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ORIGINAL ARTICLE

THE CLINICAL PRESENTATION, EPIDEMIOLOGY, AND SHORT-TERM OUTCOME OF GUILLAIN-BARRÉ SYNDROME IN TIKURANBESSA HOSPITAL: A 6-YEAR RETROSPECTIVE STUDY

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ABSTRACT

Introduction: *Gullian-Barré Syndrome (GBS) is an acute monophasic demyelinating polyradiculoneuropathy which is characterized by progressive weakness and areflexia. Different antecedent events are associated with GBS and one of those is an anti-rabies vaccine prepared from infected animal brain.*

Objective: *The study goal was to determine epidemiological features of and to describe the clinical and short-term outcomes of Gullian-Barré syndrome.*

Materials and Methods: *A cross sectional descriptive study with retrospective data collection was done on children admitted with a diagnosis of Gullian-Barré Syndrome from September 2006 to September 2012.*

Result: *112 children were identified. The male to female ratio was 1.6. All had motor weakness, only one patient (0.9%) had sensory loss, 34(30.3%) had cranial nerve involvement and 37 (32.9%) had dysautonomia. Respiratory involvement which necessitated ventilation was found in 14 (12.5%) of our cases. Antecedent events were recorded in 82 (73.2%) of children and among them; upper respiratory infection (URTI) was the most frequent (43.8%). Of the 15 patients with vaccination antecedents, 7 (6.35%) had received anti-Fermi type rabies vaccine. The GBS subtype distribution among the 31 patients who had electrodiagnostic studies performed was as follows: acute inflammatory demyelinating neuropathy (AIDP) 3 (10%), acute motor axonal neuropathy (AMAN) 24 (80%),acute motor-sensory axonal neuropathy (AMSAN) 1 (3.3%), and both axonal and demyelinating neuropathy 3 (10%). Complete recovery was noted in 31 (27.7%) patients and there were 9 (8%) deaths.*

Conclusion: *Male preponderance and presence of antecedent illness was observed in the majority of subjects. Acute motor axonal neuropathy was the commonest subtype of Guillain-Barré. Prior anti-Fermi-type rabies vaccine may have been one predisposing factor.*

Keywords: *Guillain-Barré syndrome, Rabies vaccine, Ethiopia*

INTRODUCTION

Guillain-Barré syndrome is the most frequently acquired demyelinating peripheral polyneuropathy. It is characterized by flaccid paralysis, areflexia, and cytoalbuminic dissociation in which the number of cells in the cerebrospinal fluid will be disproportionately low with respect to the protein. It is a major cause of acute flaccid paralysis worldwide especially after the decrement of poliomyelitis (1). Most studies that estimate incidence rates of GBS were done in Europe and North America and showed a similar range of 0.8–1.9 (median 1.1) cases per 100,000 people per year (2). It affects all age and sex; most studies have found that the incidence increases linearly with age and men are more likely to be affected than women (3).

Although the pathogenesis of GBS remains unclear, it is increasingly believed to be immunologic with antecedent inciting events in two thirds of the cases. It is frequently preceded by viral respiratory infections, gastrointestinal infections, vaccines and others (4, 5). After acceptance of role of immunity, plasmapheresis and intravenous immunoglobulin (IVIG) have been used for treatment. With both treatments, the mortality and morbidity of GBS decrease significantly when they are used in the early stages of neuropathy (4).

The natural course of the disease is progression of ascending motor weakness (up to 4 weeks) that reaches the maximum deficit (nadir) and remains at nadir for several weeks before improvement. 20-30% of patients with GBS require admission to the intensive care unit (ICU), associated with significant risk of morbidity, mortality and incomplete recovery. The major concerns for a patient with GBS are aspiration and respiratory failure (6,7).

The epidemiology, clinical features and outcomes of GBS in Ethiopian children has not been well studied. Though etiologies are not clear, the perception among clinicians is that there is high rate of diagnosis of GBS in our setting. Knowledge of epidemiologic features could help in predicting GBS and could also provide clues for prevention.

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Knowledge on the outcome and possible prognostic factors could affect our resource allocation for patients with GBS in intensive care units.

The main purpose of this study was to describe the demographic features, clinical characteristics, preceding events and short-term outcome of childhood GBS during the period of 2006-2013.

PATIENTS AND METHODS

Study area and period: This study was done in Tikur Anbessa Hospital and from the period of 2006-2012. Tikur Anbessa Specialized Referral Hospital is a tertiary center in Addis Ababa, Ethiopia with the highest number of postgraduate and undergraduate students. The department of pediatrics and child health is the only center in the country where pediatric neurologist, pediatric emergency and intensive care specialists are available, and manages most of the national GBS cases.

Source and sample population: This was a cross-sectional retrospective study. All children with documented acute flaccid paralysis (AFP) who were admitted from September 2006–September 2012were included.

Data analysis: Data was collected from patient charts located in all pediatric emergency, ward, and intensive care units. It was collected by the investigators using standardized data abstraction forms. The data consists of demographic characteristics, antecedent events, clinical features, treatment received, and outcomes.

