Original Article

Gender Influence on Clinical and Electrophysiological Manifestations of Guillain-Barre Syndrome (GBS), and Response to Treatment

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ABSTRACT

Objective: To study the gender influence on clinical and electrophysiological manifestations and response to treatment.

Study Design: Retrospective / cross sectional study

Place and Duration of Study: This study was conducted at the Neurology Department of Mayo Hospital Lahore for a period of seven months from October 2017 till April 2018.

Materials and Methods: Patients fulfilling the Asbury and CornBlath's Criteria for diagnosis of GBS were included in the study. Subtypes or variants of GBS were identified according to our defined operational definitions. All patients who showed progression of disease were treated with five sessions of plasmapharesis performed over 10 days. Clinical features, muscle power strength on admission and NCS/EMG and CSF findings and duration of hospital stay required for one grade improvement in MRC scale before discharge results were recorded on a specified proforma designed for this study. The results were analyzed using IBM SPSS version.

Results: Twenty nine (29) patients fulfilling the Asbury and CornBlath's Criteria for diagnosis of GBS were included in the study. There were 19 males and 10 females with M: F of 1.9:1. The mean age for male group (n=19) was 39(+16.92) with range 15 to 75 years. The mean age for female group (n=10) was 32.30(+8.05) with range 6 to 41 years. The mean muscle power in limbs on admission according to MRC grading in female group was 1.50 (+1.354) compared with mean muscle power in male group of 2.50 (+1.150). The various subtypes of GBS in male group were AMSAN 52.63% (10 out of 19 patients), AIDP 36.84% (7out of 19 patients) and AMAN 5.2% (one patient). In comparison AIDP was most common 70% (7 out of 10 patients) variant of GBS in the female group followed by AMSAN 30% and AMAN 10%. The respiratory distress requiring ventilator support occurred in 15% (3 out of 19) of male patients compared with none in female group. Bilateral facial weakness was seen in 26% (5 out of 19) male patients compared with 30% in female group. Dysphagia occurred in 21% (4 out 0f 19) in male group compared with 10% (1 put of 10) in female group. All patients with progression of disease after admission to hospital were treated with alternate day sessions of plasmapharesis for a total five sessions. For the male group mean duration of hospital stay for improvement in muscle power of limbs according to MRC grade of one from the baseline before discharge was 11.63(+ 12.584) days with range from 2-45 days. In comparison the mean duration of hospital stay for female group was 20.10 (+ 8.749) days with range from 3-30 days.

Conclusion: In conclusion our study confirms significant gender influence on the clinical and electrophysiological manifestations of Guillain-Barre syndrome (GBS), and response to treatment. AMSAN was most common subtype in males and AIDP in females. Limb weakness was severe in female on admission and required prolonged hospital stay compared with males. Bilateral facial weakness, dysphagia and respiratory involvement were more common in males. This study has small sample size and larger studies are needed to confirm our findings.

Key Words: Guillain-Barré syndrome, Gender, Male, female, muscle weakness, areflexic

Citation of articles: Javed M, Khan UA, Javed F, Abbas RZ, Javed MA. Gender Influence on Clinical and Electrophysiological Manifestations of Guillain-Barre Syndrome (GBS), and Response to Treatment. Med Forum 2018;29(7):25-28.

INTRODUCTION

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Received: May, 2018; Accepted: June, 2018

Guillain-Barre Syndrome is a group of autoimmune disorders of the peripheral nervous system characterized by rapidly progressing polyradiculoneuropathy.[1] The aberrant auto-immune response consistent with the disease process is usually triggered by a preceding infection of the respiratory or gastrointestinal tract.[2] Infectious agents with a recognized role in disease pathogenesis include Campylobacter jejuni, Cytomegalovirus (CMV), Mycoplasma pneumonia, Ebstein Barr Virus and

Influenza Virus.[3] Classic clinical presentation of GBS is sudden onset progressive symmetrical motor weakness with loss or diminution of deep tendon reflexes.[4] Clinical nadir is reached in 90% of patients by four weeks. Bulbar palsy, facial palsy, ophthalmoplegia may occur secondary to cranial neuropathies with one- third of patients requiring mechanical ventilation due to paralysis of diaphragm.[1, 5] Epidemiological studies on GBS estimate the average global annual incidence rate of the disease to be 1.1-1.8 cases per 100000 population. [6, 7, 8] Incidence of disease is seen to increase linearly with age; adults being affected more frequently than children. [6, 7] An approximate male to female preponderance of 3:2 has been appreciated. [6, 9]

