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Assessment of Risk Factors, Diagnosis and Treatment Pattern in Guillain Baree Syndrome

SK. Hazara Begum[1], Dr. Tejaswi Chillara[2*], Dr. Kamalyadav[3], Dr. E Srinivas Rao[4]

Abstract: ***Guillain -Barre syndrome (GBS) is an immune-mediated disorder of nervous system and a recognized cause of generalized progressive paralysis worldwide. The most common symptoms of GBS include Quadriparesis, paresthesia both upper and lower limbs which is ascending in nature and difficulty in standing from sitting position. Many antecedent events of GBS Ave been identified including Cytomegalovirus infection, Campylobacter jejuni gastroenteritis, Mycoplasma pneumonia, influenza virus and Epstein Barr virus infections. This study was aimed to document the clinical findings, assess the risk factors, diagnosis and treatment pattern in variants of GBS (i.e. Acute Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), and Acute Motor Sensory Axonal Neuropathy (AMSAN) amongst the patients with GBS during the hospital stay.***

Keywords: Guillain-Barre syndrome, Acute inflammatory demyelinating polyneuropathy, (AIDP), Acute Motor Sensory Axonal Neuropathy (AMAN), Acute Motor Sensory Axonal Neuropathy (AMSAN), Retro-Prospective study

1. Introduction

Guillain –barre syndrome is an auto immune disorder of nervous system of acute onset characterized by generalized progressive weakness of upper and lower limbs, paresthesia and complete areflexia. (1.1). In this autonomic dysfunction are common with conventional manifestations as loss of vasomotor control with wide fluctuation in blood pressure, postural hypotension and cardiac arrhythmias. (1.2) Oropharyngeal weakness and respiratory failure may require mechanical ventilation in about one – third of hospitalized patients making it a disease of vital importance for early management. (1.3) The report occurrence for GBS is 1-2 per 100,000 population and increases linearly with age, and men are about 1.5 times more affected than women. (9.1.) Primary infections such as upper respiratory tract infections are well known preceding event in the development of GBS have been identified including Campylobacter jejune gastroenteritis, Cytomegaly virus, Mycoplasma Pneumoniae, Epstein Barr virus and Influenza virus infections. (1.5). The common types of GBS are acute inflammatory demyelinating polyneuropathy. (AIDP), acute motor axonal neuropathy, (AMAN), acute motor sensory axonal neuropathy (AMSAN) and Miller Fisher Syndrome (MFS). (1.6). AIDP is the most prevalent form and accounts for 70-90 per cent of cases. (1.7.) Primary infection such as upper respiratory tract infection is well known event in the pathophysiology of GBS. (1.8). Many antecedent events are associated with GBS such as Campylobacter jejuni gastroenteritis, Mycoplasma pneumonia, Cytomegalovirus, Influenza virus and Epstein Barr virus infections.(1.9) The clinical manifestations of GBS is ascending, progressive, symmetrical flaccid limbs paralysis, cranial nerve involvement and hyporeflexia which is progress over the course of days to several weeks. (5.1).

Risk Factors: Age: risk increases with age. Sex: males are more likely to contract GBS. Campylobacter jejune bacterial infection, HIV, Epstein Barr virus (EBV), these are associated with cases of GBS. (2.3.) previous surgeries and childhood vaccination: these have also been linked to GBS in rare cases. (2.4)

Signs and Symptoms: The primary symptoms of this disease include varying degrees of weakness or tingling sensation in the legs. The commonest manifestation is limb weakness, more proximal than distal. (2.1) Facial palsy is the commonest type of cranial nerve involvement followed by bulbar weakness, ophthalmoplegia and tongue weakness. In many cases, the weakness and abnormal sensations spread to the upper body. (2.2)

Risk Factors: Age: risk increases with age. Sex: males are more likely to contract GBS. Campylobacter jejune bacterial infection, HIV, Epstein Barr virus (EBV), these are associated with cases of GBS. (2.3.) previous surgeries and childhood vaccination: these have also been linked to GBS in rare cases. (2.4)

