

Profile Of Children With Guillan Barre Syndrome In RSUP

Haji Adam Malik Medan: Events In 5 Years

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Abstract

Background : Guillain-Barré syndrome (GBS) is an acute demyelinating disease of the peripheral nervous system characterized clinically by flaccid paralysis. The mortality rate in children is about 3-5%. Early diagnosis and therapy important for patient's prognosis.

Objective : The aim of this study was to acquaint the profile of children with Guillain-Barré syndrome at the RSUP HAM Medan Hospital from 2016 to 2020.

Methods : This study is a descriptive study with a retrospective design. The population and sample with total sampling of the children with GBS diagnosed at the HAM Medan Hospital recorded in the medical record from January 2016 to December 2020. The data were analyzed univariately and presented with a frequency distribution.

Results: From this study, 41 children with GBS were found. There were 18 children (43.9%) with age between 10-14 year (female was 22 people (53.7%). Based on the Brighton Criteria for GBS children, most of the children was on level 2 that were 35 people (85.4%). From the results of the EMG (Electromyography) examination in GBS children, 24 people (58.5%) had the most types of GBS were Acute Motor Axonal Neuropathy (AMAN). There was no cytoalbumin dissociation was found on CSF analysis. Mostly 28 people had supportive therapy, that was the most used type of therapy. The disability scale shows that children who can walk with the help of a cane or supporting equipment (disability scale 3) was 26 people (63.4%). Based on the length of stay in the hospital, 26 children (63.4%) were treated for 8-14 days.

Conclusion: Majority the case of GBS in the RSUP HAM Medan was similar previous studies. Our results can be used as baseline data for understanding the characteristics of GBS in Indonesia.

Key word: Guillain-Barré syndrome; profile; children.

Introduction

Guillain-Barré syndrome (GBS) is an acute demyelinating disease of the peripheral nervous system characterized clinically by acute flaccid paralysis and is one of the leading causes of neuromuscular paralysis worldwide.¹ The incidence of GBS occurs in only 1 or 2 cases per 100,000 worldwide each year.^{2,3} From 1996 to 2012, the Canadian Pediatric Surveillance Program (CPSP) received 773 case reports of Acute Flaccid Paralysis (AFP), an estimated annual incidence of 0.4–1.1 per 100,000 children, of whom 69% were diagnosed as GBS.⁴ The incidence of GBS based on population-based studies is estimated to be 0.5 – 1.5 cases per 100,000 children under 16 years of age.⁵ Data from Cipto Mangunkusumo Hospital (RSCM) Jakarta showed that at the end of 2010-2011 there were 48 cases of GBS in one year with various number of cases per month.⁶

Guillain-Barré syndrome is a life-threatening disease that can cause both morbidity and mortality even with medical treatment. The mortality rate in children is about 3-5%.⁷ Respiratory insufficiency can

occur in patients with GBS and can lead to death in these patients.^{1,8} Early diagnosis of GBS affects the patient's prognosis.⁹ The Brighton Collaboration created the Brighton criteria, a novel set of case definitions for GBS that can estimate the level of diagnostic certainty based on clinical examination, cerebrospinal fluid examination, and neurophysiological examination findings.^{8,10}

GBS in children has a good prognosis, especially if intravenous immunoglobulin (IVIG) was given as soon as the clinical suspicion is established. According to research by Salehiomran MR et al, only one out of 17 children with GBS suffered from respiratory paralysis. Sixteen other patients showed complete recovery, while one patient with respiratory paralysis required a wheelchair.⁵ In 1978, Hughes et al. proposed a disability scale that has been widely used until now.¹¹

The purpose of this study was to determine the profile of children with Guillain-Barré syndrome at the HAM Hospital in Medan from 2016 to 2020.

Methods

This is a descriptive study to determine the profile of children with GBS. Researchers will use medical record data from the Haji Adam Malik Provincial General Hospital (RSUP HAM) Medan to identify all research subjects having a diagnosis of Guillain-Barré syndrome in pediatric patients from 2016 to 2020. Age, gender, Brighton Criteria Level, GBS Type, treatment, GBS Disability Scale, Length of Stay, and CSF Analysis Characteristics are among the data collected. Table 1 shows the Brighton criterion level.

