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Erythrocyte Sedimentation Rate as An Inflammatory Biomarker for Prediction of Prognosis of Guillain-Barre Syndrome

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ABSTRACT

Background: Guillain-Barre syndrome (GBS) is an acute or subacute inflammatory autoimmune postinfectious poly-radiculoneuropathy, usually triggered by antecedent infections during the preceding six weeks suggesting a humoral immune-pathogenic mechanism. Inflammation raises the erythrocyte sedimentation rate **(**ESR), which can be used to monitor the inflammatory process. **Objective:** This study aimed to find out if there is correlation between the ESR as a marker of the inflammatory process and the Erasmus GBS outcome score.

Methods: Patients were diagnosed with GBS based Asbury and Cornblath diagnostic criteria. Assessment of GBS disability score and the Erasmus GBS outcome score (EGOS) were performed.

Results: Among 37 patients with GBS; the GBS disability score was 3 in 13 patients (35.2%), and 4 in 24 patients (64.5%). None of our patients showed other grades of the GBS score. As regard the EGOS 4 patients (10.8%) scored 3, 3 (8.1%) scored 3.5, 11 (29.7%) scored 4, 6 (16.2%) scored 4.5, 10 (27.1%) scored 5, 2 (5.4%) scored 5.5, and only one patient (2.7%) scored 6. Assessed first hour ESR mean value was 42.97 ± 18.01, with minimum value of 16, maximum 110. Positive correlation between the ESR and the EGOS was detected with r value of 0.7328.

Conclusion: ESR may serve as a simple prognostic biomarker of clinical severity as higher ESR levels were associated with increase severity of GBS.

Keywords : ESR, GBS disability score, EGOS, Guillain-Barre.

INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute or subacute inflammatory autoimmune postinfectious poly-radiculoneuropathy, usually triggered by antecedent infections during the preceding six weeks suggesting a humoral immunopathogenic mechanism [1, 2]. Campylobacter jejuni is the most common pathogen associated with GBS. Several viruses have been also reported to be associated with GBS including; Epstein Barr virus, influenza A virus, cytomegalovirus and most recently COVID-19 [3, 4].

Molecular mimicry of such pathogens is responsible for triggering a humoral and cell mediated inflammatory responses that result in poly-radicular and neuropathic affection [5]. The erythrocyte sedimentation rate (ESR) is an acute phase inflammatory biomarker that measure the amount of precipitated red blood cells (RBC) in a test tube within a known time interval. It depends on the concentrations of the serum protein especially fibrinogen, in addition to the interactions of the RBC with these proteins. While the ESR is not a diagnostic test itself, however, it is used to monitor the inflammatory disease activity and treatment response [6].

The Erasmus GBS Outcome Score (EGOS) is a validated prognostic score based on assessment of multiple parameters including age, diarrhea, and GBS disability score at 2 weeks after hospital admission that accurately predicts the odd of independent motor activity at 6 months. This can be utilized to starify the disease severity among the patients and determine the high-risk groups [7, 8].

Methods:

Thirty-seven patients diagnosed as Guillain-Barre syndrome via thorough history taking including history of diarrhea or upper respiratory tract infection preceding the onset of illness. Full neurological examination, and complete laboratory profile including ESR were done. Nerve conduction studies (NCSs) were carried out and based on the deduced distal motor latencies, amplitudes, conduction velocities and F wave latencies, patients were classified into demyelinating or axonal polyradiculoneuropathy. The Asbury and Cornblath GBS diagnostic criteria were taken as the reference for the clinical diagnosis. GBS disability score and the Erasmus GBS outcome score were assessed (Table 1) [9].

Table (1): The Erasmus GBS outcome score

Age at onset (years)	> 60 41–60 ≤ 40	**1** **0.5** **0**
Diarrhea (≤4 weeks)	Absence Presence	**0** **1**
GBS disability score	**0** →A healthy state **1** → Minor symptoms and capable of running **2** →Able to walk 10 m or more without assistance but unable to run **3** → Able to walk 10 m across an open space with help **4** → Bedridden or chair bound **5** → Requiring assisted ventilation for at least part of the day	**1** **1** **2** **3** **4** **5**
Erasmus GBS outcome score		**1–7**

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Ethical considerations:

Ethical approval was obtained from Mansoura Faculty of Medicine Institutional Research Board (MFM-IRB) (approval code: R.22.09.1806).

