Background and Purpose  Guillain-Barre syndrome (GBS) is a common cause of inflammation-related acute flaccid paralysis, and is characterized by acute onset, rapid progression, and symmetrical weakness. GBS is an emergency with high morbidity and long-term disability rates. It is important to determine the prognostic factors for GBS in order to improve the disease outcomes. This study aimed to identify the correlation between the neutrophil-to-lymphocyte ratio (NLR) on day 1 of hospitalization (D1) and motor deterioration in GBS patients.

Methods  This observational analytical study applied a cross-sectional analysis to the medical records of GBS patients who were hospitalized at Dr. Soetomo General Hospital Surabaya from January 2018 to March 2020. The analysis used the chi-square bivariate test, multivariate analysis with logistic regression, and correlation analysis with the Spearman test.

Results  The study included 61 subjects. Statistical tests showed that there was no correlation between NLR and changes in the Medical Research Council sum scores (ΔMRC sum scores) during D1–D3, D1–D7, D1–D14, and D1 to the day of discharge (\(p > 0.05\)). There was a significant correlation between NLR and the Erasmus GBS outcome score (EGOS) (\(p = 0.006\)). NLR values differed significantly within each treatment group (\(p = 0.001\)). Therefore, a subanalysis within each treatment group was conducted, which revealed a significant negative correlation (\(p < 0.05\)) between NLR and the ΔMRC sum score during D1–D14 in the group treated without immunotherapy.

Conclusions  There was no correlation between NLR and motor deterioration in patients with GBS during hospitalization. However, NLR was significantly correlated with EGOS, and there was a negative correlation between NLR and motor deterioration during D1–D14 in GBS patients treated without immunotherapy.

Keywords  Guillain-Barre syndrome; neutrophil; lymphocyte; clinical deterioration; MRC sum scores.

INTRODUCTION

Guillain–Barre syndrome (GBS) is a disease that can be caused by both infectious and non-infectious agents, and involves the immune system attacking the peripheral nerves. GBS is characterized by progressive flaccid paralysis, decreased physiological reflexes, and extensive sensory, motoric, and autonomic symptoms. The most-common subtypes of GBS include acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy. A 10-year study found that the incidence rate of GBS exceeded 0.42 cases per 100,000 people. GBS has been reported to be more common in young adults, and morbidity and mortality are higher in adults aged 50 years and over. In addition, it has been reported that the mortality rate for GBS in the general population ranges from 0.89 to 1.89
cases per 100,000 people, making GBS one of the most-common causes of flaccid-type paralysis.6

In 20% of GBS cases, the reported disability and mortality rates range from 2% to 10%. In general, patients with GBS (of whom 60% are intubated) suffer from respiratory insufficiency. Intravenous immunoglobulin (IVlg) and plasmapheresis have been demonstrated to be effective treatments for GBS. However, despite receiving such treatments, many patients experience a progressive disease course, pain, and residual deficits; up to 20% of patients retain severe deficits, and approximately 5% die despite receiving immunotherapy.2,5 Variations in the rate of recovery from GBS make prognostication difficult.6 Therefore, the prognostic factors of GBS need to be identified in order to reduce mortality and morbidity.

It has been reported that the levels of serum albumin can determine the prognosis, C-reactive protein level, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio (NLR), which have been reported as biomarkers of inflammation in GBS.1,6-8 A higher NLR is an independent predictor of poor prognosis in patients with acute ischemic stroke, heart disease, or cancer.9-11

The present study aimed to identify the correlation between NLR on day 1 of hospitalization (D1) and motoric deterioration in patients with GBS at Dr. Soetomo General Hospital Surabaya from January 2018 to March 2020.

METHODS

Study subjects
This observational analytical study applied a cross-sectional approach using the medical records of patients with GBS. The target population included all patients diagnosed with GBS. The accessible population was GBS patients who were hospitalized at Dr. Soetomo General Hospital Surabaya from January 2018 to March 2020. The inclusion criteria were being older than 18 years and diagnosed with GBS as agreed by at least two neurologists. GBS was diagnosed based on the following inclusion anamnesis criteria: 1) the occurrence of sudden and progressive ascending weakness, 2) symptoms of rapid motor weakness, with a peak deficit occurring within 2 weeks, 3) relative symmetry, 4) mild sensibility symptoms, 5) cranial nerve symptoms, 6) dysautonomia, 7) no fever at the onset of neurological symptoms, and 8) preceded by a previous infection. Neurological examinations produced the following findings: 1) palsy in cranial nerves III, V, VI, VII, IX, and X, 2) weakness of limbs that tend to be symmetrical and ascending, 3) hyporeflexia or areflexia, and 4) no pathological reflexes. Lumbar puncture investigations revealed cytoalbumin dissociation (elevated protein at >0.55 g/L, and normal cell count of <10 lymphocytes/mm³), and the electrophysiological study supported a picture of GBS with an onset within the previous 14 days. Complete medical records needed to be available.

The exclusion criteria included 1) dying within 3 days of hospitalization, 2) history of hypertension and diabetes mellitus, 3) anemia, kidney disorders, liver disorders, or signs of infection on D1, or 4) history of autoimmune diseases other than GBS and tumors.

