Original Research Article

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Clinical Profile of Patients with Guillain-Barre Syndrome (GBS)

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Abstract

Antecedent infection with following organism likecytomegalovirus, Epstein Barr virus, Varicella zoster virus, Human immunodeficiency virus (HIV), Campylobacter jejuni, Mycoplasma pnemoniae and Shigella are implicated in the causation of the Guillain Barre Syndrome. In all the patients the following data were recorded: demographic data; season in which patient developed disease; detailed history of present and preceding (if any) illness; physical as well as neurological examination details; laboratory characteristics including CSF analysis (if done); electrophysiological findings, any need for assisted mechanical ventilation, duration of mechanical ventilation; duration of hospital stay; any complications; treatment given and outcome. The median duration to get admitted in hospital from disease onset was 8 (range 4-18) days, and the median time to reach nadir of the disease was 7 (range 5-14) days. The median duration of total hospital stay was 16 days, with minimum and maximum duration of hospital stay being 7 and 60 days, respectively. All patients presented with symmetrical weakness. Quadriparesis was present in 54 (88.5%) patients. Global areflexia was present in 53 (88.6%) patients.

Keywords: Guillain-Barre Syndrome; Epstein Barr Virus; Clinical Profile.

Introduction

It was Jean-Baptiste Octave Landry who first in 1859 described a case of distal sensory "formications" and ascending weakness after a prodromal fever, malaise, and pain who progressed to paralysis over 3 weeks and died from respiratory failure, in addition to another four cases. Later in 1916 Georges Guillain, Jean-Alexandre Barre , and Andre Strohl reported two cases with albuminocytologic dissociation on cerebrospinal fluid (CSF) testing and distinguished this syndrome from poliomyelitis induced paralysis. It is called by Landry-Guillain-Barre´ -Strohl syndrome or Guillain-Barre´ -Strohl syndrome or, more often, Guillain-Barre´ syndrome (GBS), after the two French army neurologists [1,2].

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The Guillain Barre Syndrome is the most common cause of acute flaccid paralysis. The annual incidence of Guillain-Barre syndrome is around 1.2 to 2.3/ 100,000 persons per year.[1] Incidence increases with age, with maximum peak in older age group. GBS is rare in infancy. Males are more frequently affected than females. 65 to 70 % have an antecedent event 1-4 weeks before onset of weakness: They include respiratory infection, gastroenteritis, respiratory and gastrointestinal infection, exanthematous illness, vaccination especially swine flu vaccine, surgery and rarely pregnancy.

Seasonal clustering of the GBS patients is very well known entity. Kalita et al in 324 patients observed the seasonal clustering of AIDP cases in winter and AMAN in summer. Seasonal clustering may be a reflection of preceding infection during that season [3].

Antecedent infection with following organism likecytomegalovirus, Epstein Barr virus, Varicella zoster virus, Human immunodeficiency virus (HIV), Campylobacter jejuni, Mycoplasma pnemoniae and Shigella are implicated in the causation of the GuillainBarre Syndrome. Antecedent infection is related to the Subtype of GBS for e.g., Campylobacter jejuni infection has been reported in 30% of patients

with GBS. AMAN is the common subtype and is associated with anti-GM1 and anti-GD IaIgG antibodies. It is associated with slower recovery and residual deficit [4].

Antecedent infection provokes autoimmune response through molecular mimicry which results in host mounting the immune response against the infectious agent that share common antigen with peripheral nerve. At the onset of the disease activated T cells play pivotal role by causing break in the blood nerve barrier leading to the exposure of the circulating auto-antibodies in blood to the peripheral nerve antigens.T-cell activation markers (interleukin [IL]-6, IL-2, soluble IL-2 receptor, and interferon gamma [IFN-γ]) and tumor necrosis factor alpha (TNF-α), a proinflammatory cytokine released by T cells and macrophages, particularly IL-23 are increased in patient serum. In addition adhesion molecules and matrix metalloproteinases are critically involved in facilitating recruitment and transmigration of activated T cells and monocytes through the blood-nerve barrier further adding to the damage. This form of cell mediated immune response in pathogenesis of AIDP is supported from animal models of experimental allergic neuritis generated from active immunization with peripheral myelin protein components [5].

GBS is more common in males than females. Age distribution follows a bimodal fashion with peaks in 2nd and 5th decade. Antecedent infection within 4 weeks of onset of symptoms is present in around 70-75% of cases. Classical case of GBS present with flaccid weakness with or without paresthesia sensation. Typically starts as symmetrical weakness of lower limbs proximally, ascends up to involve trunk, neck, oro-pharyngeal and respiratory muscle in severe cases. Progression may take hours to days and reaches peak by 4 weeks following which it reaches a plateau. Hyporeflexia or areflexia is invariably present apart from weakness. Rarely weakness may start in the cranial nerves descends to upper limbs and lower limbs mimicking botulism.

