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Clinical Features, Role of Mobile Plasmapharesis Unit and Outcome in Patients with Acute Inflammatory Demyelinating Polyradiculoneuropathy (Guillain-Barré Syndrome)

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ABSTRACT

Objective: To study the clinical features, role of mobile plasmapharesis unit and outcome in patients with acute inflammatory demyelinating polyradiculoneuropathy (AIDP).

Study Design: Retrospective Cross Sectional Study

Place and Duration of Study: This study was conducted at Neurology Department, KEMU, Lahore from July 2008 till June 2012.

Materials and Methods: Patients from various hospitals (both public and private) fulfilling the Ashbury and Cornblath's Clinical Diagnostic Criteria for GBS and requiring plasmapharesis were included in the study. For this purpose a special proforma was designed to be filled by the primary physician at the time of request for mobile plasmapharesis service. This service was provided by a donor organization namely Pakistan Myasthenia Gravis Welfare Organization (PMWO) based at a public hospital in Lahore. Plasmapharesis was started according to the guidelines, as soon as possible after admission, if patient had history of progressive weakness. The protocol of this treatment was to exchange 200 to 250 ml of plasma per kilogram of body weight in five sessions within 7 to 10 days. The replacement fluids most often consist of 0.9% normal saline, haemaccel and/or albumin. Recovery was assessed by modified Hughes Guillain-Barré syndrome disability scale.

Results: A total of 152 patients were included in the study with 94 (61.8%) males and 58 (38.2%) females and M: F ratio of 1.62:1. The mean age was 32.66 (SD 15.89) with range from 7-80 years. One hundred and nine (72%) cases presented between 11-40 years of age. All patients were treated with five sessions of plasmapharesis. Drop out rate for plasmapharesis was 1.5% implying its good tolerability.

Out of the total of 152 cases, 149 (98%) cases presented with progressive areflexic weakness and 3 (2%) patients with bilateral external Ophthalmoplegia, areflexia and ataxia (Miller-Fisher variant). Sensory symptoms were present in 31(20.4%), bulbar weakness in 29(19.1%), and bilateral facial weakness in 25(16.4%) cases. Severe respiratory distress requiring ventilatory support occurred in 36(23.7%) cases. Pearson's correlation revealed that gender and age were not risk factors for the development of ventilatory failure (p=0.354; 0.803), bilateral facial weakness (p = 0.121; 0.473) or bulbar weakness (p= 0.383; 0.745) respectively.

Overall mortality was 5% and all these cases developed severe respiratory distress and needed ventilatory support. Complete recovery occurred in 90% cases and 5% had residual deficit (Hughes disability scale severity 1 & 2) at mean follow up of six months.

Conclusions: Our study showed that GBS is statistically more frequent in males than females in our local population with maximum frequency between 11-40 years of age range. However, the two factors i.e. gender and age has no significant association with the development of ventilatory failure, bilateral facial weakness and bulbar weakness. Areflexic motor weakness was the commonest presenting feature. Plasmapharesis remained very effective therapeutic option which is cheaper and affordable in our poor socio-economic setting. Mobile unit service provided an excellent opportunity to treat most of these patients at their native hospitals. We recommend that government and donor organizations should develop more mobile plasmapharesis services in all major cities which can cover nearby district and tehsil hospitals.

Key Words: Acute inflammatory demyelinating polyradiculoneuropathy; Areflexic weakness; Respiratory distress; Intravenous immune globulin (IVIg); Plasmapharesis.

INTRODUCTION

'Guillain-Barré Syndrome (GBS) or Acute Inflammatory Demyelinating Polyradiculo-neuropathy (AIDP)' is characterized by an acute monophasic, non-febrile, post-infectious illness manifesting as ascending weakness and areflexia.[1] The syndrome is named after the French physicians Georges Guillain and Jean Alexandre Barré, who described it in 1916. Sensory and autonomic abnormalities may also be seen.

GBS is subdivided into four distinct forms based on histopathological and neurophysiological basis: Acute inflammatory demyelinating polyradiculoneuropathy

(AIDP); Acute motor axonal neuropathy (AMAN); Acute motor and sensory axonal neuropathy (AMSAN) and Miller-Fisher syndrome (MFS).[2,3,4] All forms of Guillain–Barré Syndrome are autoimmune diseases due to an immune response to foreign antigens (such as infectious agents). Immune response, instead, is mistargeted at host nerve tissues, a phenomenon called 'molecular mimicry'.[5] The most common antecedent infection is the bacterium Campylobacter jejuni, followed by cytomegalovirus (CMV).[6,7,8]

Supportive care is the cornerstone of successful management in the acute patient. Of greatest concern is respiratory failure due to paralysis of the diaphragm. Intubation may be needed when there is evidence of impending failure of the muscles of breathing.

Subsequently, main therapeutic options consist of either plasmapharesis (filtering antibodies out of the blood stream) or administration of intravenous immune globulin (IVIg) to neutralize harmful antibodies and inflammation causing disease. These two treatments are equally effective and a combination of the two is not significantly better than either alone. [9, 10] Glucocorticoids have not been found to be effective in GBS.[10] Treatment is usually begun as soon as the diagnosis is made.

