Addis Ababa University

College of Health Sciences

Department of Neurology

RESEARCH THESIS

A two-yearretrospective review on theclinical and electrophysiologic profiles of Guillain-Barre Syndrome at two centers in Addis Ababa,Ethiopia

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Abstract

Background: The clinical manifestations and electrophysiologic patterns of Guillain-Barre Syndrome(GBS) have been established with several studies previously.Nerve conduction study has been known to be one of the diagnostic tool complementing the clinical presentation of GBS patients. The aim of this study was to assess the clinical characteristicsand electrophysiologic pattern of GBSpatients at two facilities in Addis Ababa,Ethiopia.

Methods:A retrospective cross-sectional study was conducted from October 1-30, 2020 upto by reviewing the medical record of GBS patientswho visited the neurology clinics at two facilities in Addis Ababa between from September 01, 2017 and September 30, 2019. Demographic, clinical, biochemical and electrophysiologic data were collected and analyzed.

Results:A total of 59 GBS patients' medical records were reviewed.Majority 46(72.8%) of the patients were male.The dominant age category was from 21-35 years of age having 26(44.1%) share.The mean age of the participants was 32.96 (15.04) years .Preceding illnesses were documented in 21patients wherediarrheal illness was reported by the majority (38%) followed by upper respiratory tract infections. Quadriparesis was the most frequent presenting symptom with 38(64.4%) patients. .Following the Nerve conduction test the two most common GBS variants identified were Acute Motor Axonal Neuropathy variant(AMAN)and AcuteInflammatory Demyelinating Polyneuropathy variants of GBS.

Conclusion: The majority of GBS patientsincluded in our study were young adults who presented with quadriparesis, with the most common variant of GBS being AMAN variant.

Key words:Guillain-Barre Syndrome, Quadriparesis, variants of GBS,Nerve conduction study

Table of Content

1.Introduction

1.1Background

Guillain-Barre Syndrome (GBS) is one of the most common cause of severe acute paralytic polyradiculoneuropathy,with an estimatedincidence of 100,000 people developing the disorder every yearworldwide.[1]Two thirds of GBS are preceded by infection or immune modulation factors which will induce auto-immune response targeting the spinal roots and peripheral nerves.[1]

Several studies have commented on a bimodalpattern of incidence by age the peaks occurring inyoung adults and the elderly with male predominance. However some studies witnessed a linear increase in incidence with age.[2]

Reports showed that there is a temporal relationship between Campylobacter Jejuni(C. jejuni) infection and GBS that neurologic symptoms typically occur 10 days to 3 weeks after onset of diarrhea. The longest reported latency between the onset of C. jejuni enteritis and GBS symptoms is 23 days.[3]The variant ofGBS that occurs after Campylobacter infection is more severe and result in more irreversible neurologic damage than GBS associated with other triggering factors[3]

In a typical case of GBS,the patient clinical presentation includes progressivelimb weakness with sensory and cranial involvement with in1-2 weeks after immune stimulation.[4]The first symptoms are pain, numbness orparaesthesia, which is followed by limb weakness which usually progress in a symmetric “ascending pattern” with most patients presenting initially with leg weakness and later spreading to the arm[5,6].Fifty percent of the patients experience involvement of the cranial nerves which can manifest as weakness of facial muscles, difficulty of swallowing and weakness of the eye muscles,In only 8% the weakness affects only the legs.[7]

A quarter of GBS cases result in weakness of the respiratory muscles which necessitatesassistance withartificial ventilation. Autonomic involvement is also common and can be manifested as urine retention, ileus, sinus tachycardia, hypertension, cardiac arrhythmia, and

postural hypotension[6].The disease reaches its maximum point by 2nd week in half of the patients and by 4th weekin almost all cases which is followed by a recovery phase. [6,8]

In addition to patient's clinical history electrophysiologic and cerebrospinal fluid examinations as well asexcluding otherdiseases that have a similar clinical picture is needed.[9]

GBS can be divided into at least 4 main subtypes of diseasebased on the type of nerve fiber involved: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the axonal subtypes, i.e. acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome, the main symptoms of which are oculomotor dysfunction, ataxia and areflexia.[10]

In North America and Europe, around 5% of patients with GBS have the axonal subtypes, whereas in Central and South America, Japan and China axonal subtypes account for 30–47% of casesdue to high prevalence of C. Jejuni infection.[11] Miller-Fisher syndrome has been found to account for around 5% of cases of GBS[11,12]

Patients with GBS need meticulous monitoring and supportive care which helps stabilize the patient by preventing and treating various complications of the disease like respiratory distress and autonomic disturbances. Early initiation of Intravenous immunoglobulins (IvIg) or plasma exchange has proven benefits [13].