Data obtained from the study was coded and entered using the SPSS version 20.0. Data was summarized using mean and standard deviation for continuous variables, and percentages for nominal variables.

Operational Definitions:

***Diagnosis of typical GBS*:** the diagnosis of GBS in this study is based on the following National Institute of Neurological and Communicative Disorders and Stroke (NNCDS) diagnostic criteria (8).

1. Progressive weakness of more than one limb due to neuropathy,
2. Areflexia or hyporeflexia
3. Duration of progress less than 4 weeks
4. The absence of a sharp sensory level on the trunk
5. The absence of other causes of acute neuropathy
6. Less than 50 mononuclear leukocytes per mm^3in cerebral spinal fluid.

Nerve Conduction Studies (NCSs) were performed within the second week of hospitalization. The study included median, ulnar, common peroneal, tibial and sural nerves using conventional techniques. In our study, the patients were classified into AIDP, AMAN, and AMSAN based on criteria which was been used in previous studies (9).

An antecedent triggering event was defined as the presence of respiratory, gastrointestinal, febrile illness or vaccination for the previous 4 weeks. Short-term outcome was defined as the patients' disability upon discharge using Hughes functional grading (Table 1). Grades 0-2 were considered a good outcome, those above 2 as a bad outcome (10).

Table 1: Hughes Scale

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

Ethical Considerations: This study was approved by the Institutional Ethics and Review Board of Addis Ababa University. No respondent's name was recorded and information obtained from medical records was kept confidential.

RESULTS

The demographic features of the GBS patients are listed in Table 2. Our GBS patients were classified into four age groups. The age of onset varied from 5 months to 13 years, average 4.3 years (standard deviation 3.2). The most frequent age group affected was 25 months to 60 months of age in 42 patients (37.5%). Antecedent events at the beginning of the clinical picture were well documented in 82(73.2%) patients, and among them, upper respiratory infection (URTI) was the most frequent (43.8%). The remaining 30(26.8%) did not have documented antecedent events. Regarding the 15 patients with vaccination antecedents, 7(6.35%) of them had received anti-Fermi type rabies vaccine (Table 2).

Table 2. Demographic features, seasonality and preceding events in children with Guillain-Barre´ syndrome, September 2006 to September 2012 to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Variable	No (%)
Age in months	
0-24	35 (31.3)
25-60	42 (37.5)
61-96	21 (18.7)
97-156	14 (12.5)
Sex	
Male	70 (62.5)
Female	42 (37.2)
Residence	
Addis Ababa	52 (46.4)
Oromia	40 (35.7)
SNNP	12 (10.7)
Preceding events	
Upper respiratory tract infection	49 (43.2)
Gastroenteritis	17 (15.2)
Rabies vaccine	7 (6.3)
Other events	2 (1.7)
No preceding event	8 (7.1)
Undocumented	20 (17.8)

The initial symptoms of these patients were listed in Table 3. The most common symptom was limb weakness. An ascending pattern of motor weakness was observed among 92(82.1%) patients, whereas 7(6.3%) had a descending pattern, with the remaining 11.6% of patients with no particular involvement. Ataxia was a presenting feature in only 6 (5.4%) patients. Autonomic dysfunction was found as a form of labile hypertension among 35 (31.3%) of patients and fluctuating pulse in 2(1.6%). The remaining patients had no form of autonomic involvement. Sphincter involvement occurred in 15(13.4%), but sensory involvement was noted in only one (0.9%) of the cases. 44(39.2%) patients were screened for HIV and none found to be reactive.

Involvement of cranial nerve was present in 21 patients (18.7%) with the commonest nerve involved being the glossopharyngeal nerve (11.6%) as shown in Table 2. Cytoalbuminological dissociation was found in 45 of patients (40.2%). Electrophysiologic studies were done in 30(27%) patients with clinical GBS and 3 (10%) had a demyelinating, 3 (10%) had a mixed axonal and demyelinating type, but the remaining (80%) had axonal type. Among the axonal group, almost all had a pure motor axonal degeneration except one who has shown mixed motor and sensory type. Among patients given specific therapies, 14 (12.5%) were given intravenous immunoglobulin (IVIG), and glucocorticoid were given in 5 (4.4%). Of those treated with IVIG two (14%) died. Complications included primarily aspiration pneumonia, among 37(33%) patients. One patient had an infection and acute renal failure. The mean length of hospital stay was 14.6 days (range 1 to 150, standard deviation 21.6 days). Forty-two (37.5%) patients required ICU admission, half of these 18.6%) needed mechanical ventilatory support. There were 9 (8%) deaths.