Motor Dysfunction	*Sensory Dysfunction*	*Autonomic Dysfunction*
Areflexia	Pain	Hyper salivation
Neck muscle weakness	Ataxia	Tonic pupils
Cranial nerve palsies	Numbness	Gastric disturbances
Symmetrical limb weakness	Paresthesia	Hypertension and postural hypotension
	Loss of joint position sense	Urinary sphincter disturbances
	Touch and pain sensation	Wide fluctuation of pulse and blood pressure
		Cardiac arrhythmia

Pathophysiology:
The pathophysiology of GBS is complex. The exact pathophysiology of GBS is still not clear, but molecular mimicry shows a possible mechanism of pathogenesis. (2.5)The important surface molecules of the nervous system is Gangliosides. (2.6) Based on the concept of molecular mimicry, antibodies are formed against the Gangliosides in the lipopolysaccharide moiety of Campylobacter jejuni which cross react with peripheral nerves causing

damage.(2.7)In cytomegalovirus infection more often Anti-GM2 antibodies are found.(2.8)

AIDP

The classic pathological picture of Guillain -Baree syndrome is of multifocal mononuclear cell infiltration throughout the peripheral neurons system in which the distribution of inflammation corresponding to the clinical shortage. (6.1) Then macrophages invade the myelin sheaths and deprive the axons. (6.2) According to one hypothesis, the activated macrophages are targeted to antigens, on the surface of Schwann cells or the myelin sheath by activated T lymphocytes, which are major actors in experimental autoimmune neuritis.

AMAN

In AMAN, the pathological process is different, probably targeted by their Fc-receptor-mediated binding of antibodies directed against ganglioside antigens on the axolemma, macrophages invade the nodes of Ranvir where they insert between the axon and the surrounding Schwann cell axolemma, leaving the myelin sheath intact (6.5). In severe cases, the axons are damaged in the ventral root, which may cause severe degeneration of the whole axon. In AMAN patient are quickly recover than patient in AIDP. This is because of in AMAN the pathological process blocks conduction but not severe the axon (6.6).

AMSAN

The pathology in AMSAN resembles that in AMAN, with the same pattern of macrophage invasion of the perinodal space. However, with AMSAN, the dorsal, as well as the ventral, roots are affected (6.7).

Fisher's syndrome

The pathophysiology of the Fisher's syndrome is not clear so far. Since it is benign condition, uncomplicated cases do not come to autopsy, and the affected parts of the nervous system cannot be biopsied. The primary electro physiological finding in Fisher's syndrome is an abnormality of sensory conduction (6.8).

VARIANTS OF GBS	RELATED ANTIBODIES
Acute inflammatory demyelinating polyneuropathy (AIDP)	Unknown
Acute motor axonal neuropathy (AMAN)	GM1, GM1b, GD1a, GalNac-GD1a
Acute motor sensory axonal neuropathy (AMSAN)	GM1, GM1b, GD1a.
Fisher's syndrome	GQ1b, GD1a
Fisher's syndrome overlaps with Guillain-Barre syndrome	GQ1b, GM1, GM1b, GD1a, GalNac-GD1a

Epidimiology:

The reported incidence of the Guillain –Barre syndrome in western countries ranges from 0.89 to 1.89 cases per 100,000 person per years, rise in age although an increase of 20% is seen with every 10-year rise in age after the first decade of life. (7.1)

The incidence of the Guillain-Barre syndrome is estimated to be 0.25 to 0.65 per 1000 cases of Campylobacter jejuni infection, and 0.6 to 2.2 per 1000 cases of primary cytomegalovirus infection. (7.3)

Diagnosis:

GBS is a clinical diagnosis, with areflexia and progressive weakness evolving over less than four weeks. (9.2)

CSF Analysis:

In this test an elevated protein levels and fewer mononuclear cells/mm3 are strongly support the diagnosis. During the first week CSF protein levels are normal (2.6). In one of the studies 12% of patients were found to have more than 5 cells / microliter in the CSF. (2.7).