The objective of our study was to assess the Clinical and electrophysiologic profiles of Guillain-Barre syndrome patients who visited the neurology clinics at TikurAnbessa Specialized Hospital and YehuleshetSpeciality clinic in Addis Ababa, Ethiopia.

1.2 Literature review

A systematic literature review done on the epidemiology of GBS worldwide published on December 2008,most of the incidence rates of GBS reported were between 1.1/100,000/year and 1.8/100,000/year with lower rates reported in children (16 years) of 0.4/100,000/year to 1.4/100,000/year[12].Most of the studies included were from Europe and North America where the rates found were similar.

A number of studies have commented on a bimodal pattern of incidence by age, with peaks occurring in young adults and the elderly. In this review, only 1 study (out of 24) found a peak incidence in young adults, although the rates were not adjusted and a high proportion of young adults in this area could have biased the incidence rates found.[14]In this review It was not possible to determine whether there was a geographical difference between incidence of AIDP, AMAN and AMSAN.[14]

A research report on epidemiology of GBS in Finland from 2004-2014incidence rate of 1.69/100,000 person-years. Slightly over half (57%) of the patients were male [15]. The mean age of the entire population was 51 years (SD 20.1; range 1–89); there was no difference between the genders (p=0.12). Total annual GBS incidence increased steadily from birth to 40 years of age, and again from 50 to 70 years [15].

A multicentre prospective study of Guillain-Barré Syndrome in Japan: A focus on the incidence of subtypes they performed a prospective multicenter survey over 3 years (2007–2010) [14]. Clinical and electrophysiological findings were collected from 184 patients with GBS in 23 tertiary neurology institutes.Anti-ganglioside antibodies were measured by ELISA. Also surveyed the incidence of Fisher syndrome (FS). By electrodiagnostic criteria patients were classified as having AIDP (40%), or AMAN(22%), or unclassified (38%). Anti-GM1 IgG antibodies were found for 47% of AMAN patients, and 18% of AIDP patients. There were no specific regional trends of the electro diagnosis and anti-GM1 positivity. During the same study period, 79 patients with FS were identified; the percentage of FS cases out of all cases (FS/(GBS+FS)) was 26%.[16]

A continental and national data primarly targeting the assessment of prevalence of variants of GBS is lacking A ten years retrospective study conducted to assess the clinical profile and outcome of Guillain-Barré Syndrome (GBS) in Ethiopian patients done at TikurAnbessa University Hospital, Addis Ababa, Ethiopia during the period September 1992 to September 2001.[15] The commonest electrophysiologic abnormality encountered was demyelinating picture in 26(55.3%) followed by mixed and axonal in 12 (25.5%) and 9 (19.1%) respectively)[17].

As the shortage of local studies evidenced by the prior data, this study will try to establish a valid and vital information on the pattern of GBS variants among our population

1.3 Statement of the Problem

GBS is a significant cause for morbidity worldwide and in our country since the advent of better neurologic set ups. Multiple studies in the western part of the world have tried to identify the prevalence of variants of GBS.

Electrophysiology is a developing area of neurology. Adequate data on the electro physiologic findings of GBS is not available for our setup.

Therefore this study will try to provide information on the prevalence of variants of GBS based on data collected from two centers.

1.4 Significance of the Study

Accurate data on prevalence of variants of GBS is useful for many reasons. The prevalence of variants of GBS are not well documented in Ethiopia, Very little is known about the general pattern and prevalence of each variants of GBS particularly in Addis there is no published data of the topic under the study.

This study is therefore aimed at assessing the pattern of GBS variants so that the result of study can be used to know the prevalence of each variant in our population.

