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RESEARCH

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The early clinical and laboratory predictors of GBS outcome: hospital-based study, Assiut University, Upper Egypt

Eman M. Khedr[1,2*], Mohamed Zayed Mohamed[1] and Mohamed Mostafa M. Shehab[1]

Abstract

Background This study was designed to identify factors that influence outcomes in a large group of well-defined Guillain–Barré syndrome (GBS) patients with a 3-month follow-up period. Sixty-two cases of GBS with a mean age of 37.15 ± 17.60 years (33 males and 29 females) were recruited in the first 2 weeks after onset. Clinical history, examination, and a variety of rating scales including Medial Research Council sum score (MRC), Erasmus Guillain-Barré respiratory insufficiency score (EGRIS), at admission and 10 days later were performed. Follow-up investigations at 3 months included the Hughes Disability Scale (HDS), and Overall Neuropathy Limitation Scale (ONLS).

Results 64.5% of participants had cranial nerve deficits, 45% had neck muscle weakness, 30.6% had dysautonomia, and 8.1% were mechanically ventilated. C-reactive protein was elevated in 38.7%, and hyponatremia was recorded in 30.6% of patients. Older age, antecedent events particularly diarrhea, neck muscles weakness, low MRC sum score, impaired cough reflex, dysautonomia, and hyponatremia, were all significantly associated with poor outcomes at 3 months using HDS and ONLS. Regression analysis with dependent variables of HDS outcome showed that the presence of an antecedent event particularly diarrhea, neck muscle weakness, hyponatremia and the presence cytoalbuminous dissociation of CSF at onset, and low MRC sum score at 10th day after treatment, were predictors of poor outcome.

Conclusion Clinical and laboratory predictors of poor outcome were older age, the presence of an antecedent event particularly diarrhea, low MRC sum score at the 10th day, elevated CRP, hyponatremia and the presence cytoalbuminous dissociation.

Keywords Guillain–Barré syndrome (GBS), Outcomes, HDS and/or ONLS, Predictors, Electrolyte, Medial Research Council sum score

Background

Guillain–Barré syndrome (GBS) is an acute polyradiculoneuropathy, characterized by a rapidly progressive, nearly symmetrical, flaccid weakness of the limbs [1, 2]. The clinical presentation, course, and the clinical recovery and outcome of GBS all are variable. In addition, GBS varies considerably between geographical regions [2–4]. In the acute phase, about 1/5 of GBS patients require mechanical ventilation and 3–4% of patients die of complications [1]. Despite therapy with intravenous immunoglobulin (IVIG) or plasma exchange, about 10–20% of patients remain severely disabled [2, 5]. The recovery from GBS takes a long time and is highly variable, therefore information on the nature, and early predictors of patient-perceived disability after GBS could be of help

*Correspondence:
Eman M. Khedr
emankhedr99@aun.edu.eg; emankhedr99@yahoo.com
[1] Department of Neurology, Faculty of Medicine, Assiut University, Assiut, Egypt
[2] Department of Neuropsychiatry, Faculty of Medicine, Assiut University Hospital, Assiut, Egypt

for patients, doctors, and caregivers both in the acute and chronic phase of disease.

Previous studies found a relationship between outcome and recent preceding infections (antecedent events), clinical presentation, electrophysiological subtype and laboratory findings [6–9]. Yao and colleagues studied the clinical presentation of GBS in four regions of China and found that a higher proportion of the axonal subtype in central and southwest China; progression in the latter region was more served at nadir and patients had the longest hospital stay [10]

Zhai and their colleagues [11] in their retrospective study of 294 patients with GBS found that the AMAN subtype was predominant in northern China (40.1%) and had shorter time to nadir, with prolonged hospitalization, and worse prognosis at discharge than AIDP. A higher GDS score on admission was a strong predictor for poor outcome at discharge and short-term follow-up, independent of treatment type or in-hospital management (Ruiz-Sandoval and their colleagues) [12]. Luijten and their colleagues found that clinical predictors of the need for mechanical ventilation (MV) were a shorter time from onset of weakness until admission, the presence of facial muscle weakness, bulbar palsy and neck muscle weakness [13].

However, most of the previous studies were retrospective, and the findings were derived from relatively small series or selected groups of patients with a limited set of suboptimal outcome measures [6–9].

The current study was designed to address these problems using a prospective study design to identify factors that influence outcomes in a large group of well-defined GBS patients with a 3-month follow-up period.

Methods

Sixty-two cases of GBS were recruited and diagnosed according to criteria of the National Institute of Neurological Disorders and Stroke (NINDS) (revised form 1990) [14] and the Brighton Collaboration in 2014 [15] during the period from October 20th 2020 to September 20th 2021.

Cases were recruited within the first 2 weeks of onset, with progressive bilateral weakness of upper and lower limbs, absent or decreased tendon reflexes in affected limbs (at some point in clinical course) as well as other features that support a diagnosis of GBS with the same inclusion and exclusion NINDS criteria.

At admission each patient underwent the following procedures.

History included age, sex, onset, time elapsed between onset of symptoms and admission, presence of other comorbidites and preceding antecedent events including upper respiratory tract infection, flu-like symptoms or gastrointestinal tract infection (diarrhea or vomiting) and vaccination.

Clinical examination, vital signs including blood pressure, heart and respiratory rates, as well as arterial blood gases (ABG). Neurological assessment included cranial nerve examination and neck muscle weakness.

