Assessment of Serum Inflammatory Markers and their Correlation with Clinical Severity and Electrophysiological Subtypes of Guillain Barre Syndrome, and Investigating their Use as Prognostic Markers of Guillain Barre Syndrome

Dear Editor,

Guillian Barre Syndrome (GBS), which is an acute inflammatory demyelinating polyneuropathy, exhibits varying immune responses affecting both humoral and cell-mediated systems.[1] Autoimmune disorders such as GBS are known to stimulate the production of a high level of inflammatory markers.[2] It is believed that levels of markers of inflammation, such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP), and albumin levels, should rise or fall in accordance with disease progression or regression. The variation in levels of these markers could also correlate with disease severity and type.[3,4] Levels of these inflammatory markers and their variation before and after plasmapheresis may also serve as prognosticating markers of the disease.[5,6] There is a lack of knowledge regarding the role of biochemical and immunological markers in the diagnosis of GBS. This research delves into the correlation between disease severity and novel markers of inflammation, namely, NLR, PLR, CRP, and albumin levels. Moreover, the study seeks to determine whether varying levels of these markers can predict response to treatment.

Fifty patients in a tertiary care hospital who were diagnosed with GBS based on the Brighton criteria participated in this study. Among the 50 patients, 34 were females and 16 were males. Patients were aged between 18 and 56 years, with a mean age of 25 and a median age of 23. Hughes disability scores of the patients, which were used to measure the clinical severity of the disease,[7] ranged between 1 and 5, with a score of 1 corresponding to mild symptoms and a score of 5 corresponding to severe symptoms. One patient had a Hughes score of 1, 10 patients had a Hughes score of 2, eight patients had a Hughes score of 3, 15 patients had a Hughes score of 4, and 16 patients had a Hughes score of 5. NLR, CRP, PLR, and albumin values were recorded from each of the patients on admission. Based on nerve conduction studies carried out at the time of admission, patients were also categorized according to the three main electrophysiological subtypes of GBS namely acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor–sensory axonal neuropathy (AMSAN).[8] NLR, CRP, PLR, and albumin values were recorded from all patients twice, once on admission to the hospital and again 2 weeks after completion of five cycles of plasmapheresis, which is the routinely carried out treatment modality for GBS.[9]

The NLR, PLR, CRP, and albumin levels were compared between patients with different Hughes disability scores on admission using analysis of variance (ANOVA). Values of the inflammatory markers across different electrophysiological subtypes were also compared using ANOVA. Finally, inflammatory marker levels on admission were compared among patients with good (Hughes score >3) and bad (Hughes score ≤2) outcomes,[10] which were measured after five cycles of plasmapheresis, using the independent sample *t*-test.

Comparison of NLR values among patients with GBS showed that patients with a Hughes score of 1 had an NLR value of 5 (n = 1), those with a Hughes score of 2 had an NLR value of 101.2 ± 45.36 (n = 10), those with a Hughes score of 3 had an NLR value of 11.5 ± 3.38 (n = 8), those with a Hughes score of 4 had an NLR value of 11.13 ± 5.41 (n = 15), and those with a Hughes score of 5 had an NLR value of 11.94 ± 5.01 (n = 16) at the time of admission, showing a statistically significant (0.033) increase in NLR values with increasing disease severity.

A comparison of PLR values among patients with GBS showed that patients with a Hughes score of 1 had a PLR value of 48 (n = 1), those with a Hughes score of 2 had a PLR value of 101.2 ± 45.36 (n = 10), those with a Hughes score of 3 had a PLR value of 124.5 ± 48.16 (n = 8), those with a Hughes score of 4 had a PLR value of 129.13 ± 55.38 (n = 15), and those with a Hughes score of 5 had a PLR value of 132.18 ± 47.46 (n = 16) at the time of admission, showing a nonstatistically significant (0.308) increase in PLR values with increasing disease severity.

Table 1: Variation of NLR, PLR, CRP and Albumin levels with Hughes disability scores

	Hughes Score - 1	Hughes Score - 2	Hughes Score - 3	Hughes Score - 4	Hughes Score - 5	*P*
NLR	5	6±4.899	11.5±3.38	11.13±5.41	11.94±5.01	0.033
PLR	48	101.2±45.36	124.5±48.16	129.13±55.38	132.18±47.46	0.308
CRP	0.4	0.39±0.13	1±1.62	0.327±0.19	2.43±3.28	0.044
Albumin	4.9	4.56±0.74	4.12±1.24	3.47±1.29	3.1±1.45	0.043