Data obtained from the research has been used to improve on the quality of patient care. Moreover,the results of the study will be a valuable input for future researches and as a reference material.

This study is useful to put base line information for clinicians caring and treating patients inour set up; as well as to forward recommendations to initiate other investigators to work further on the same and/or other related issues.It will also try asses the presence of comorbidity and outcome among GBS patients in the study period.

2.Objective

2.1 General Objective

To assess the clinical and electrophysiologic profile of GBS patients who are reffered to electrophysiology labratory at TASUH and YSC from September 2017-september 2019.

2.2 Specific Objectives

To assess the relation of the independent variable such as demographic data,Preceding illnesses, Presence of comorbidities,length of stay,Lab results,Ventilator requirement with variants of GBS

3.Methodology

An institutional based retrospective cross-sectional study among GBS patients who were evaluated at TASH and YSC neurology clinics between September 2017-September 2019 was conducted .Data was collected through revision of their medical records starting from October 1-30, 2020.All GBS patients with no age limit and whose diagnosis were confirmed by electrophysiologictest were included.Patients with clinical diagnosis of GBS but without or with inconsistent nerve conduction test, and those with incomplete clinical records were excluded.

Patients data were collected through a structured format.Datawas analyzed by SPSS 26.Results were presented with Tables, graphs and charts.The association between categorical variables were tested using Chi-square or Fisher's exact test. . Significance level was set at $p<0.05$.

3.1 Study variables

3.1.1. Dependent

1.Electrophysiology profile of GBS patients

3.1.2. Independent

1. Socio-demographic variables like age, gender, address of the patient.
2. Preceeding illnesses
3. Pattern of weakness
4. Length of stay in the wards
5. Lab results
6. Need for in patient management
7. Ventilator and oxygen requirement

4.RESULTS

4.1Socio-demographic characteristics of the study participants

A total of 59 patients with the diagnosis of GBS who visited TASH and YSC electrophysiology laboratory within the study period were included. The majority (42) were from YSC.

There were 43(72.9%)males and 16(27.1%)females giving the male to female ratio of 2.7:1. Age of the participants ranged from4 years to 70 years with mean(SD)age of 32.96(15.04)years.Thirty two (54.2%) patients were from urban areas while 27 (45.8%) were from rural areas.

4.2Clinical characteristics of participants

From the total 59patients 21(35.6%) had a recording of where 9(42.8%) patients had diarrheal illness,8(38%) had upper respiratory tract infection,3(14.2%) gave a history of recent vaccinationanda single patient reporteda non-specific febrile illness.

The majorityof our study participants presented with quadriparesis38(64.4%) followed by paraparesis10(16.9%) patients.Various Cranial nerve deficits were also major presenting symptoms as depicted in table 2

Duration of symptoms at presentation ranged from 2 to 30 days with the mean(SD) being 11.9(9.3) days.

The pattern of admission was assessed and 37(62.7%) patients needed inpatient management while the rest 22(37.3%) patients were managed in outpatient basis.The duration of their hospital stay ranged from 2 days to 41 days with a mean(SD) of 8.9(1.3)days.Only 5(8.5%) of the patients had a documented comorbidity including Hypertension and Diabetes Mellitus.

Among those admitted for inpatient care6(10.2%) patients needed an oxygen therapy due to respiratory embarrassment. Dysautonomia was documented in 11 patients where sinus tachycardia was picked in 5(8.5%) patientswhile labile BP was seen 6(10.2%) participants. Thirteen (22%) patients weretreatedwith Intravenous Immunoglobulin as a GBS specific treatment in addition to the supportive care provided.