Nerve Conduction Studies

These studies are helpful to diagnose Guillain -Barre syndrome in clinical practice . It's needed to meet all criteria's of Brighton for Guillain Barre syndrome. (2.8).

NCS are essential for classification of Guillain Barre syndrome in AIDP or AMAN.(2.9)

In this AIDP features of demyelination is prolonged distal motor latency, decreased motor nerve conduction velocity, temporal depression ,conduction blocks and increased F – wave latency . (2.10). In other hand AMAN shows no features of demyelination, one demyelinating feature in one nerve, if distal CMAP amplitude is less than10%LLN, can be found ; distal CAMP amplitude less than 80% LLN in at least two nerves .(2.11) . Conduction block of Transient motor nerve might be present. (2.12)

LLN- lower limit of normal

CAMP – compound muscle action potential

AIDP	*AMAN*	*AMSAN*
Reduced conduction velocity Conduction block or abnormal temporal dispersion Prolonged terminal latency Absent F wave or prolonged F wave latency.	Absent or reduced compound muscle action potential (CMAP) amplitude Normal motor terminal latency and conduction velocity Normal sensory nerve action potential (SNAP)	Absent or reduced SNAP amplitude Absent or reduced CMAP amplitude Normal motor terminal latency and conduction velocity

2. Treatment

Plasmapheresis:

Both plasma therapy and IVIG shows good outcomes in GBS

About Intravenous Immunoglobulin therapy:

IVIG is used in the treatment of several immunologically mediated disorders. It is supposed to act through several mechanisms including anti-idiotypic suppression of autoantibodies.(8.10). The IVIG mechanism of action is probably multifactorial and uncertain, including the provision of anti-idiotype antibodies, interference with

complete activation and blocked of Fc receptors. Antibodies increased catabolism may also play a part.(8.11). A large, randomised, multicentre trial compared Intravenous Immunoglobulin, plasma exchange, and combination of both there was no significant difference in efficacy between plasma exchange and IVIG. No evidence was in significant advantage in combined treatment. (8.12) 0.4 mg/kg / day for five days gives significant outcomes in GBS.

Contraindications of IVIG	Adverse effects of IVIG
Severe congestive Cardiac failure Selective IgA deficiency Anaphylaxis following previous IVIG infusion Renal insufficiency	Nausea, vomiting Vasomotor symptoms, Myalgia, myalgia, Transient increase in liver enzymes

Corticosteroids:

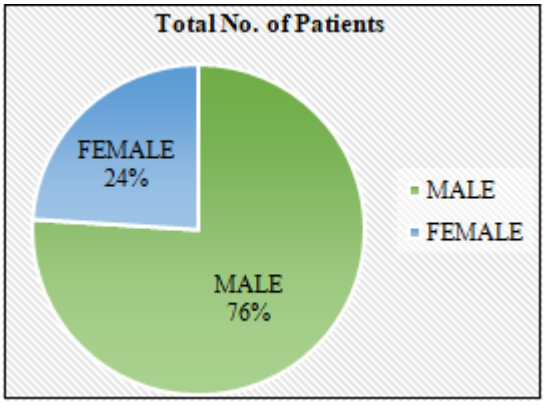
"A pilot study suggested that combined treatment with intravenous methylprednisolone (0.5g/d) and IVIG (0.4g/kg body weight /d) for five days was more beneficial than IVIG alone. ''(8.14).