The total sampling method was applied in this study: all subjects who met the inclusion criteria were included in this study and followed during their hospitalization period. This study was performed in accordance with the guidelines from the Health Research Ethics Committee of Dr. Soetomo General Hospital Surabaya with a letter of exemption (ref: no: 0367/LOE/301.4.2/II/2021). The requirement to obtain informed consent from the subjects was waived.

Clinical and laboratory assessments
NLR corresponds to the number of neutrophils relative to the number of lymphocytes in a routinely obtained 5-mL blood sample. The numbers of neutrophils and lymphocytes were measured in venous blood serum samples mixed with EDTA (ethylenediaminetetraacetic acid). The blood sample was taken on D1; that is, the day on which the GBS patient was admitted to the hospital. Examinations and calculations were automatically carried out at the Clinical Pathology Laboratory, using a flow cytometry method with the Celldyn Ruby Abbott machine (Abbott Laboratories, Abbott Park, IL, USA). A nominal scale with a serum NLR cutoff was used, with the receiver operating characteristic (ROC) curve or the area under the ROC curve used to evaluate and compare NLR values in GBS groups treated with and without immunotherapy. The ROC coordinates in Fig. 1 show that the cutoff value for NLR of 2.45 mg/L used in this study had a sensitivity of 80% and a specificity of 80.6%.

NLR was obtained from each patient on D1 during a complete hematological examination. Meanwhile, the motor deterioration was assessed based on the Medical Research Council (MRC) sum score during the hospitalization days. The MRC sum scores on D1, D3, D7, and D14 were obtained from the patients’ medical records. This study also compared NLR with the Erasmus GBS outcome score (EGOS).

Statistical analysis
The correlation between NLR on D1 and motor deterioration as assessed by the changes in the MRC sum score (ΔMRC sum score) in patients with GBS was analyzed using the Spearman correlation statistical test, as was the correlation between NLR on D1 and EGOS. Those two variables within
each treatment group were also compared and subanalyzed using the Mann-Whitney test and the independent t-test. A p value of <0.05 was considered significant. Logistic regression multivariate analysis was used to identify independent factors in this study. The data analysis was performed using SPSS software (version 24.0.0; IBM Corp., Armonk, NY, USA).

RESULTS

Demographic and clinical characteristics

The demographic and clinical characteristics of the 61 study subjects who met the inclusion criteria are presented in Table 1: 25 (41.0%) subjects were treated with immunotherapy and 36 (59.0%) subjects were treated without immunotherapy. The former group comprised 22 (88%) who received IVIg therapy and 3 (12%) who received plasmapheresis. The entire study subjects were predominantly male (55.7%), aged 41–50 years (29.5%), and had an acute respiratory infection (44.3%) among those with a history of infections, an onset of 1–5 days (54.1%), and MRC sum scores on D1 of 31–40 (31.1%).

The clinical presentations of the subjects included 13 subjects (21.3%) with and 48 subjects (78.7%) without cranial nerve paresis, 59 subjects (96.7%) with motor symptoms and 33 subjects (54.1%) with sensory symptoms, 14 subjects (23%) who experienced and 47 subjects (77%) who did not experience respiratory failure during hospitalization, and 10 subjects (16.4%) who were treated in the ICU. The most-common range of hospitalization durations was 8–15 days (52.5%).

Eight subjects (13.1%) died, while the remaining 53 survivors (86.9%) were discharged from the hospital. Most subjects (26.2%) had MRC sum scores after discharge of 20 (60% in the immunotherapy group and 1% in the no-immunotherapy group). EMG indicated that 30 subjects (49.2%) were the demyelinating type, which was a higher proportion than the axonal type. EGOS was 1–3 in 26 subjects (42.6%).

Correlation data

NLR was found to be significantly but weakly correlated with EGOS (p=0.006 and r=0.351). There were also negative correlations between NLR and MRC sum scores on D1 and D3, with p values of 0.003 and <0.001, respectively, but not on the D7, D14, or the day of discharge, with p values of 0.116, 0.338, and 0.193, respectively. There was no correlation between NLR and ΔMRC sum scores during D1–D3, D1–D7, D1–D14, and D1 to the day of discharge, with p values of 0.164, 0.715, 0.611, and 0.710, respectively.

There were negative correlations between NLR and MRC sum scores on D1 and D3 in patients treated with immunotherapy, with p values of 0.029 and 0.003, respectively, but not on D7, D14, or the day of discharge, with p values of 0.170, 0.925, and 0.721, respectively. There was no correlation between NLR and ΔMRC sum scores in patients treated with immunotherapy during D1–D3, D1–D7, D1–D14, and D1 to the day of discharge, with p values of 0.558, 0.808, 0.111, and 0.223, respectively.

There were negative correlations between NLR and MRC sum scores on D1, D3, and the day of discharge in patients treated without immunotherapy, with p values of 0.017, 0.009, and 0.037, respectively, but not on D7 or D14, with p values of 0.469 and 0.073, respectively.