Table 3: Clinical features in children with Guillain-Barré syndrome, September 2006 to September 2012, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

Variable	No (%)
Pattern of Weakness	
Ascending	92 (82.1)
Descending	7 (6.3)
No specific pattern	13 (11.6)
Other manifestation	
Autonomic dysfunction	37 (32.9)
Sensory abnormality	1 (0.9)
Cranial nerve palsy (glossopharyngeal, facial nerve and others)	21 (18.7)
Bulbar involvement	13 (11.6)
Sphincter involvement	15 (13.4)
Ataxia	6 (5.4)
Electrophysiologic studies	
AIDP	3 (10)
AMSAN	1 (3.3)
AMAN	23 (76.7)
Mixed axonal and demyelinating	3 (10)
Not done	82
Mean duration of hospitalization	18 days
Need for mechanical ventilator	14 (12.5)
Outcome	
Good	31 (27.7)
Bad	41(36.6)
Mortality	9 (8)
Unknown	31(27.7)
Treatment applied	
IVIG	14(12.5)
Steroids	5(4.5)
No specific therapy	93(83)

Table 3: Clinical features in children with Guillain-Barré syndrome, September 2006 to September 2012, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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DISCUSSION

Guillain-Barre syndrome is a global disease seen in all age groups including neonates. It is known as the major cause of non-polio AFP, particularly after the global decrement of poliomyelitis (11).Reviewing the literature it was observed that GBS can affect childhood and adolescent age groups (12-14). In our study as well, 68.8% of the patients were below 5 years of age. It might be attributable to exposure to several infections in this age group and greater susceptibility to demyelination (15). It was found to be slightly more common in males in the current study and this finding is similar to other studies done in India in 2014 and in the northwest Greece in 2007(16, 17).

Prior infections should always be searched for, particularly when trying to define the presence of etiologies more frequently associated with GBS. In this series, there was a report of a preceding clinical event before the first symptoms of GBS in two-thirds of the cases, a finding consistent with a report from India of20 patients (16) and from Greece done on 46 patients over 9 years (17). Among these events, upper respiratory infection was the most frequent followed by gastrointestinal infections.

There has been an ongoing debate regarding the possible contribution of vaccines to the etiology of GBS. Associations with oral polio vaccine, influenza vaccine and rabies vaccine were described in a review of reports appearing in peer-reviewed literature between 1950 and 2008 (18, 19). In our study only 15 (13.4%) patients had preceding vaccinations and 7(6.3%) of them had reported antecedent rabies vaccination in the previous two to three

weeks of symptoms. The association between rabies vaccine and GBS is not clear but rabies vaccines prepared from the infected brain tissues of adult animals carried an increased risk of inducing GBS, probably because of contamination with myelin antigens (19), and henceforth WHO has recommended rabies vaccines be prepared not from infected brain tissue (as is the case for Fermi type vaccines) but embryonic cells lines.

The pattern of the motor deficit was relatively more severe in our study in which 88% had quadriparesis. This is more severe when it is compared with previous studies from Senegal where paraparesis was reported in 63.2% and quadriparesis in 36.8% (20). About 93% of our patients had an ascending pattern of progression. Cranial nerve involvement was 40% in our study, less than that of other studies. The most common nerve affected in other studies was the facial nerve whereas in our study the glossopharyngeal nerve was more commonly affected (13). Studies reported an autonomic disturbance in 66% and ventilatory support in 30% of GBS patients (21,22). In our study, the incidence of both autonomic disturbance and ventilatory support was lower, at 32.7 % and 18.6%, respectively.

According to electrophysiologic findings, 23(76.7%) of our cases had axonal type while AIDP accounted for 10% and AMSAN accounted for 3.3%. There was no Miller-Fisher variant in our study. This is quite different from studies from other sites. In the Western part of the world, most patients with GBS had demyelination of both sensory and motor nerves (AIDP), which accounted for 80-90% of cases (23, 24). A retrospective study in a medical center in Taiwan reported a high proportion of MFS (18%), whereas in China the axonal and AMSAN types of GBS were up to 65% (25, 26). In a prospective study from Italy, the axonal type accounted for 25% and cases with MFS accounted for 19% (27).

The difference could be partly accounted for by variations in the environmental factors, pathogenic mechanisms, genetic susceptibility, and other triggering factors such as different infections operating in different populations. The electrophysiological features evolve over time and may be misleading in early stages of the disease. Serial recordings in a previous study revealed a change of diagnosis in 24% of patients (28). This may be due to the fact that in early AMAN, reversible conduction failure mimicking demyelinating neuropathy can occur which may erroneously lead to the diagnosis of AIDP (29). These anomalies in the electrophysiological diagnosis may play a major role in false interpretation of the prevalence of subtypes in various regions of the world.

In this study it was found that the prognosis was generally unfavorable with relatively high mortality rates (8%) and frequency of residual deficits (37%). The mortality rate, however, was significantly lower compared with a study done previously in the same hospital in 2006, reporting a frequency of 16.4% (30). The decrement in mortality could be explained by the establishment of pediatric intensive care units and availability of IVIG. Residual disabilities in our patients approximated 37% which was relatively high compared with studies from Europe and Asia (31-33). Only about 28% had complete or partial improvement as the rehabilitation service is not well developed in the hospital.

The major limitation of this study, as a retrospective chart review, was incomplete patient record documentation with respect to outcomes and the unavailability of electrodiagnostic tests for all patients. This could be improved in a prospective study among children.

In conclusion, we have seen male predominance and upper respiratory infections as the most common antecedent event. Acute motor axonal neuropathy is the commonest subtype among those who had nerve conduction tests.

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