Table 1: frequency and percentage of presence of preceding illness,major presenting symptoms and presence of comorbidities of participants

Variables	**frequency**	**percentage**
Presence of preceding illness		
Yes	21	35.6
No	38	64.4
Type of illness		
Diarrheal disease	9	15.3
URTI	8	13.6
Recent vaccination	3	5.1
Nonspecific febrile illness	1	1.7
Major presenting symptoms		
Quadriparesis	38	64.4
Paraparesis	10	16.9
Hemiparesis	1	1.7
Facial diplagia	3	5.1
Quadriparesis with facial diplegia	1	1.7
Ophthalmoparesis	1	1.7
Swallowing difficulty	4	6.8
Sphincter dysfunction(transient)	1	1.7
Neeed for MV		
Yes	5	8.5
No	40	67.8
Not Documented	14	23.7

4.3Laboratory data of the study participants

From the study participants AMAN was the predominating variant with 35(59.3%) patients followed by AIDP pattern seen in 18(30.5%) patients and the 1(1.69%) patient categorized in the other variants showed a mixed pattern of Axonal and demyelinating neuropathy

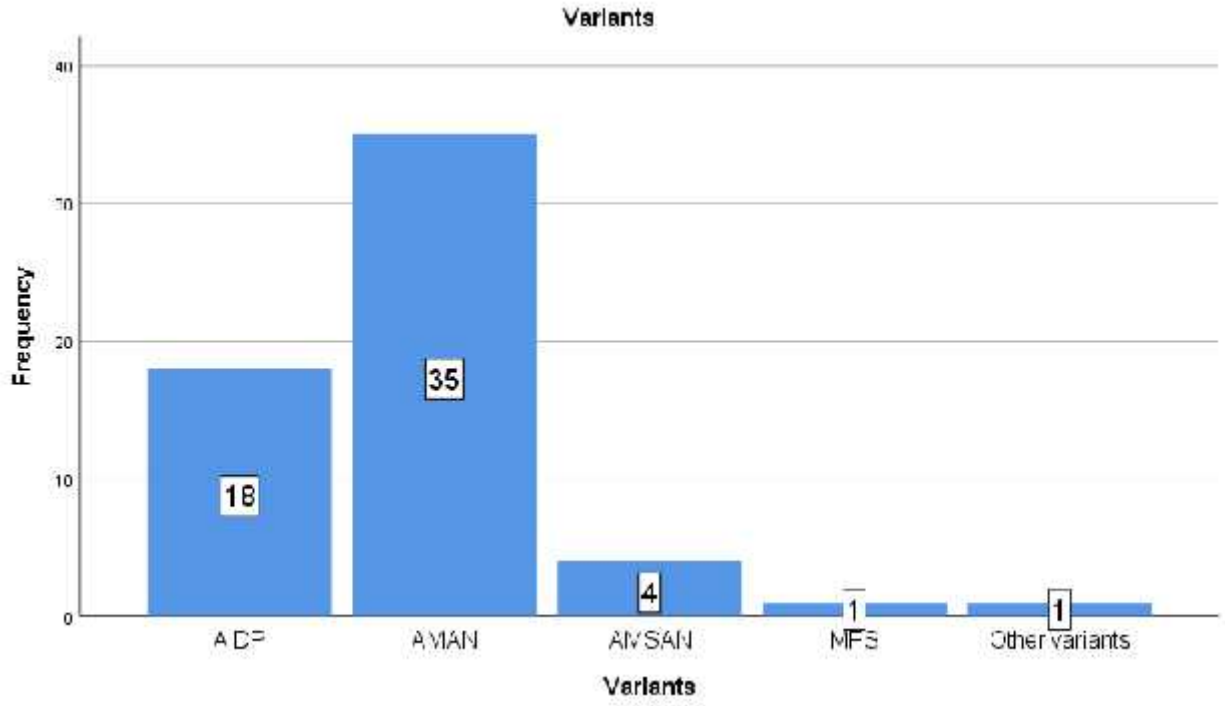

Figure 1:Bar graph showing frequency of electrophysiologic variants of GBS

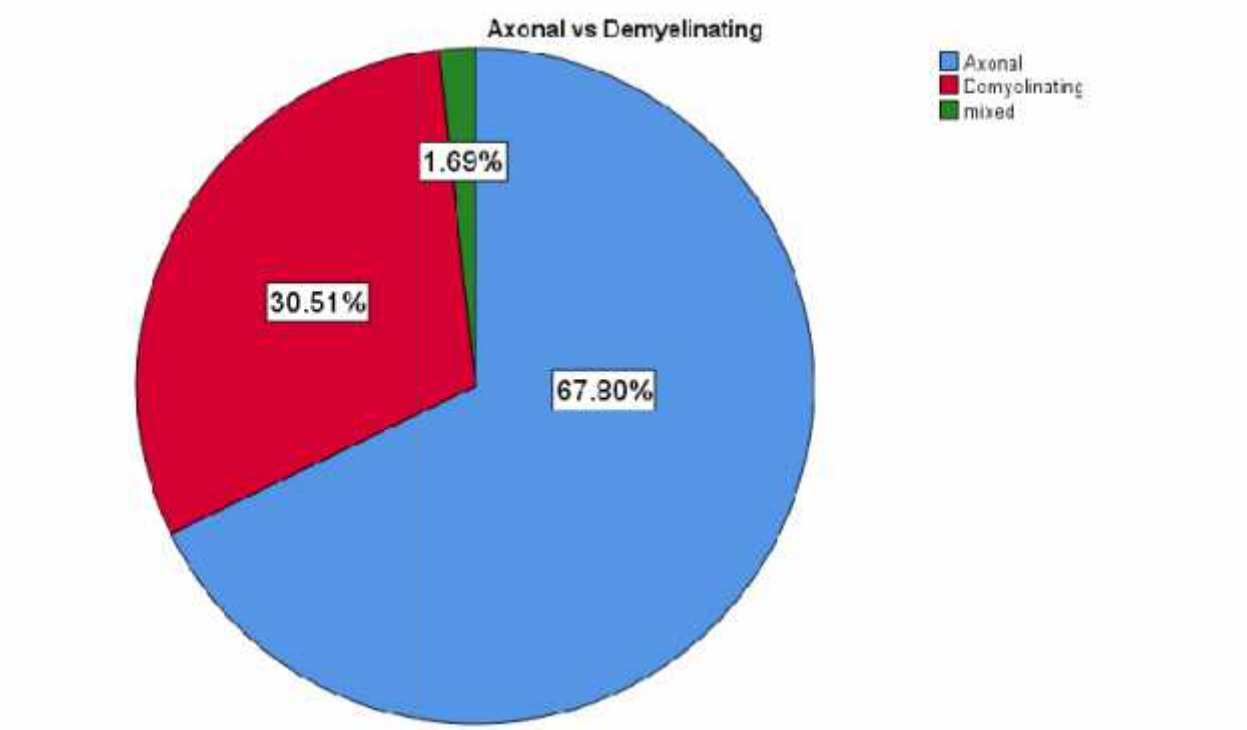

Figure 2: Pie chart showing Axonal, Demyelinating and Mixed pattern on NCS

Table 2:CSF profile of participants

Variables	frequency	percentage
Was CSF done		
Yes	10	16.9
No	42	71.2
Not documented	7	11.9
Albuminocytologic dissociation		
Yes	8	80
No	2	20

4.4 Association between sex and variants

The association between variants of GBS and Gender were assessed. Axonal variant of GBS was seen in 30(50.8%) male patients while 10(19.9%)female participantshad demyelinatingvariant of GBS. There was no significant association of sex with GBS variants (p value=0.249)

Table 3 :Association between Genders of participants with variants of GBS

						Pearson chi square	**P-Value**
			Axonal	Non axonal	Total		
sex	Male	Count (% within sex)	30(69.8%)	13(30.2%)	43	**2.782**	**0.249**
	Female	Count (% within sex)	10 (62.5%)	6(37.5%)	16		
Total		Count (% within sex)	40(67.8%)	19(32.2%)	59		

4.5 Association between patient's age category and major presenting symptoms

We performed Pearson's Chi-square test or Fisher exact test to see the association between age category and major presenting symptoms.Participants were categorized with age group using 18 years as a cutoff value,Fifty(84.7%) patients were in the age group ≥18 from which 33(66%) of them presented with quadriparesis while5(55.6%) patients from theunder 18 years of age category presented with the same symptom. There was no significant association between the two variables which gave a Pearson chi-square value of 7.23 with p-value of 0.045