Autonomic dysfunction included variation in arterial blood pressure, arrhythmia, attacks of diarrhea, vomiting, and sweating. Hughes Disability Scale (HDS) [5, 16] as this scale has six levels ranges from 0 point (healthy), up to 6 points (dead) depending on the disability of lower limbs (capable of running, walking without assistant, walk with assistance, bedridden, need ventilation, and dead) [5, 16].

Medial Research Council sum score (MRC) [17–19] as this scale ranges from zero power up to 60 full powers and is scored as the sum of six muscle power in both upper and lower limbs in points. This scale was assessed at onset, at nadir and 10 days of treatment [17–19].

The Erasmus GBS Respiratory Insufficiency Score (EGRIS) is a model developed to estimate the risk of respiratory failure. At admission and according to EGRIS, three clinical factors are explored, the time from onset of weakness to admission, presence of facial and/or bulbar weakness, and severity of muscle weakness [7].

Overall Neuropathy Limitation Scale (ONLS), this scale is used to assess the limitations of patients with immune-mediated peripheral neuropathies; it is reliable, responsive and has construct validity in people with GBS, chronic inflammatory demyelinating polyneuropathy and paraprotein-associated demyelinating neuropathy. [20]

Laboratory investigations at admission, complete blood count (CBC), blood urea, creatinine, serum electrolytes (Na, k, Ca), total protein, albumin, and C-reactive protein (CRP). Arterial blood gases (ABG) included PaO2, PaCo2, pH, and SPo2 were also assessed.

Cerebrospinal fluid analysis (CSF) as 42 patients underwent analysis during the first 3 days of admission.

Treatment options as all patients received treatment immediately after diagnosis either by plasmapheresis (plasma Exchange 5 sessions one every other day) or intravenous immunoglobulin (IVIG) 0.4 g/kg/day for 5 consecutive days.

Patients were assessed on admission, at nadir and 10 days after the end of plasma exchange and IVIG, using the MRC sum score and EGRIS. HDS and ONLS GBS scales were assessed 3 months after the onset of illness. All patients received a conventional neurophysiological assessment (distal latency, nerve conduction study and F-wave of four limbs) within 1–3 days of admission in order to confirm the diagnosis.

Statistical analysis used SPSS (Statistical Package for the Social Science, version 17, IBM, and Armonk, New

York). Because the data distributions did not differ statistically from normality (using Shapiro–Wilk test, $P > 0.05$), continuous variables are given as means ± SD; categorical variables are summarized as counts (percentage). Spearman's correlations were calculated between HDS, and ONLS scales outcome (at 3 months follow-up) and clinical or laboratory variables at baseline. Multiple ordinal and linear regression analysis was used to identify best predictors of outcome graded according to HDS score and ONLS score, respectively.

Results

Sixty-two cases of GBS were recruited with a mean age of 37.15 ± 17.60 years (33/29 male/female ratio). 43 (69.4%) patients recorded an antecedent event before the onset of GBS symptoms, the commonest of which were high grade of fever 38 (61.3%), and upper respiratory tract infection while diarrhea with or without vomiting were observed in 13 cases (21%) (see Table 1). Clinical variants included sensory motor (47 patients 75.8%), pure motor (12 patients 19.4%), paraparetic (2 patients 3.2%), and Miller Fisher (1 case 1.6%). A number of specific clinical features were noted including 40 (64.5%) patients with involvement of cranial nerves, 28 (45%) patients with neck muscle weakness, 13 (21%) patients with papilledema, 19 (30.6%) patients with autonomic affection, and 5 (8.1%) mechanically ventilated patients and in ICU. C-reactive protein was positive in 24 (38.7%) patients, hypoalbuminemia and hyponatremia were observed in 20 (32.3%) and 19 (30.6%) patients, respectively, and cytoalbuminous dissociation in CSF was found in 24 (57.1%) patients. Details of outcome according to HDS are illustrated in Table 1. Table 2 shows correlations between clinical data and laboratory findings at baseline assessment and their relation to outcomes using both HDS and ONLS scales at 3 months.

Poor outcomes were associated with older age, comorbidities, antecedent events (especially diarrhea), neck muscle weakness, low MRC sum score at onset, nadir and at the 10th day of treatment, papilledema, impaired cough reflex and dysautonomia (Fig. 1).

Of the laboratory findings, only hyponatremia, hypoalbuminemia (Fig. 2), elevated CRP and cytoalbuminous dissociation in CSF were significantly correlated with poor outcomes (Table 2).

Multiple ordinal regression analysis (Table 3) was used to identify the best clinical and laboratory predictors of poor HDS outcome. These were the presence of an antecedent event particularly diarrhea, neck muscle weakness as well as elevated CRP, and low serum sodium at onset. Linear regression analysis was used to identify the best clinical and laboratory predictors of the ONLS Outcome Scale (Table 4) with cytoalbuminous dissociation and treatment plan as factors in addition to all those predictive of HDS outcome.

The best predictor of clinical rating scales of HDS outcome and ONLS (Table 5) using multivariate ordinal regression analysis and multivariate linear regression analysis, respectively, showed that low MRC sum score at the 10th day of treatment was the best single factor.

Discussion

Most previous studies have been retrospective, and the outcomes derived from relatively small series or selected variants of patients with relatively short follow-up and limited outcome measures [6–9]. The present study was a prospective longitudinal study involving a relatively large group of GBS recruited at an early stage of the disease.