Statistical Analysis

Data were analyzed using the **SPSS**. After the data being tested for normality by Kolmogorov Smirnov test, parametric data were presented in mean ± SD, while non-parametric data were presented as median and range. Pearson correlation was used to measure correlation between the ESR and the EGOS score. Receiver operating characteristic (ROC) curves were performed to determine the cut-off value of ESR in prediction of the neuropathic affection type.

RESULTS

Out of our 37 patients, 21 patients were males (56.7%), 16 patients were females (43.3%), with mean age of 44.76 ± 18.75 years. Nine patients had prior history of diarrhea (24.3%), 25 patients had history of upper respiratory tract infection (URTI) (67.5%), while 3 patients had neither (8.2%).

The nerve conduction studies (NCS) showed demyelinating neuropathic affection in 29 patients (78.4%), and axonal neuropathic affection in 8 patients (21.6%). Intravenous immunoglobulin (IVIG) was used in the treatment of 29 patients (78.4%), while plasmapheresis was used in 8 patients (21.6%)**.**

The GBS disability score was 3 in 13 patients (35.2%), and 4 in 24 patients (64.8%). None of our patients showed other grades of the GBS score. As regard the EGOS, 4 patients (10.8%) scored 3, 3 (8.1%) scored 3.5, 11 (29.7%) scored 4, 6 (16.2%) scored 4.5, 10 (27.1%) scored 5, 2 (5.4%) scored 5.5, and only one patient (2.7%) scored 6. Assessed first hour ESR mean value was 42.97 ± 18.01, with minimum value of 16, maximum 110 **(table 2).**

Table (2): Descriptive statistical analysis of the study participants

Sex	• Male • Female	**N (%)** 21 (56.7) 16 (43.3)
Age (years)	Mean ± SD Median Min max	44.76 ± 18.75 45 12-82
Preceding symptoms	• Diarrhea • URTI • None	**N (%)** 9 (24.3) 25 (67.5) 3 (8.2)
NCS	• Demyelinating • Axonal	**N (%)** 29 (78.4) 8 (21.6)
Treatment	• Plasmapheresis • IVIG	**N (%)** 8 (21.6) 29 (78.4)
GBS disability score at 2 weeks	0-1 2 3 4 5 6	**N (%)** 0 0 13 (35.2) 24 (64.8) 0 0
EGOS score	<3 3 3.5 4 4.5 5 5.5 6	**N (%)** 0 4 (10.8) 3 (8.1) 11 (29.7) 6 (16.2) 10 (27.1) 2 (5.4) 1 (2.7)
First hour ESR:	Mean ± SD	42.97±18.01

Positive correlation between ESR and EGOS was detected with r value of 0.7328 (figure 1).

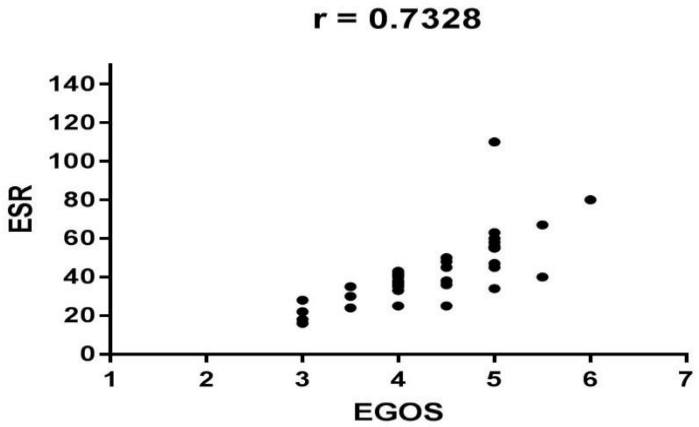

Figure (1): Positive Pearson correlation analysis on scattered plot

As regards the relation between ESR and the type of the neuropathic affection, ROC curve deduced that ESR at cut-off value of 37.5 showed 87.5 % sensitivity and 51.7% specificity for axonal neuropathic affection (AUC = 0.59, 95% CI=0.384-0.806, P=0.42) (Figure 2).

