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ACCURACY OF SYSTEMIC INFLAMMATORY IMMUNE INDEX (SII) IN ASSESSING MYASTHENIA GRAVIS SEVERITY

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ABSTRACT

Objective: To determine the accuracy of systemic inflammatory immune index in assessing myasthenia gravis severity using MGFA classification as gold standard.

Study Design: Descriptive cross-sectional study.

Place And Duration Of Study: Neurology department of Mayo Hospital Lahore from June 2025 to September 2025.

Methodology: This study was done after taking ethical approval from IRB. This study was done on 178 patients diagnosed with MG, recruited from Neurology and Medicine department. Data collection was done using pre-designed proforma. Prior to enrollment written consent was obtained from patients. Blood samples were collected prior to treatment, and SII was calculated (>1105.412 was considered as elevated) and MGFA IV & V was considered as severe MG. Data were analyzed using SPSS v26, and diagnostic performance metrics were calculated.

Results: Mean age was 37.12 ± 7.80 years, with 68% females. MGFA classification identified 24.2% severe cases, mean SII was 878.71 ± 237.16, and 23.6% exhibiting raised values. Sensitivity, specificity and accuracy of SII for predicting severe MG were 88.37%, 97.04%, and 94.94%. Subgroup analysis showed consistent diagnostic performance: accuracy was 95.92% in patients ≤30 years and 94.57% in those >30 years, 95.87% in females versus 92.98% in males, and sensitivity was higher in patients with MG-ADL >12 (90%) compared to those with MG-ADL ≤12 (66.67%).

Conclusion: The study demonstrates that systemic immune-inflammation index is highly accurate biomarker for identifying severe myasthenia gravis. These findings suggest that SII could be a valuable tool for early risk stratification and clinical decision-making in patients with myasthenia gravis.

Keywords: Systemic inflammatory immune index, Myasthenia gravis, Severity

INTRODUCTION

Myasthenia gravis, a chronic autoimmune disorder characterized by skeletal muscle weakness resulting from antibody-mediated damage to postsynaptic membrane. (1) The global prevalence of MG has been increasing, with reported estimates ranging from approximately 100 to 200 cases per million population.(2)

Although its exact cause remains unclear, inflammation is considered as central mechanism in disease development.(3) Within microenvironment, abnormal expression of inflammatory mediators promotes B-cell activation and leads to increased production of pathogenic autoantibodies.(4) Current management strategies primarily focus on suppressing inflammation and reducing circulating antibodies; however, response to therapy is often variable.(5) Consequently, accurate assessment of inflammatory activity is essential for optimizing individualized treatment approaches.

Several systemic inflammatory markers derived from routine blood cell counts; have been increasingly utilized.(6) These indices are considered reliable indicators of systemic inflammatory response and have demonstrated clinical relevance in various autoimmune conditions.(7)

The systemic immune-inflammation index (SII), calculated using platelet, neutrophil, and lymphocyte counts, has recently gained attention as novel inflammatory biomarker.(8) Previous studies have demonstrated its association with disease severity and therapeutic response in autoimmune encephalitis.(9) Additionally, recent evidence suggests that this index is useful tool for assessing disease activity and aiding diagnosis in rheumatological disorders. (10)

Although these systemic inflammation markers are widely used to evaluate the severity and prognosis of autoimmune diseases, there is paucity of local evidence to clarify the role of SII in MG patients specifically for its severity. This research aims to assess the accuracy of SII in assessing MG severity, aiming to improve early detection strategies, enable more timely interventions, and ultimately reduce morbidity and mortality associated with complications in MG.

METHODOLOGY

This validation, descriptive cross-sectional study was conducted at Neurology Department, Mayo Hospital, Lahore from June 2025 to September 2025. Data were collected using structured, pre-formed proforma and were maintained by the principal investigator. Written informed consent was obtained from all participants prior to enrollment. A total sample size of 178 patients was calculated using 95% confidence level, 8% margin of error, expected sensitivity of 64.3%, specificity of 88.4%, and prevalence of raised SII score as 29.8%.(11) Patients were enrolled through non-probability consecutive sampling.