There was a negative correlation between NLR and the ΔMRC sum score during D1–D14 in patients treated without immunotherapy, with a p value of 0.022, but not during D1–D3, D1–D7, or D1 to the day of discharge, with p values of 0.301, 0.432, and 0.539, respectively. The correlation data are presented in Table 2.

Comparison between patients treated with and without immunotherapy

NLR differed significantly between patients treated with and without immunotherapy, with a p value of 0.001. The ΔMRC during D1–D3 differed significantly between patients treated with and without immunotherapy, with a p value of 0.017 (Table 3).

Bivariate analysis of other variables in GBS patients with and without immunotherapy

Bivariate analysis was applied to other variables in GBS patients treated with and without immunotherapy using the
Table 1. Demographic and clinical characteristics of GBS patients during hospitalization

| Variable                                | Total (n=61) | With immunotherapy (n=25) | Without immunotherapy (n=36) |
|-----------------------------------------|--------------|----------------------------|------------------------------|
| **Age, years**                          |              |                            |                              |
| <20                                     | 1 (1.6)      | 1 (4.0)                    | 0 (0)                        |
| 20–30                                   | 13 (21.3)    | 6 (24.0)                   | 7 (19.4)                     |
| 31–40                                   | 14 (23.0)    | 3 (12.0)                   | 11 (30.6)                    |
| 41–50                                   | 18 (29.5)    | 8 (32.0)                   | 10 (27.8)                    |
| 51–60                                   | 14 (23.0)    | 7 (28.0)                   | 7 (19.4)                     |
| >60                                     | 1 (1.6)      | 0 (0)                      | 1 (2.8)                      |
| **Sex**                                 |              |                            |                              |
| Male                                    | 34 (55.7)    | 16 (64.0)                  | 18 (50.0)                    |
| Female                                  | 27 (44.3)    | 9 (36.0)                   | 18 (50.0)                    |
| **History of previous infection**       |              |                            |                              |
| Diarrhea                                | 13 (21.3)    | 5 (20.0)                   | 8 (22.2)                     |
| Acute respiratory infection             | 27 (44.3)    | 10 (40.0)                  | 17 (47.2)                    |
| Swallowing pain                         | 3 (4.9)      | 1 (4.0)                    | 2 (5.6)                      |
| Fever                                   | 8 (13.1)     | 3 (12.0)                   | 5 (13.9)                     |
| Others                                  | 10 (16.4)    | 6 (24.0)                   | 4 (11.1)                     |
| **Onset, days**                         |              |                            |                              |
| 1–5                                     | 33 (54.1)    | 13 (52.0)                  | 20 (55.6)                    |
| 6–10                                    | 23 (37.7)    | 11 (44.0)                  | 12 (33.3)                    |
| 11–14                                   | 5 (8.2)      | 1 (4.0)                    | 4 (11.1)                     |
| **MRC sum score on D1**                 |              |                            |                              |
| 20                                      | 9 (14.8)     | 5 (20.0)                   | 4 (11.1)                     |
| 21–30                                   | 12 (19.7)    | 4 (16.0)                   | 8 (22.2)                     |
| 31–40                                   | 19 (31.1)    | 8 (32.0)                   | 11 (30.6)                    |
| 41–50                                   | 16 (26.2)    | 6 (24.0)                   | 10 (27.8)                    |
| 51–60                                   | 5 (8.2)      | 2 (8.0)                    | 3 (8.3)                      |
| **Cranial nerve paresis**               |              |                            |                              |
| Yes                                     | 13 (21.3)    | 6 (24.0)                   | 7 (19.4)                     |
| No                                      | 48 (78.7)    | 19 (76.0)                  | 29 (80.6)                    |
| **Clinical presentation on admission with motor symptoms** | | | |
| Yes                                     | 59 (96.7)    | 24 (96.0)                  | 35 (97.2)                    |
| No                                      | 2 (3.3)      | 1 (4.0)                    | 1 (2.8)                      |
| **Clinical presentation on admission with sensory symptoms** | | | |
| Yes                                     | 33 (54.1)    | 13 (52.0)                  | 20 (55.6)                    |
| No                                      | 28 (45.9)    | 12 (48.0)                  | 16 (44.4)                    |
| **Respiratory failure**                 |              |                            |                              |
| Yes                                     | 14 (23.0)    | 9 (36.0)                   | 5 (13.9)                     |
| No                                      | 47 (77.0)    | 16 (64.0)                  | 31 (86.1)                    |
| **ICU treatment**                       |              |                            |                              |
| Yes                                     | 10 (16.4)    | 7 (28.0)                   | 3 (8.3)                      |
| No                                      | 51 (83.6)    | 18 (72.0)                  | 33 (91.7)                    |
| **Length of stay, days**                |              |                            |                              |
| 0–7                                     | 14 (23.0)    | 1 (4.0)                    | 13 (36.1)                    |
| 8–15                                    | 32 (52.5)    | 15 (60.0)                  | 17 (47.2)                    |
| 16–23                                   | 11 (18.0)    | 6 (24.0)                   | 5 (13.9)                     |
| 24–31                                   | 3 (4.9)      | 2 (8.0)                    | 1 (2.8)                      |
| >32                                     | 1 (1.6)      | 1 (4.0)                    | 0 (0)                        |
chi-square test, with significant differences found for the MRC sum score after discharge ($p<0.001$), EGOS ($p<0.001$), outcome after 3 months ($p<0.001$), and outcome after 6 months ($p<0.001$). The complete data from the bivariate analysis are presented in Table 4.