The main findings were significant correlations between HDS and ONLS outcomes at 3 months and age at onset, the presence of antecedent events (especially diarrhea), low MRC sum score at onset, nadir, and the 10th day after treatment, neck muscle weakness, papilledema, impaired cough reflex, and dysautonomia. With regard to laboratory findings; hyponatremia, hypoalbuminemia and elevated CRP were correlated with poor outcomes.

Of these factors, multiple ordinal regressions showed that the best predictors for poor prognosis in both outcome measures were the presence of diarrhea, elevated CRP, and hypoalbuminemia. In addition, a low MRC sum score at the 10th day following admission was a predictor of poor HDS outcomes.

Regarding age, a total of 62 patients with GBS enrolled in our study with an average age of 37.15 ± 17.60 years (10–75) with more than half of them ≤ 40 years (54.8 ٪). These distributions are consistent with Sudulagunta SR and colleagues, and Abdelkader Tunç [21, 22]. The age of the patients in years was significantly correlated with outcomes of HDS and ONLS scores meaning that older age was associated with poorer outcomes, as reported in several previous studies [8, 22–28]. There was no influence of sex on HDS or ONLS outcomes.

According to antecedent Events, an antecedent event was recorded in 43 (69.4%) patients of which 38 (61.3%) had fever, 30 (48.4%) had upper respiratory tract infection, and 13 (21%) had gastrointestinal infection including diarrhea with or without vomiting. Siddiqui and their colleagues [29] found a lower frequency of various antecedent events was recorded in 33 patients, including respiratory tract infection in 9 (14%) and diarrhea/vomiting in 13 (21%) patients. In contrast, Sudulagunta and colleagues, 2015 found that 80% of patients had a predisposing infection which was higher than our study; however, gastrointestinal infection was more common in that study (47.25%) than upper respiratory infection (34.73%) [21].

Table 1 Demographic, clinical, laboratory, and outcome data among studied patients

Variables	
Demographic data	
Age mean SD (range of age years)	37.15 ± 17.60 (10–75)
Age group	
≤ 40 years	34 (54.8%)
40–60 years	20 (32.3%)
≥ 61 years	8 (12.9%)
Sex: male/female Number (%)	33/29 (53.2/46.8%)
Residency: urban/rural Number (%)	24/38 (38.7/61.3%)
Comorbidity	
No	48 (77.4%)
DM	2 (3.2%)
HTN	5 (8.1%)
DM + HTN	7 (11.3%)
Duration of each event	
Number of days between the antecedent event and onset of neurological manifestations Mean ± SD (range (days)	7.95 ± 7.095 (0–28)
Duration of antecedent event Mean ± SD (range 0–5 days)	1.82 ± 1.52
Number of days between onset of symptoms and nadir Mean ± SD (range 1–7 days)	3.32 ± 1.64
Number of days between onset of weakness and admission Mean ± SD (range)	6.69 ± 4.51 (1–18)
Type of antecedent event number = 43 (69.4%)	
Presence	
Upper respiratory tract infection Number (%)	30 (48.4%)
Fever Number (%)	38 (61.3%)
Gastrointestinal infection: diarrhea with or without vomiting Number (%)	13(21%)
Absent antecedent event Number (%)	19 (30.6%)
Days between onset and admission	
> 7 days	23 (37.1%)
4–7 days	12 (19.54%)
< 3 days	27 (43.5%)
MRC at nadir	
51–60 = 0	4 (6.5%)
41–50 = 1	6 (9.7%)
31–40 = 2	10 (16.1%)
21–30 = 3	17 (27.4%)
< 20 = 4	25 (40.3%)
Clinical variant	
Sensory motor	47 (75.8%)
Pure motor	12 (19.4%)
Para paretic	2 (3.2%)
Miller Fisher	1 (1.6%)
Specific clinical presentation	
Cranial nerves affection	
Presence	40 (64.5%)
Absence	22 (35.5%)

Table 1 (continued)

Variables	
Papilledema and visual affection (blurred vision)	
Present	13 (21%)
Intact	49 (79%)
Neck muscle	
Affected	28 (45.2%)
Not affected	34 (54.8%)
Sensory affection	
Hypoesthesia	46 (74.2%)
Intact sensation	16 (25.8%)
Cough reflex and affection of respiratory muscle	
Impaired cough reflex	32 (51.6%)
Preserved	30 (48.4%)
Erasmus Guillain–Barre Respiratory Insufficiency Score EGRIS risk	
Low risk	12 (19.4%)
Intermediate risk	15 (24.2%)
High risk	35 (56.5%)
Mechanical ventilation	
Mechanical ventilated	5 (8.1%)
Not ventilated	57 (91.9%)
Autonomic affection (dysautonomia)	
Presence	19 (30.6%)
Absence	43 (69.4%)
Laboratory findings (normal range)	
Total leukocyte count TLC (normal range 4000–10,000/L)	
Within normal range	23 (37.1%)
Leukocytosis	39 (62.9%)
Serum protein level (normal range 64-83 g/l)	
Within normal protein level	41 (66.1%)
Hypoproteinemia	21 (33.9%)
Serum albumin level (34-50 g/l)	
Within normal range	42 (67.7%)
Hypoalbuminemia	20 (32.3%)
C-reactive protein (CRP)	
Negative	38 (61.3%)
Elevated	24 (38.7%)
Serum sodium NA level (136-145 mmol/L)	
Within normal level	43 (69.4%)
Hyponatremia	19 (30.6%)
PCO2 in PH and respiratory acidosis	
Normal	55 (88.7%)
Respiratory acidosis and Co2 retention	7 (11.3%)
Cytoalbuminous dissociation in CSF (total 42 cases)*	
Negative	18 (42.9%)
Positive	24 (57.1%)
Outcome according to HDS	
Outcome according to HDS	
Healthy	27 (41.5%)
Minor symptoms and capable of running	10 (15.4%)
Able to walk 10 m without assistance but unable to run	11 (16.9%)