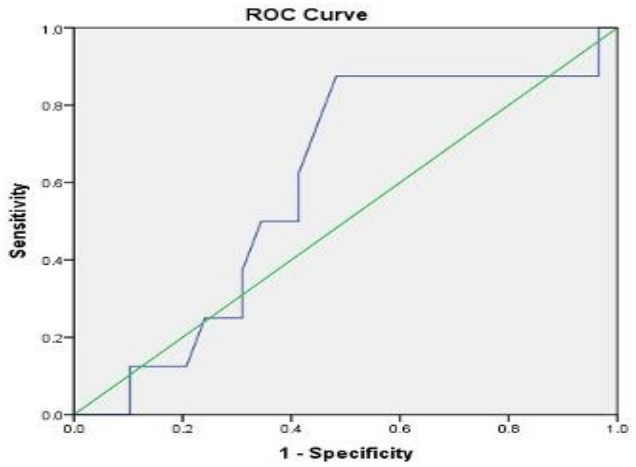

Figure (2): ROC curve analysis of ESR in the prediction of type of neuropathic affection.

DISCUSSION

As regard the demographic data, our sample criteria were homogenous with the general demographic distribution of GBS, with males being affected more than females [10], with mean age of onset 44.76 ± 18.75 years [11], with antecedent URTI in 67.5 %, diarrhea in 24.3%, neither in 8.2 %, which is almost similar to previously reported percentages (upper respiratory illness in 41.3% of the antecedent events and acute gastroenteritis in 34.4% [12].

The GBS disability score of all our patients fell in score 3 and 4 exclusively, 35.2 % of the patients scored 3, while 64.8 % scored 4. The selection criteria of the inpatient admission in our hospital, pre-hospitalization malpractice and delay in the diagnosis may have contributed to miss patients in less severe conditions (score 0,1,2), while the unavailability of data of the patients initially admitted to the ICU as it is not exclusively related to our department led to missing patients requiring assisted ventilation (score 5).

This is also acceptable in the highlight of the previously reported results by **Walgaard and his colleagues [7]** who recoded GBS disability score among 394 patients, 91 patients (23.1%) scored 3, 265 (67.2%) scored 4, 38 (9.7%) patients scored 5, and none scored 0 or 1 or 2.

Upon the basis of the assessed GBS disability score, age at onset, and the antecedent events, EGOS score was calculated where 10.8% of the cases scored 3, 8.1% scored 3.5, 29.7% scored 4, 16.2% scored 4.5, 27.1% scored 5, 5.4% scored 5.5, and 2.7% scored 6.

Erythrocyte sedimentation rate (ESR) is a rapid, simple, inexpensive biomarker have been recommended all the time in the GBS work up, as a screening for the underlying inflammatory process. Many studies reported elevated ESR levels on the sideline of their investigations [13-18]. Among the Egyptian patients, our results were comparable to the results reported by Hashim and their colleagues who found that ESR levels showed statistically significant higher levels in GBS patients than in healthy subjects (p=0.017) [18].

Our results showed positive correlation between ESR and EGOS (r= 0.7328). No available studies focused on ESR levels as the primary predictor. Most of the interest was focused on the C-reactive protein (CRP) [19-20]. This may be explained by the limitations of the ESR measurements including the presence of multiple influencing factors including age, sex, RBCs shape, hemoglobin concentration, and serum antibodies levels. Also, the blood sample must be manipulated appropriately and analysed within few hours to ensure accurate results [6]. But generally, there is no evidence or consensus that favor one over the other [21].

Both CRP and ESR are acute phase inflammatory reactants. However, the pattern of response differs for each. CRP usually becomes elevated few hours after the onset of an infectious or inflammatory condition and normalizes within 3 to 7 days. In contrary, ESR rises slowly and remains high for a longer period of time [21]. Based on this we felt that ESR will be more representative biomarker for our patients, because of the usual delay before being presented to our department. On comparison of the prognostic value of ESR with that of the CRP, the value of the ESR for predicting improvement with

plasmapheresis (CI 0.39–0.73, AUC 0.56, p = 0.57) was higher than CRP value (CI 0.33–0.67, AUC 0.50, p = 1.1) [18].

Higher ESR levels were found to be associated with the axonal neuropathic affection variant of GBS, which is usually associated with worse outcome and slower recovery [15]. Up to our knowledge there are no studies that evaluated the relation between ESR and the type of neuropathic affection. However there are some reports about the higher CRP levels to be associated with absence of responses of both motor and sensory nerves denoting axonal affection [20].

CONCLUSION

ESR may serve as a simple prognostic biomarker for clinical severity as higher ESR levels were associated with increased severity of GBS.

Limitations and recommendations: Our study had some limitations. The sample size was relatively small. Further large sized studies to compare the predictive value of ESR, CRP and neutrophils to lymphocytes ratio are warranted.

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