Serum Neurofilament Light Chain Associated With Outcome In Guillain-Barré Syndrome Across Regional And Disease Spectrums

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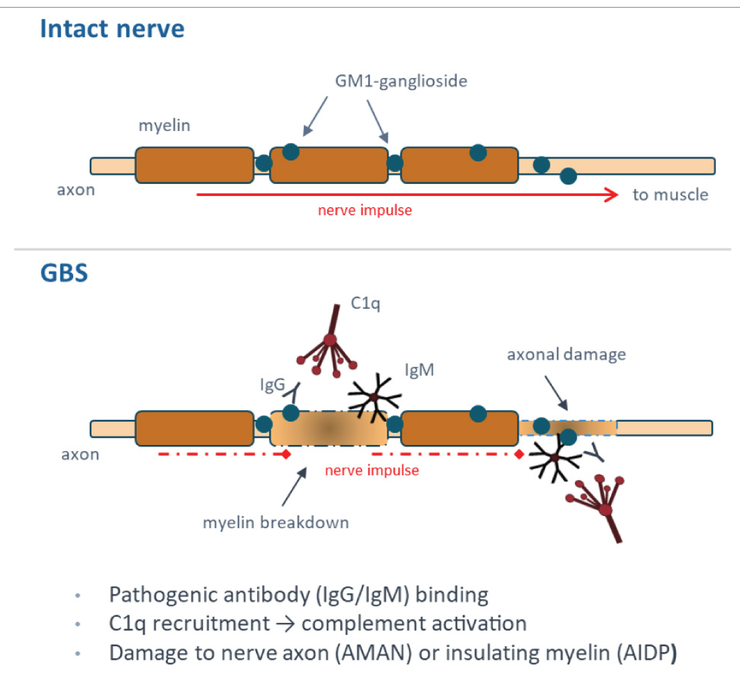
Introduction:

- Guillain-Barré Syndrome (GBS) is an acute classical complement-mediated peripheral nerve disease that has a diverse presentation globally and is characterized by rapidly progressive muscle weakness, impaired mobility, and respiratory distress[1]
  - Early identification of GBS is important to avoid poor prognosis, as treatment initiation within 2 weeks of disease onset has been associated with improved outcomes[2]
- In GBS, auto-antibodies (IgG and IgM) target surface antigens on peripheral nerves and nerve roots, causing axonal damage (**Figure 1**)[1,3]

Figure 1. Pathogenic Antibody Binding to Nerves Causes Axonal Damage in GBS



- Pathogenic antibody (IgG/IgM) binding
- C1q recruitment → complement activation
- Damage to nerve axon (AMAN) or insulating myelin (AIDP)

- The level of axonal damage is an important determining factor in poor prognosis in GBS outcome, but no early predictive fluid biomarkers are currently available[2,4]
- Neurofilament light chain (NfL) is a serum biomarker that is elevated following axonal damage in many neurological diseases, suggesting a role for serum NfL in predicting outcomes in patients with GBS[4]
- The objective of this study was to evaluate serum NfL (sNfL) as a prognostic biomarker in patients with GBS from different geographical areas

Methods:

- Serum samples were collected prospectively from 35 healthy controls and 97 GBS patients, 82 from Bangladesh and 15 from Europe and North America (EU/NA)
- Eligible patients included those ≥17 years of age with onset of weakness ≤2 weeks prior to admission and a GBS disability score (GBS-DS) of ≥3 (**Table 1**)

Table 1. GBS Disability Score (modified)[5]

