SERUM CXCL13 LEVELS ASSOCIATE WITH EDSS SCORE AND SPINAL CORD LESION NUMBER IN MS

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OBJECTIVES

There are prognostic data recommended for MS patients, however our knowledge so far lacks parameters that would give definite information about the prognosis of an individual with MS [1]. Cytokines are intracellular polypeptides that play an active role in the area of inflammation [2]. Chemokines are small protein superfamily and are involved in the migration of many different cell types, including lymphocytes, to the site of inflammation. [3].
Our study aims to determine a biomarker that reflects the disease activity at the disease onset by evaluating the cytokine and chemokine levels from the serum and CSF samples of patients with poor prognostic data and patients without poor prognostic data when diagnosed with Multipl Sclerosis.

METHODS

Patients who applied to Marmara University Pendik Training and Research Hospital Neurology Clinic diagnosed either with MS according to 2017 McDonald criteria or non-inflammatory neurological diseases for which lumbar puncture is indicated included in our study.
Treatment naïve MS patients were divided into two classes according to their clinical and radiological findings as those with poor prognostic expectation and those without. Any of the following factors was sufficient to include the patient in the poor prognostic expectation patient group:

- Late onset [4] [5], presence of multifocal relapses affecting motor, cerebellar and sphincter functions [4][6], EDSS score reaching 4.0 points in 5 years after disease onset [7], presence of new or expanding lesion on T2-weighted images or an active lesion showing Gadolinium uptake on T1-weighted images [8], presence of black hole or atrophy on T1-weighted images [8], presence of spinal cord or brain stem lesion on MRI [9].

After the clinical and radiological evaluation of each patient, serum and CSF samples were obtained simultaneously. IL-8, IL-12 / IL-23p40, IL-21, CHI3L1 and CXCL13 levels were measured using ELISA method.
Data were evaluated using Stata version 15.1 (StataCorp, College Station, Tex). A *P*-value lower than 0.05 was considered significant.
Our study was approved by Marmara University Faculty of Medicine Clinical Research Ethics Committee.

RESULTS

Demographic Data and Clinical Characteristics

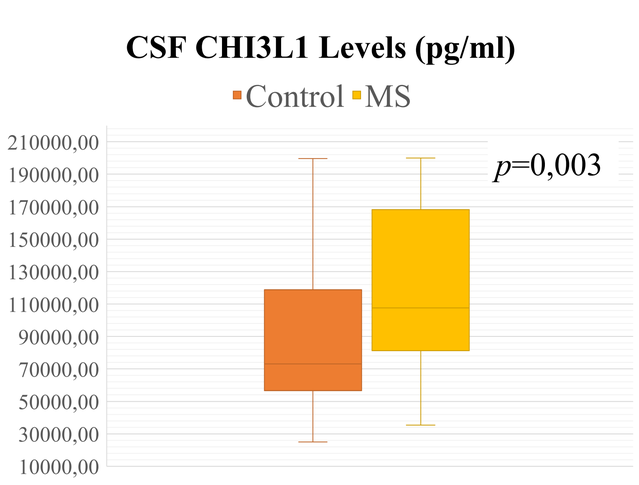
A total of 56 patients included to our study. Of those patients 21 were MS patients with poor prognostic data (PP), 8 had MS without poor prognostic data (WPP) and 27 were control patients. It was observed that there may be a marginal significance for the PP group in terms of the frequency of relapses affecting the pyramidal system (p= 0.05). EDSS scores of the patients in the PP group were found to be significantly higher than the patients in the WPP group (p=0.04). The number of lesions in the spinal cord in the PP group was significantly higher than in the WPP group (p<0.001).
Demographic data and clinical characteristics were summarized in table 1.

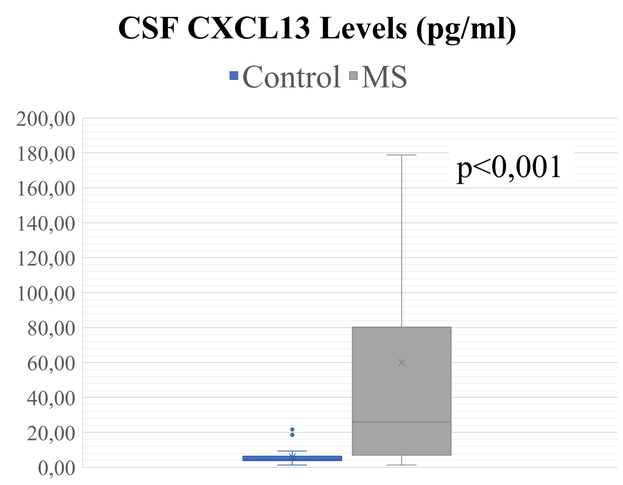
Table 1. Demographic Data and Clinical Characteristics

	Control	PP	WPP	p
Female, n (%)	25 (93)	13 (62)	5 (63)	0,02
Age, Median (Range)	37,2 (21,9 – 53,1)	36,4 (22,9 – 63,1)	33,0 (22,0 – 47,3)	0,60
Number of Previous Relapses, Median (Range)	-	1 (0 – 4)	1 (0 – 4)	0,22
EDSS, Median (Range)	-	1 (0 – 3,5)	0 (0 – 1)	0, 04

Serum and CSF Chemokine Levels for Multiple Sclerosis and Control Patients

CHI3L1 and CXCL13 levels in CSF of MS patients were found to be significantly higher than control patients, no significant difference was found between serum levels.