While the diagnosis of GBS is made on clinical grounds, electro-diagnostic studies are essential for predicting prognosis and for classifying the disease into its distinct variants.[10] GBS has three common subtypes: Acute inflammatory demyelinating neuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN). Predominant subtype varies geographically; AIDP is more prevalent in Europe and North America while AMAN is the common form in East Asia.[10, 11]

Being an autoimmune disease, the impact of gender in defining clinical picture of Guillain-Barre Syndrome should be significant.[10] Yet, of the innumerable studies conducted on GBS, little has been done to investigate the degree of sex influence on the presentation of GBS and electrophysiological pattern. The objective of this study was to ascertain the role of gender, if any, on the clinical and electrophysiological manifestations of GBS, and response to treatment.

MATERIALS AND METHODS

This was a retrospective cross sectional study designed to see Gender influence on Clinical and electrophysiological manifestations in patients presenting with Guillain-Barre Syndrome (GBS). The study was conducted at the Neurology Department of Mayo Hospital Lahore for a period of seven months from October 2017 till April 2018. Medical records of the patients with clinical diagnosis of GBS were reviewed. A special proforma was designed to record clinical features, demographic details, nerve conduction findings, CSF abnormalities and duration of hospital stay required for one grade improvement in muscle power of limbs as per MRC scale before discharge.

Patients fulfilling the Asbury and CornBlath's Criteria for diagnosis of GBS were included in the study.[12] Features necessary for diagnosis included progressive motor weakness of both lower and upper limbs which developed over few days to 4 weeks associated with areflexia. Other supportive diagnostic features were abnormal nerve conduction studies consistent with various types of GBS and CSF cytoalbuminologic dissociation. Diagnosis was excluded in the presence of any one of the following features; recent history of hexacarbon abuse, abnormal porphyrin metabolism, recent diphtheritic infections, lead neuropathy with evidence of lead intoxication, purely sensory syndromes or a definitive diagnosis of similar conditions: poliomyelitis, botulism, hysterical paralysis, toxic, metabolic, drug induced or vasculitic neuropathy.[12] Patients with paraneoplastic or paraproteinemic neuropathy were also excluded from the study.

Assessment of Motor weakness of the upper and lower limbs was made using the MRC scale for muscle power (Table 1)[13]. The lowest power grade for any of the four limbs was then used for comparative purposes.

Duration of hospital stay was taken as number of days spent in hospital required for at least one grade improvement in muscle power according to MRC scale. Response to treatment was considered negative with a decrease in the MRC power grade by one or more points. Assessment of cranial nerve involvement was made on purely clinical grounds.

Electrophysiological classification into distinct subgroups was done using the suggested electrodiagnostic protocols[14]. Criteria used for classification into AIDP, AMAN, and AMSAN is as follows[15].

AIDP: At least one of the following in each of at least two nerves, or at least two of the following in one nerve if all others inexcitable and distal compound muscle action potential (dCMAP) >10% lower limit of normal (LLN).

- Motor conduction velocity<90% LLN (85% if dCAMP <50% LLN)
- Distal motor latency >110% upper limit of normal (ULN) (>120% if dCMAP <100% LLN)
- pCMAP/dCMAP ratio <0.5 and dCMAP >20% LLN
- F-response latency >120% ULN

AMAN:

- None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP <10% LLN
- Sensory action potential amplitudes normal.

AMSAN:

- None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP <10% LLN.
- Sensory action potential amplitudes less than LLN.

RESULTS

Twenty nine (29) patients fulfilling the Asbury and CornBlath's Criteria for diagnosis of GBS were included in the study There were 19 male and 10 female patients with M: F of 1.9:1.