Table 1 (continued)

Variables	
Able to walk 10 m across open space with help	4 (6.2%)
Bed ridden or wheel chair bound	6 (9.2%)
Required assisted ventilation at least part of the day	2 (3.1%)
Dead	2 (3.1%)
Outcome according to Overall Neuropathy Limitation Scale (ONLS)	2.87 ± 3.59

MRC Medical Research Council score, *HDS* Hughes Disability Scale, *CSP* cerebrospinal fluid

* 42 cases only underwent CSF analysis

In the present study, the presence of a preceding antecedent event especially diarrhea was correlated with outcomes of HDS, and ONLS and was considered as one of the predictors for poor outcome. Hadden and colleagues, van Koningsveld and colleagues, and Rajabally and colleagues found similar results [24, 26, 27]. In contrast, Tunç and colleagues [22] found no correlations between outcome and the presence or absence of antecedent events although this may be related to the small sample size.

In the current study the duration of the antecedent event was 1.82 ± 1.52 days and the number of days between onset of symptoms and nadir was 3.32 ± 1.64 days. Twenty-seven patients (43.5%) presented with weakness within 3 days of onset; 23 additional patients were weak (37.1%) within 7 days or more. Similarly, Walgaard and colleagues, 2010 found that 35% of patients presented with weakness within 3 days from onset [7].

Comorbidities had little effect on outcome. Fourteen patients (22.6%) had diabetes and/or hypertension, but this was not related to outcome.

Low MRC sum scores at onset, at nadir and 10th day of treatment were associated with poor outcomes. Chiò A and colleagues, and McKhann GM and colleagues reported similar findings [23, 25]. Rajaballys and colleagues found that a low MRC sum score at admission or 7 days after admission predicted the need for mechanical ventilation [27]. Wen and colleagues found that MRC sum scores on admission and at nadir were significantly different between severe GBS and non-severe GBS groups [28], while Singh NK and colleagues found that severe weakness at nadir, and rapid onset of weakness were poor prognostic features [30]. Gonzalez-Suarez and colleagues reported that older age, severe deficits at onset, and cranial nerve involvement were poor prognostic factors [31].

More than three-quarters of the patients (47 patients with 75.8%) presented with the classic sensory–motor variant, while 12 patients (19.4%) presented with a pure motor variant, 2 patients (3.2%) had paraparesis and one patient (1.6%) had Miller Fisher syndrome. The pure motor type had significantly poorer outcome compared with classic sensory motor neuropathy consistent with other studies [15, 32–34].

Involvement of cranial nerves was observed in 40 patients (64.5%) with either unilateral or bilateral facial palsy, bulbar palsy or both but neither correlated with outcome. Other studies reported a lower incidence of cranial nerve involvement ranging from 25 to 34% [21, 22, 35, 36], while several previous reports found that involvement of cranial nerves was more common in severe forms of GBS and was associated with poor prognosis [27, 28, 31]. Verma, Chaudhari, Raut and colleagues found that cranial nerve involvement was associated with mechanical ventilation [36].

Neck muscle weakness was observed in 28 patients (45.2%) and was significantly correlated with HDS and ONLS outcomes. Malaga and their colleagues [37] showed that two clinical parameters (bulbar and neck weakness) early at onset are strongly associated with the risk of respiratory failure.

Malaga and their colleagues found that the frequency of respiratory failure in GBS was 14% [37]. In the present study, 32 patients (51.6%) had respiratory muscle involvement and an impaired cough reflex, but only 5 (8.1%) were intubated and mechanically ventilated (MV) which was lower than that reported by Sudulagunta and colleagues who found that 38.5% of patients were mechanically ventilated [21]. The impaired cough reflex and respiratory muscle involvement significantly correlated with poor outcomes using HDS and ONLS ($p = 0.01$, $p = 0.035$, respectively). However, neither was considered as predictor of poor prognosis. In contrast, EGRIS risk total score at onset for respiratory insufficiency significantly correlated with poor outcomes of HDS and ONLS at 3 months ($p = 0.008$, $p = 0.000$). The Erasmus GBS Outcome Scale also correlated with poor outcomes in HDS and ONLS. Respiratory problems may well arise because bulbar weakness leads to reduced protection of the airway and difficulty in clearing secretions. It can also cause upper airway collapse, which increases airway resistance and respiratory muscle load causing fatigue, and ultimately respiratory failure.

