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Clinical Profile of Pediatric Guillain-Barré Syndrome: A Study from National Referral Hospital in West Java, Indonesia

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Diagnosing Guillain-Barre syndrome (GBS) in children is challenging due to its highly variable clinical presentation. However, the clinical profile still becomes the hallmark of diagnosis. Thus, this study was aimed at exploring the clinical profile of pediatric GBS. This is a retrospective study of clinical profile at a national referral hospital in West Java, Indonesia from January 2011?December 2015. From a total of 40 patients, 27 complete medical records were included in the study. The gender distribution, females were outnumbered, male. Most patients were in preschool (4-5 years) and school-age (6-12 years) category. All patients had bilateral, progressive, and ascending pattern muscle weakness. Muscle weakness limited in legs was evident in 29.6% of patients. Sensory deficits were presented in 37%, autonomic dysfunction 14.8%, cranial nerve involvement 29.6%, and respiratory failure 11.1%. Most patients were discharged from the hospital with improvement. GBS profile in our pediatric patients has wide-ranging manifestation thus diagnosis criteria covering all patients are very important.

Keywords: Clinical profile; Pediatric Guillain-Barre syndrome.

Near elimination of polio worldwide another etiology of acute flaccid paralysis (AFP) in children that takes major importance is Guillain-Barre syndrome (GBS), which now becomes the leading cause of AFP that account for nearly 50% cases worldwide.[1–4] GBS is considered as an emergency case as well.[5] A common mistaking is that GBS has a good outcome but a recent study showed that severe, generalized manifestation and respiratory involvement affect 20-30% cases of GBS.[6,7] Other studies also showed that despite standard treatment given nearly 20% of patients die or have a persistent disability that may be caused by delayed diagnosis or standard treatment that not given timely.[7] Thus, early and accurate diagnosis of GBS is indeed needed.

GBS is a post-infectious autoimmune disease that attacks peripheral nerves component

such as motor, sensory, autonomic, or cranial nerves.[6] Its pathogenesis is molecular mimicry between microbial and nerve antigen that triggers the patient's immune response, thus antecedent infection such as flu or respiratory tract infection (URTI), gastroenteritis (*C.jejuni* infection) and others before the symptoms occurred.[1,6] The incidence rate in children ranged between 0.82–3.25 per 100.000 person.[8–10] GBS has several subtypes such as Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor and Sensory Axonal Neuropathy (AMSAN), and Miller-Fisher Syndrome (MFS).[6,11,12] These different subtypes contribute to the heterogeneous clinical manifestations and severity of GBS such as differences in rate of progression, time of recovery, sensory deficit involvement, autonomic dysfunction, cranial involvement, and others.[13] The clinical presentation is also diverse in children as some cases are atypical such as patient experienced pain preceding the motor weakness, which different with the typical one.[10,13] Despite its heterogeneity, clinical manifestation still becomes the hallmark of diagnosis as there is no pathognomonic sign and typical biomarker for each variants and other supportive examination such as cerebrospinal fluid (CSF), electromyography is used only for supporting purpose.[6,10,13]

In Indonesia, the incidence of GBS at National Refferal Hospital, Cipto Mangunkusumo, since 2010-2014 is 7.6 case/year.[14] An epidemiology study in Surabaya reported GBS mostly affected children aged under 15 y.o. from 2014-2017.[15] The rarity of GBS in children, its main symptom of acute flaccid paralysis (AFP) that may mimicked by another causes of GBS, diagnosis criteria that were developed but rarely validated and may not cover all patients especially children because of the clinical presentation diversity, make diagnosis based on clinical profile even more difficult and challenge for the physician.[1,3,16] Existing GBS diagnosis criteria refer to adults patients,[13] and to our knowledge there are no specific criteria used in pediatric cases. However, this problem can be overcome through the knowledge of clinical profiles acquired from many regions worldwide. Therefore, through those information validated diagnostic criteria could be developed and helped physician in making early and accurate diagnoses and poor outcomes of the patients can be reduced. This study was aimed to know the clinical profile of pediatric GBS in Indonesia, especially in West Java.

MATERIAL AND METHODS

This study was a retrospective design exploring the clinical profile of GBS in children at the largest tertiary care and referral hospital in West Java, Indonesia, in Dr. Hasan Sadikin General Hospital from January 2011 December 2015. Demographic data, length of stay, duration between onset of symptoms and hospital admission, clinical profile (motor disturbances, sensory deficits, dysautonomic sign and symptoms, cranial nerve and respiratory involvement) and condition at hospital discharge were collected from medical records after approval from the local ethics committee. The inclusion criterion was all complete medical records of GBS patients in the department of the child health of the hospital. Medical records with inadequate information were excluded from this study.

