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Original Article

Erasmus Guillain-Barre Syndrome Outcome Score (EGOS) to predict functional outcomes

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Abstract

Background Guillain-Barre syndrome (GBS) has a highly diverse clinical course and prognosis. Predicting functional outcomes is needed in order to give appropriate treatment and counseling. *Erasmus Guillaine-Barre Syndrome Outcome Score* (EGOS) is simple scoring based on age onset, pre existing diarhea and GDS score obtained from medical record and physical findings that can be used by clinician to predict the functional outcomes of the child with GBS.

Objective To assess the usefulness of EGOS to predict functional outcomes of GBS patients.

Methods A retrospective cohort study to see the functional outcomes which was walking or not walking of children with GBS aged 6 months to 18 years hospitalized in RSUP Dr. Sardjito, Yogyakarta from 2014 to 2019, were enrolled by a purposive sampling method. Bivariate and logistic regression multivariate backward method analyses were used to assess for possible correlations between predictive factors and functional outcomes in GBS patients.

Results A total of 33 patients were enrolled and analyzed. After six months of weakness, 57.1% of patients with high EGOS (> 4) had poor functional outcomes according to the Hughes scale, scoring to asses functional outcomes. Patient with high EGOS (> 4) had greater risk of poor functional outcomes compared to patients with lower EGOS (≤ 4) (OR 33.3; 95%CI 2.74 to 404.94; P=0.006). Poor functional outcomes of GBS patients was not influenced by preceding upper respiratory tract infection, cranial nerve involvement, use of ventilator, autonomic dysfunction, immunotherapy, complicating disease, rehabilitation, or nutritional status.

Conclusion High EGOS of >4 is a predictor for poor functional outcomes in children with GBS. [Paediatr Indones. 2022;62:130-7 DOI: 10.14238/pi62.1.2022.130-7]

Keywords: EGOS; Guillain-Barre syndrome; functional outcomes

uillain-Barre Syndrome (GBS) is an autoimmune polyneuropathy disease with variable course of disease and prognosis. The incidence of GBS increases with age, and is 0.4-1.4 cases per 100,000 children aged less than 15 years worldwide. The estimated incidence of GBS in Indonesia is 1 to 2 cases per 100,000 population under 18 years of age in a one-year period, and predominantly affecting males. The functional outcomes of GBS patients in children is good, but 20% of patients who recover have remaining disabilities.

Functional outcomes at 6 months in patients with GBS which is ability to walk independently can be predicted by using a scoring system EGOS that consists of age at onset of weakness, diarrhea preceding the weakness, and Guillain-Barre disability score (GDS).² Other factors that may influence outcomes are acute respiratory infection (ARI) before weakness, cranial nerve involvement, ventilator use, autonomic dysfunction, immunotherapy use, presence

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of comorbidities, rehabilitation, nutritional status, and interval of onset of weakness to admission.² Interval onset of weakness to admission define as time (how many days) needed from the first weakness symptom untill the child brought to the hospital.

Erasmus Guillaine-Barre Syndrome Outcome Score (EGOS) has not consistently been found useful for predicting functional outcomes in GBS patients.^{2,3} Thus, we undertook this study, the first in Indonesia to our knowledge, to assess EGOS for predicting functional outcomes of GBS patients in the pediatric population.

Methods

This retrospective cohort observational study was done in Dr. Sardjito Hospital, Yogyakarta. The study period was January 2014 to December 2019 and subjects were enrolled by purposive sampling. Medical records were assessed by a pediatric neurologist to determine if patients met the inclusion criteria, which were children aged 6 months - 18 years diagnosed with GBS by Asbury criteria⁴ with available data on functional outcomes at 6 months of weakness documented in the medical records. If not, the author telephoned the family to obtain uncomplete information. Patients with incomplete data, Miller Fisher GBS subtype, and the inability to walk before suffering GBS, such as patients with cerebral palsy or post-traumatic conditions, as well as other preexisting neuromuscular diseases were excluded.