**Multivariate logistic regression analysis to identify independent factors**

The variables included in the multivariate analysis were the length of stay (in days), respiratory failure, MRC sum score after discharge, EGOS, outcome after 3 months, and outcome after 6 months, for which the $p$ value was $<0.25$. The complete data from the multivariate analysis are presented in Table 5.

**DISCUSSION**

Immunotherapy including IVIg and plasmapheresis therapy was applied to 25 of 61 subjects in this study. This follows the current guidelines for GBS therapy, namely IVIg and

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**Table 1. Demographic and clinical characteristics of GBS patients during hospitalization (continued)**

| Variable                        | Total (n=61) | With immunotherapy (n=25) | Without immunotherapy (n=36) |
|---------------------------------|-------------|---------------------------|-----------------------------|
| **Attack time**                 |             |                           |                             |
| January–June 2018               | 21 (34.4)   | 8 (32.0)                  | 13 (36.1)                   |
| July–December 2018              | 6 (9.8)     | 6 (24.0)                  | 0 (0)                       |
| January–June 2019               | 18 (29.5)   | 5 (20.0)                  | 13 (36.1)                   |
| July–December 2019              | 7 (11.5)    | 4 (16.0)                  | 3 (8.3)                     |
| January–March 2020              | 9 (14.8)    | 2 (8.0)                   | 7 (19.4)                    |
| **Cytoalbumin dissociation**    |             |                           |                             |
| Yes                             | 13 (21.3)   | 4 (16.0)                  | 9 (25.0)                    |
| Did not undergo lumbar puncture | 48 (78.7)   | 21 (84.0)                 | 27 (75.0)                   |
| **Electromyography**            |             |                           |                             |
| Axonal                          | 15 (24.6)   | 7 (28.0)                  | 8 (22.2)                    |
| Demyelinating                   | 30 (49.2)   | 10 (40.0)                 | 20 (55.6)                   |
| Not performed                   | 16 (26.2)   | 8 (32.0)                  | 8 (22.2)                    |
| **Patient’s outcome**           |             |                           |                             |
| Survived                        | 53 (86.9)   | 21 (84.0)                 | 32 (88.9)                   |
| Deceased                        | 8 (13.1)    | 4 (16.0)                  | 4 (11.1)                    |
| **MRC sum score after discharge**|          |                           |                             |
| 20                              | 16 (26.2)   | 15 (60.0)                 | 1 (2.8)                     |
| 21–30                           | 10 (16.4)   | 5 (20.0)                  | 5 (13.9)                    |
| 31–40                           | 10 (16.4)   | 1 (4.0)                   | 9 (25.0)                    |
| 41–50                           | 8 (13.1)    | 0 (0)                     | 8 (22.2)                    |
| 51–60                           | 9 (14.8)    | 0 (0)                     | 9 (25.0)                    |
| Patient died                    | 8 (13.1)    | 4 (16.0)                  | 4 (11.1)                    |
| **Erasmus GBS outcome score**   |             |                           |                             |
| 1–3                             | 26 (42.6)   | 1 (4.0)                   | 25 (69.4)                   |
| 3.5–4.5                         | 7 (11.4)    | 3 (12.0)                  | 4 (11.1)                    |
| 5                               | 7 (11.4)    | 4 (16.0)                  | 3 (8.3)                     |
| 5.5–7                           | 21 (34.4)   | 17 (68.0)                 | 4 (11.1)                    |
| **Outcome after 3 months**      |             |                           |                             |
| Death                           | None        | None                      | None                        |
| Incomplete recovery             | 15 (28.3)   | 12 (57.2)                 | 3 (9.3)                     |
| Complete recovery               | 38 (71.7)   | 9 (42.8)                  | 29 (90.7)                   |
| **Outcome after 6 months**      |             |                           |                             |
| Death                           | None        | None                      | None                        |
| Incomplete recovery             | 8 (15.1)    | 6 (28.6)                  | 2 (6.3)                     |
| Complete recovery               | 45 (84.9)   | 15 (71.4)                 | 30 (93.7)                   |

Data are $n$ (%) values.

GBS, Guillain–Barre syndrome; MRC, Medical Research Council.
plasmapheresis, which have been demonstrated to be effective for GBS; moreover, no other procedures or drugs are effective in treating GBS. The demographic characteristics of the subjects in this study indicated that most were male (55.7%) and aged 41–50 years (29.5%). These results are broadly consistent with those of a multicenter study in Japan by Yamagishi et al. in 2017 and a study by Geyik et al. in 2016, which found that more males than females suffered from GBS (59% and 53.5%, respectively). Moreover, a large-scale cohort study conducted in a United States hospital also found that most GBS patients were in the age range of 18–50 years (50.4%), which is classified as the productive age by the Central Bureau of Statistics.