Statistical analysis

Categorical data were presented as percentages, continuous data as means and standard deviations if normally distributed and as medians and interquartile ranges (IQR) if not normally distributed. Statistical analysis was done on Microsoft Excel and SPSS Statistics 16.0 for Windows.

Ethical clearance

Ethical approval for this study was obtained from the Health Research Ethics Committee (KEPK) Faculty of Medicine Universitas Padjadjaran with registration number: 593/UN6.C1.3.2/KEPK/PN/2016.

RESULTS

From a total of 40 GBS patients at the Department of Child Health Dr. Hasan Sadikin General Hospital from January 2011 December 2015, 27 complete medical records were being included in the study. Demographic data are illustrated in Table 1. There is a slight predominance in female patients with a ratio of 1.45:1. In female, the median age was 5 (1 13), and male was 9 (range 3 13). The length of stay

was ranged from 0–91 days with a median 7. The median of duration between onset of symptoms and hospital admission was 5 with range 6 hours 120 days.

Females were outnumbered males with a percentage 59.3%. Most patients were in the "preschool" and "school-age" category. The presence of antecedents before the beginning of the clinical sign and symptom was mentioned in 10 (37%) patients (Table 1); among them, the most frequent were upper respiratory tract infection (18.5%).

All patients had bilateral and progressive muscle weakness with ascending pattern (Table 2). The site of muscle weakness was predominated by upper and lower extremities involvement as it experienced by 19 (70.4%) patients. Muscle weakness limited in lower extremities was referred in 8 (29.6%) patients. Most patients had decreased muscle tone and tendon reflex in affected limbs.

Sensory deficits were presented in 10 (37%) patients with the details presented in Table 2. There was one patient who had both pain and paresthesia. Cranial nerve involvement was noted in 4 (14.8%) patient with CN VII and X as the most frequently affected nerve. There was 1 (3.7%) patient who CN VII, X, IX, and XII were affected and 1 (3.7%) patient who CN IX and X were affected. Dysautonomic signs were evident in 4 (14.8%) patients that consist of 2 (7.4%) gastrointestinal disturbance and 2 (7.4%) urinary retention. Respiratory involvement was disclosed in 3 (11.1%) patients. Most patients (85.2%) were discharged from the hospital with improvement.

Table 1. Demographic Status of GBS Patients at Child Health Departement of Dr. Hasan Sadikin General Hospital from January 2011 December 2015 (n=27)

Variables	n	%
Gender		
Male	11	40.7
Female	16	59.3
Age category		
Infancy (0 1 year)	1	3.7
Toddlerhood (2 3 years)	4	14.8
Preschool (4 5 years)	8	29.6
School Age (6 12 years)	8	29.6
Early Adolescence (13 14 years)	6	22.2
Antecedent Event		
Unknown	17	63.0
Upper Respiratory Tract Infection	5	18.5
Diarrhea	2	7.4
Unspecified Fever	2	7.4
Varicella-Zoster Infection	1	3.7

Table 2. Clinical Sign, Symptoms, and Condition at Hospital Discharge (n=27)

Clinical Sign and Symptom	n	%
a. Motor Sign and Symptom		
Site of Muscle Weakness		
Upper extremities	0	0
Lower extremities	8	29.6
Upper and Lower extremities	19	70.4
Symmetry		
Bilateral	27	100
Unilateral	0	0
Progressive		
Yes	27	100
No	0	0
Muscle Tone		
Normal	8	29.6
Increase	2	7.4
Decrease	17	63.0
Tendon Reflex		
Normal	4	14.8
Increase	0	0
Decrease	20	74.1
Absent	3	11.1
b. Sensory Sign and Symptom		
Hypesthesia	3	11.1
Paresthesia	2	7.4
Hyperesthesia	1	3.7
Pain at:-		
Inferior Limb	2	7.4
Shoulder Girdle	1	3.7
Back	1	3.7
Head	1	3.7
c. Dysautonomic Sign and Symptom		
Gastrointestinal Disturbance	2	7.4
Urinary Retention	2	7.4
d. Cranial Nerve Involvement		
CN VII	3	11.1
CN IX	2	7.4
CN X	3	11.1
CN XII	1	3.7
e. Respiratoy Involvement		
Yes	3	11.1
No	0	0
f. Condition at hospital discharge		
Improvement	23	85.2
Unrecovered	4	14.8

