagulant. (23)

Management of respiratory failure:GBS is the most frequent peripheral neuropathy that causes respiratory paralysis, and it is the most prevalent cause of respiratory failure. One-third of the patients will require mechanical ventilation. (23) Percutaneous dilatational tracheostomy may be preferable to regular tracheostomy because it reduces the danger of inadvertent extubation and provides a more attractive appearance. Weaning off of ventilatory assistance usually takes 2–6 weeks. (24)

Nutrition: Early and gradual introduction of nasogastric or gastric tube feeding is recommended. To decrease muscle wasting and aid respiratory weaning, a high-energy (40–45 non-protein kcal) and high-protein (2–2.5 g/kg) meal has been advised. In these individuals, continuous enteral feeding appears to be more tolerated than bolus feeding. (24)

Psychological: Patients with GBS have a significant prevalence of depression. It is critical that the patient and their family have access to support groups if they are accessible. Counselling and mental assistance should also be offered if necessary. (25)

Rehabilitation: Appropriate pain medication and a comprehensive approach to rehabilitation, as well as patient education, are critical during the gradual but steady recovery, with benefits expected for up to two years. (26)

AYURVEDIC MANAGEMENT

Medicines to treat nerve damage: Drugs that cure nerve injury include, YograjGuggulu, KaisoreGuggulu, TrayodasangaGuggulu, PanchtiktagritaGuggulu, MahavatVidhwansanRasa, VataGajankusha Rasa, LashunadiVati, ChitrakadiVati, HinguvadiVati, KupiluhinguvadiVati, Kapikacchu. (27)

Herbal medicine: Yastimadhu, Manjistha, Mandukaparni, Nirgundi, and Dashamula are all effective in the treatment of this illness. Punarnavamandura, Tapyadilauha, Guduchi, Amalaki, and Mustaka are all medicines that work on the Majja dhatu of the body and are particularly successful in treating this illness. In addition, for the treatment of GBS, localised Panchakarma therapy can be performed.

Only medicated steam fomentation is recommended during the acute period, which lasts 3 to 6 weeks. After this time, the body is massaged with medicinal oils, followed by medicated steam fomentation. Mahanarayana oil, Mahahamasa oil, Mahasaindhava oil, DashamulaKvathandNirgundiKwath are some of the medicines used in these operations. To address immunological dysfunction in the body, Ashwagandha, Yastimadhu, Tulasi, and Bhringaraja are taken. To offset the mental pressures, assurance treatment is often recommended. (28)

THE FUTURE

Eculizumab is going to begin a new randomised placebo-controlled study in individuals with early GBS who are unable to walk. Antiganglio side antibodies cause complement-dependent destruction at the nodes of Ranvier, nerve terminals, and presynaptic Schwann cells, according to results in an animal model of GBS. Many more studies are being anxiously awaited, such as those looking into pain therapy, nerve regeneration, and other variables that may enhance the prognosis of GBS patients. (29)

ACKNOWLEDGEMENT:

Nothing to disclose.

CONCLUSION:

Guillain Barre Syndrome is a type of autoimmune disease in which symptoms increase the chance of major long-term consequences considerably. Historically, corticosteroids have been used to treat inflammation associated with Guillain-Barré syndrome. They're no longer in use. There is no evidence that they promote healing or impact long-term prognosis. More research is needed to identify potential molecular intervention targets, create novel diagnostics, and develop effective and cost-efficient therapeutics.

REFERENCES:

[1] Hemal Tandel, Jigar Vanza, Nilima Pandya et.al. Guillain-Barré Syndrome (GBS): A Review. European Journal of Pharmaceutical and Medical Research. 2016, 3(2), 366-371.

[2] Anand B. Pithadia, Nimisha Kakadia. Guillain-Barré syndrome (GBS). Pharmacological Report 2010, 62, 220-232.

[3] Dr. Anjana Tom, Dr.Manasa R et.al.Guillain-Barre Syndrome - In Brief. World Journal of Pharmaceutical Research.11 August 2021.Volume 10, Issue 11, 393-404.

[4] Sahu Abhilasha1, Vyas O. A Critical Review On Guillain Barre Syndrome (Acute Inflammatory Demyelinating Polyneuropathy-AIDP) And Their Management.International Journal of Ayurveda and Pharma Research. November2020, Vol 8, Issue 115.