The mean age for male group (n=19) was 39(+16.92) with range 15 to 75 years. The mean age for female group (n=10) was 32.30(+8.05) with range 6 to 41 years. The mean muscle power in limbs on admission according to MRC grading in female group was 1.50 (+1.354) compared with mean muscle power in male group of 2.50 (+1.150). The various subtypes of GBS in male group were AMSAN 52.63% (10 out of 19 patients), AIDP 36.84% (7out of 19 patients) and AMAN 5.2% (one patient). In comparison AIDP was most common 70% (7 out of 10 patients) variant of GBS in the female group followed by AMSAN 30% and AMAN 10%. The respiratory distress requiring ventilator support occurred in 15% (3 out of 19) of male patients compared with none in female group. Bilateral facial weakness was seen in 26% (5 out of 19) male patients compared with 30% in female group. Dysphagia occurred in 21% (4 out 0f 19) in male group compared with 10% (1 put of 10) in female group. All patients with progression of disease after admission to hospital were treated with alternate day sessions of plasmapharesis for a total of five sessions. For male group the mean duration of hospital stay for improvement in muscle power of limbs according to MRC grade of one from the baseline before discharge was 11.63(+ 12.584) days with range from 2-45 days. In comparison the mean duration of hospital stay for female group was 20.10 (+ 8.749) days with range from 3-30 days.

Table No.1: MRC Scale of Muscle Power

0	No contraction
1	Flicker or trace of contraction
2	Active movement, with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

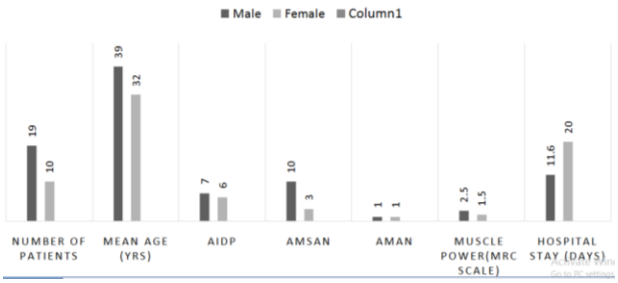

Figure No.1: Gender influence on different variables of GBS

DISCUSSION

This is first study from Pakistan to assess the gender influence on various clinical and electrophysiological features of GBS. Most published studies report male preponderance for GBS with an approximate M: F ratio of 1.9:1.[16-18] Our study also confirm this finding with males being affected more than females. This is in contradiction to studies that a definite female predominance is found in many autoimmune diseases. Gender has been also associated with differences in clinical presentation, onset, progression and outcome of autoimmune diseases such as multiple sclerosis.[19] HLA associations are also found to differ with the gender of the patient in some autoimmune diseases. McCombe et al investigated whether there were gender-related HLA associations in Guillain–Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), both of which occur more frequently in male patients than in females. His study showed no particular HLA associations in GBS except for a slight negative association for carriage of HLA-DR5 in both males and females. In a new study to determine *Campylobacter jejuni* infection in GBS patients before onset of neurologic symptoms, it was found that male patients were three times more likely to have serologic evidence of *C. jejuni* infection ($P = 0.009$)[21]. In yet another study factors found to be associated with poorer current level of functioning and wellbeing outcomes in survivors of Guillain–Barre syndrome (GBS) included females, older patients (57+ years), acute hospital stay >11 days, those treated in intensive care and those discharged to rehabilitation. No associations were found between the Medical Research Council (MRC) Motor Scale Rating scores at admission [22]. In line with these findings, results of our study show that female patients have a low mean MRC grading on admission and also prolonged hospital stay compared with males. However contradictory to this are results of Italian Guillain-Barre Study Group showing that the chance of recovery is significantly affected by age, antecedent gastroenteritis, disability, electrophysiological signs of axonopathy, latency to nadir and duration of active disease with no gender influence on outcome[23].

CONCLUSION

In conclusion our study is the first study of its kind designed to see the gender influence on the clinical and electrophysiological features and outcome of GBS. We found that AIDP was most common variant of GBS (70%) in female gender and AMSAN (52.63%) in male patients. This finding has not been reported before. Similarly we found that cranial nerve palsies especially bilateral facial weakness and dysphagia occurred more commonly in males compared with females. This observation has also not been published before. Finally, limb weakness was more severe in female group (mean MRC grade 1.5) compared with male group (mean MRC grade 2.5) and as a result the mean hospital stay was prolonged in female group than in male group. All these sex gender differences in GBS has not been reported before. Keeping in view of small sample size

of our study, lager studies are needed to confirm our findings.

Author's Contribution:

Concept & Design of Study:	Maryam Javed
Drafting:	Usman Ali Khan, Fatima Javed
Data Analysis:	Raja Zaigham Abbas,
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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