Table 1. Guillain-Barré syndrome based on Brighton criteria²⁶

Level 1	• Acute onset of bilateral and relatively symmetric flaccidity • Weakness/paralysis of the limbs • Decreased or absent deep tendon reflexes • Monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death • Electrophysiologic findings consistent with GBS • Presence of cytoalbuminologic dissociation (elevation of cerebrospinal fluid (CSF) protein level above laboratory normal value, and CSF total white cell count <50 cells / μl) • Absence of alternative diagnosis for weakness
Level 2	• Acute onset of bilateral and relatively symmetric flaccidity • Weakness/paralysis of the limbs • Decreased or absent deep tendon reflexes • Monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death • Cerebrospinal fluid (CSF) with a total white cell count <50 cells / mm³ (with or without CSF protein elevation above laboratory normal value)

	• If CSF not collected or results not available, electrodiagnostic studies consistent with GBS
Level 3	• Absence of alternative diagnosis for weakness • Acute onset of bilateral and relatively symmetric flaccidity • Weakness/paralysis of the limbs • Decreased or absent deep tendon reflexes at least in affected limbs • Monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death
Level 4	• Absence of alternative diagnosis for weakness • More than one criteria of: – Acute onset of bilateral and relatively symmetric flaccidity – Weakness/paralysis of the limbs – Decreased or absent deep tendon reflexes at least in affected limbs • Absence of alternative diagnosis for weakness

This study has been approved by the Health Research Ethics Committee, Faculty of Medicine, University of North Sumatra number. Univariate analysis used SPSS version 20.0 by displaying the size of frequency distribution and percentage.

Study Results

This study included 41 children with Guillain-Barré syndrome who were hospitalized at the HAM Hospital in Medan from January 2016 to December 2020. Table 2 lists the characteristics of the research sample.

Table 2. Age, Gender, GBS Type, Treatment, and Length of Stay Distribution in Children with Guillain-Barré at H. Adam Malik Hospital Medan

Demography Characteristics	Frequency	%
Age		
0 – 4 years old	6	14.6
5 – 9 years old	14	34.1
10 – 14 years old	18	43.9
15 – 18 years old	3	7.3
Gender		
Male	19	46.3
Female	22	53.7
GBS Type		
AIDP	9	22
AMSAN	8	19.5
AMAN	24	58.5
Treatment		
Intravenous Immunoglobulin	13	31.7
Supportive	28	68.3
Length of stay		

1-7 days	8	19.5
8-14 days	26	63.4
> 14 days	7	17.1

Based on Brighton criteria for GBS in children (Table 3), mostly subjects (82.9%) were at level 2, while the rest were at level 1 (17.1%).

Table 3. Frequency Distribution of Brighton Criteria Level in Children with Guillain-Barré Syndrome at H. Adam Malik Hospital Medan

Brighton Criteria	Frequency	%
Level 1	7	17.1
Level 2	34	82.9
Total	41	100

Disability scale in children with GBS. Table 4 shows that most of the children had disability scale 3 (63.4%) and the least were disability scale 2 and 5 (4.9%).

Table 4. Frequency Distribution of Disability Scale in Children with Guillain-Barré Syndrome at H. Adam Malik Hospital Medan

Disability Scale	Frequency	%
Can walk without the help of cane, but cannot do manual work	2	4.9
Can walk with the help of cane or supportive equipment	26	63.4
Limited activity in bed/chair	11	26.8
Need mechanical ventilation	2	4.9
Total	41	100

Lumbar puncture was only performed on 7 children (17.1%), while 34 children (82.9%) did not have one. Lumbar puncture results of the 7 children with GBS (Table 5) showed that there was no increase in protein (>45mg/dL) (100%) in, however there was an increase in leukocyte count in 5 children (71.4 percent). There was no cytoalbumin dissociation.

