

exploring its serum and CSF levels in multiple sclerosis

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Background

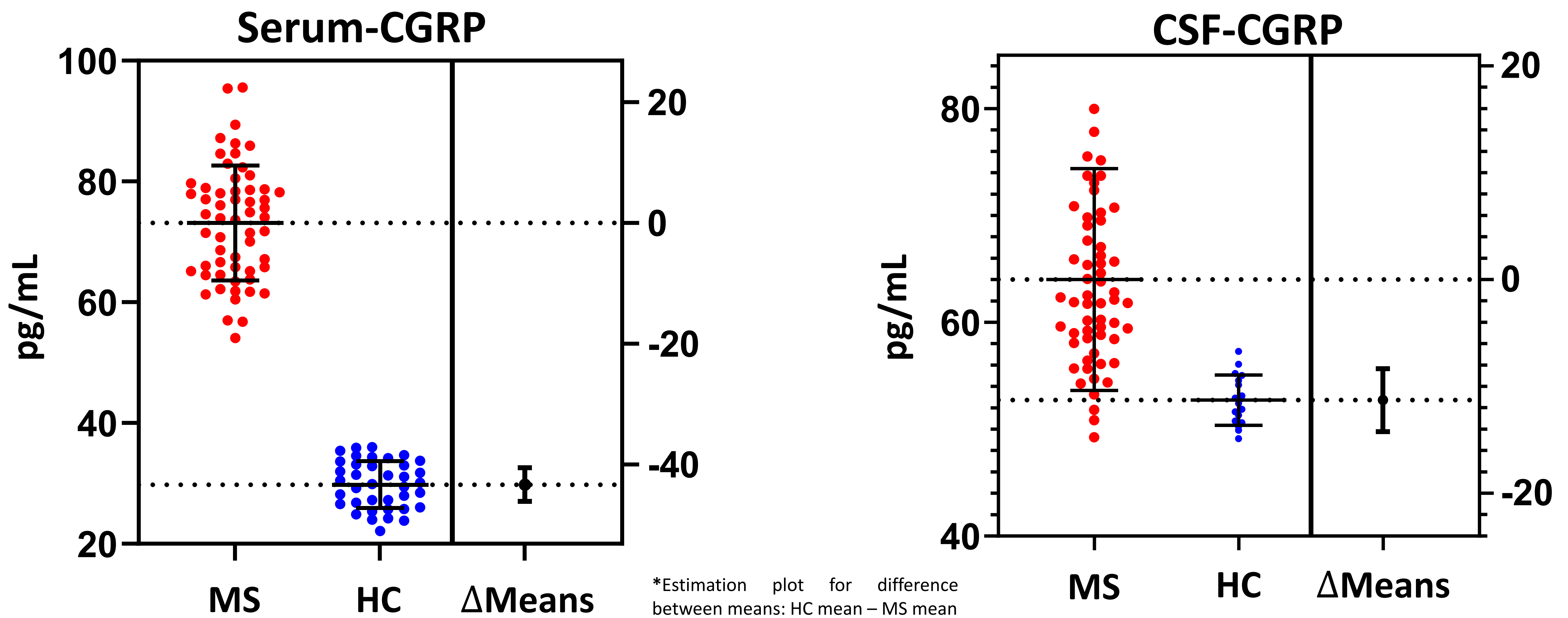
Multiple Sclerosis (MS) is a disease of the central nervous system (CNS) characterized by progressive demyelination and inflammatory process. While the exact etiology of MS remains unknown, it relies on an autoimmune process that includes the activation of microglia and localizes at the perivenular site. **Calcitonin Gene Related Peptide (CGRP)** is a neuropeptide ubiquitous in the peripheral and CNS, mostly known for the role in vasodilation and pain signal transmission during migraine attacks. Recent studies have been unraveling its **immunomodulatory properties**, showing both anti and pro-inflammatory effects.

Objective

In this study we evaluated soluble CGRP, determined at MS diagnosis in cerebrospinal fluid (CSF) and serum, and correlated its levels with progression and short-term disease severity.

Patients and Methods

We enrolled for a prospective study **59 MS patients** (39 females, mean age at diagnosis 38.79 years ± standard deviation or SD 9.89) with Radiological Isolated Syndrome (RIS), Clinical Isolated Syndrome (CIS) and Relapsing-Remitting (RR) MS. During the diagnostic work-up were collected clinic-demographic data, serum and CSF. Patients were followed with regular clinical visits (minimum 2 year?). CGRP levels were determined through an ELISA commercial kit (MyBioSource Inc, MBS267126, San Diego, CA, USA). **None** had a history of **migraine** at diagnosis. **Healthy control (HC)** CCGRP values were published by Papiri et Al.¹ and Han et Al.² Statistical analyses were conducted with STATA software to determine Mann–Whitney, Kruskal-Wallis test and Spearman's rank correlation coefficient significance.