Based on the history of infections, most of the subjects in this study had previous acute respiratory infections (44.3%), which is similar to the history of infections of the subjects in the cohort study of Wang et al. in 2017, for which respiratory tract infection was the most-common infection preceding GBS (29.25%).

NLR could serve as a simple index of the immune function. It may be of prognostic significance and be correlated with EGOS. We assumed that certain inflammatory factors are related to the disease. The white blood cell count and its subtypes are involved and are markers of systemic inflammation, while neutrophils play pivotal roles in innate immune responses.

Most subjects (54.1%) had experienced symptom onset within the range of 1–5 days. This is similar to the multicenter study conducted by Yamagishi et al. finding that most GBS patients were hospitalized at 4–7 days after onset (42%).

Most of the present subjects (31.1%) had MRC sum scores ranging from 31 to 40 on D1. Ishaque et al. found in 2017 that most GBS patients (54%) had MRC sum scores >20 at the time of admission.

The clinical presentations of the subjects in this study indicated that most of them (78.7%) presented without cranial nerve paresis. Moreover, 59 subjects (96.7%) presented with motor symptoms, while the remaining 33 subjects (54.1%) presented with sensory symptoms. This differs slightly from a study by Altaweel et al. in 2018, which found that 79.2% of GBS patients presented with cranial nerve paresis, 100% with motor symptoms, and 100% with sensory symptoms. Meanwhile, Bhargava et al. found in 2014 that 98% of GBS patients presented with motor symptoms, 70% with sensory

### Table 2. Correlation data between NLR vs. EGOS and motoric deterioration (MRC sum score, ΔMRC sum score) in GBS patients with and without immunotherapy

| Variable | With immunotherapy | Without immunotherapy | p |
|----------|--------------------|-----------------------|---|
| NLR vs. EGOS | 0.351 ± 0.006 | 0.37 ± 0.049 | 0.001* |
| D1 vs. MRC sum scores | -0.372 ± 0.033 | -0.412 ± 0.053 | 0.017* |
| D3 vs. MRC sum scores | -0.473 ± 0.001 | -0.412 ± 0.053 | 0.174* |
| D7 vs. MRC sum scores | -0.215 ± 0.116 | -0.215 ± 0.116 | 0.849† |
| D14 vs. MRC sum scores | -0.188 ± 0.338 | -0.188 ± 0.338 | 0.849† |
| At discharge | -0.184 ± 0.193 | -0.184 ± 0.193 | 0.174* |
| NLR vs. ΔMRC sum scores during hospitalization | | | |
| D1–D3 vs. ΔMRC | -0.180 ± 0.164 | -0.180 ± 0.164 | 0.849† |
| D1–D7 vs. ΔMRC | 0.050 ± 0.715 | 0.050 ± 0.715 | 0.849† |
| D1–D14 vs. ΔMRC | 0.101 ± 0.611 | 0.101 ± 0.611 | 0.849† |
| D1 to discharge vs. ΔMRC | 0.053 ± 0.710 | 0.053 ± 0.710 | 0.849† |
| NLR vs. ΔMRC sum scores for treatment with immunotherapy | | | |
| D1 vs. ΔMRC | -0.438 ± 0.029 | -0.438 ± 0.029 | 0.174* |
| D3 vs. ΔMRC | -0.568 ± 0.003 | -0.568 ± 0.003 | 0.174* |
| D7 vs. ΔMRC | -0.290 ± 0.170 | -0.290 ± 0.170 | 0.174* |
| D14 vs. ΔMRC | -0.025 ± 0.925 | -0.025 ± 0.925 | 0.174* |
| At discharge vs. ΔMRC | 0.085 ± 0.721 | 0.085 ± 0.721 | 0.174* |
| NLR vs. ΔMRC sum scores for treatment without immunotherapy | | | |
| D1 vs. ΔMRC | 0.123 ± 0.558 | 0.123 ± 0.558 | 0.174* |
| D1–D3 vs. ΔMRC | 0.052 ± 0.808 | 0.052 ± 0.808 | 0.174* |
| D1–D7 vs. ΔMRC | 0.401 ± 0.111 | 0.401 ± 0.111 | 0.174* |
| D1–D14 vs. ΔMRC | 0.285 ± 0.223 | 0.285 ± 0.223 | 0.174* |
| D1 to discharge vs. ΔMRC | 0.739 ± 0.100 | 0.739 ± 0.100 | 0.174* |
| NLR vs. ΔMRC sum scores for treatment without immunotherapy | | | |
| D1 vs. ΔMRC | -0.394 ± 0.017 | -0.394 ± 0.017 | 0.174* |
| D3 vs. ΔMRC | -0.427 ± 0.009 | -0.427 ± 0.009 | 0.174* |
| D7 vs. ΔMRC | -0.135 ± 0.469 | -0.135 ± 0.469 | 0.174* |
| D14 vs. ΔMRC | -0.590 ± 0.073 | -0.590 ± 0.073 | 0.174* |
| At discharge vs. ΔMRC | 0.370 ± 0.037 | 0.370 ± 0.037 | 0.174* |
| NLR vs. ΔMRC sum scores for treatment without immunotherapy | | | |
| D1–D3 vs. ΔMRC | -0.177 ± 0.301 | -0.177 ± 0.301 | 0.174* |
| D1–D7 vs. ΔMRC | -0.146 ± 0.432 | -0.146 ± 0.432 | 0.174* |
| D1–D14 vs. ΔMRC | -0.708 ± 0.022 | -0.708 ± 0.022 | 0.174* |
| D1 to discharge vs. ΔMRC | -0.113 ± 0.539 | -0.113 ± 0.539 | 0.174* |