Table 2 Spearman correlations of clinical data and baseline laboratory findings with 3-month outcome using the Hughes Disability Scale (HDS) and Overall Neuropathy Limitation Scale (ONLS)

Clinical and laboratory variables	HDS at 3 months outcome (0–7)	ONLS at 3 months outcome (0–12)
Age groups		
Correlation coefficient	0.253*	0.299*
Sig0. (2-tailed)	0.047	0.02
Gender		
Correlation coefficient	− 0.015	− 0.012
Sig. (2-tailed)	0.907	0.93
Comorbidity		
Correlation coefficient	0.264*	0.287*
Sig. (2-tailed)	0.038	0.03
Duration between antecedent event and onset of weakness		
Correlation coefficient	− 0.114	− 0.134
Sig. (2-tailed)	0.379	0.306
Number of days of antecedent event		
Correlation coefficient	− 0.066	− 0.001
Sig. (2-tailed)	0.612	0.99
Days between onset and admission scale		
Correlation coefficient	0.173	− 0.015
Sig. (2-tailed)	0.178	0.91
Presence of antecedent event		
Correlation coefficient	0.395**	0.418**
Sig. (2-tailed)	0.001	0.001
Respiratory antecedent event		
Correlation coefficient	0.046	0.047
Sig. (2-tailed)	0.720	0.719
Presence of diarrhea (antecedent)		
Correlation coefficient	0.391**	0.426**
Sig. (2-tailed)	0.002	0.001
MRC sum score at nadir		
Correlation coefficient	0.368**	− 0.446***
Sig. (2-tailed)	0.003	0.0001
MRC sum score at onset		
Correlation coefficient	− 0.367**	− 0.456***
Sig. (2-tailed)	0.003	0.0001
MRC sum score at the 10th days of treatment		
Correlation coefficient	− 0.626***	− 0.71***
Sig. (2-tailed)	0.0001	0.0001
EGRIS risk total score at onset		
Correlation coefficient	0.378*	0.350**
Sig. (2-tailed)	0.002	0.006
Mechanical ventilation		
Correlation coefficient	0.242	0.305*
Sig. (2-tailed)	0.059	0.018
ICU admission		
Correlation coefficient	0.307*	0.273*
Sig. (2-tailed)	0.015	0.035
Impaired cough reflex		
Correlation coefficient	0.307*	0.273*
Sig. (2-tailed)	0.015	0.035

Table 2 (continued)

Clinical and laboratory variables	HDS at 3 months outcome (0–7)	ONLS at 3 months outcome (0–12)
Autonomic affection		
Correlation coefficient	0.425**	0.41**
Sig. (2-tailed)	0.001	0.001
Cranial nerve affection		
Correlation coefficient	0.235	0.188
Sig. (2-tailed)	0.065	0.15
Neck muscle affection		
Correlation coefficient	0.401**	0.347**
Sig. (2-tailed)	0.001	0.007
Sensory onset		
Correlation coefficient	− 0.186	− 0.146
Sig. (2-tailed)	0.148	0.264
Leukocytosis (WBC)		
Correlation coefficient	0.136	0.08
Sig. (2-tailed)	0.291	0.49
Serum protein level		
Correlation coefficient	− 0.220	− 0.18
Sig. (2-tailed)	0.086	0.169
Serum albumin level		
Correlation coefficient	− 0.380**	− 0.263**
Sig. (2-tailed)	0.002	0.042
Serum sodium level		
Correlation coefficient	− 0.310**	− 0.404**
Sig. (2-tailed)	0.014	0.001
C-reactive protein (CRP)		
Correlation coefficient	0.287*	0.223
Sig. (2-tailed)	0.024	0.125
Cytoalbuminous dissociation		
Correlation coefficient	0.347*	0.418**
Sig. (2-tailed)	0.024	0.006
Management plan		
Correlation coefficient	− 0.144	− 0.31*
Sig. (2-tailed)	0.264	0.016

*P value < 0.05, **P < 0.01, ***P < 0.0001

MRC Medical Research Council score, *EGRIS* Erasmus GBS respiratory insufficiency score

In the present study, an impaired cough reflex was correlated negatively with poor outcomes but was not considered as a predictor. Thirty-five (56.5%) patients were considered high-risk according to EGRIS which is consistent with Rajabally and colleagues. They found 65% patients had a high-risk score, 24% intermediate and 4% low-risk scores [27]. Shangab and their Colleagues found that 20 cases (24.4%) required MV at onset and axonal type was presented in 11 (55%) patients requiring intubation [38].Dysautonomia occurred in 19 patients (30.6%) and was significantly correlated with poorer outcomes in HDS and ONLS ($P=0.001$, $P=0.001$, respectively). Puyuan Wen and colleagues considered dysautonomia as a risk factor for severity with a significant difference in outcome in the severe GBS and non-severe GBS groups [28]. Islam and colleagues identified autonomic involvement as an important risk factor for mechanical ventilation and poor outcome [39]. Netto and colleagues found that older age, dysautonomia, and pulmonary complications were predictors of mortality in MV patients with GBS [40]. Zhai and their colleague [11] found that HDS (at admission), dysphagia, and dysautonomia were independent risk factors for GBS patients requiring MV.