Aetiology :	**Clinical features** :
Cytomegalovirus Previous gastrointestinal infection Campylobacter jejuni infection **Biochemical markers :**	Older age Longer time to clinical improvement Greater disability and disease severity. **Electrophysiology** :
Neuron specific enolase and S-100 b protein in CSF Anti -GM1 antibodies	Inexcitable nerves Absent or reduced CMAP (<20% of the lower limit of normal)

3. Methodology

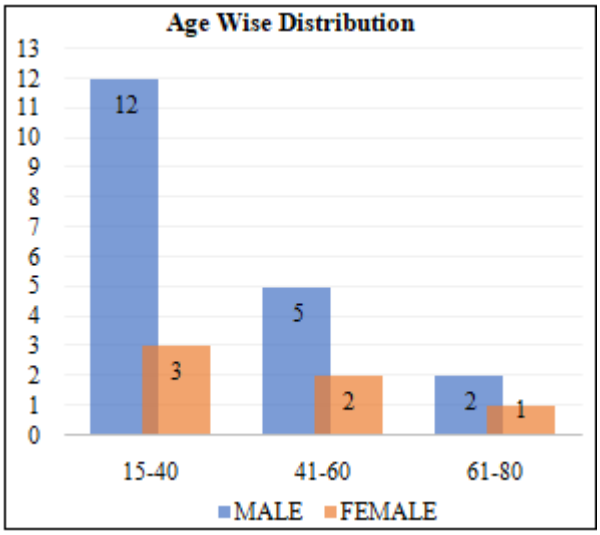
A Retro-Prospective observation study was conducted in inpatient department of neuro care center for a period of six months.

4. Results



Gender Wise Distribution

Gender	Total No. of Patients
Male	19(76%)
Female	6(24%)

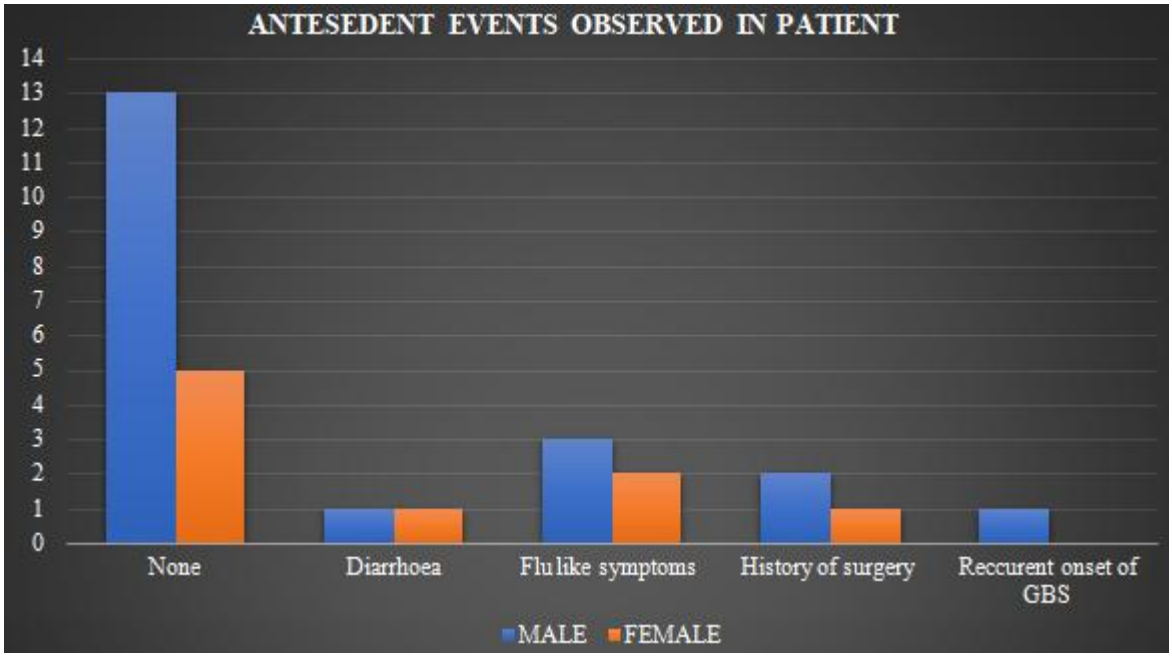


Age Wise Distributions

Age	Male	Female	Total
15-40	12(48%)	3(12%)	15(60%)
41-60	5(20%)	2(8%)	7(28%)
61-80	2(8%)	1(4%)	3(12%)