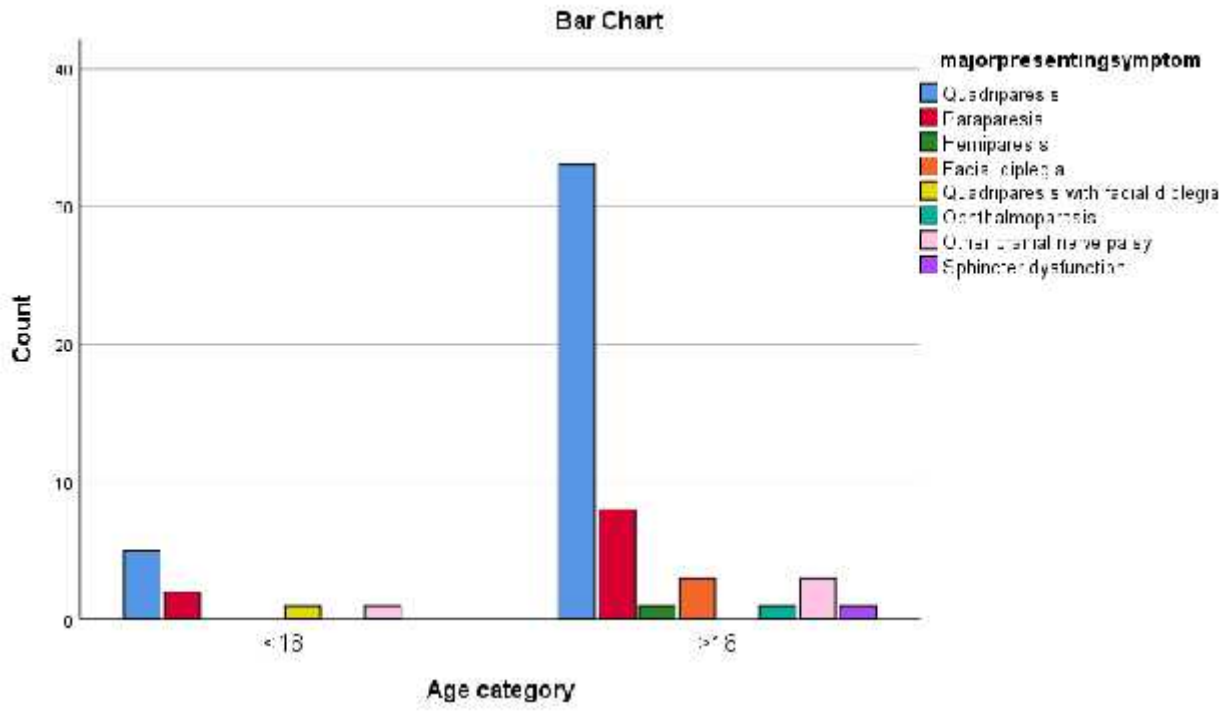

Figure 3: Bar chart on the distribution of major presenting symptoms among age category

4.6Association between major presenting symptoms and variants

From the 38 quadriparetic patients 25(71.4%) were classified as AMAN variant while among the patients with paraparesis both AIDP and AMAN variants were represented equally by 4 patients, each making 40% of the patients presenting with paraparesis. Association between major presenting symptoms and variants of GBS was done using Pearson chi-square whichshowed a strong association between the two variables(P- value<0.01) that Quadriparetic patients are more likely to have AMAN variant of GBS.

4.7Association Between need for in patient management and GBS variants

From the 59 study participants 37(62.7%) patients needed inpatient management. From the inpatient managed patients 27(73%)of them had axonal variant and 9(24.3%) showed demyelinating pattern on NCS.Correlation was assessed between the need for in patient management and variants of GBS which turned out to show no significance having a P-value of0.328

Table 4 :Association between need for inpatient management and variants of GBS

						Pearson chi-square	P-Value
			Axonal	Non Axonal	Total		
Needforinpatientmanagement	Yes	Count (% within Needforinpatientmanagement)	27(73.0%)	10(27%)	37	**2.231**	**0.328**
	No	Count (% within Needforinpatientmanagement)	13(59.1%)	9(40.9%)	22		
Total		Count (% within Needforinpatientmanagement)	40(67.8%)	19(32.2%)	59		

Association between variants of GBS (axonal vs non axonal) and age,sex and need for in patient managent was done using binomial logistic regression which gave a Cox and Snell r^2 value of 0.32

5. Discussion

Our study showed the Majority 42(71.2%) ofthe participants were from YSC.Participants age ranged from 4 years to 72 years with a mean age of 33.1 year.The result of gender distribution showed a male to female ratio of 2.7:1.The limited number of study participants shows the limitation of access to electrophysiology laboratories in the country.The study showed most of the participantswere from the urban areas representing the 54.2% of the total participants.The assessment of a possible association between sociodemography of patients with variants of GBS didn't show any significant association.