Data were collected by case report form (CRF) guidelines. All patients underwent EGOS assessment at day 14 of hospitalization. The components of EGOS were calculated according to Table 1 and Table 2; age of onset was defined as age when the child start suffer from GBS, preceeding diarrea was diarrhea that happened within 4 weeks before the onset, and GDS was a scale that used to asses the functional status of the GBS patient as described in Table 2.5 EGOS > 4 was considered to be high, while \leq 4 was considered to be low. Other factors that may influence outcomes are acute respiratory infection (ARI) before weakness, cranial nerve involvement, ventilator use, autonomic dysfunction, immunotherapy use, presence of comorbidities, rehabilitation, nutritional status, and interval of onset of weakness to admission.² Interval

onset of weakness to admission was defined as time (how many days) needed from the first weakness symptom untill the child brought to the hospital.

The functional outcomes were assessed using Hughes' criteria (Table 3) at 6 months after weakness onset; subject with score <2 according to the Hughes scale⁶ were considered to have good functional outcomes, which was the ability to walk independently; subject with score >2 was considered to have poor prognosis.⁷

Table 1. EGOS assessment5

Prognostic factors	Score
Age at onset	
> 60 years	1
41-60 years	0.5
≤ 40 years	0
Preceding diarrhea	
No	0
Yes	1
GDS (at 14 days after admission)	
0-1	1
2	2
3	3
4	4
5	5
EGOS	1-7

Table 2. Guillain-Barre Disability Score (GDS)2

Score	Condition
0	Healthy
1	Mild symptoms, can still run
2	Can walk 10 meters or more without assistance but cannot run
3	Can walk more than 10 meters with assistance
4	Lie in bed or in a wheelchair
5	Requires assistance with ventilation at least several times a day
6	Died

Table 3. Hughes' criteria for functional⁶

Score	Condition
0	Healthy
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Data were analyzed using the Statistical Package for the Social Science (SPSS) version 25 software. Fisher's exact test was used for bivariate data and followed by multivariate analysis for variables with P<0.25, using the logistic regression backward method. The study was approved by the Ethics Committee of the Universitas Gadjah Mada Medical School, Indonesia.

Results

Of 43 GBS patients, 33 met the inclusion criteria. Baseline characteristics of subjects are shown in **Table** 4. Male gender was predominated and the mean age was under 5 years.

Table 4. Baseline characteristics of subjects

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Characteristics	(N=33)
Mean age (SD), months	106.7 (56.43)
Gender, n Male Female	21 12
Mean LoS (SD), days	21.97 (23.42)
Preceding diarrhea, n Yes No	6 27
Preceding upper respiratory infection, n Yes No	14 19
Cranial nerve involvement, n Yes No	9 24
Use of a ventilator, n Yes No	9 24
Autonomic dysfunction, n Yes No	11 22
Immunotherapy use, n None IVIG PE	5 20 8
Comorbidities, n Yes No	9 24
Rehabilitation, n Yes No	32 1
Mean interval of onset of weakness to admission (SD), days	7.18 (23.42)

Table 4. Baseline characteristics of subjects (continued)

Characteristics	(N=33)
Nutritional status, n Severe malnutrition Malnutrition Normal Overweight Obese	0 6 26 1 0
Mean GDS (SD)	3.73 (0.80)
Mean EGOS (SD)	3.94 (1.00)
EGOS, n > 4 ≤ 4	7 26
Functional outcomes at 6 mo, n Poor (not walking) Good (walking)	5 28
ENMG, n AMAN AMSAN AIDP CIDP Miller Fisher Bulbar type Normal Not specific Not done	15 4 5 3 1 2 1 7 5

LoS=length of stay; GDS=Guillain Barre disability score; AMAN=acute motor axonal neuropathy; AMSAN=acute motor and sensory axonal neuropathy; AIDP=acute inflammatory demyelinating polyradiculopathy; CIDP=chronic inflammatory demyelinating polyradiculopathy; ENMG=electroneuromyography; IVIG=intravenous immunoglobulin; PE=plasma exchange