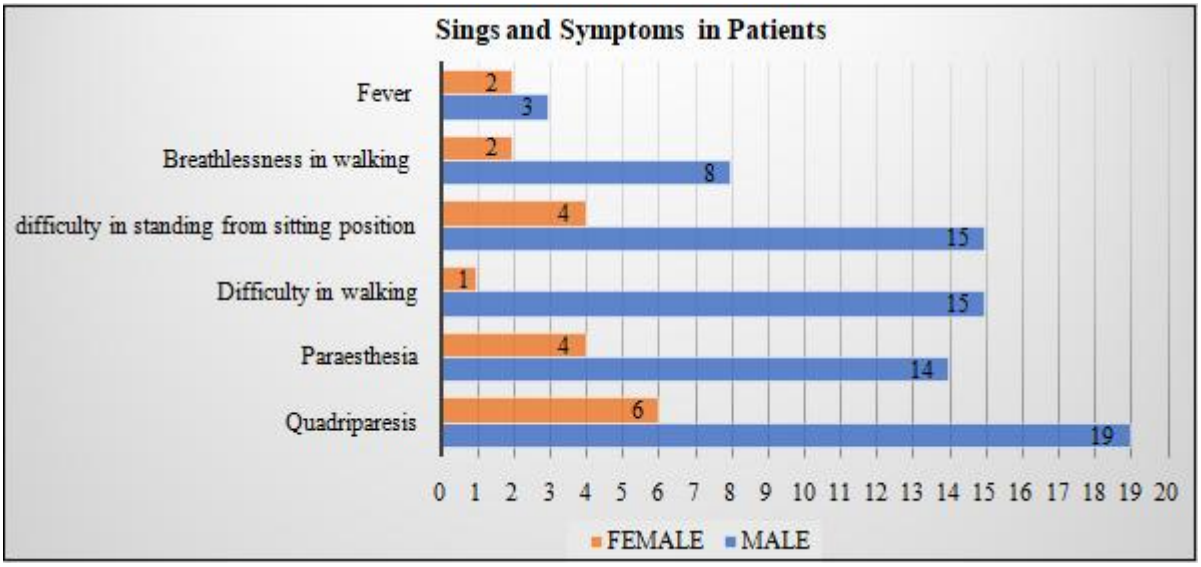
Antecedent Events Observed in Patients

Illness	Male	Female	Total
None	13(52%)	5(20%)	18(72%)
Diarrhoea	1(4%)	1(4%)	2(8%)
Flu like symptoms	3(12)	2(8%)	5(20%)
History of surgery	2(8%)	1(4%)	3(12%)
Recurrent onset of GBS 1(4%)	0(0%)		1(4%)



Sings and Symptoms in Patients

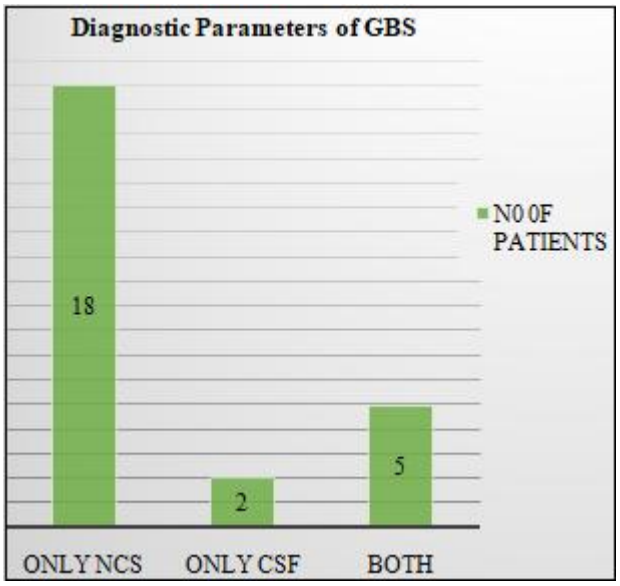
SIGNS AND SYMPTOMS	MALE	FEMALE	TOTAL
QUADRIPARESIS	19(76%)	6(24%)	25(100%)
PARAESTHESIA	14(56%)	4 (16%)	18(72%)
DIFFICULTY IN WALKING	15(60%)	1(4%)	16(64%)
DIFFICULTY IN STANDING FROM SITTING POSITION	15(60%)	4(16%)	19(76%)
BREATHLESSNESS IN WALKING	8(32%)	2(8%)	10(40%)
FEVER	3(12%)	2(8%)	5(20%)