The results of the study showed 21(35.6%) of the study participants had a preceding event prior to the onset of symptoms of GBS.According to unpublished local study done at the same center 04 years back on the clinical profile and predictors of mortality among GBS patients which included a total of 82 cases preceding events which were predominantly acute gastroenteritis and upper respiratory tract infections were seen in 36 cases.Comorbidities were identified in 22(26.8%) cases from which Hypertension and Retroviral infection were the commonest in order [18].The study also looked for other comorbidities like HIV,cardiac disease and renal disease but there was no study participant with documentation of the above mentioned conditions.

The major 64.4% presenting symptom of GBS patients in this study isquadriparesis followed by paraparesis.The result of this study is comparable to a retrospective study on clinical manifestations done in a tertiary setup in Indiaover a period of six years which showed that the main clinical presentation was bilateral ascending weakness and areflexia which resulted in quadriparesis was seen in 69.2% of patients.[19] The rest of the patients presented with Hemiparesis,Facial diplagia,Quadriparesis with facial diplegia,Ophthalmoparesis,Other cranial nerve palsies and Sphincter dysfunction. Even though sphincter dysfnction is uncommon manifestation of GBS which even urges a consideration of an alternate diagnosis, a research published on journal of neurology, neurosurgery and psychiatry on micturitional disturbance in patients with GBS documented urinary dysfunction in 7(25%) of 28 patients.[20]Among the participants only 5(8.5%) had comorbidities 3(5.08%) of them having Hypertension while 2(3.4%) of them were diabetic,there was no documentation or positive history of comorbid illnesses in the rest 54 patients.

The result of this paper showedmore than half (62.7%) of the participants needed in patient management among which only 6 of them needed an oxygen therapy and 5(8.5%) required mechanical ventilation support. GBS specific treatment was given to 13(22%) patients that all of the participants received IVIG none of the patients in this study received plasma exchange therapy.The result of our study with regard to GBS specific treatment is too low when compared from a study done in india which reported a GBS specific treatment rate of60.7% that IVIG treatment had a share of the 49.2%.[19] Cardiovascular complications were seen in 11 patients from which 6(10.2%) had labile blood pressure while being followed in the inpatient facilities and 5(8.5%) had changes on their ECG,In our study the ECG changes picked in all 5 patients was sinus tachycardia.

The relevant laboratory data that was tried to be seen in this study was the electorophysiologic pattern of GBS patients according to their NCS results and the frequency of cerebrospinal fluid analysis among the study participants in addition with the pattern of albuminocytologic dissociation.

From the result of this study the majority of GBS variant according to the NCS results from the respective electrophysiologic laboratories was AMAN variant which was represented by 35(59.3%) patients followed by AIDP 18(30.5%),AMSAN 4(6.8%), MFS 1(1.7%) and mixed variants 1(1.7%).The classification of mixed variant was used in a study done at the same setup previously.[17]The results of this study is supported with a retrospective study done on The clinical presentation ,epidemiology and short term outcome of GBS in children atTASH over 06 years period which showed predominance of AMAN variant 23(76.7%) of their study population.[21]Which would be attributed to large number of antecedent diarrheal illnesses or as TASH is the largest referral center where most severe cases of GBS were usually referred.

A study done in Pakistan to determine the frequency of axonal variants among GBS patients also demonstated the predominace of AMAN type representing 40 % of the study participants.[22]

The association between variants of GBS with major presenting symptoms in the study was shown to be strong with a p value of< 0.01.As shown in the results AMAN variant of GBS was more associated withquadriparesis as a major presenting symptom that from 38quadriparetic patients in the study 25(65.8%) of them showed AMAN variant of GBS.while thesecond more

common presenting symptom which is paraparesis showed equal number of represention in AMAN and AIDP variants with 4(40%) patients for bothcategory.This result is supported by a research done to compare electrophysiologic findings in axonal and demyelinating variants of GBS which reported that at early times in patients with AIDP prominent CMAP amplitude reduction was observed in lower limbs while in axonal types the reduction was the same in both upper and lower limbs.[23]

In this study only 10(16.9%) patients had CSF analysis results in their medical records while 7 of them had an information that CSF analysis was done but the result was either undocumented,not collected or lost from their charts.From the 10 patients 8(80%) of them showed albumunocytologic dissociation.