EGOS, Erasmus GBS outcome score; MRC, Medical Research Council; NLR, neutrophil-to-lymphocyte ratio; ΔMRC, changes in Medical Research Council sum score.
Table 4. Results of bivariate analysis of other variables in GBS patients with and without immunotherapy

| Variable                                | With immunotherapy | Without immunotherapy | OR  | 95% CI      | p    |
|-----------------------------------------|--------------------|-----------------------|-----|-------------|------|
| Sex                                     |                    |                       |     |             |      |
| Male                                    | 16 (64.0)          | 18 (50.0)             | 1.78| 0.62–5.06   | 0.281|
| Female                                  | 9 (36.0)           | 18 (50.0)             |     |             |      |
| Age, years                              |                    |                       |     |             |      |
| ≤40                                     | 10 (40.0)          | 18 (50.0)             | 1.08| 0.39–3.01   | 0.878|
| >40                                     | 15 (60.0)          | 18 (50.0)             |     |             |      |
| Diarrhea                                |                    |                       |     |             |      |
| Yes                                     | 5 (20.0)           | 8 (22.2)              | 0.56| 0.13–2.44   | 0.444|
| No                                      | 20 (80)            | 28 (77.8)             |     |             |      |
| Acute respiratory infection             |                    |                       |     |             |      |
| Yes                                     | 10 (40.0)          | 17 (47.2)             | 1.01| 0.32–3.15   | 0.985|
| No                                      | 15 (60)            | 19 (52.8)             |     |             |      |
| Swallowing pain                         |                    |                       |     |             |      |
| Yes                                     | 1 (4.0)            | 2 (5.6)               | 0.87| 0.25–3.07   | 0.835|
| No                                      | 24 (96)            | 34 (94.4)             |     |             |      |
| Fever                                   |                    |                       |     |             |      |
| Yes                                     | 3 (12.0)           | 5 (13.9)              | 1.45| 0.45–2.56   | 0.786|
| No                                      | 21 (84)            | 31 (86.1)             |     |             |      |
| Other infections                         |                    |                       |     |             |      |
| Yes                                     | 6 (24.0)           | 4 (11.1)              | 0.39| 0.99–1.58   | 0.190|
| No                                      | 19 (76)            | 32 (88.9)             |     |             |      |
| Onset, days                             |                    |                       |     |             |      |
| ≤5                                      | 13 (52.0)          | 20 (55.6)             | 1.89| 1.24–4.72   | 0.254|
| >5                                      | 15 (24.6)          | 16 (26.2)             |     |             |      |
| MRC sum score on D1                     |                    |                       |     |             |      |
| ≤30                                     | 9 (14.8)           | 12 (19.7)             | 2.56| 0.46–5.73   | 0.288|
| >30                                     | 16 (26.2)          | 24 (39.3)             |     |             |      |
| Cranial nerve paresis                   |                    |                       |     |             |      |
| Yes                                     | 6 (24.0)           | 7 (19.4)              | 1.04| 0.28–3.73   | 0.957|
| No                                      | 19 (76.0)          | 29 (80.6)             |     |             |      |
| Clinical presentation on admission with motor symptoms |                   |                       |     |             |      |
| Yes                                     | 24 (96.0)          | 35 (97.2)             | 0.68| 0.04–11.5   | 0.793|
| No                                      | 1 (4.0)            | 1 (2.8)               |     |             |      |
| Clinical presentation on admission with sensory symptoms |                   |                       |     |             |      |
| Yes                                     | 13 (52.0)          | 20 (55.6)             | 0.78| 0.20–3.04   | 0.731|
| No                                      | 12 (48.0)          | 16 (44.4)             |     |             |      |
| Respiratory failure                     |                    |                       |     |             |      |
| Yes                                     | 9 (36.0)           | 5 (13.9)              | 1.28| 0.82–1.99   | 0.050|
| No                                      | 16 (64.0)          | 31 (86.1)             |     |             |      |
| ICU treatment                            |                    |                       |     |             |      |
| Yes                                     | 7 (28.0)           | 3 (8.3)               | 2.41| 0.66–8.73   | 0.666|
| No                                      | 18 (72.0)          | 33 (91.7)             |     |             |      |
| Length of stay, days                    |                    |                       |     |             |      |
| ≤14                                     | 16 (64.0)          | 30 (83.3)             | 0.35| 0.11–1.18   | 0.091|
| >14                                     | 9 (36.0)           | 6 (16.7)              |     |             |      |
| Cytosalbumin dissociation               |                    |                       |     |             |      |
| Yes                                     | 4 (16.0)           | 9 (25.0)              | 1.13| 0.76–3.56   | 0.768|
| Did not undergo lumbar puncture         | 21 (84.0)          | 27 (75.0)             |     |             |      |
Correlation of NLR With Motoric Deterioration in GBS

symptoms, and 62.3% with cranial nerve paresis.