Medication Adherence

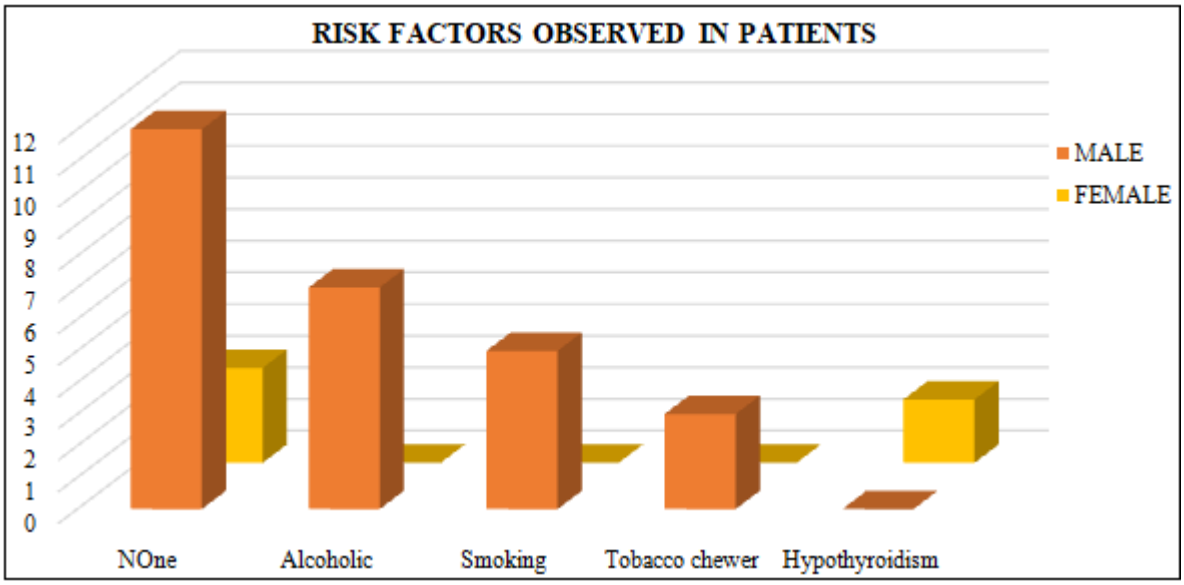
Diagnostic Parameter	No. of Patients
NCS	18(72%)
CSF	2(8%)
BOTH	5(20%)

Note: NCS (Nerve Conduction Study), CSF (Cerebrospinal Fluid)