Bivariate analysis results of potential predictive factors of functional outcomes are shown in Table 5. Variables that had significant associations with functional outcomes were EGOS, ventilator use, comorbidities, and less interval of onset. Variables that had P values < 0.25 in bivariate analysis were further analyzed by multivariate logistic regression backward method, by excluding variables which were not significant. Variable that being analyzed in multivariat were EGOS, use of a ventilator and interval of onset. The variable of comorbidities was having significant values but having incomplete cells in cross tabulation, so it was not able to analysis in multivariate due to risk relative value that would be so high and the infinity of the confidence interval. Only EGOS had a significant association with functional outcomes (P=0.006) in the multivariate analysis. Patients with high EGOS had 33.3 times higher risk of poor functional outcomes than patients with low EGOS (OR 33.3; 95%CI 2.74 to 404.94; P=0.006) according to **Table 6**.

Table 5. Bivariate analysis of variables and the outcomes

Variables	Functional outcomes		Bivariate			Multivariate (backward method)		
Variables	Poor	Good	RR	95%CI	P value	OR	95%CI	P value
EGOS			14.86	1.96 to 112.69	0.004*	33.33	2.74 to 404.94	0.006*
> 4	4	3						
≤ 4	1	25						
Diarrhea			1.13	0.15 to 8.35	1.000			
Yes	1	5						
No	4	23						
Upper respiratory infection			0.91	0.17 to 4.71	1.000			
Yes	2	12						
No	3	16						
Cranial nerve involvement			1.78	0.35 to 8.96				
Yes	2	7						
No	3	21						
Use of a ventilator			10.67	1,37 to 83,11	0.013*			
Yes	4	5						
No	1	23						
Autonomic dysfunction			3.00	0.58 to 15.41	0.304			
Yes	3	8						
No	2	20						
Immunotherapy					1.000			
None	0	5						
IVIG	4	16						
PE	1	7						
Comorbidities					0.001*			
Yes	5	4						
No	0	24						
Rehabilitation					1.000			
Yes	5	27						
No	0	1						
Nutritional status			1.13	0.15 to 8.35	1.000			
Malnutrition	1	5						
Normal	4	23						
Mean interval of onset (SD), days	2.00 (1.00)	8.11 (6.99)			0.000*			

^{*}significant P<0.25

Table 6. Multivariat analysis

Variables	Model I			Model II			Model III		
Variables	OR	CI 95%	P value	OR	CI 95%	P value	OR	CI 95%	P value
EGOS >4	6.48	0.31 to 136.43	0.229	14.69	1.09 to 197.58	0.043	33.33	2.74 to 404.94	0.006
Use of ventilator	5.84	0.29 to 118.37	0.250						
Interval of onset	0.76	0.43 to 1.35	0.350	0.68	0.34 to 1.39	0.294			

EGOS=Erasmus Guillaine Barre Outcome Score, OR=odd ratio, CI=confidence of interval

As a tool limitation of SPSS, the result was presented in OR. According to the type of retrospective cohort study, the OR was converted to risk ratio (RR). However, due to only EGOS being significant in the multivariate analysis, the RR was the same as the bivariate result (RR 14.86).

Discussion

In our study, 57.1% of patients with high EGOS had poor outcomes (OR 33.33; 95%CI 1.96 to 112.69). EGOS was evaluated to predict the ability to walk independently as a functional outcomes in GBS patients 6 months after weakness. The prediction is needed

for appropriate management and comprehensive counseling (information and education) regarding the prognosis. Preceding infections such as ARI and diarrhea, or other conditions such as immunization before weakness should be documented briefly in medical records to ensure the accuracy of EGOS evaluation.