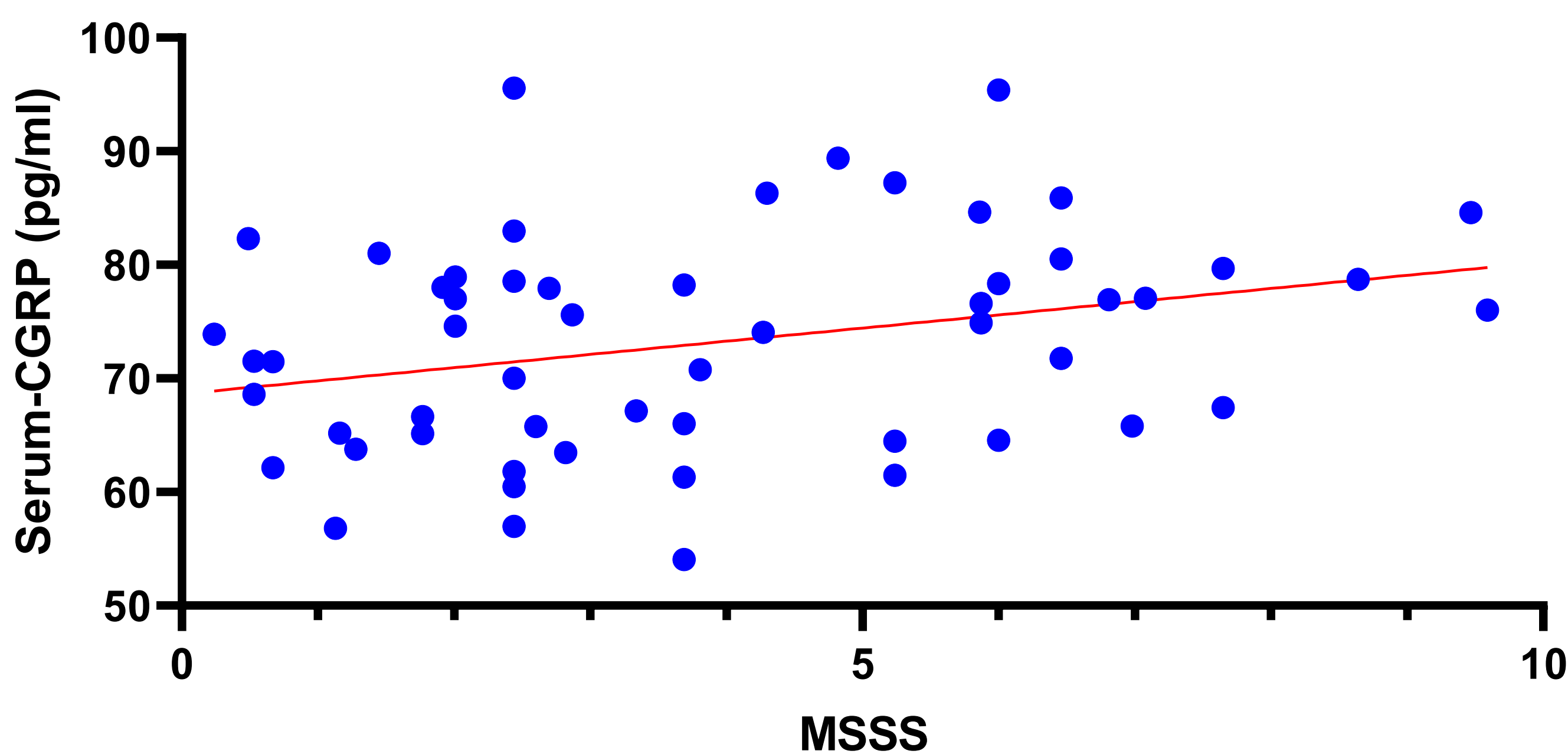


Results

CGRP levels were significantly higher in MS patients if compared to healthy controls published by Papiri et Al. [1] and Han et Al. [2]. Mean values resulted 73.10 pg/ml in serum (±9.42 vs 29.50 ± 8.91, p<0.05 t-test) and 64.01 in CSF (± 10.39 vs 52.05 ± 5.70, p<0.05 t-test). CGRP levels did not relate to clinical variables at diagnosis: age, gender, Expanded Disability Status Scale (EDSS), number of T2, gadolinium enhancing and spinal cord lesions. However, there was a positive correlation between serum CGRP and the **Multiple Sclerosis Severity Score (MSSS)** at the last follow up ($r^2 = 0.27$, p<0.05 Spearman's rank correlation).

Spearman's rank correlation

$r^2=0.27$ p<0.05



Discussion

We observed an **increased CGRP level** in the CSF and serum of MS patients at diagnosis. Our study firstly evaluated this **biomarker** both in CSF and serum and subsequently confirmed and expanded on its possible role in identifying cases **with poor prognosis**, as suggested by the work of Al-Keilani et Al. [3]. However further research is needed to better understand the potentials of this neuropeptide in MS.

- Papiri, G. et al. Cerebrospinal Fluid α -Calcitonin Gene-Related Peptide: A Comparison between Alzheimer's Disease and Multiple Sclerosis. *Biomolecules* 12, (2022).
- Han, D. Association of Serum Levels of Calcitonin Gene-related Peptide and Cytokines during Migraine Attacks. *Ann. Indian Acad. Neurol.* 22, 277 (2019).
- Al-Keilani, M. S., Almomani, B. A., Jaradat, S. A., Al-Sawalha, N. A. & Qawasmeh, M. Al. Alpha Calcitonin Gene-related Peptide, Neuropeptide Y, and Substance P as Biomarkers for Diagnosis and Disease Activity and Severity in Multiple Sclerosis. *CNS Neurol. Disord. Drug Targets* 22, (2023).