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, CRP: C- reactive protein

Table 2: Mean Hughes disability scores of patients with good outcomes and bad outcomes after treatment

	n	Mean Hughes score, Mean±SD
Good outcome	35	3.91±1.067
Bad outcome	15	3.2±1.032

Table 3: Relationship between age, NLR, CRP, and Albumin levels at presentation with outcome after treatment

	Outcome	*n*	Mean±SD
Age	Good Outcome	35	25.4±9.27
	Bad Outcome	15	24.2±7.58
NLR	Good Outcome	35	10.57±5.35
	Bad Outcome	15	9.67±5.2
Albumin	Good Outcome	35	3.56±1.30
	Bad Outcome	15	4.02±1.39
CRP	Good Outcome	35	1.11±2.17
	Bad Outcome	15	1.15±2.13

NLR: Neutrophil to lymphocyte ratio, CRP: C- reactive protein

Table 4: Variation of NLR, PLR, CRP, and Albumin levels across AMAN, AMSAN, and AIDP subtypes of GBS

	AIMSAN	AIDP	AMAN	*P*
NLR	9.40±4.23	9.96±5.47	12.50±6.023	0.32
PLR	109.47±46.7	122.24±51.55	141.0±51.01	0.31
CRP	1.32±2.71	0.556±0.94	2.24±2.94	0.098
Albumin	3.66±1.47	3.79±1.27	3.52±1.39	0.85

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, CRP: C-reactive protein. All values are represented as Mean±SD

A comparison of CRP values among patients with GBS showed that patients with a Hughes score of 1 had a CR*P* value of 0.4 ($n = 1$), those with a Hughes score of 2 had a CR*P* value of 4.56 ± 0.74 ($n = 10$), those with a Hughes score of 3 had a CR*P* value of 4.12 ± 1.24 ($n = 8$), those with a Hughes score of 4 had a CR*P* value of 0.327 ± 0.19 ($n = 15$), and those with a Hughes score of 5 had a CR*P* value of 2.43 ± 3.28 ($n = 16$) at the time of admission, showing a statistically significant (0.044) increase in CR*P* values with increasing disease severity.

A comparison of albumin values among patients with GBS showed that patients with a Hughes score of 1 had an albumin value of 4.9 ($n = 1$), those with a Hughes score of 2 had an albumin value of 0.39 ± 0.13 ($n = 10$), those with a Hughes score of 3 had an albumin value of 1 ± 1.62 ($n = 8$), those with a Hughes score of 4 had an albumin value of 3.47 ± 1.29 ($n = 15$), and those with a Hughes score of 5 had an albumin value of 3.1 ± 1.45 ($n = 16$) at the time of admission, showing a statistically significant (0.043) decrease in albumin values with increasing disease severity [Table 1].

To summarize, a comparison of NLR and CR*P* values among patients with different Hughes disability scores on admission showed a statistically significant ($P = 0.033$ and $P = 0.044$, respectively) positive correlation between the inflammatory marker level and disease severity, while the levels of albumin, a known negative phase reactant, showed a statistically significant ($P = 0.043$) negative correlation, and there was no correlation between PLR level and disease severity. The findings were consistent with several studies done till date, which demonstrated a reliable correlation between NLR values and severity of GBS. However, CRP and albumin, which have been relatively less studied, also show promise in serving as reliable indicators of disease severity. PLR, on the other hand, does not seem to hold much promise in this regard.

Upon analysis of response to treatment, we did not find any correlation between pretreatment NLR, CRP, or albumin values with treatment outcome.

However, an incidental finding that we noted was patients with a higher Hughes disability score (3.91 ± 1.07) ($n = 35$) at admission were found to have a better outcome defined as a Hughes score of ≥3 after five cycles of plasmapheresis, while those with a lower Hughes score (3.2 ± 1.03) ($n = 15$) on admission had significantly ($P = 0.049$) worse outcome to treatment, indicating that a less-severe disease manifestation at the outset is more likely to have a better outcome after treatment [Tables 2 and 3].

Comparison of NLR, PLR, CRP, and albumin levels across the AMAN, AMSAN, and AIDP subtypes of GBS showed some variation among the subtypes; however, the variations were not statistically significant [Table 4].

The findings suggest that NLR, CRP, and albumin levels correlate well with disease severity. NLR, an already well-studied marker of GBS severity, used in conjunction with CRP and albumin, could serve as a good indicator of disease severity. The study proposes the potential of combined inflammatory biomarker readings in assessment of clinical

severity of GBS. The study also revealed that patients with a clinically milder disease at the initial presentation had better posttreatment outcomes than those with a clinically more severe disease at presentation.

The role of these markers as prognostic agents and their variability between subtypes, however, require further studies.

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Conflicts of interest
There are no conflicts of interest.

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