STUDY OF EPIDEMIOLOGICAL AND CLINICAL PROFILE OF CHILDHOOD GUILLAIN-BARRE SYNDROME AT THE CHILDREN'S HOSPITAL, LAHORE

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ABSTRACT

Objective: To ascertain the demographic profile, diversity of clinical aspects of Guillain-Barre Syndrome (GBS) along with its prognosis.

Study Design: Cross sectional study.

Place and Duration of Study: Department of Pediatric Neurology, The Children's Hospital Lahore, from Jul 2015 to Dec 2016.

Material and Methods: One hundred and twenty five patients of both genders from the age of 1 to 15 years, fulfilling the inclusion criteria were included in the study. The clinical data were entered into proforma.

Results: Out of the total, 77 (61.6%) were males and 48 (38.4%) were females. History of preceding illness was recorded in 57.6% of the patients and Upper Respiratory Tract Infection (URTI) 31.2% was the most common. 54.4% of the patients had cranial nerve paralysis. Upon electro diagnostic studies including electromyography (EMG) and nerve conduction studies (NCS) and clinical examination, there were 49 patients with acute inflammatory demyelinating polyradiculoneuropathy variant (AIDP), 67 had acute motor axonal neuropathy variant (AMAN), 6 patients having mixed and 3 patients with Miller Fischer syndrome (MFS). Treatment with intravenous immunoglobulins (IVIG) was given keeping in mind the indication. At 6 months follow up visit 89.6% of the patients had good outcome while 10.4% patients had poor outcome.

Conclusion: The results of our study show that GBS is a disease with diverse clinical presentation. With the help of diagnostic facilities like EMG/NCS, well-equipped treatment and IVIG clinical outcome is good.

Keywords: Antecedent illness, Guillain-Barre syndrome, Polyradiculoneuropathy.

INTRODUCTION

Guillain-Barre syndrome (GBS) is an immune mediated polyradiculoneuropathy that is one of the common causes of acute flaccid paralysis (AFP). It is characterized by ascending paralysis, areflexia and raised protein in cerebrospinal fluid. The disease was noticed way back in 1859 by Landry having a disease with acute progressive paralysis of lower motor neuron type. Later on, in 1916 same illness was described by three French neurologists, George Guillain, Jean Alex Barre and Andrea Strohl, who noticed acute flaccid paralysis with absent deep tendon reflexes and later on spontaneous improvement in two soldiers[1].

GBS can present at any age group i.e. neonatal period to late adolescent but some of them can present in adult life. The disease has its prevalence worldwide with an incidence of 1.1 to 1.8 per 100,000 populations. But this figure is slightly lower in children i.e. 0.9 to 1.1 case/ 100,000 children[2,3] but in North America incidence of GBS in pediatric age group was seen as high as 1.37/100,000 per year[4].

Unlike other autoimmune diseases, GBS is more common in males. With a dramatic decline in incidence of polio worldwide, GBS has become the most common cause of AFP in children[5]. This illness is usually followed by antecedent infection which activates immune response that produces some antibodies that target the myelin or axons of peripheral nerves ultimately leading to neuropathy. The immune mediated nature of the disease has been confirmed by the presence of different antibodies in patients of GBS.

The disease typically starts with acute onset of bilateral symmetrical ascending paralysis of

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lower motor neuron (LMN) type involving upper and lower limbs. The disease is usually rapidly progressive and may involve cranial nerves and may even cause respiratory failure. GBS may also affect sensory as well as autonomic nervous system. The natural pattern of the disease is categorized into 3 phases: progressive phase in which there is continuous increase in weakness leading to maximum weakness lasts for 2 to 4 weeks. The second phase is the plateau phase which lasts for about 2 to 4 weeks and followed by recovery phase which usually takes 2 weeks but it can take months to years for full recovery.

There are multiple subtypes of disease. Acute inflammatory demyelinating radiculo-neuropathy (AIDP) is most common variant of acute GBS. It is due to involvement of myelin sheath and Schwann cells of sensory and motor nerves. This is in contrast of axonal variety, the second most occurring form of GBS in which there is damage to axons directly with relative sparing of the Schwann cells. The axonal involvement may take the form of acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal nuropathy (AMSAN) depending upon the nature of nerve fibers involved. Miller Fischer is fourth variant characterized by extra ocular eye muscle involvement, ataxia and areflexia. It is present in 10% of cases of GBS. It usually has better outcome[6].