Respiratory failure during hospitalization occurred in 14 subjects (23%), and 10 subjects (16.4%) were treated in the ICU. Ceylan and Sonkaya\(^1\) similarly found that as many as 25.5% of GBS patients experienced respiratory failure. Studies by Yuki and Hartung\(^5\) in 2012 and van den Berg et al.\(^2\) in 2014 found that up to 30% of GBS patients required treatment in the ICU, which are higher proportions than in the present study.

Most of the patients (52.5%) were hospitalized for 8–15 days. This is consistent with Alloush et al.\(^23\) reporting in 2019 that the most-common duration of hospitalization (75%) for GBS patients was <4 weeks. Most of the subjects in the present study (86.9%) survived and were discharged from the hospital. A multicenter study in Serbia by Stojanov et al.\(^24\) in 2020 found that 5.6% of patients died during the acute phase of the disease, while Alsheklee et al.\(^18\) found that 2.58% died during hospitalization within 5 years in a large-scale cohort study in the United States. The mortality rate in the present study was therefore higher than in these two previous studies.

Worsening physical conditions such as secondary lung infections can also cause respiratory failure and lead to death.

The overall demographic and clinical characteristics of the subjects in this study are similar to those in previous studies. However, there was a significant difference in that the present subjects mostly presented without cranial nerve paresis, and their mortality rate was quite high.

Table 4. Results of bivariate analysis of other variables in GBS patients with and without immunotherapy (continued)

| Variable                              | With immunotherapy | Without immunotherapy | OR     | 95% CI          | p     |
|---------------------------------------|--------------------|-----------------------|--------|----------------|-------|
| Electromyography                      | 1.23               | 0.37–4.10             | 0.729  |
| Axonal                                | 7 (28.0)           | 10 (16.4)             |
| Demyelinating                         | 10 (40.0)          | 17 (27.8)             |
| Patient’s outcome                     | 2.09               | 0.42–10.31            | 0.363  |
| Survived                              | 21 (84.0)          | 32 (88.9)             |
| Deceased                              | 4 (16.0)           | 4 (11.1)              |
| MRC sum score after discharge         | 86.67              | 9.64–778.88           | <0.001 |
| ≤30                                   | 20 (95.3)          | 6 (18.8)              |
| >30                                   | 1 (4.7)            | 26 (81.2)             |
| Erasmus GBS outcome score             | 20.0               | 5.3–74.4              | <0.001 |
| ≤4.5                                  | 4 (16.0)           | 29 (80.5)             |
| >4.5                                  | 21 (84.0)          | 7 (19.5)              |
| Outcome after 3 months                | 2.06               | 0.05–3.24             | <0.001 |
| Incomplete recovery                   | 12 (57.2)          | 3 (9.3)               |
| Complete recovery                     | 9 (42.8)           | 29 (90.7)             |
| Outcome after 6 months                | 2.05               | 0.01–3.24             | <0.001 |
| Incomplete recovery                   | 6 (28.6)           | 2 (6.3)               |
| Complete recovery                     | 15 (71.4)          | 30 (93.7)             |
| Neutrophil-to-lymphocyte ratio        | 0.85               | 0.20–3.53             | 0.819  |
| ≤2.45                                 | 4 (16.0)           | 5 (13.8)              |
| >2.45                                 | 21 (84.0)          | 31 (86.1)             |

Data are \(n\) (%) values.

CI, confidence interval; GBS, Guilain-Barre syndrome; MRC, Medical Research Council; OR, odds ratio.

Table 5. Results from multivariate logistic regression analysis

| Characteristic                        | Adjusted OR | 95% CI          | p     |
|---------------------------------------|-------------|----------------|-------|
| Step 1                                |             |                |       |
| Other infections                      | 0.39        | 0.99–1.58      | 0.190 |
| Length of stay                        | 0.35        | 0.11–1.18      | 0.091 |
| Respiratory failure                   | 1.28        | 0.82–1.99      | 0.050 |
| MRC sum score after discharge         | 86.67       | 9.64–778.88    | <0.001 |
| EGOS                                  | 20.00       | 5.3–74.4      | <0.001 |
| Outcome after 3 months                | 2.06        | 0.05–3.24      | <0.001 |
| Outcome after 6 months                | 2.05        | 0.01–3.24      | <0.001 |
| Step 2                                |             |                |       |
| MRC sum score after discharge         | 56.67       | 9.64–778.88    | <0.001 |
| EGOS                                  | 13.00       | 5.3–74.4      | <0.001 |
| Outcome after 3 months                | 1.06        | 0.02–2.24      | <0.001 |
| Outcome after 6 months                | 1.05        | 0.01–2.24      | <0.001 |

CI, confidence interval; EGOS, Erasmus GBS outcome score; GBS, Guilain-Barre syndrome; MRC, Medical Research Council; OR, odds ratio.
cally significant relationship between NLR of GBS patients and the MRC sum score at the time of admission ($p=0.005$).