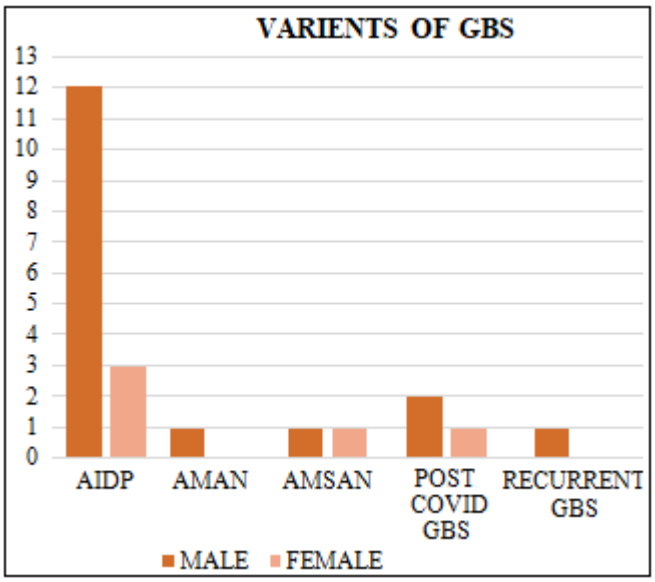
Risk factors observed in patients

Risk Factors	Male	Female	Total
None	12(48%)	3(12%)	15(60%)
Alcoholism	7(28%)	0(0%)	7(28%)
Smoking	5(20%)	0(0%)	5(20%)
Tobacco chewer	3(12%)	0(0%)	3(12%)
Hypothyroidism	0(0%)	2(8%)	2(8%)



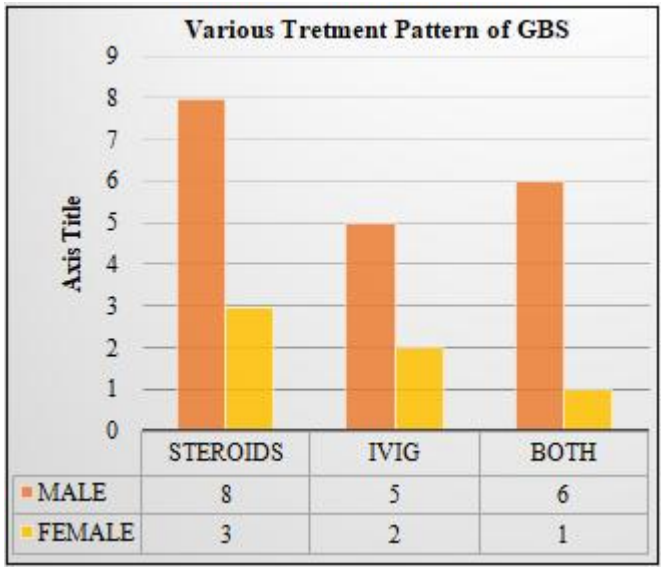
Variants of GBS

Variant	Male	Female	Total
AIDP	12(48%)	3(12%)	15(60%)
AMAN	1(4%)	0(0%)	1(4%)
AMSAN	1(4%)	1(4%)	2(8%)
POST COVID GBS	2(8%)	2(8%)	4(16)
RECURRENT GBS	1(4%)	0(0%)	1(4%)



Treatment Pattern

Drugs	Male	Female	Total
CORTICOSTEROIDS	8(32%)	3(12%)	11(44%)
IVIG	5(20%))	2(8%)	7(28%)
Both	6(24%)	1(4%)	7(28%)



5. Discussion

Guillain-Barre syndrome is a condition, which is rarely occurs in 1-2/100,000 population. Still the exact cause of this disease is unknown. In our study most of the male patients were analyzed due to chronic alcoholism. This study provides the exact treatment pattern in variants of GBS i.e. AIDP, AMAN, and AMSAN. In six months study, treatment pattern was analyzed based on the patient's response among 25 samples.

1) Gender

Of total study population, male (76%) were predominant over female (24%). Our results are similar to the study conducted by Shrivastava, (2017) where in among 66 patients, 47 were male & 19 were female. This could be due to unhealthy lifestyle (Alcoholism and smoking) and antecedent events of infections disease (COVID -19)

2) Age

In our study the prevalence of the prevalence of GBS low in elder people 61-80 years age group (12 % in which male were 8% & female were 4%); 28% (20% were male & 8% in female) in 41-60 years age group and 60% (48% were male & 12 % were female) in 15-40 years. This could be due to alcohol abuse in men and COVID-19 infection.