Electromyography (EMG) and nerve conduction studies (NCS) are the main diagnostic tools of the disease. In cerebro spinal fluid (CSF), proteins are raised without increase in white cell count. Moreover antibodies to GM1, GD 19, GQ1, GD1, GT1a are present in serum of patients with GBS with frequency of about 30 to 70%[7,8].

The treatment of disease is supportive as well as specific. Supportive treatment includes care of bed ridden patients. Treatment of autonomic complications and ventilator care where required. Specific treatment includes Intravenous immunoglobulin (IVIG) and plasmapheresis. IVIG is preferred in pediatric age group[9]. The recovery and outcome of GBS in children is better as compared to adults with minimal residual damage.

The Children's Hospital Lahore is the largest public sector tertiary care pediatric hospital in Pakistan where we come across large number of AFP cases per year. Most of which turn out to be GBS. No such study has been done combining clinical, epidemiological and outcome data in our country. This study will help us to know about diversity of clinical pattern, response along with its prognosis.

MATERIAL AND METHODS

This cross sectional survey was done in the department of Neurology, The Children's Hospital and Institute of Child Health, Lahore from July 2015 till December 2016. We selected 125 patients by taking 95% confidence level, 10% margin of error and expected percentage of GBS 50%. Patients of both genders from the age of 1 to 15 years, with suspicion of AFP fulfilling the clinical criteria of GBS were enrolled for this study. All patients were clinically evaluated and investigated by neurophysicians. Patients with co-morbid diseases, any periodic weakness and previous history of GBS were excluded. Permission was taken from hospital Ethical Review Committee, informed written consent was taken from parents. Detailed neurological assessment was done and later NCS/EMG were performed in one of upper as well as one of the lower limb by using standard nerve conduction techniques, studying atleast two motor and one sensory nerve in each limb. Depending upon the results of EMG/NCS, the variants of GBS were labeled as demyelinating or axonal, using criteria adapted from Flachenecker *et al*[6]. Patient's functional motor deficits were analyzed by keeping in view the widely accepted disability scale by Hughes *et al*. This disability scoring is as follows. grade 0: healthy state, grade 1: minor symptoms, grade 2: ability to walk 10 meters or more without help but unable to run, grade 3: Able to walk 10m across an open space with assistance, grade 4: chair bound or confined to bed, grade 5: requiring assisted ventilation for some part of the

day, grade 6: dead. grade 0-2 classified as good outcome while grade 3-6 documents poor outcome. This disability score was also recorded at the time of discharge, and subsequently on regular follow up at 1, 3 and 6 months to assess for functional disability in patients. All the clinical data were entered into a pre-designed proforma.

Table-I: Patient distribution according to the age groups.

Age Group	Frequency	Percentage
1-5 years	50	40.0
6-10 years	62	49.6
more than 10 years	13	10.4
Total	125	100.0

Table-II: Demographic and clinical profile of the patients with GBS.

	Number (n)	Percentage
Male	77	61.6
Female	48	38.4
Mean Age ± S.D	6.59 ± 2.84	
Mean duration of illness	3.9 ± 0.303	
Duration of stay	4-43 days (Mean = 11.5 days)	
Antecedent illness	72	57.6
Motor weakness	125	100
Sensory involvement	85	68
Cranial nerve involvement	68	54.4
Autonomic involvement	80	64
Respiratory involvement	73	58.4
Assisted ventilation	60	48
IVIG	75	60
Variants		
(AIDP)	49	39.2
(AMAN)	67	53.6
(Axonal+Demyelinating)	6	4.8
(MFS)	3	2.4

Data was analyzed by SPSS version 23. Frequency and percentage were calculated for qualitative variable. Mean ± SD calculated for quantitative variable.

RESULTS

During this period, a total of 125 patients were enrolled. There were 77 (61.6%) males and 48 (38.4%) females. Age range for these patients was 18 months to 13 years with mean age of 6.59 years. We divided our patients in three age groups with the age group of 6 to 10 years is the most common group to be presented with GBS (table-I). The demographic and clinical profile of the enrolled patients was summarized in table-II.