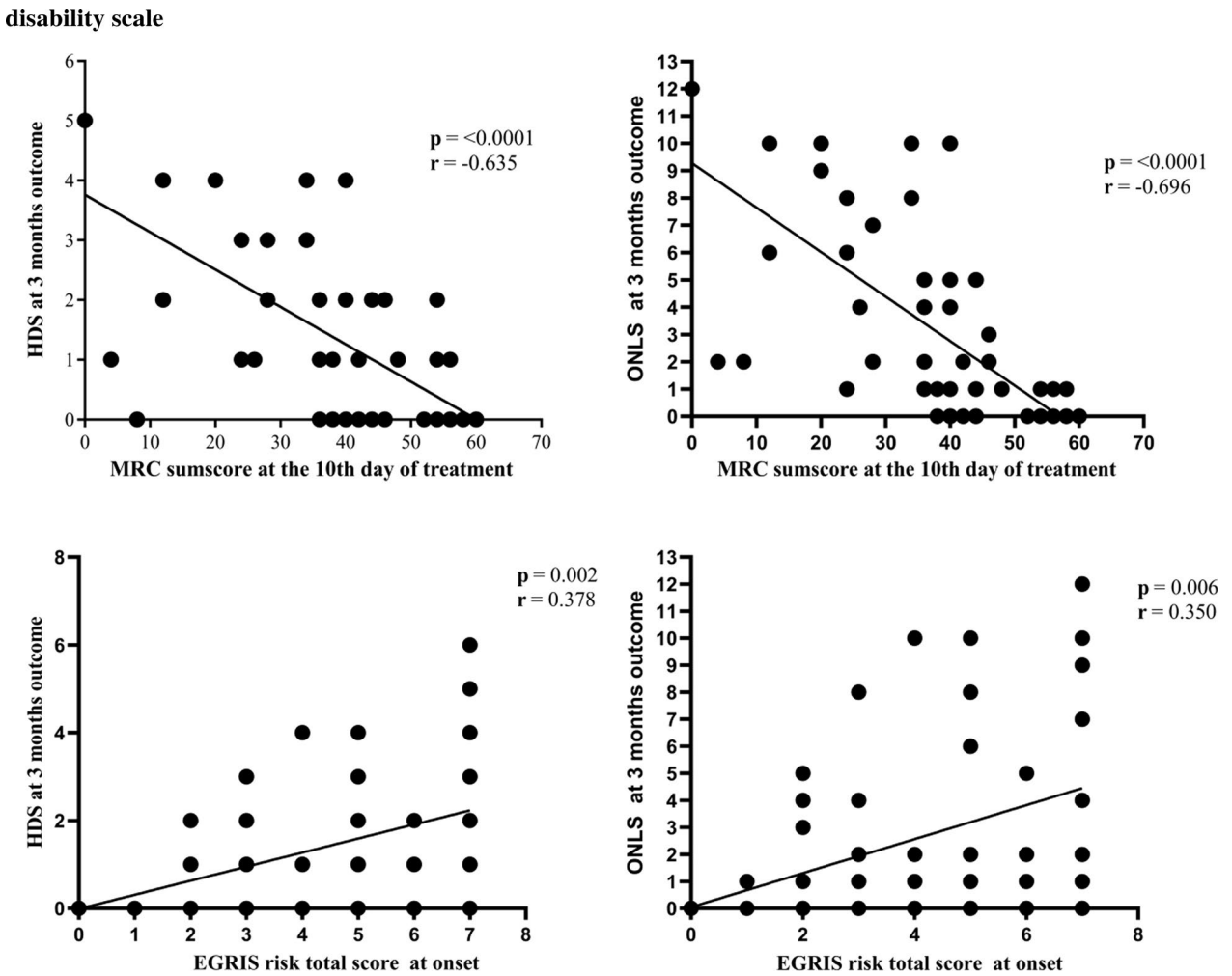

Fig. 1 Spearman correlations of MRC sum score at the 10th day after treatment and Erasmus Guillain–Barré Respiratory Insufficiency Score (EGRIS) at onset with 3-month outcome measured with the Hughes Disability Scale (HDS) and Overall Neuropathy Limitation Scale (ONLS). Outcomes in both scores were significantly correlated with MRC sum score at the 10th day of treatment and EGRIS at onset

Hyponatremia occurred in 19 (30.6%) patients and was significantly correlated with HDS and ONLS outcomes ($p=0.002$, $p=0.001$, respectively) and was considered as a predictor of poor prognosis, consistent with previous studies [41–43].

In GBS, inflammation, demyelination, and axonal damage produce reactive oxygen species associated with free radical toxicity [44, 45]. In the present study, 20 patients (32.3%) had hypoalbuminemia which was significantly correlated with poor outcomes of HDS and ONLS ($p=0.002$, $p=0.017$, respectively) but was not considered as one of the predictors for poor outcome. Tunç and colleagues found that serum albumin levels decreased consistently with the progression of the disease severity whils Su and colleagues demonstrated that high albumin was a protective factor for GBS patients [22, 46].

Elevated C-reactive protein occurred in 24 (38.7%) patients and was significantly correlated with poor outcomes only in HDS ($p=0.024$). It was also predictive of poor outcome. Abdulkadir Tunç and colleagues demonstrated the negative impact of higher age and higher CRP levels measured at the end of the first month [22]. Although elevated CRP levels have been reported to be potential biomarkers for some inflammatory diseases [47], the association of GBS and CRP is still lacking [48].