3) Antecedent Events

In our study, the patients are observed with none antecedent events are a bout 72% (in which male were 52% & female were 20%); diarrhoea in 8% (in which male were 4% & female were 4%); Flu like symptoms are in 20%(in which male were 12% & female were 8%); History of surgery in 12%(in which male were 8% & female 4%); and Recurrent onset of GBS in only 4% of male were noted. Our results are similar to the study conducted by Shrivastava, (2017) where in among 66 patients. This could be due past history of infectious disease and surgery.

4) Signs & Symptoms

In our study, sings & symptoms are observed in patients about Quadriparesis is 100% (in which male were 76% & female were 24%), Paraesthesia is 72% (in which male were 56% & female were 16%), Difficulty in walking is 64%(in which male were 60% & female were 4%), Difficulty in standing from sitting position is 66 % (in which male were 76% & female were 16 %), Breathless in walking is 40%(in which male were 32% & female were 8%), and fever is 20% (in which male were 12% & female were 8%). These are common sings & symptoms of GBS.

5) Diagnostic Parameters

In our study, we assess the chiefly two parameters, which are Nerve conduction studies (NCS) & Cerebrospinal fluid analysis (CSF). We observed that 72% of patients diagnosed with NCS, 8% were diagnosed with CSF and 20% of patients with both parameters. This could be due to the NCS are shown accurate results and they also helpful to categories the variants of GBS in clinical practice.

6) Risk Factors of GBS

In our study, we observe the patients of none risk factors are about 60%(in which male were 48% & female were 12%), Alcohol abuse is 28%(total male), smoking is 20% (total male), tobacco chewer is 12% (total ale), Hypothyroidism is 8% (only female). The exact cause of GBS is still unknown, these are few risk factors we observed in our study.

7) Variants of GBS

In our study, we observed that few variants of GBS in among 25 patients, they are AIDP about 60% (in which male were 48% & female were 12%), AMAN is 4%(total male), AMSAN is 8% (in which male were 4 % & female were also 4 %), post COVID GBS is 16%(in which male were 8% & female were 8%), Recurrent onset of GBS is 4% (only male). AIDP is most common variant of GBS.

8) Various Treatment Patterns

In our study, we observed that most of the patients cured with corticosteroids (methylprednisolone 8mg – 4mg), about 44% (in which male were 32% & female were 12%), IVIG is 28% (in which male were 20% & female were 8%) and

both is 28% (in which male were 24% & female were 4%). This is due the patient condition and based on their response to the drugs.

Along with this drugs the physician prescribed the Neuroprotectives, antibiotics and anticoagulants in hospital stay.

Table 14

Drug	*Dose*	*Frequency*
Methylprednisolone(MP)	4mg – 8mg	BD for five days
IVIG	0.4mg/kg/day	BD for five days

Note: If patient is not respond to MP, then the physician prescribed the IVIG, in some patients the physician also prescribed the both drugs for better results.

Along with above drugs routinely prescribed drugs are in below table.

Table 15

Drug Name	Dose	Frequency
APIXABAN	2.5mg	BD for 5 days
DOXYCYCLINE/ LACTOBACILLUS	100mg	BD for 5days
VITAMIN- C	500mg	BD for 1 month
GABAPENTIN/ NORTRYPTILINE	400mg	OD for 10 days
ACETYLCHOLINE	600mg	BD for 10 days
CITICOLIN	500mg	OD for 10 days
MVT	500mg	OD for 10 days
VITAMIN-D3	1tab(50,000IU)	Once in week for 1 month
PIRACETAM	400mg	OD for 10days

In our study, Neuroprotectives also play vital role to recovery from this condition

6. Conclusion

In this study we observed that the Nerve conduction studies are play vital role in clinics to know the severity of disease and variants of GBS. By assessing the risk factors and antecedent events the causes of GBS can be assessed. Based on the findings from the study, in few patients along with medication adherence, complete stoppage of alcohol abuse is very important to recover quickly from the condition and non-pharmacological measures to be taken to prevent further complications and recurrent onsets of GBS. In this study corticosteroids also shows better outcomes in all variants of GBS. In those patients who are not respond to corticosteroids, were treated with IVIG or combination of both.

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