There were 35% cases of GBS in the months of February till April in our study population. Antecedent illness was recorded in 72 (57.6%) patient and respiratory tract infection (RTI) (31.2%) was the most common antecedent illness followed by gastroenteritis (16%) as shown in table-III.

The time interval between this antecedent illness and onset of GBS symptoms varied from 13 to 26 days with the average of 17.5 days. Hospital stay duration ranges between 4 to 43 days with mean of 11.5 days.

Out of the 125 patients studied, all patients had motor weakness in different forms most commonly ascending weakness, quadripresis, walking difficulties, hoarseness of voice and ataxia. Three patients had ataxia and opthalmoplegia thus labeled as Miller Fischer Syndrome (MFS). Sensory involvement was seen in 85 (68%) of the patients. Autonomic nervous system abnormalities were observed in 80 (64%) patients. Blood pressure derangements were seen more frequently as shown in table-III.

Out of 125 patients, 68 (54.4%) of the patients had cranial nerve palsies. Cranial nerve IX and X are the most common cranial nerve to be involved followed by VI and III cranial nerve as shown in table-III. Assisted ventilation was required in 60 (48%) of the admitted patients. Intravenous immunoglobulin (IVIG) were given in 75 (60%) of the enrolled patients.

Table-III: Distribution of antecedent illness.

Illness	Frequency	Percentage
RTI	39	31.2
G/E	20	16.0
Fever	8	6.4
Chicken pox, Measles, Vaccine	5	4.0
No antecedent illness	53	42.4
Total	125	100.0
Distribution of autonomic involvement.		
Autonomic involvement		
Hypo/hypertension	65	52.0
Bradycardia /tachycardia	30	24.0
Sweating, Cardiac arrhythmia	20	16.0
no autonomic involvement	45	36.0
Distribution of cranial nerve involvement.		
Cranial nerves		
IX, X cranial nerves	46	36.8
VI cranial nerve	18	14.4
III cranial nerve	4	3.2
No cranial nerve involvement	57	45.6
Total	125	100.0
Distribution of different variants of GBS.		
Variants		
AIDP	49	39.2
AMAN	67	53.6
Anxonal + Dermyelinating	6	4.8
MFS	3	2.4
Total	125	100.0

Table-IV: Outcome of patients at follow up.

Follow up	Grade 0-2 (good outcome) N (%)	Grade 3-6 (poor outcome) N (%)
1 month	25 (20%)	100 (80%)
3 months	64 (51.2%)	61 (48.8%)
6 months	112 (89.6%)	13 (10.4%)

EMG/NCS tests were done in all of the enrolled patients. The median time between onset of weakness and EMG/NCS was 13 days. Upon electro diagnostic studies and examination, the GBS variants distribution was as follows: Acute inflammatory demyelinating polyradiculo-neuropathy variant (AIDP) in 49 (39.2%) of the patients, acute motor axonal neuropathy (AMAN) variant in 67 (53.6%), 6(4.8%) patients having mixed (axonal + demyelinating) variety as shown in table-IIII.

There was no death reported in any of our patient enrolled for this study. These enrolled 125 patients were checked and kept on follow up until 6 months after the discharge. At 1 month follow up only 25 (20%) children had good outcome (grade 0-2), while rest were having grade between 3 and 5. At 6 months follow up visit 112 (89.6%) of the patients had good outcome while 13 (10.4%) patients had poor outcome as depicted in table-IV.

DISCUSSION

There is male predominance in our study as 61.6% are male, which matches with the results described by the Alter *et al*[7] and Kannan *et al*[8] but contrary to that Linden *et al*[9] observed GBS in 46% male patients. The disease can affect patients of any age group but usually it is more common in the adult age group[10,11]. Enrolled patients had age range from 18 months to 13 years with an average of 6.5 years while Linden *et al* had patients from 7 months till 13 years in their study[9]. We came across more cases of GBS in months of February till April where there is more propensity of upper respiratory infection due to allergic illness, while Ho *et al*[12] noticed a summer peak in cases of GBS due to prevalent campylobacter jejuni infection in north china[12]. Kannan *et al*[8] observed a peak incidence between August and September while many other authors in literature also revealed a uniform distribution of GBS patients throughout the year.