Methodology

This prospective observational study conducted among consecutive patients diagnosed to have Guillain Barre Syndrome at the neurology department.

Inclusion Criteria

- Fulfilment of clinical criteria proposed by GBS study group.
- All patients who give consent.

Exclusion Criteria

- Those who decline to give consent.

In all the patients the following data were recorded: demographic data; season in which patient developed disease; detailed history of present and preceding (if any) illness; physical as well as neurological examination details; laboratory characteristics including CSF analysis (if done); electrophysiological findings, any need for assisted mechanical ventilation, duration of mechanical ventilation; duration of hospital stay; any complications; treatment given and outcome. All the details were recorded in a structured proforma. Patient's disability at admission and at discharge was evaluated using Hughes functional grading scale. Muscle power was expressed using MRC Sumscore.

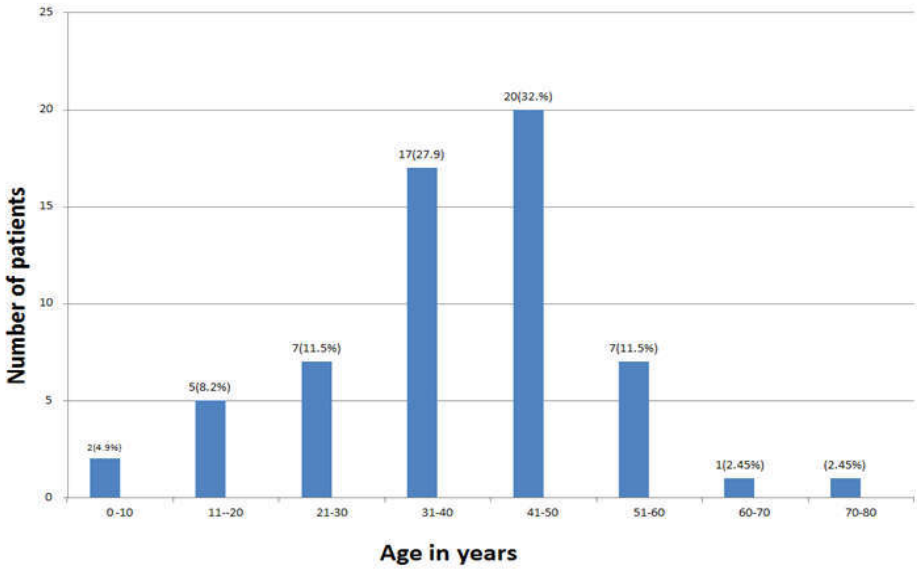

Fig. 1: Age distribution of the study population

Results

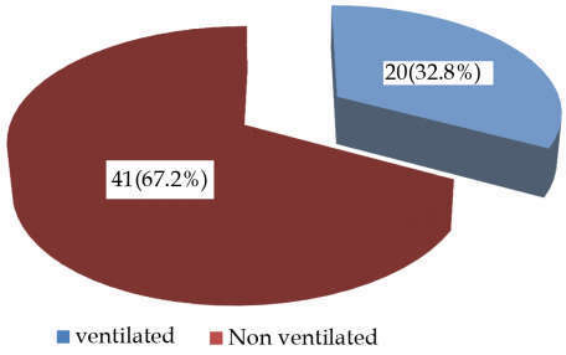

Fig. 2: Sex distribution of study population

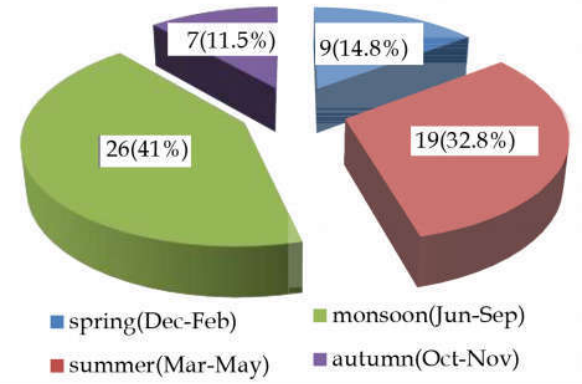

Fig. 3: Seasonal distribution

Most of the patients belong to the 5th decade (n=20), followed by 4 th decade (n=17).The mean age was 38.4±14.1 years with range from 4 to 74 years. Three were children less than 13 years.

Males (n=38) outnumbered the females (n=23) by constituting 62.3% out of 61 patients. Male: female ratio was 1.7: 1.