Serum and CSF Chemokine Levels for PP, WPP and Control Patients

CHI3L1 and CXCL13 levels in CSF were found to be significantly higher in the PP and WPP groups compared to the control group. There was no difference between the 3 groups for serum CHI3L1 and CXCl13 levels. No statistically significant difference was found between PP and WPP for any parameter in serum or CSF. (Table 2)

Table 2. Serum and CSF Chemokine Levels for Control, PP and WPP Patients in pg/mL

	Control, Median (IQR)	PP, Median (IQR)	WPP, Median (IQR)	p
Serum CHI3L1	44366 (41189)	38118 (24273)	52445 (36073)	0,27
Serum CXCL13	93,5 (80,5)	75,2 (108,4)	36,4 (49,2)	0,07
CSF CHI3L1	73120 (62145)	120130 (93905)	106020 (62546)	0,009
CSF CXCL13	4,6 (2,5)	26 (79,8)	27,8 (47,9)	<0,001

Correlation Analyzes with Clinical and Radiological Data

A positive correlation was detected between EDSS and serum CXCL13 (p=0.04, r=0.39), however no similar correlation was found between EDSS and CSF CXCL13 level (p=0.98). (Figure 1)
75% of MS patients (n=21) with spinal cord lesions were identified and a moderate positive correlation was found between the number of spinal cord lesions and serum CXCL13 (p=0.009, r=0.48). No correlation was found with the number of lesions in the spinal cord for CSF CXCL13 (p=0.67). (Figure 2)

Fig 1. Serum CXCL13 LEVEL AND EDSS

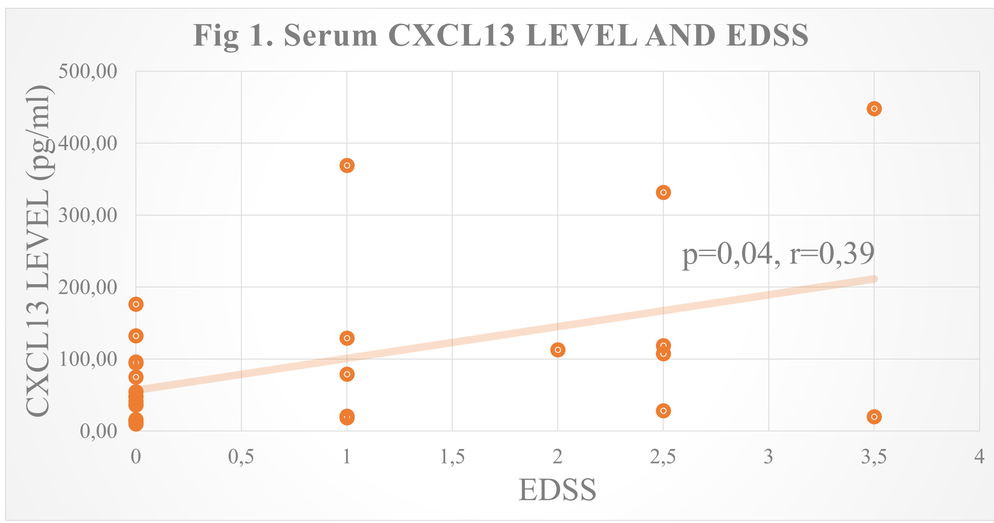
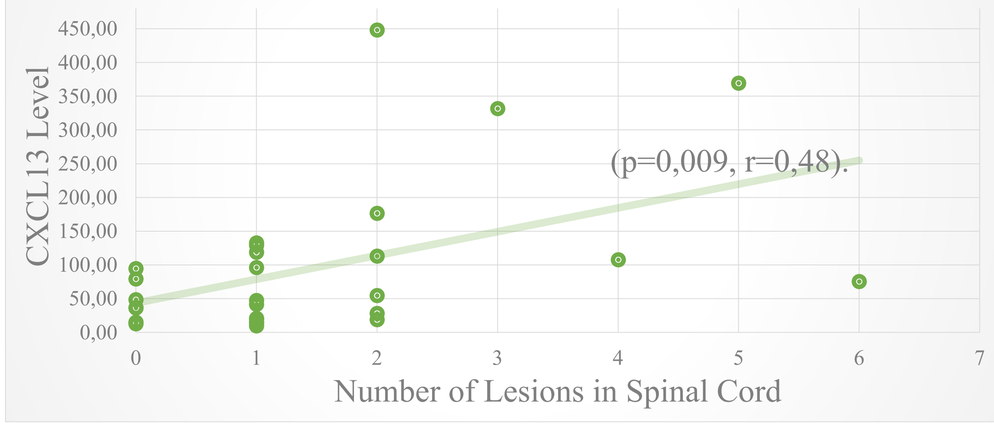


Fig 2. Serum CXCL13 and Number of Lesions in Spinal Cord



CONCLUSION

This study showed that the EDSS increases with the increasing level of CXCL13 in serum for Multiple Sclerosis patients. Supporting this data, a positive correlation was found between the number of spinal cord lesions and serum CXCL13 level. The negative effects of spinal cord lesions on disability are known [10]. Considering the results of this study and the ease in obtaining serum samples CXCL13 level in serum could be a biomarker with the potential to reflect disease activity through studies to be conducted in larger patient and healthy control groups.

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