Inclusion Criteria

Patients of either gender, aged 18 to 60 years, with confirmed diagnosis of myasthenia gravis were included. Diagnosis was established based on clinical features (muscle weakness worsening with activity and improving with rest), supported by positive acetylcholine receptor antibodies or anti-MUSK antibodies and/or decremental response on RNS].(12)

Exclusion Criteria

Patients were excluded if they had evidence of active infection within the preceding one month, other autoimmune disorders, severe cardiac, hepatic, or renal disease, active malignancy or hematological disorders, or if they had received immunosuppressive therapy within the past three months. Pregnant and lactating females were also excluded.

All eligible patients admitted to neurology ward were evaluated at the time of admission. Demographic information including age, gender, body mass index, and disease duration was recorded. Disease severity was assessed at admission using Myasthenia Gravis Foundation of America clinical classification, and patients were categorized into non-severe (types I, II, and III) and severe disease (types IV and V).(13) The impact of myasthenia gravis on daily functioning was evaluated using Myasthenia Gravis Activities of Daily Living score.(14) Blood samples were obtained at admission prior to initiation of treatment, and complete blood counts were analyzed using standard laboratory techniques. The systemic immune-inflammation index was calculated using the formula *(platelet count × neutrophil count) / lymphocyte count*. An index value greater than 1105.412 was considered indicative of high systemic inflammation. True positive cases were defined as patients with elevated systemic immune-inflammation index and severe myasthenia gravis (types IV and V).

Data analysis was performed using SPSS version 26. Quantitative variables were expressed as mean and standard deviation and qualitative variables as frequencies and percentages. A 2 × 2 contingency table was constructed to calculate sensitivity, specificity, positive and negative predictive value, and overall diagnostic accuracy of SII for predicting severe myasthenia gravis. Stratification was performed for age, gender, and activity scores, and post-stratification diagnostic accuracy was determined.

RESULTS

Total 178 patients with confirmed myasthenia gravis were enrolled in the study. As shown in table 1, mean age of participants was 37.12 ± 7.80 years, with predominance of females 121 (68%) compared to males 57 (32%). The average BMI was 23.76 ± 1.54 kg/m², and mean duration of disease was 2.46 ± 0.81 years. At admission, MG-ADL score was 11.87 ± 2.56. According to MGFA clinical classification, 135 patients (75.8%) had non-severe disease (Grade I: 4 [2.2%], Grade II: 63 [35.4%], Grade III: 68 [38.2%]), while 43 patients (24.2%) had

severe disease (Grade IV: 35 [19.7%], Grade V: 8 [4.5%]). The mean systemic immune-inflammation index (SII) across all participants was 878.71 ± 237.16, with 42 patients (23.6%) exhibiting raised SII.

Table 1: Characteristics of participants (N=178)

Age (years)			37.123 ± 7.802
Gender	**Male**		57 (32%)
	Female		121 (68%)
BMI (kg/m2)			23.76 ± 1.537
MG duration (years)			2.457 ± 0.805
MG-ADL Score at admission			11.870 ± 2.555
MGFA Grade	**Non-severe**	**Grade I**	4 (2.2%)
		Grade II	63 (35.4%)
		Grade III	68 (38.2%)
		Total	135 (75.8%)
	Severe	**Grade IV**	35 (19.7%)
		Grade V	8 (4.5%)
		Total	43 (24.2%)
SII			878.707 ± 237.157
Raised SII			42 (23.6%)

MG: Myasthenia Gravis; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGFA: Myasthenia Gravis Foundation of America; SII: systemic immune-inflammation index

The diagnostic performance of SII for identifying severe myasthenia gravis is summarized in Table 2. Among patients with severe disease, 38 of 43 (88.4%) had raised SII, while 131 of 135 (97.0%) patients with non-severe disease had normal SII values. The overall sensitivity and specificity of SII for predicting severe MG were 88.37% (95% CI: 74.92–96.11%) and 97.04% (95% CI: 92.59–99.19%), respectively. Positive and negative predictive values were 90.48% (95% CI: 78.24–96.17%) and 96.32% (95% CI: 91.99–98.35%), respectively, with overall diagnostic accuracy of 94.94% (95% CI: 90.62–97.66%).