History of preceding illness was seen in 72 (57.6%) patients. Similarly Winer *et al* suggested that about 75% of patients have a history of preceding symptoms of infection[13] and Linden *et al* showed antecedent illness as high as 62% of the patients[12].

Out of the antecedent illnesses, upper respiratory tract infection was most common followed by gastroenteritis while Rees *et al*[14] and Jacobs *et al*[15] observed the campylobacter jejuni infection in about 26% and 32% respectively in their studies. There is time lapse of about 2 to 4 weeks with an average of 17.5 days between antecedent illness and onset of symptoms of GBS.

The progression of the symptoms were seen in more than 75% of our patients during first 2 weeks of hospital stay and then there is a plateau phase in which there is no further progression of the symptoms. Similar progression of symptoms was also narrated by Asurby in literature[16] except two patients of axonal variety who showed progression of symptoms until 7th week of illness. Cranial nerve involvement were found in 68 (54.4%) of our patients while literature review revealed involvement of cranial nerves in 45 to 55% of the patients[9,17]. The most common cranial nerve to be involved is IX & X in our study as well as by Jin *et al*[17] but surprisingly Linden *et al*[9] noticed VII cranial nerve as most common nerve to be involved in their study population.

Respiratory involvement was seen in 73 (58.4%) of our patients while many authors mentioned about 25 to 35% respiratory involvement[9,18,19] in GBS. A large number of our patients (64%) showed autonomic involvement which do not match with results of Kannan *et al* where they found autonomic nervous system involvement in about 13.9% of patients[8]. The most frequent dysautonomia found in our patients was blood pressure derangements either in the form of hypo or hypertension while literature review revealed that there can be any autonomic derangement like hypotension, hypertension, tachyarrythmias and bradyarrhythmias in patients of GBS[20-23].

Lumbar puncture was done in all of the patients which showed normal cell count along with increased proteins which is same as documented in literature and fulfills the diagnostic criteria of GBS as well.

On electrophysiological studies, we found AMAN as the most common variant in our population which is about 53.6% followed by AIDP (39.2%) and our results matches with Ho *et al*[12], who observed AMAN variant in 65% of the study population. While many other authors like Jin *et al*[17] and Paradiso *et al*[24] documented AIDP variant in 74.2% and 70.4% of study population respectively.

One hundred and six of these 125 patients reported back for regular follow up until 1 year after the discharge. Almost 90% of our patients had grade 0-2 at the end of one year thus favoring good outcome which shows quiet good recovery for GBS in pediatric population.

No death was reported in any of our enrolled patients for this study as we gave IVIG where indicated and shifted the patients to our ICU for ventilator support where needed. Previously most of the cases with acute flaccid para-

lysis in children were not diagnosed and differentiated clinically but with a significant decline in incidence of polio worldwide, GBS has become the most common cause of AFP in children. There were multiple studies already done on GBS with each showing heterogeneity of clinical features and association of different variants with outcome and prognosis. There is significant statistical difference between different variants and their outcome. During last few years, new prognostic clinical scoring scales, the Erasmus GBS outcome score (EGOS)[25], the Erasmus GBS Respiratory Insufficiency Score (EGRIS) and modified EGOS, were reported. These advanced scoring methods are more accurate and authentic for predicting need of mechanical ventilation outcome, or aided walking being based on multiple clinical factors but not solely on electrophysiological findings. There are usually multiple follow up visits of the discharged patients in which disability scoring monitored which is cumbersome for the parents and families. Moreover there can be prolonged hospital admissions of such patients with different complications, adding financial burden to healthcare system and the families.