GBS is an inflammatory disease that attacks the peripheral nervous system due to molecular mimicry processes and cross-reactive immune responses. NLR is a dynamic parameter defined as the ratio of the numbers of neutrophils and lymphocytes, which reflect inflammation. Neutrophils show active nonspecific inflammatory processes and are one of the body’s first defense mechanisms, while lymphocytes are regulatory and protective components of inflammation. Therefore, a higher NLR in a person with GBS indicates a higher level of inflammation. Inflammatory processes that attack the nervous system can cause muscle weaknesses in GBS patients, as represented by the MRC sum score.25,26

The main result of this study was that there was no correlation between NLR on D1 and motoric deterioration in patients with GBS, where the $\Delta$MRC sum score reflected motoric deterioration during D1–D3, D1–D7, D1–D14, and D1 to the day of discharge. However, the NLR values of GBS patients differed significantly between those who received and did not receive immunotherapy ($p=0.001$). Therefore, a subanalysis within each treatment group (with and without immunotherapy) was conducted, since the administration of immunotherapy could have affected the MRC sum scores in patients during the treatment period and the $\Delta$MRC sum scores that describe motor deterioration in this study.

In the immunotherapy group, significant negative correlations ($p<0.05$) were found between NLR on D1 and the MRC sum scores on D1 and D3, meaning that a higher NLR was associated with a lower MRC sum score. However, there was no correlation between NLR on D1 and the $\Delta$MRC sum scores during hospitalization. This may be due to immunotherapy (both IVIg and plasmapheresis) still being the only therapy that has been demonstrated to be effective for GBS.

Meanwhile, in the group that did not receive immunotherapy, significant negative correlations ($p<0.05$) were found between NLR on D1 and the MRC sum scores on D1 and D3. Moreover, there was a significant negative correlation ($p<0.05$) between NLR on D1 and the $\Delta$MRC sum score during D1–D14. The higher level of inflammation in the peripheral nervous system of patients with GBS indicated by a higher NLR will result in muscle weaknesses as indicated by the $\Delta$MRC sum scores.

We found no correlation between the overall NLR values on D1 and motoric deterioration in GBS patients during hospitalization. However, the subanalysis results for the two treatment groups showed a significant negative correlation between NLR on D1 and motoric deterioration in GBS patients who were treated without immunotherapy. NLR on D1 can therefore be used as a prognostic factor for predicting motoric deterioration in GBS patients during the treatment period. The monitoring of NLR will allow therapies to be applied early so as to prevent more-severe disabilities, especially among patients in remote areas where immunotherapy is less available.

Financial factors resulted in 36 patients with GBS in this study not receiving immunotherapy (59.0%). The cost of IVIg was about 200,000,000 Indonesia rupiah (IDR) per day, while plasmapheresis therapy cost about IDR 50,000,000/day. A lack of insurance and a good clinical condition are factors contributing to not receiving immunotherapy. The mortality rate in this study was affected by respiratory complications, cardiovascular or autonomic complications, and secondary infections. We identified the following risk factors for mortality: older age, greater muscle weakness at entry, and use of ventilation. Patients died of cardiovascular or autonomic complications during the acute progressive phase. However, eight of the deceased GBS patients died during the recovery phase after neurological improvement; these patients mainly died of pulmonary infections or cardiovascular complications.2 Remarkably, some recovering patients died relatively shortly after being transferred from the ICU to the general ward, where monitoring facilities are less intensive. Only four patients died shortly after the start of treatment.

There was a significant correlation between NLR and EGOS, with a $p$ value of 0.006. This is consistent with EGOS being an accurate and validated model for predicting the outcome at several timepoints in GBS.11 An important advantage of existing models is that EGOS can be used in the early phase of the disease when the process of nerve damage is ongoing and possibly reversible. The independent prognostic factors for GBS are the MRC sum score after discharge, EGOS, outcome after 3 months, and outcome after 6 months.

The strengths of our study include it being the first to use $\Delta$MRC sum scores—which represent motoric deterioration—in patients with GBS during hospitalization. This study additionally conducted a subanalysis in the groups treated with and without immunotherapy. However, several limitations remain. First, the data used were secondary and from a single center; it would have been better to use primary data. Second, this study had a cross-sectional design, and it would have been better if it was conducted in a cohort that could be followed prospectively. Third, this study did not differentiate or analyze the different subtypes of GBS. Future studies with a prospective cohort design should explore, differentiate, and analyze primary data for the different GBS subtypes.

In conclusion, no correlation was found between NLR on D1 and motor deterioration in patients with GBS during hospitalization. However, there was a significant negative correlation between NLR on D1 and motor deterioration during hospitalization. However, several limitations remain. First, the data used were secondary and from a single center; it would have been better to use primary data. Second, this study had a cross-sectional design, and it would have been better if it was conducted in a cohort that could be followed prospectively. Third, this study did not differentiate or analyze the different subtypes of GBS. Future studies with a prospective cohort design should explore, differentiate, and analyze primary data for the different GBS subtypes.
D1–D14 in GBS patients treated without immunotherapy.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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