6. Conclusion

According to this study demographic data showed predominance of male and urban population of young age, most of GBS cases present with paralysis of all limbs which also has a concomitant cardio- respiratory embarrassment.Significant number of patients required a close follow-up and monitoring while some needed an intensive care including mechanical ventilator.From the results of the study we have seen AMAN variant of GBS is the commonest variant in the two study centers.

7. Recommendation

Proper clinical evaluation and documentation would improve the clinical care,as well as NCS for patients presenting with symptoms of GBS.We also recommend screening for cardiopulmonary complications upon encountering a patient with GBS since the result of our study showed a higher rate of need for admission and supportive care.

8.Strength of the study

This study gives a general picture on the clinical manifestations,complications and pattern of severity for patients with GBS.It also showed the electrophysiologic variants and their distribution in our setup. Data was obtained from two different facilities with in depth revision of individual patient’s medical record.

7.Limitation of the study

The number of NCS done was limited with respect to the total number of GBS cases in the two facilities which limted the sample size.The limited duration of study period was due to limitation of accessability of electrophysiologic results and patients medical chart in times prior to the studyalso there was a nine year study on the same setup which covered the prior time. There was also a lack of information about reasons for admission.

Generalization of the study result to the general population will be challenged by the relatively small number of participants in the research.Interpretation of the result of this study should be with caution because both pediatric and adult patients were included in our study

8. Operational definitions

Prevalence--Prevalence is the proportion of a population with a disease or a particular condition at a specific point in time or a specific period of time. [22]

GBS---patients with clinical and electrophysiological evidence of poly radiculoneuropathy with diagnosis of either variant of GBs like AMAN, AMSAN, AIDP and MFS [24]

AIDP-GBS variant due to acute demyelination process evidenced by electrophysiologic studies with findings of motor conduction blocks and reduced conduction velocity [24]

AMAN-GBS variant caused by an immune mediated motor axonal disorderelectophysiologic studies demonstrate normal SNAP,motor distal latency and conduction velocity but reduced CMAP[10]

AMSAN-A subtype of axonal disorder which involves both motor and sensory fibers with electophysiologic features of reduced or absent CMAP and SNAP without significant conduction slowing[25]

MFS-A variant of GBS characterized by the classic triad of ophthalmoplegia, ataxia and areflexia.[25]

Urban- of, relating to, characteristic of, or constituting a city [26]

Rural-of or relating to the country, country people or life, or agriculture [26]

Abbreviations

AIDP Acute Inflammatory Demyelinating Polyneuropathy

AMAN Acute Motor Axonal Neuropathy

AMSAN Acute Motor Sensory Axonal Neuropathy

CMAPCompound Muscle Action Potential

ECGElectro Cardio Gram.

GBS GullianBarre syndrome

MFS Miller-Fisher Sndrome

NCS Nerve Conduction Study

SNAP Sensory Nerve Action Potential

TASH TikurAnbessaSecialized Hospital

YSC YehuleshetSpeciality Clinic

9.Declarations

Ethical approval and consent to participate

Official letter was written to TASUH and YSC to secure permission. Since data collection is done by the investigator through review of medical records of patients the study did not directly involve patients in anywayin the study. The investigator made sure that confidentiality of the information is assured in such a way that no disclosure of any name of the patient, the health care provider or drug product in relation to the finding was made. Ethical clearance was obtained from the Addis Ababa University College of Health sciences, Department of Neurology ethical Clearance Committee in the month of August, 2020.

Consent for publication

Not applicable. No person's details, images, or videos are being used in this study.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Competing interests

The authors declare that they have no competing interests.

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Authors Contribution

All the stated authors are equally involved in the study together with the corresponding author. All authors read and approved this manuscript.

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