24 (38.7%) of the 42 patients who underwent CSF analysis had cytoalbuminous dissociation and elevated protein in CSF protein, both of which were correlated with poor outcome although not considered as predictors. High CSF protein concentration is thought to indicate disruption of the blood–nerve barrier [49], but few previous studies have demonstrated that it is related to poor prognosis [49–51]. DiCapua DB and colleagues 2015

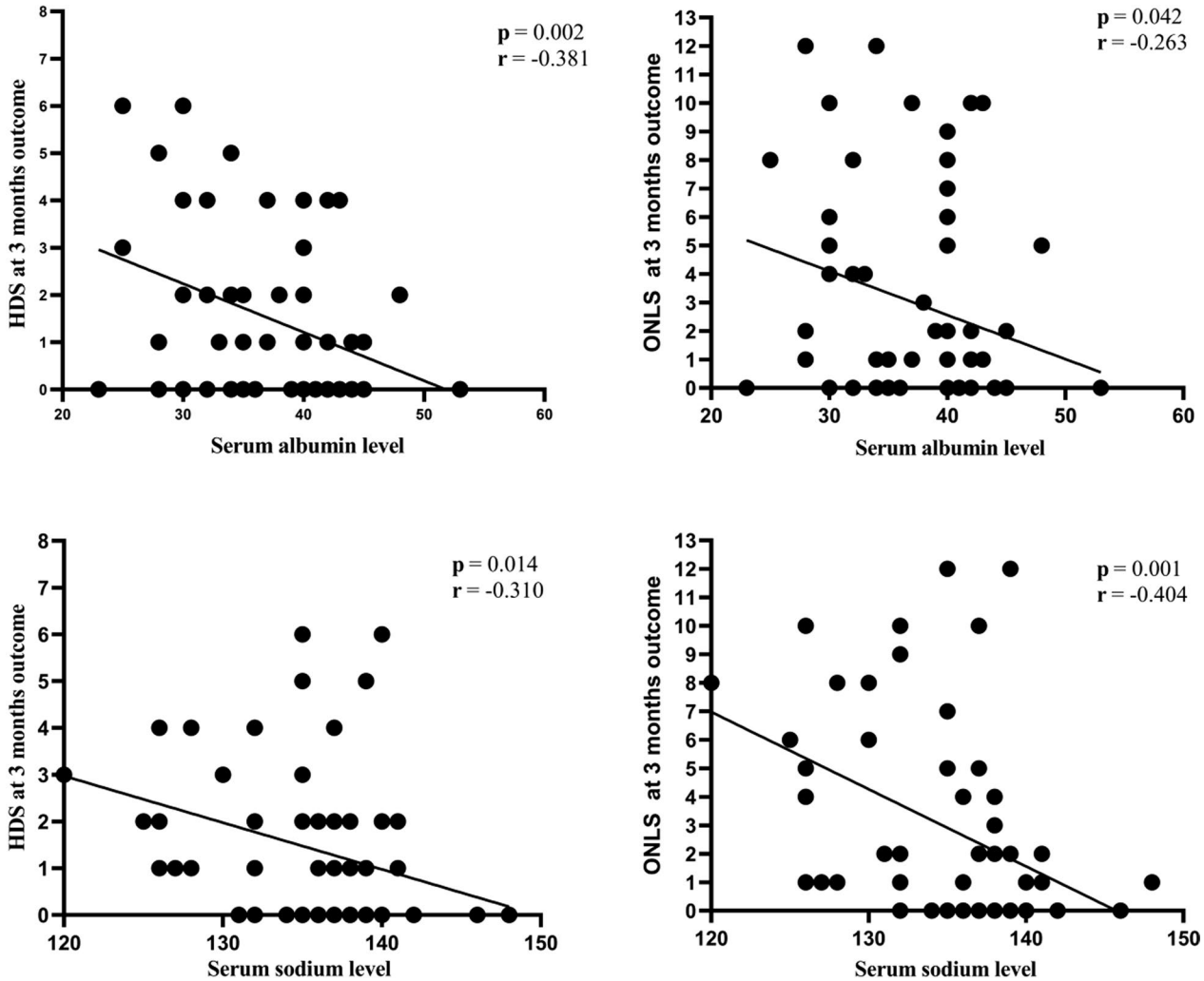

Fig. 2 Spearman correlations between serum sodium and albumen and outcomes using both HDS and ONLS at end of 3 months. There are significant negative correlations between serum sodium and albumen at onset with both outcome scores

Table 3 Multiple ordinal regression analysis to identify the best clinical and laboratory predictors of HDS outcome

Clinical and laboratory/HDS outcome	Estimate	Std. error	Wald	*df*	Sig	95% Confidence interval	
						Lower bound	Upper bound
Serum protein level	0.017	0.037	0.217	1	0.641	− 0.056	0.090
Serum sodium level	− 0.131	0.055	5.624	1	0.018	− 0.240	− 0.023
CRP	1.346	0.603	4.984	1	0.026	0.164	2.528
Serum albumin level	− 0.091	0.057	2.569	1	0.109	− 0.201	0.020
Gender	− 0.537	0.634	0.716	1	0.397	− 1.780	0.706
Age group ≤ 40 years	− 1.572	0.862	3.324	1	0.068	− 3.262	0.118
Age group (41–60 years old)	− 2.128	0.953	4.990	1	0.025	− 3.995	− 0.261
Antecedent event	− 1.568	0.764	4.213	1	0.040	− 3.065	− 0.071
Cough reflex impaired	0.659	0.934	0.498	1	0.481	− 1.172	2.490
Autonomic affection	− 1.067	0.724	2.174	1	0.140	− 2.486	0.352
Neck muscle weakness at onset	− 1.939	0.862	5.061	1	0.024	− 3.628	− 0.250