[5] Ambed Mishra1, Sai Krishna G, Komal Krishna T. Guillain-Barré Syndrome (Gbs) – An Orphan Disease. World Journal of Pharmaceutical Research. Volume 6, Issue 5, 393-400. 6.

[6] GantalaAlekhya Reddy, Gangadhara Tejaswini, Rakam Niharika et.al. An Overview on Guillain Barre Syndrome. Asian Journal of Pharmaceutical Research and Development. 2019; 7(5): 103-112.

[7] Udaya Seneviratne. Guillain-Barré syndrome. Post Graduate Medical Journal. Volume 76, Issue 902.

[8] Bianca van den Berg, Christa Walgaard, et.al, Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nature Reviews Neurology volume 10, pages469–482 (2014).

[9] Mazen M. Dimachkie, M.D.Guillain-Barré Syndrome and Variants. Elsevier, Neurologic Clinics. Volume 31, Issue 2, May 2013, Pages 491-510.

[10] J B Winer. Guillain Barré syndrome Mol Pathol. 2001 Dec;54(6):381-5.

[11] https://about-guillain-barre.com/guillain_barre_treatment

[12] J Bayry1, N Misra. Mechanisms of action of intravenous immunoglobulin in autoimmune and inflammatory diseases. Neurol Sci (2003) 24:S217–S221.

[13] V. Patil,S. V. Kaveri. The mechanisms of action of IVIG in autoimmune and inflammatory diseases. ISBT Science Series (2013) 8, 185–188.

[14] Satoshi Kuwabara.Guillain-Barr´e Syndrome Epidemiology, Pathophysiology and Management. Therapy In Practice. 17 September 2012, volume 64, 597–610.

[15] Benjamin Chaignea, LucMouthon. Mechanisms of action of intravenous immunoglobulin. TransfusApher Sci. 2017 Feb;56(1):45-49.

[16] Yi Guo, Xin Tian, Xuefeng Wang. Adverse Effects of Immunoglobulin Therapy. Front Immunol. 2018; 9: 1299. 2018 Jun 8.

[17] Anand B. Pithadia, Nimisha Kakadia.Guillain-Barré syndrome (GBS)Review. Pharmacol Rep Mar-Apr 2010;62(2):220-32.

[18] Hughes RAC, Brassington R, Gunn AA et.al. Corticosteroids for Guillain-Barré syndrome (Review).Review Cochrane Database System Rev. 2016 Oct24;10(10):CD001446.

[19] Muhammad Yasir; Amandeep Goyal; Sidharth Sonthalia. Corticosteroid Adverse Effects. StatPearls. July 8, 2021.

[20] Burns TM, Lawn ND, Low PA et.al. A dynamic Ileus in severe Guillain–Barré syndrome. Muscle Nerve 2001;24:963-5.

[21] Truax BT. Autonomic disturbances in the Guillain–Barré syndrome. Semin Neurol1984;4:462-8.

[22] Eelco F. M. Wijdicks.Guillain–Barre´ Syndrome. Review Mayo Clin Proc. 2017 Mar;92(3):467-479.

[23] Meena A. K., S. V. Khadilkar1, J. M. K. Murthy. Treatment guidelines for Guillain–Barré Syndrome. Ann Indian Acad Neurol. 2011 Jul;14(Suppl 1):S73-81.

[24] Lawn ND, Wijdicks EF. Post-intubation pulmonary function test in Guillain–Barré syndrome. Muscle Nerve 2000;23:613-6.

[25] Roubenoff RA, Borel CO, Hanley DF. Hypermetabolism and hypercatabolismin Guillain-Barre´ syndrome. J Parenter Enteral Nutr.1992; 16(5):464-472.

[26] Jane Pritchard. Guillain-Barré syndrome. Lancet 2004 Jun 26;363(9427):2186-8.

[27] Dr. L. Mahadevans. Ayrvedic Clinical Practice. Vol2.Tamilnadu; Sarada mahadeviyerAyur.

[28] Dr. P. S. Byadgi, Dr. A. K. Pandey. A text book of Kayachikitsa. Vol3. New Delhi; Chaukhambha publication; 2014. p.140.

[29] https://www.clinicaltrials.gov/ct2/show/NCT02029378