The seasonal distribution of the patients showed highest clustering in the monsoon (n =26) with 41% followed by summer season (n=19) with 32.8%.

The history of antecedent infection was noted in 34 (55.73%)of the subjects. The most common antecedent events observed were fever without focus in 21 (34.4%) patients, followed by gastroenteritis in 7 (11.5%) patients.

Mean duration from antecedent illness to onset of neurological symptoms is 11 days with a range of 7-20 days.

URTI= Upper respiratory tract infection GE=gastroenteritis FF =fever without focus NIL= No antecedent event

Hypertension was present in 4 (6.6%) patients, diabetes mellitus in 3 (4.9%) patients, and coronary artery disease in 3 (4.9%) patients. 3 (4.9%) patients were smokers and 4(6.6%) were alcoholics.

The median duration to get admitted in hospital from disease onset was 8 (range 4-18) days, and the median time to reach nadir of the disease was 7 (range 5-14) days. The median duration of total hospital stay was 16 days, with minimum and maximum duration of hospital stay being 7 and 60 days, respectively. All

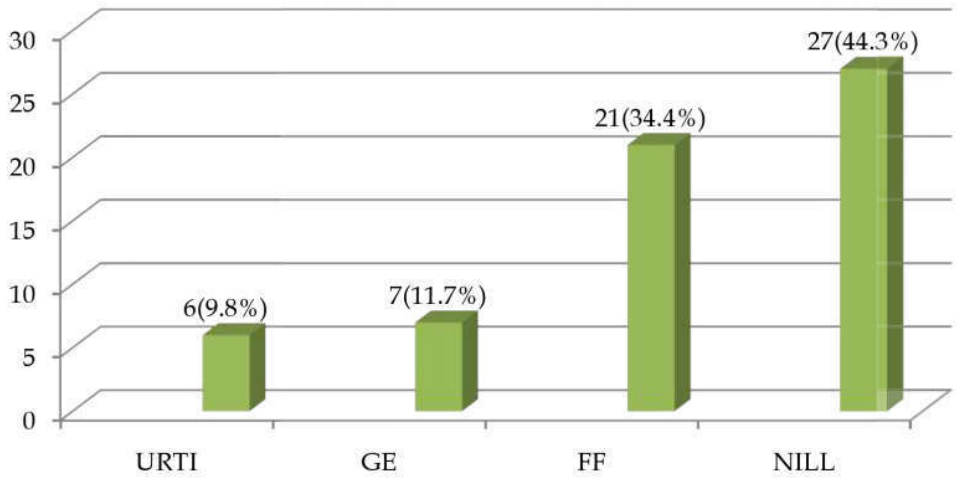

Fig. 4: Spectrum of antecedent events in the study population

Table 1: Clinical features of the study population at admission

Clinical Feature	Frequency
Limb weakness	
-Quadriparesis	54 (88.5%)
-Paraparesis	6(11.4%)
- no weakness	1(1.6%)
Reflexes	
-Global areflexia	53(88.6%)
-Retained upper limb reflexes	7(11.4%)
-Normal reflexes	1(1.6%)
Cranial nerve weakness	
-Facial weakness	41(67.2%)
-Ophthalmoplegia	2(3.2%)
-Bulbar weakness	24(39.3%)
Sensory involvement	25(41%)
Respiratory failure	20(32.8%)
Autonomic disturbance	19(31%)

patients presented with symmetrical weakness. Quadriparesis was present in 54 (88.5%) patients. Global areflexia was present in 53 (88.6%) patients. Bilateral facial palsy was the most common cranial nerve involvement presenting in 41 (67.2%) followed by bulbar weakness in 24 (39.3%) patients.

Applying GBS study group clinical criteria 52 (85.2%) patients were classified into classical GBS, 6 (9.8%) patients into paraparetic-GBS, 1 (1.6%) patients into GBS-Miller-Fisher Syndrome overlap, 1 (1.6%) patient into Bickerstaff brainstem encephalitis(BBE), and 1 (1.6%) patient is classified into Miller Fisher Syndrome(MFS).

Lumbar puncture was done in 32 patients (52.4%). The time interval between onset of disease and lumbar puncture was at a median of 12 (range of 6-18) days. The classic 'albuminocytologic dissociation', defined as the combination of an increased protein concentration and a cell count of <50 cells/uL, was observed in 18/32 (56.2%) of these patients.

Other laboratory features observed were: neutrophilicleucocytosis [(n=24/61 (39.3%)], elevated ESR [n=19/61 (31.14%)], and elevated hepatic transaminases [(n=15/97 (24.5%)].