Dependent variable: HDS at 3 months

HDS Hughes Disability Scale, *CRP* c reactive protein

Table 4 Linear regression analysis to identify the best clinical and laboratory predictors of ONLS outcome

Clinical and laboratory/ONLS outcome	Unstandardized coefficients		Standardized coefficients	*t*	Sig.
	B	Std. error	Beta		
Serum protein	− 0.035	0.077	− 0.082	− 0.462	0.648
Serum sodium	− 0.238	0.110	− 0.343	− 2.168	0.039
Serum albumin	0.074	0.148	0.107	0.501	0.620
Gender	0.760	1.065	0.099	0.714	0.481
Age group	0.053	0.717	0.010	0.074	0.941
Antecedent event	3.556	1.238	0.412	2.873	0.008
Mechanical ventilation	2.892	2.357	0.224	1.227	0.230
Impaired cough reflex	− 1.442	1.569	− 0.188	− 0.919	0.366
Autonomic affection	− 0.362	1.282	− 0.045	− 0.282	0.780
Neck muscle weakness	3.714	1.685	0.487	2.204	0.036
Cyto albuminous dissociation	2.731	1.106	0.356	2.470	0.020
Management plan	− 1.644	0.542	− 0.369	− 3.033	0.005

Dependent variable: ONLS at 3 months

Table 5 Multiple ordinal and linear regression between baseline clinical rating scales and HDS and ONLS outcome after controlling for age and sex

HDS outcome/different rating scales	Estimate	Std. error	Wald	*df*	Sig.
MRC sum score at nadir	− 0.041	0.794	0.003	1	0.959
MRC sum score at onset	− 0.051	0.065	0.601	1	0.438
MRC sum score at 10th days after treatment	− 0.155	0.042	13.510	1	< 0.0001
EGRIS RISK onset	− 0.190	0.419	0.207	1	0.649
EGRIS RISK 10 days	− 0.172	0.427	0.161	1	0.688
Age	− 0.016	0.017	0.915	1	0.339
Sex	0.154	0.534	0.083	1	0.773
ONLS outcome/ different rating scales	**Estimate**	**Std. error**	**Wald**	***df***	**Sig.**
MRC sum score at nadir	− 0.337	1.013	− 0.116	− 0.332	0.741
MRC sum score at onset	− 0.016	0.083	− 0.066	− 0.189	0.851
MRC sum score at 10th days after treatment	− 0.136	0.047	− 0.581	− 2.904	0.005
EGRIS RISK onset	0.020	0.557	0.011	0.035	0.972
EGRIS RISK 10 days	− 0.026	0.537	− 0.014	− 0.048	0.962
Age	0.825	0.699	0.161	1.180	0.244
Sex	− 0.364	0.703	− 0.051	− 0.517	0.607

MRC Medical Research Council score, *EGRIS* Erasmus GBS respiratory insufficiency score, *HDS* Hughes Disability Scale

found that elevated levels of CSF protein occur in 50% of patients after the first week and in 80% of patients in the second week [49]. Sevki Sahin and colleagues reported a positive association between low baseline levels of CSF protein and good prognosis [52]. Vidrio-Becerra and colleagues, 2018 reported that CSF can be used as a prognostic indicator of severity, and that proteins greater than 100 translate into a torpid evolution with more complications [53]. Sahin and colleagues, 2017 found that CSF protein level was a prognostic indicator as it was negatively correlated with MRC outcome at 6 months follow-up, and it was an independent factor on regression analysis [52].

In the present study, 49 patients were treated with plasma exchange, while 13 were treated with IVIG according to the availability. There were no significant differences in outcomes of HDS between the two lines of treatment, however better outcome was recorded with

IVIG than plasma exchange in relation to ONLS outcome ($p = 0.016$).

Conclusions

Clinical and laboratory predictors of poor outcome were older age, antecedent events (particularly diarrhea), low MRC sum score at the 10th day, elevated CRP, hyponatremia and cytoalbuminous dissociation.

Abbreviations

CBC	Complete blood count
Na	Sodium
K	Potassium
CA	Calcium
CRP	C-reactive protein
ABG	Arterial blood gases
ICU	Intensive care unit
MV	Mechanical ventilation
CMAPs	Compound muscle action potentials
GBS	Guillain–Barré syndrome
IVIG	Intravenous immunoglobulin
CSF	Cerebrospinal fluid
NINDS	National Institute of Neurological Disorders and Stroke
NCS	Nerve conduction study
MRC	Medical Research Council sum score
EGOS	Erasmus GBS Outcome Score
HDS	Hughes GBS Disability Scale
ONLS	Overall Neuropathy Limitation Scale

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Author contributions

EMK, MM, MS contributed to study concept and design, acquisition of data, draft and revision of the report, statistical analyses, and interpretation of data. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author reasonable on request.

Declarations

Ethics approval and consent to participate

An informed written consent was obtained from all the patients after approval by the institutional review board of Assiut University's Faculty of Medicine. The Ethical approval of this study was done with number: 17101401 and registered on Clinicaltrials.gov ID: NCT04927598 with posted date: 16/06/2021-(Retrospectively registered)- https://clinicaltrials.gov/ct2/show/NCT04927598. The confidentiality of patients' information was maintained during all steps of the study. The research design adheres to the ethical principles outlined in the Helsinki Declaration of 1975.

Consent for publication

Not applicable.

Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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