Table 5. Lumbar Puncture Fluid Examination Results

Laboratory Results	n (%)	Average (SD)	Median (Min – Max)
LDH, U/L		29.86 (4.34)	30 (22 – 37)
< 200 U/L	7 (100)		
Total Protein, mg/dL		16.11 (8.71)	16 (0.8 – 28)
≤45 mg/dL	7 (100)		
Leukocyte Count		0.06 (0.11)	0.005 (0.001 – 0.284)
≥ 0.003	5 (71.4)		
< 0.003	2 (28.6)		
Erythrocyte Count		0.0001 (0.0004)	0 (0 – 0.001)

+	1 (14.3)		
-	6 (85.7)		
Glucose, mg/dL		76.43 (28.98)	64 (47 – 119)
Normal (40-76)	5 (71.4)		
Increased (>76)	2 (28.6)		
pH		8.29 (0.49)	8 (8 – 9)
7-8	5 (71.4)		
>8	2 (28.6)		
MN Cells		79.74 (33.36)	97.7 (20.8 – 100)
PMN Cells		20.26 (33.36)	2.3 (0 – 79.2)

Discussion

The initial characteristic data in this study showed that the proportion of female gender (53.7%) was higher than male (46.3%). According to a study by Mahmoud et al. in 2019, there was no difference in the proportion of male and female sex.¹² Several investigations on the characteristics of children with GBS, however, revealed that male outnumbered females (54-58 %: 46-42 %).¹³⁻¹⁸ The patients in this study were predominantly 10-14 years old (43.9%); study by Levinson in Denmark and Sandip in India both found the same result. GBS was most commonly diagnosed in children under the age of ten years old. The average length of stay for children with GBS was 14 days in studies conducted in Bangladesh and Turkey.^{15,16} In this study, the longest length of stay was 8-14 days. One study from the United States reported shorter hospitalizations (5-13 days, median: 7 days).¹⁹ Study from Oman, on the other hand, showed longer hospital stays (range: 5-116 days, median: 20.4 days).²⁰ The difference in length of stay is mainly due to differences in the treatment obtained, where in developed countries such as the United States, treatment for children with GBS is in accordance with the recommendations for managing GBS in children.

In this study, the frequencies of AMAN, AIDP and AMSAN were 58.5%, 22%, and 19.5%, respectively. This is similar to studies published from China, Spain, India, Malaysia, Japan, Mexico, and Bangladesh, where the axonal type is more common than the demyelinating type.^{16-18,22} In a study of 108 children with GBS conducted in India by Sandip et al, AIDP was seen in 52.8% (n=57), the axonal pattern in 33.3% (n=36), and a normal EMG pattern in 5.6% (n=6).²³ A study in India found that children with GBS with axonal variation had higher Hughes disability scores at presentation, at the peak of illness, at discharge and at follow-up at eight weeks and six months.²³ The axonal type has a higher incidence rates of gastrointestinal symptoms, while upper respiratory tract disease was more common in AIDP according to some studies.^{24,25,26} Several studies showed that axonal variants are associated with higher ventilation requirements. Other investigations reported no significant changes in axonal type or demyelination on the frequency of respiratory support device use or the outcome of children with GBS.^{17,27,28}

Treatment with intravenous immunoglobulin (0.4 g/kg for 5 days) and plasmapheresis (typically five sessions at 200-250 ml/kg) has been shown to be effective for GBS.^{4,11,30,31} In general, IVIG is considered the first choice of treatment because it is easy to administer, widely available and associated with less side effects compared to plasmapheresis.^{30,32} However, plasmapheresis is less expensive than IVIG and could theoretically be the preferred treatment option in low-income countries.^{34,35,36} The lack of national treatment guidelines and the high costs of existing treatment contribute to poorer prognostic outcomes and higher GBS mortality rates in low-income countries compared to high-income countries.³⁷

Cytoalbumin dissociation is one of the validated diagnostic criteria for GBS, reflecting impaired blood-CSF barrier due to neuroinflammation. However, inflammation in GBS varied between patients and elevated protein levels were not found in all cases.³⁸ The percentage of cytoalbumin dissociation was shown to vary between 44 and 81% depending on lumbar puncture (LP) time, with a lower rate early in the disease course (sensitivity 50% during the first week).^{10,39} Furthermore, protein levels in CSF have been demonstrated to be age dependent, and when age-adjusted values are utilized, the sensitivity of total protein (TP) for diagnosing albuminocytologic dissociation decreases.^{38,39} Based on the data collected in this study (Table 5), lumbar puncture was only performed on 7 children (17.1%). This is because there are some subjects that refused the procedure.