The immune globulin (IVIg) has important practical advantages, since it can be administered without delay in every hospital. Furthermore, treatment with immune globulin is well tolerated and is considered safe, especially with respect to viral transmission.[11,12,13] On the other hand, plasmapharesis facility may not be available in every hospital, requires a double lumen central catheter and each session lasts for 3-4 hours. The procedure is technically difficult to perform in children, and it may be contraindicated at any age because of cardiovascular instability; the largest trial of plasma exchange had a 10 percent dropout rate.[14] Furthermore, cost of IVIG is about 0.6 - 1.2 million PKR (U.S$ 6,400 – 12,500) compared with five sessions of plasmapharesis which is around PKR 60,000 (U.S$ 640) and is much cheaper.

The availability of mobile plasmapharesis unit made it possible to provide this facility to patients admitted in different hospitals, even, in various cities. We undertook this prospective study to analyze the clinical features, role of mobile plasmapharesis service unit and outcome in patients of GBS in our local population.

MATERIALS AND METHODS

This was a retrospective cross sectional study on all cases of Guillain-Barré syndrome that required plasmapharesis between July 2008 and June 2012. A special proforma was designed to record the clinical features to be filled by the primary physician at the time of request for plasmapharesis. Recruitment was done from various hospitals in Lahore and other cities including public and private hospitals. Patients fulfilling the Ashbury and Cornblath's clinical diagnostic criteria for GBS (Table 1) were included in the study[15]. Exclusion criteria included all cases with asymmetric motor weakness, bladder or bowel dysfunction at onset, distinct sensory level suggestive of transverse myelitis, and >50 mononuclear leukocytes/mm^3 or presence of polymorphonuclear leukocytes in CSF.

As per guidelines of Consensus Conference[16], an updated plasmapharesis service was provided to all the patients by the donor organization named Pakistan Myasthenia Gravis Welfare Organization (PMWO). Plasma exchange was started, as soon as possible after admission under optimal conditions, if patient had history of progression of weakness. The protocol of this treatment was to exchange 200 to 250 ml of plasma per kilogram of body weight in five sessions within 7 to 10 days. The replacement fluids most often consists of 0.9% normal saline, haemaccel and/or albumin.

Follow up was done by regular clinical review of all patients admitted in Mayo and National Hospitals, Lahore by the authors. Clinical information about patients admitted in other hospitals was obtained through telephonic communications with the primary physicians. Follow up at six months was done by authors in outpatient or telephonic communication to the patients and their relatives. Recovery was assessed by modified Hughes Guillain-Barré syndrome Disability scale (Table 2).[17] Statistical analysis was done by SPSS version 16.

RESULTS

A total of 152 patients of GBS were included in the study with 94(61.8%) males and 58(38.2%) females and M:F 1.62:1. The mean age was 32.66 (SD 15.89) with range from 7-80 years. One hundred and nine (72%) cases presented between 11-40 years of age (Table 3).

Out of the total 152 cases 149 (98%) cases presented with progressive areflexic motor weakness and 3 (2%) with bilateral external ophthalmoplegia, areflexia and ataxia (Miller Fisher variant). Severe sensory symptoms were present in 31 (20.4%), bulbar weakness in 29 (19.1%), and bilateral facial weakness in 25 (16.4%) cases. Severe respiratory distress requiring ventilatory support occurred in 36 (23.7%) cases (Table 4). Gender based analysis of various manifestations revealed that out of 94 male patients, 25 (26.5%) required ventilatory support, 12(12.8%) developed bilateral facial weakness and 20 (21%) had bulbar weakness. In female patients with GBS (n=58), 11 (18.9%) required ventilatory support, 13 (22%) developed bilateral facial weakness and 9 (15.5%) had bulbar weakness. Pearson's correlation revealed that gender and age was not a risk factor for the development of ventilatory failure (p=0.354; 0.803), bilateral facial weakness (p = 0.121; 0.473) or bulbar weakness (p= 0.383; 0.745) respectively.

Table No.1: Asbury & Cornblath's Diagnostic criteria for Guillain-Barré Syndrome

Required features
• Progressive weakness in both arms and legs • Areflexia (or hyporeflexia)
Features supportive of diagnosis
• Progression of symptoms over days to 4 weeks • Relative symmetry • Mild sensory signs or symptoms • Cranial nerve involvement, especially bilateral facial weakness • Recovery beginning 2 to 4 weeks after progression ceases • Autonomic dysfunction • Absence of fever at onset • Typical CSF (albuminocytologic dissociation) • EMG/nerve conduction studies (characteristic signs of a demyelinating process in the peripheral nerves)
Features casting doubt on the diagnosis
• Asymmetrical weakness • Persistent bladder and bowel dysfunction • Bladder or bowel dysfunction at onset • >50 mononuclear leukocytes/mm^3 or presence of polymorphonuclear leukocytes in CSF • Distinct sensory level
Features that rule out the diagnosis
• Hexacarbon abuse • Abnormal porphyrin metabolism • Recent diphtheria infection • Lead intoxication • Other similar conditions: poliomyelitis, botulism, hysterical paralysis, toxic neuropathy.