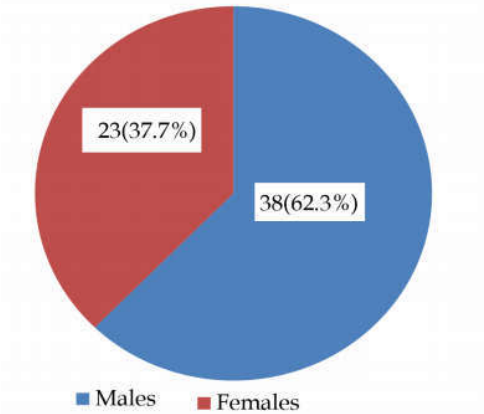

Fig. 5: Proportion of patients ventilated and non- ventilated

One patient serum tested positive for Hepatitis B antigen.

During the course of hospital stay 20 (32.8%) patients required ventilatory support.

During hospital course 5 (8.2%) patients developed complications. Two patients developed deep venous thrombosis, two developed pneumonia and one patient developed atelectasis.

Discussion

Guillain Barre Syndrome is the most common cause of acute flaccid paralysis. Nerve conduction studies (NCS) play a vital role in establishing the diagnosis of GBS, classification in to subtypes and prognostication. There is disparity among the studies in India and rest of the world regarding incidence of subtypes of GBS.

Single nerve conduction study is not sufficient to accurately establish the subtype of GBS. Recently it was recognised that early in the course of the disease electrophysiological changes in AMAN subtype mimics AIDP subtype leading to over estimation of the AIDP. Hence serial nerve conductions are necessary for the accurate classification of GBS in to subtypes. Data regarding the serial nerve conduction studies in GBS patients is sparse and there are no published Indian studies of this type.

The present study is undertaken to accurately estimate the incidence of subtypes of GBS by serial nerve conduction studies performed at admission and 3-8 weeks after the onset of illness. Present study is a prospective observational study which is conducted between April 2014 and December 2015. A total of 61 patients of GuillainBarre Syndrome admitted in neurology intensive care unit and neurology ward were included in the study.

Majority of the patients in the present study were in their 3rd and 4 thdecade of life with mean age of 33 years similar to previous studies from India [6,7]. This is in contrast to other studies from Australia (median age-52 years) (78), Mexico (mean age-48 years) (79), and Iran (mean age-39 years) (80). Men were more frequently affected similar to that observed in most of the other studies worldwide [6,7].

The present study showed bimodal seasonal distribution with maximum peak in rainy season (41%) and another peak in summer season (32.8%). Most of the studies from other parts of India also showed higher incidence of GBS in rainy season,

while a meta-analysis of 42 studies showed that incidence of GBS was greater in winter season in Western countries, the Far East and Middle East [8].

The heterogeneity between these studies may be due to the different geographical regions, the difference in nature and duration of seasons based on latitude and longitude, seasonal and geographical variability in the incidence of antecedent infectious diseases.

With regard to antecedent infections, non specific fever (fever without focus) (34.3%) was the most common antecedent event observed in the present study, followed by gastroenteritis (10%) and respiratory tract infections (3%). Studies from Northern India and Japan also showed higher frequency of fever (Indian study-22.3% and Japanese study-52%) as antecedent event in patients with GBS, followed by respiratory tract infection and gastroenteritis [9,10].

In the present study, 52.4% of patients underwent lumbar puncture, because of unwillingness of patients as well as non-suspicion of alternative diagnosis. The time interval between onset of disease and lumbar puncture was at a median of 12 (IQR 8-16) days. CSF albumin-cytological dissociation was observed in 18/32 (56.2%) ofpatients. CSF albumin-cytological dissociation was observed in 68% of patients with GBS in a study from Northern India andin a study from Netherlands, it was observed in 64% of patients with GBS (49% at the first day to 88% after 2 weeks). These findings suggests that the CSF is examined mainly to exclude disorders that are associated with pleocytosis, instead of seeking confirmation of the diagnosis GBS.

Conclusion

- 61 out of the 84 patients satisfying GBS study group clinical criteria underwent the serial nerve conduction studies were included in the study.
- Majority of the patients were in their $4^{th}$and 5^{th} decade. The mean age was 38.4±14.1 years with range from 4 to 74 years.
- Males (n=38) outnumbered females (n=23) (male: female=1.7:1).
- Most of the patients presented in monsoon (41%) and summer (32.8%) season.
- History of antecedent infections was present in more than half of the study population (55.7%) patients and the median interval between antecedent infection and onset of disease was 11 (IQR 7-20) days. Non specific fever (fever without localisation) (44.3%) was the most common antecedent event observed in the present study, followed by gastroenteritis (11.7%) and respiratory tract infections (9.8%).

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