The Brighton criteria are the criteria used to diagnose children with GBS according to the modalities available at the health center in the area. Brighton criteria are divided into 4 levels of diagnostic certainty. In this study, the majority of the subjects were at level 2 (85.4%), where at this level only one examination was carried out, namely nerve conduction study (NCS) and lumbar puncture. For level 1, only 14.6% were found. This is because the subject's family mostly does not approve of the lumbar puncture, and only relies on one modality, the nerve conduction study. In a study aimed at validating the Brighton criteria for diagnosing GBS in Pakistan, it was concluded that the Brighton criteria for the diagnosis of GBS could be used with acceptable sensitivity for level 3 certainty (does not require clinical laboratory testing), level 2 certainty (using CSF examination or NCS), and level 1 certainty (using both tests).⁴⁰

The completeness of the data about the primary diagnostic characteristics is required for the classification of GBS using the Brighton criteria. As a result, the criteria were validated independently for each patient subgroup using the entire data set as well as the entire patient cohort.⁴¹ Neuro-electrophysiological examination and CSF examination were positively correlated with the diagnostic certainty level of the Brighton criteria ($P < 0.01$).²¹ When the Brighton criteria and the National Institute of Neurological Disorders and Stroke (NINDS) were compared in a cohort analysis, a diagnostic certainty of at least Level 3 of the Brighton criteria (95 percent) exhibited a sensitivity comparable to the NINDS criteria.²²

The sensitivity of the Brighton criteria in the GBS patient population has been studied in numerous research. Sensitivity ranged from 60% to 98% in different groups.^{9,10,41,42} In the Malaysian study by Chen et al regarding the validity of the Brighton criteria in GBS patients, the highest level of diagnostic certainty (Level 1) was achieved in 67% of patients, followed by 25% at Level 2, 4% at Level 3 and 5% at Level 4.²¹ The findings in Malaysia are comparable to studies from the Netherlands where Level 1 diagnostic certainty was achieved in 61% of their adult GBS population.^{10,21} High diagnostic rates have been reported in GBS cohorts in Bangladesh and China, where level 1 was achieved in 91% and 79% of patients, respectively.^{42,43} There are several reasons for this difference. The interval from GBS onset to CSF examination was longer in both countries (Bangladesh: median 11 days; China: mean 13 days) compared to the Malaysian cohort (median 8 days). This results in a higher probability of obtaining CSF albuminocytological dissociation patterns.^{22,42,44}

Jafari et al. conducted research on 79 children with GBS aged 4 to 14 years in India using the Brighton criteria. According to the study, children with GBS usually met the Brighton level 3 criteria (86%) without any CSF or NCS studies. In this investigation, there was no difference in sensitivity between levels 2 and 3 (84% vs 86%, $p > 0.05$).⁴⁵ Although most of the cases met the level 3 criteria, 11 cases failed to meet the level 3 criteria due to lack of data and documentation. Level 1 criteria were found in 62% of patients. In that cohort study, 17 individuals (22%) met the level 2 criteria after CSF analysis revealed no cytoalbumin dissociation in the second week after acute flaccid paralysis (AFP). The study concluded that the Brighton criteria could be used in low-income countries with moderate to high sensitivity.⁴⁵

Conclusion

According to studies on children with GBS from 2016 to 2020, the majority are females between the ages of 10 and 14, with an average stay of 8 to 14 days. Axonal type (AMAN) was the most common, followed by demyelinating type (AIDP), with 31.7 percent receiving intravenous immunoglobulin treatment. Based on Brighton criteria, majority of children were diagnosed with a diagnostic level 2 and the majority of children on a disability scale with disability scale 3 were able to walk with the assistance of a cane or supportive equipment.

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