Table No. 2: Guillain-Barré Syndrome Disability Scale (Hughes)

0	Healthy
1	Minor symptoms or signs of neuropathy but capable of manual work/capable of running
2	Able to walk without support of a stick (5m across an open space) but incapable of manual work/running
3	Able to walk with a stick, appliance or support (5m across an open space)
4	Confined to bed or chair bound
5	Requiring assisted ventilation (for any part of the day or night)
6	Death

Table No.3: Age and sex distribution.

Age	Males	Females	Total
1-10	1	0	1
11-20	33	10	43
21-30	20	22	42
31-40	18	06	24
41-50	08	12	20
51-60	09	03	12
61-70	04	03	07
71-80	01	02	03
Total	94	58	152

Table No.4: Presenting symptoms and complications

Symptoms	Males	Females	Total
Areflexic motor weakness of limbs	90 (95.7%)	56(96.5%)	146 (96%)
Severe sensory symptoms	23(24.4%)	08(14.8%)	31(20%)
Respiratory muscle weakness requiring ventilatory support	25(26.9%)	11(18.9%)	36 (23.6%)
Bilateral facial weakness	12(12.7%)	13(22.4%)	25(16.4%)
Bulbar weakness	20(21.2%)	09(15.5%)	29(19%)
Miller fisher variant	03(3.1%)	00	3(2%)

All patients were treated with five sessions of plasmapharesis done at their native hospital from various cities (Table 5). There was drop out of two patients (1.5%) due to hypotension and severe hypoalbuminemia. Overall mortality was 5% and all these patients developed severe respiratory distress. Complete recovery occurred in 90% cases and 5% had residual deficit (Hughes disability scale severity 1 & 2) at mean follow up of six months.

Table No.5: Number hospital covered by single mobile plasmapharesis unit.

City	Public hospitals	Private hospitals	Total
Lahore	5	11	16
Faisalabad	1	1	02
Bahawalpur	1	0	01
Total	7	12	19

DISCUSSION

To our knowledge this is the largest study on patients suffering from GBS who were treated with plasmapharesis in Pakistan. Our study showed that GBS is more common in males compared with female with M: F ratio of 1.62:1. This male preponderance has been previously reported in various international and local publications both in adult and pediatric population.[18-21] In our series maximum number of cases [86/152 (72%)] occurred between 11-40 years of age. In the United States, age distribution is apparently bimodal, with most patients presenting from 15-35 years or 50-75 years. In China (and other countries), frequent outbreaks in children aged 2-12 years have been reported.[22]

Acute onset areflexic motor weakness was present in 98% cases. The reported incidence of motor weakness as presenting symptom varied from 75-95%.[23,24] In our study bulbar involvement was seen in 29 (19%). Bulbar involvement was noted in 29-35% of cases in another series.[25] Ventilatory support was required in 36 (23.7%) cases in our study. A previous study from Karachi

showed that 55.9% patients developed respiratory muscle weakness support requiring intubation. [26] This low frequency of respiratory muscle weakness may be because most of the patients presented early in the course of the disease and immediately treated with plasmapharesis. In our study isolated Miller-Fisher variant was seen in 3 (2%). This variant has been reported in 5% of GBS cases.[27]

Since all the patients in our study had plasmapharesis, the clinical features and course of the disease may be different from other published studies which included all the cases of GBS (treated with IVIg or plasmapharesis and those not requiring any treatment).

Response to plasmapharesis was excellent in our study. Only 5% patients died and 90% recovered completely with 5% had residual deficit. Drop out rate directly related to plasmapharesis was 1.5% (2 cases) and was due to severe hypotension and hypoalbuminemia. Advantages of mobile plasmapharesis unit included broad coverage of hospitals in and outside Lahore (Table 4), low cost and good tolerability. Most patients were treated at native places without the need to shift to tertiary care neurology center and thus avoiding further inconvenience to their relatives.

A previous study had shown immunoglobulin to be superior to plasmapharesis.[28] However it is generally agreed that both treatments are equally effective for GBS. There are reports where plasmapharesis was done in patients who did not respond to immunoglobulin and showed significant improvement.[29]

In summary, our study showed that GBS is more common in males than females in our local population with maximum frequency between 11-40 years of age. Areflexic motor weakness is most common presenting feature. Plasmapharesis remained good therapeutic option for all ages and sex, which is also much cheaper, affordable and effective. Mobile unit service provided an excellent opportunity to treat most of these patients at their native hospitals. The above results are related to only one center. If we can develop such centers at various major city hospitals, this will be a great service to treat this potentially fatal condition, and also help decrease disability and hasten recovery time for patients with GBS. We recommend that government and donor organizations should develop more mobile plasmapharesis services in all major cities which can cover nearby district and tehsil hospitals.

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