DISCUSSION

GBS is known having a diverse clinical presentation and severity. Thus, there are a lot of challenges in making early and accurate diagnosis such as clinical presentation diversity, another possible etiology that may mimic GBS, rarity of the disease, atypical cases found in children, clinical pattern, and diagnosis criteria of GBS in children that is rarely validated. In addition, the problems may also be complicated by other conditions such as found in developing countries like Indonesia which financial consideration still takes a major part in giving a supportive examination. The physician may only use the clinical profile as diagnostic tools. Thus, the knowledge about the clinical profile of GBS is indeed needed.[6] Based on results that evident in this study the clinical presentations generally resemble the typical cases of GBS that are found in other studies and literatures but there are still characteristics that are different from many studies that have been conducted before.[1,6,9,12]

In our series, female patients were outnumbered male, this is consistent with previous study.[17] While in another study male is more commonly being affected.[18,19] Whether the difference is meaningful or not needs further evaluation but the association between gender and GBS is rarely being proposed.[3,6,16,20] In this study, GBS most occurred in preschool and school-age, this was in line with the previous study.[1,12,21] This age group is suspected to be vulnerable to previous infections and susceptible to demyeliniation.[1,22] GBS is a syndrome caused by acute inflammation of the peripheral nerves and preceded by respiratory system or gastrointestinal tract infection.[11,23,24] Kalra et. al.[3] and Sharma[2] reported antecedent infections were an upper respiratory infection and diarrheal episode. In this study 25.9% patients had antecedent infection, whose upper respiratory infection (URTI) as the most common (18.5%). A prospective study in North India reported AMAN had preceding gastroenteritis, and AIDP had upper respiratory infections.[25]

Pathogenesis underlies the clinical picture found in GBS. Muscle weakness with ascending pattern experienced by most subjects resembles the typical case of GBS, and also reported by Ramirez.[21] Eight (29.6%) patients experienced muscle weakness that was limited in legs until the hospital discharge which does not meet features needed for diagnosis of a typical case. In typical case, diagnosis criteria is progressive muscle weakness with arm and legs involvement.[6]The sensory function disturbances presented in this study are paesthesia (7.4%), hypesthesia (11.1%), and pain (18.5%). Some patients also had dysautonomia (14.8%) and reflex disturbances (85.2%). These inline with other symptoms that have been reported as limb pain,[12,26] sensory symptoms,[2,3,27] cranial nerves involvement,[3,12,26,27] dysautonomic,[2,3,12,26,27] and reflex disturbances.[2,12] According to WHO, manifestation caused by cranial nerve involvement and respiratory failure occur in severe form of Guillain-Barré Syndrome. In this study, 29.6% patients presented cranial nerve involvement. CN VII and CN X is the most affected nerves in this study. Similar compared to the literature that CN VII,IX,X was known as the most often cranial nerve involved.[10]Respiratory involvement was found in 3 (11.1%) fewer compared to several studies that range between 17-38%.[3,13] This result revealed that some GBS patients especially children have a variable clinical presentation, thus diagnosis criteria that can cover all patients are most needed.

Most patients were discharged from the hospital with improvement. Four (14.8%) patients were discharged from the hospital with under-recovery conditions. The factor that may affect outcome which generally good in our series is an early diagnosis of the disease, as described before.[6] 81.5% of patients were admitted to the hospital before the acute progressive phase (< 2 weeks). A full hospital condition and financial problem contributed to the early discharge of under-recovery patients. Because there is no follow-up about the disease progression, whether the patients have persistent muscle weakness, relapse, or death after hospital discharge is unknown.

The limitation of this study is the subtype is unknown because only 2 patients were subjected to electromyography due to financial considerations. The patients in this study were also not being followed-up so the information about the progression after a hospital discharged is unknown. Recalling the clinical presentation of GBS patients that still variable, a further study exploring diagnosis criteria that can cover all

patients is very important. It is expected that from information about the clinical profile of GBS children patients worldwide validated diagnostic criteria for pediatric GBS might be necessary.

CONCLUSION

Motor disturbances found in this study which is bilateral, symmetry muscle weakness with ascending pattern generally resembles the typical case of GBS but there are still some patients who experienced muscle weakness that does not meet the features needed for typical case diagnosis. This may be influenced by the highly variable clinical presentation in children. Sensory deficits, autonomic dysfunction, cranial nerve, and respiratory involvement findings were generally similar to other studies.

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