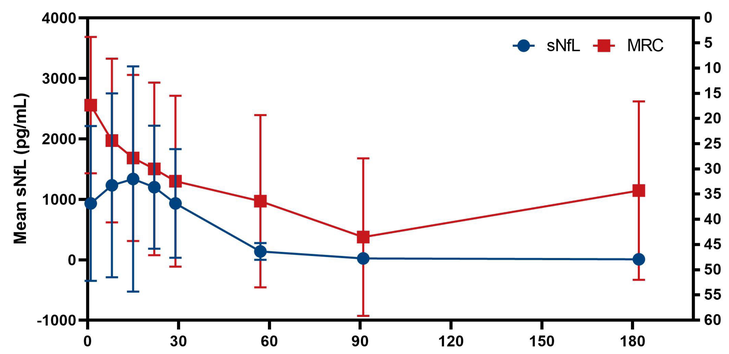
GBS-DS Score	Patient State
0	A healthy state
1	Minor symptoms and capable of running
2	Able to walk 10 meters or more without assistance but unable to run
3	Able to walk 10 meters across an open space with help
4	Bedridden or chairbound
5	Requiring assisted ventilation for at least part of the day
6	Dead

- sNFL was measured by single-molecule array, and its association with GBS-DS was evaluated by Spearman's coefficient, unadjusted for known prognostic factors and irrespective of treatment administered

Results:

- All patients had elevated sNfL at baseline, with a mean sNfL ± SD of 932.1 ± 1281 pg/mL (1-1200x controls)
- The average peak sNfL was higher than at baseline (1561 vs 932 pg/mL)
- sNfL levels mirrored the monophasic course of disease, peaking 12.5 days after admission, declining by day 29, and normalizing by day 182 (**Figure 2**)

Figure 2. Mean sNfL and MRC at Baseline Through Day 182

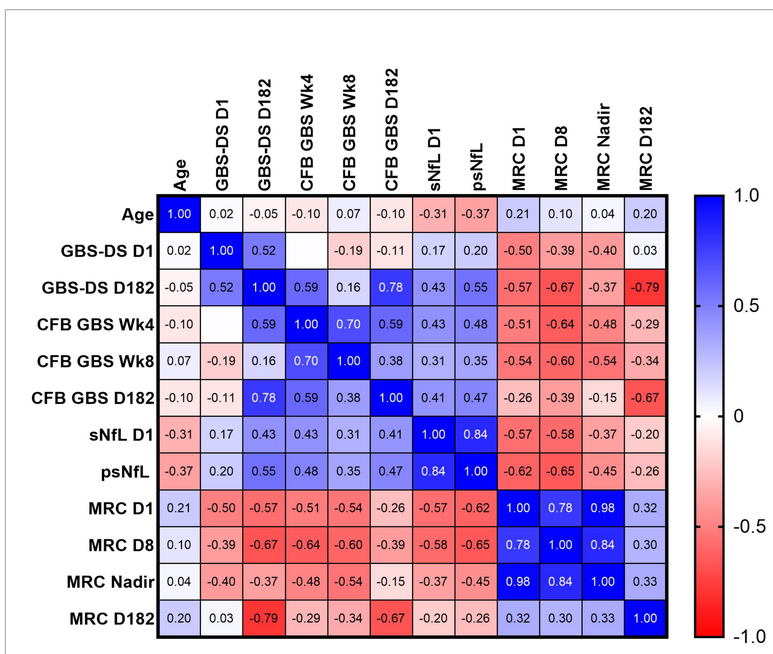


	Day	1	8	15	22	29	57	91	182
N	sNfL	96	95	94	64	95	82	45	38
	MRC	84	84	84	64	84	84	34	69

For the included studies, not all endpoints were recorded for all patients at each timepoint.
MRC, Medical Research Council sum score; sNfL, serum neurofilament light chain.

- Mean patient sNfL correlated with GBS-DS (r=0.5395, p<0.0001)
- In this monophasic disease, peak sNfL (psNfL) provided stronger correlations than baseline sNfL regarding baseline GBS-DS (r=0.202, p=0.0482 vs. 0.17, p=0.098), change in GBS-DS by day 29 (r=0.480, p<0.0001 vs 0.431 p<0.0001) or day 57 (r=0.351, p<0.001 vs 0.309, p<0.001), and final GBS-DS outcome at day 182 (r=0.55, p<0.0001 vs 0.431, p=0.003) (**Figure 3**)