The EGOS components consist of age, preceding diarrhea and GDS at the 14th day from of admission (day 14th of hospitalization). Previous studies have concluded that younger age, absence of preceding diarrhea, and low GDS at day 14 of admission are predictive of good functional outcomes.⁸ However, previous studies on using EGOS to predict functional outcomes in children have had inconsistent results.³ The EGOS was initially thought to be inappropriate for children due to the age classification, as children would always have scores of 0 (zero) (i.e., age \leq 40 years). However, the age component only has a weight of 1 from the total score, so it was still considered useful in some studies.²

The multivariate logistic regression backward method analysis revealed that EGOS was the only variable that had a significant association with functional outcomes in children with GBS. We noted that only 3.8% of patients with low EGOS score (<4) had poor functional outcomes, which was consistent with findings from a previous study which reported that 55% of patients with high EGOS and 7% with low EGOS had poor functional outcomes.⁸

In our study, 23% of the sample population was less than 5-year-old consistent with the incidence of GBS patients that can occur at any age, not only in the elderly. Our subjects were predominantly male, in accordance with the global GBS prevalence and in agreement with an Indian study (male to female ratio of 2 to 3: 1). ¹⁰ In contrast, a study in Indonesia found no such difference. Male predominance in GBS patients remains poorly understood. ¹¹

The ENMG revealed that AMAN was the most prevalent subtype. A study also reported that in Asian countries such as China and Bangladesh, the AMAN subtype was predominant. Although the pathogenesis is not clear, AMAN type is thought to be caused by host factors, individual susceptibility, and preceding infectious agents.1²

There were 7 children with non-specific ENMG results, which we concluded were due to

spinal irritation and healing features. Most of the non-specific GBS features were came from previous hospitalizations, before referral to Dr. Sardjito Hospital. One patient had a normal ENMG result, which may have been due to the early timing of the examination, such that the demyelination process and axonal damage could not yet be seen. Five children (11.6%) did not undergo ENMG due to equipment problems, death before the examination, or discharge before the ENMG was scheduled, as there tended to be long queues for ENMG at our hospital. Hence, due to such data limitations we could not perform a subgroup analysis of ENMG and functional outcomes.

The preceding event of weakness could be upper respiratory infections, gastrointestinal infections manifesting as diarrhea, or vaccinations (polio).¹³ In our study, 20/33 children had preceding infection within 4 weeks before the onset of weakness. This result was lower than in a previous study, which noted that 70% of GBS patients had preceding infections.¹³

In our study, upper respiratory infection was the most common preceding infection, in agreement with Muid *et al.*¹¹ who reported that 84.21% of patients had preceding upper respiratory infection. In contrast, Akbayram *et al.*¹⁴ found no difference in the incidences of preceding upper respiratory and gastrointestinal infections (diarrhea). Infection prevalences can be influenced by seasonal and geographic conditions. A study in Asia noted that two-thirds of patients had preceding diarrheal infections mainly caused *C. jejuni.*¹⁴

Neither cranial nerve involvement nor autonomic dysfunction were significantly associated with the functional outcomes of children with GBS (P<0.05). Cranial nerve involvement manifested as facial muscle weakness, difficulty speaking or swallowing, and eye muscle weakness, that were not related to the degree of extremities weakness; and it is often recognized as a sign of Miller Fisher subtype that overlaps with other GBS subtypes such as AMAN and AMSAN.1 If the Miller Fisher subtype occurs in isolation, patients often have good functional outcomes due to minimal or no manifestation of extremity weakness. Autonomic dysfunction manifests as the inability to control micturition and defecation. In PICU patients, it also manifests as tachycardia or hypertension. Severe autonomic dysfunction can lead to multiple organ dysfunction and death.

The use of a ventilator was not significant in predicting functional outcomes (OR 5.84; 95%CI 0.29 to 118.37; P=0.250). In contrast, a previous study reported that the use of ventilator was a poor predictor of walking ability in children. In our study, 3 patients who used ventilators died before the day 14 after admission, so the EGOS could not be evaluated. This result suggests that ventilator use could be worsen GBS patient survival, such that the functional outcomes would be absolutely poor (death before 6 months). Of 9 patients with comorbidities (urinary tract infection, pneumonia, electrolyte imbalance), 5 patients had poor functional outcomes, but associations were deemed to be not significant.