CONCLUSION

The result of our study shows that GBS is a disease with diverse clinical presentation. Initial presentation is critical in the form of paraplegia or quadriplegia but with well-equipped treatment and diagnostic facilities like EMG/NCS, ventilator and IVIG, clinical outcome is good.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Guillain G, Barré J, Strohl A. Sur un syndrome de radiculonevrite avec hyperalbuminose du liquid ecephalora chidien sans reaction cellulaire. Remarquessur les characters cliniqueetgraphique des reflexes tendinaux. Bulletins et Memories de la Societe Medicale des Hopitaux de Paris 1916; 40: 1462–70.
2. Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis: Its role in pathogenesis. Medicine (Baltimore) 1969; 48(3): 173-215.
3. Olive JM, Castillo C, Castro RG, de Quadros CA. Epidemiological study of Guillain-Barre syndrome in children <15 years of age in Latin America. J Infect Disease 1997; 175(Suppl): S160-4.
4. Molinero MR, Varon D, Holden KR, Sladky JT, Molina IB. Epidemiology of childhood Guillain-Barré syndrome as a cause of acute flaccid paralysis in Honduras. J Child Neurol 2003; 18(11): 741-47.
5. Hughes RA, Cornblath DR. Guillain-Barre syndrome. Lancet 2005; 366(9497): 1653-66.
6. Flachenecker P, Toyka KV, Reiners K. Cardiac arrhythmias in Guillain-Barre syndrome. An overview of the diagnosis of a rare but potentially life-threatening complication. Nervenarzt 2001; 72(8): 610-7.
7. Alter M. The epidemiology of Guillain-Barré syndrome. Ann Neurol 1990: 27(suppl): S7–12.
8. Kannan MA, Ch RK, Jabeen SA, Mridula KR, Rao P, Borgohain R. Clinical, electrophysiological subtypes and antiganglioside antibodies in childhood Guillain-Barré syndrome. Neurol India 2011; 59(5): 727-32.
9. Van der Linden VV, Albino da Paz JA , Casella EB, Marques-Dias MJ. Guillain-Barré syndrome in children. Arq Neuropsiquiatr 2010; 68(1): 12-17.
10. Johnson RT (ed). Viral infections of the nervous system, 2th Ed. Philadelphia: Lippincott-Raven Publ 1998; 181-210.
11. Ryan MM. Guillain-Barré syndrome in childhood.J Paediatr Child Health 2005; 41: 237-41.
12. Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR et al. Guillain-Barré syndrome in northern China. Relationship to campylobacter jejuni infection and anti-glycolipid antibodies. Brain 1995; 118 (3): 597-605.
13. Winer JB, Hughes RA, Anderson MJ. A prospective study of acute idiopathic neuropathy. Antecedent events. J Neurol Neurosurg Psychiatry 1988; 51(5): 613-18.
14. Rees JH, Soudain SE, Gregson NA, Hughes RA. Campylobacter jejuni Infection and Guillain–Barré Syndrome. N Engl J Med 1995; 333(21): 1374-79.
15. Jacobs BC, Rothbarth PH, van der Meché FG, Herbrink P, Schmitz PI, de Klerk MA et al. The spectrum of antecedent infections in Guillain-Barré syndrome: A case-control study. Neurology 1998; 51(4): 1110-5.
16. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol 1990; 27(Suppl): S21-24.
17. Jin K, Keong W, Vaithialingam M, Tan T. A clinical and electrophysiological study of Guillain-Barré syndrome in Malaysia. Neurol J Southeast Asia 1999; 4: 67-72.
18. Berg B, Walgaard C, Drenthen J, Fokke C. Jacobs BC. vanDoorn PA. Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014; 10(8): 469-82.
19. Cosi V, Versino M. Guillain-Barré syndrome. J Neurol Sci 2006; 27(1): 47-51.
20. Birchfield RI, Shaw CM. Postural hypotension in the Guillain-Barre syndrome. Arch Neurol 1964; 10: 149-57.
21. Lichtenfeld P. Autonomic dysfunction in the Guillain Barre syndrome. Am J Med 1971; 50(6): 772-80.
22. Kusunoki S. Autonomic involvement in Guillain-Barré syndrome. Clinc Neurol 2006; 46(11): 878-80.
23. Tuck RR, McLeod JG. Autonomic dysfunction in Guillain-Barré syndrome. J Neurol Neuro surg Psychiatry 1981; 44(11): 983-90.
24. Paradiso G, Tripoli J, Galicchio S, Fejerman N. Epidemiological, clinical, and electrodiagnostic findings in childhood Guillain-Barré syndrome: A Reappraisal. Ann Neurol 1999; 46(5): 701-7.
25. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC et al. Clinical prognostic scoring system for GBS. Lancet Neurology 2007; 6(7): 589-94.