Table 2: Accuracy of SII for MG severity

			Severe MG		
			Yes	**No**	**Total**
SII Raised	**Yes**	**Frequency**	38	4	42
		%	90.5%	9.5%	100.0%
	No	**Frequency**	5	131	136
		%	3.7%	96.3%	100.0%
Total		**Frequency**	43	135	178
		%	24.2%	75.8%	100.0%

Statistic	**Value**	**95% CI**
Sensitivity	88.37%	74.92% to 96.11%
Specificity	97.04%	92.59% to 99.19%
Positive Predictive Value	90.48%	78.24% to 96.17%
Negative Predictive Value	96.32%	91.99% to 98.35%
Accuracy	94.94%	90.62% to 97.66

As shown in Table 3, the overall diagnostic accuracy of SII remained high across different subgroups. Among patients aged ≤30 years, SII demonstrated an accuracy of 95.92%, while in those aged >30 years, the accuracy

was 94.57%, indicating consistent performance across age groups. When stratified by gender, females exhibited slightly higher accuracy (95.87%) compared to males (92.98%). Analysis based on MG-ADL scores at admission revealed that patients with scores ≤12 had lower sensitivity (66.67%), whereas those with scores >12 demonstrated higher sensitivity (90%), reflecting better detection of severe MG in patients with more pronounced functional impairment.

Table 3: Data stratification with respect to effect modifiers

Groups	Subgroups	Specificity %	Sensitivity %	PPV %	NPV %	Accuracy %
Age	**Upto 30 years**	95.24	100	77.78	100	95.92
	>30 years	97.85	86.11	93.94	94.79	94.57
Gender	**Male**	93.33	91.67	78.57	97.67	92.98
	Female	98.89	87.10	96.43	95.70	95.87
MG-ADL Score at admission	**Upto 12**	98.17	66.67	50	99	97.32
	>12	92.3	90	94.74	85.71	90.91

DISCUSSION

In current study, mean age of MG participants found was 37.12 ± 7.80 years, with female's predominance (68%). Aguirre & Villa, reported similar mean age of 38 years, with women starting earlier at 32 years vs 48 years for men.(15) Sobieszczuk et al, also supported female predominance, with ratios such as 1.65:1.(16) According to MGFA clinical classification 24.2% had severe disease (grade IV & V). Voháňka et a, found lower prevalence (13.3%) of severe MG. (17) Pesa et al, in line with current findings found severe MG among 23.3% MG partcipants.(18) In our study, SII across all participants was 878.71 ± 237.16, with 42 patients (23.6%) exhibiting raised SII. Huang et al, reported median SII 483 (among non-severe) vs 860 (severe).(11) In this study, we have found that, among patients with severe disease, 88.4% had elevated SII. Chen et al, has shown association of SII with respiratory failure, major cause of mortality in patients with MG, ranging from 54.8%-61.3%.(19) In current study, overall sensitivity (88.37%) and specificity (97.04%), and diagnostic accuracy (94.94%) of SII for severe MG further supports its utility in routine clinical assessment. Huang et al, in contrast has shown that, SII at cut-offvalue 1105.412 has sensitivity 64.3%, and specificity 88.4%.(11) In some studies, SII found to be inferior to SIRI, comparable to PLR and LMR.(20) Huang et al, (2022) supported that, in MG patients, NLR, PLR, and SII were significantly elevated compared to healthy controls, and SII was identified as independent predictors of severity, also found to be associated with poor clinical outcomes.(21) Mangoni et al, in their pooled review showed that SII has good diagnostic accuracy for immune disorders, with an overall AUC of 0.85.(8) Overall, the results support the role of SII as a simple, accessible, and effective biomarker for assessing MG severity. Its high diagnostic accuracy, combined with consistency across patient subgroups, suggests it could aid clinicians in early risk stratification and timely intervention, potentially reducing morbidity associated with severe MG. Future studies may explore its prognostic value and role in monitoring treatment response.

CONCLUSION:

The study demonstrates that the systemic immune-inflammation index is a highly accurate biomarker for identifying severe myasthenia gravis. These findings suggest that SII could be a valuable tool for early risk stratification and clinical decision-making in patients with myasthenia gravis.

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