Most patients received immunotherapy. Intravenous immunoglobulin (IVIG) was preferred in younger children, due to the inability to perform plasmapheresis (difficulty inserting catheter). In addition, IVIG is considered easier to administer due to the need for peripheral venous access only and the higher likelihood of completing the therapy dose. However, 5/33 patients did not receive immunotherapy (either IVIG or plasmapheresis) due to insurance problems, as the hospital did not approve IVIG because the patients did not meet the criteria. Despite this, all had good functional outcomes. Similarly, Wang *et al.*¹⁶ reported that the use of immunotherapy, IVIG or plasmapheresis, did not affect the long-term outcomes of GBS patients.

Rehabilitation was found to have no significant effect on patient outcomes. With RR that could not be calculated due to incomplete medical record data. However, early rehabilitation programs could have prevented secondary disabilities caused by immobility in GBS patients.¹⁷ Rehabilitation was performed as indicated, either oral or nerve stimulation using faradization, or general physiotherapy.

The mean interval onset of weakness to admission was 2.0 (SD 1.0) days in poor functional outcomes subjects and 8.11 (SD 6.99) days in good functional outcomes subjects, but the result was not significant on multivariate analysis. This result was consistent with that of a previous study which concluded that short interval periods of less than seven days, and especially less than 3 days, were poor predictors of functional outcomes. The mechanism was due to the severity of acute phase that the weakness occurs progressively in shorter period

indicating more extensive and progressive damage that leads to progressive ascending weakness and paralysis of respiratory muscle. In this progressive weakness and paralysis of respiratory muscle the patient has a higher risk of ventilator use and higher risk of comorbidities during hospitalization, ultimately affecting the functional outcomes.¹⁸

Malnutrition can increase the risk of infection and general weakness, which in turn affect functional outcomes. ¹³ Most of our subjects had good nutritional status (78.8%); nutritional status was significantly associated with outcomes in bivariate, but not in multivariate analysis. However, none of our subjects had severe malnutrition, which can affect the immunologic and healing processes. Children with good nutritional status likely have normal immunity and healing. ¹⁷

Overall, 5/33 of subjects had poor functional outcomes. This rate was lower compared to a previous study in which 20% were unable to walk independently at 6 months of weakness. The lower rate may have been due to neurological recovery, which is the theory that children have greater ability to regenerate nerve cells than adults. In children with GBS, the mechanism of disease is similar to other neurological diseases, so the concept of age-dependent capacity to recover from acute neurological disease in children also applies to GBS patients. However, the healing process of GBS patients is also influenced by the extent of neural damage and the degree of clinical severity in the acute phase.8 Other study suggest that geographical conditions, seasonality, race, and individual susceptibility factors can influence the functional outcomes of GBS, but the mechanism has not been clearly explained. 18

As we used secondary data, incomplete information was a problem in collecting data. The sample size was also inadequate, so that subgroup analysis of the GBS subtypes, based on ENMG results, and functional outcomes could not be performed. Prospective studies with a larger sample size as well as multicenter studies are needed to address the weaknesses of this study.

The advantage of the EGOS is its simple format and applicability in limited resource areas, since scoring information can be obtained from medical records and other sophisticated examinations are not required. The weakness of this scoring is that it is to be applied at 14 day after admission, so it would be rather late for severe cases who might need more immediate intense intervention or therapy.¹⁹

The strength of this study is that we showed EGOS to be a practical instrument for clinicians to predict the outcomes of walking at 6 months in pediatric patients with GBS. Prediction is urgently needed for appropriate management, as patients with poor prognoses should receive a second dose of immunoglobulin to improve the outcomes. 19 In addition, the family should receive counseling, information, and education regarding the prognosis. For children with predictions of poor functional outcomes, the family should be informed in order to prepare for the next treatment and home care, so that the family will be mentally and physically ready to properly care for children with long-term disabilities.²⁰ In conclusion, early use of the EGOS tool can be predictive of functional outcomes of GBS patients at 6 months after the onset of weakness.

Conflict of Interest

None declared.

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