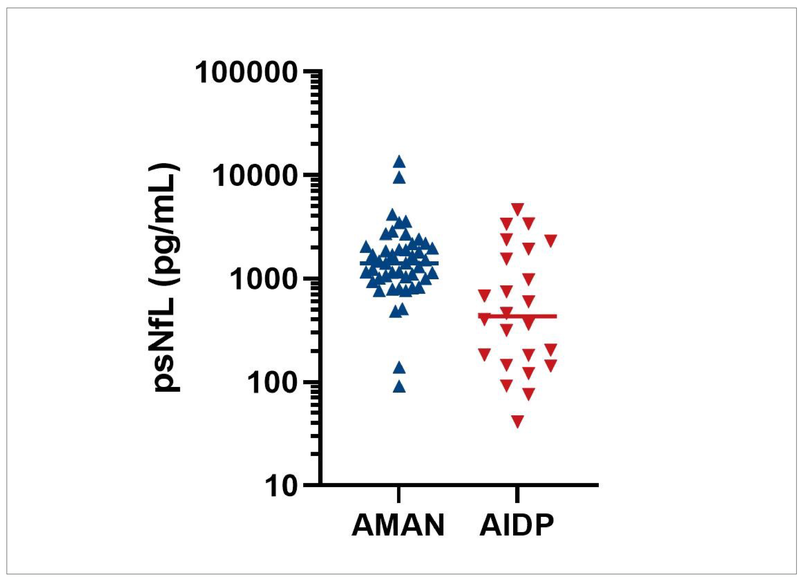
Figure 3. Spearman r Coefficients for Correlation Between Endpoints



CFB, change from baseline; GBS-DS, Guillain-Barré Syndrome disability score; MRC, Medical Research Council sum score; psNfL, peak serum neurofilament light chain; sNfL, serum neurofilament light chain.

- Higher psNfL was seen in patients with acute motor axonal neuropathy (AMAN) vs acute inflammatory demyelinating polyneuropathy (AIDP) (1986.0 vs 1050.0 pg/mL; p=0.07) (**Figure 4**)

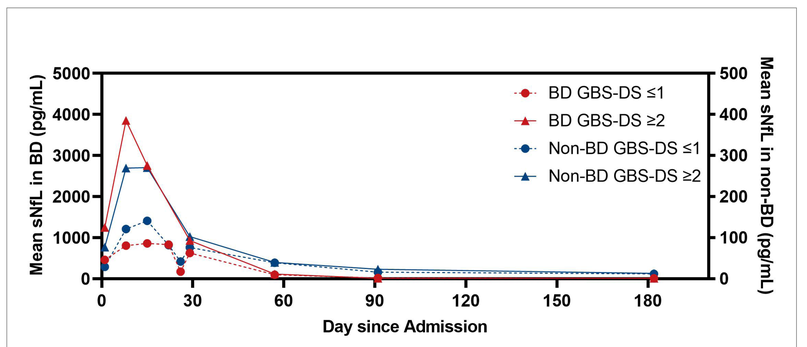
Figure 4. Peak sNfL in AMAN and AIDP



AIDP, acute inflammatory demyelinating polyradiculoneuropathy; AMAN, acute motor axonal neuropathy; psNfL, peak serum neurofilament light chain.

- At day 182, patients able to run or better (GBS-DS ≤ 1) displayed a median psNfL of 362 vs 1417 for patients unable to run (p=0.0025)
- At day 182, 34% of patients (11 of 32) in Bangladesh could run compared to 71% (10 of 14) in Europe/North America (EU/NA)
- At day 182, patients able to run or better had a lower psNfL than those unable to run, both in Bangladesh (766.0 vs 2298.0 pg/mL [p=0.088]) and in EU/NA (182.2 vs 455.1 pg/mL [p=0.142]) (**Figure 5**)

Figure 5. Mean sNfL by Geography and GBS-DS Through Day 182



BD, Bangladesh; GBS-DS, Guillain-Barré Syndrome disability score; sNfL, serum neurofilament light chain.

Conclusions:

- **sNfL levels mirrored disease course and correlated with disease severity, axonal variants, and functional outcome across a heterogeneous population from different geographic regions**
- **Integration of sNfL in a universal GBS disease model is warranted**

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