Serum BDNF levels in SARS-CoV-2 patients are associated with lymphocyte count, ferritin and D-dimer levels

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Background & Objective

- Brain-derived neurotrophic factor (BDNF) is a neuronal growth factor that transported within platelets in the peripheral blood and exerts survival effect on neuronal cells
- The role of BDNF in SARS-CoV-2 infection, is largely unknown
- Recently, we provided the first preliminary data on serum BDNF levels in SARS-CoV-2 patients and their correlations with ferritin levels
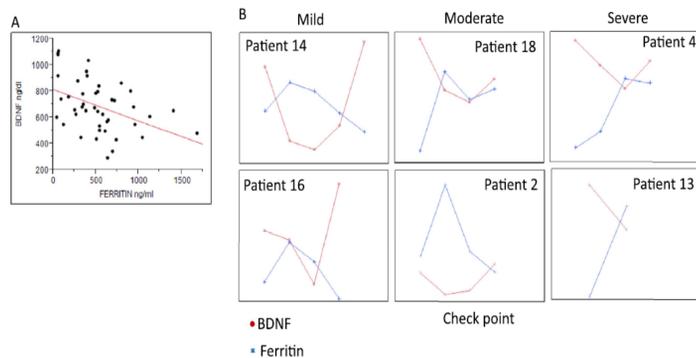

Fig. 1. BDNF and Ferritin levels in SARS-CoV-2 patients. a. a. Linear regression between BDNF and Ferritin levels (r = −0.42, p< 0.003). b. BDNF (ng/dL) (red line) and Ferritin (ng/ml) (blue line) levels upon hospital admission (left check point) and at several time points during hospitalization and hospital discharge (right check point) in selected individual patients.

- Here, we aim to extend these observations and study the potential link between BDNF, lymphopenia and other inflammatory indices in SARS-CoV-2 patients

Methods

- Serum BDNF levels were measured in 73 patients with SARS-CoV-2 infection
- The total BDNF level was quantified using the DuoSet ELISA Development System kit (R&D System DY278) according to the manufacture instructions
- We investigated the proportion and absolute count of different lymphocyte subsets by flow cytometry in the peripheral blood of SARS-CoV-2 patients.
- The correlations between BDNF levels and peripheral blood cell count, C-reactive protein, ferritin, fibrinogen and D-dimer levels were assessed.

Conclusions and Limitations

- BDNF positive association with lymphocytes count and negative association with ferritin and D-dimer production suggests beneficial effect in SARS-CoV-2 infection
- The role of BDNF as a lymphocyte survival factor and a mediator of coagulopathy in SARS-CoV-2 patients should be further studied
- The limitations of our study are the relatively low patients' number, especially in the severe disease group. Additionally, our study includes two different cohorts of patients from the current and the previous pandemic waves in Israel. During this period, some differences emerged in the guidelines of determining the disease severity and treatment protocols between the two cohorts, that could have an influence on the results.

Results

Serum BDNF levels are positively correlated with absolute lymphocytes count and inversely correlated with ferritin and D-dimer levels.

Table 1: SARS-CoV-2 patients characteristics and variables by disease severity according to the NEWS system

Parameter	All patients	Mild	Moderate	Severe	P-value
N (F:M)	73 (34:39)	30 (17:13)	26 (8:18)	17 (9:8)	N.S
Age (Years): Mean ± SD (range)	61.46±20.00 (16-98)	59.17±18.64	59.35±20.8	70.17±19.25	N.S
WBCs (x10³/µL): Mean ± SD (range)	7.07±4.07 (1.2-33.3)	6.98±4.52	6.76±3.85	7.02±3.49	N.S
Abs Lympho (x10³/µL): Mean ± SD (range)	1.21±0.77 (0.1-5.11)	1.27±0.49	1.11±0.54*	1.0±0.64**	*P value (Mild vs. Moderate) = 0.05, **P value (Mild vs. Severe) = 0.01
Neutrophils Lymphocyte Ratio (NLR) (range)	6.33±6.10 (5.55-7.12)	5.16±5.38	5.70±5.66	7.49±6.04*	*P value (Mild vs. Severe) = 0.02
PLT (x10³/µL): Mean ± SD (range)	213±101.98 (11.4-704)	236.72 ±97.46	205.09* ±80.19	201.3±93.48	*P value (Mild vs. Moderate) = 0.02
Serum BDNF (ng/ml): Mean ± SD (range)	7.51±2.63 (1.93-16.63)	7.26±2.17	7.67±2.74	7.48±2.92	N.S
D-dimer (ng/ml):Mean ± SD (range)	2,931.26±7,087.73 (12.3-67,837)	1,240.66 ±1,335.81	2,847.25 ±8,316.13	4,972.28* ±7,986.34	*P value (Mild vs. Severe) = 0.02
Fibrinogen (mg/dL):Mean ± SD (range)	527.18±181.75 (53-1,174)	528.27±214.72	531.75±161.01	517.26±186.33	N.S
Ferritin (ng/ml):Mean ± SD (range)	803.56±828.56 (38.89-3877)	470.31 ±496.81	906.14 ±832.94*	1,007.04 ±1,026.36**	*P value (Mild vs. Moderate) = 0.0064, **P value (Mild vs. Severe) = 0.0045
CRP (mg/L):Mean ± SD (range)	42.91±56.57 (0.03-295)	23.11±33.38	49.04±60.44*	59.7±67.0**	*P value (Mild vs. Moderate) = 0.0034, **P value (Mild vs. Severe) = 0.0005

Table 2: Relative and absolute count of Lymphocytes subsets in Non-SARS-Cov-2, SARS-Cov-2, EBV and HIV patients

Parameter	Non-SARS-Cov-2 (N=10)	SARS-Cov-2 (N=10)	P-value SARS-Cov-2 vs. non-SARS-Cov-2	EBV (N=7)	P-value SARS-Cov-2 vs. EBV	HIV (N=5)	P-value SARS-Cov-2 vs. HIV
Abs Lympho (x10³/µL)	1.66±0.74	0.78±0.43 *	0.007	7.91±3.83 **	<0.0001	0.48±0.17	0.16
% T cells	71.15±10.39	58.64±11.04 *	0.02	83.6±8.44 **	0.0002	58.46±21.5	0.98
Abs T cells (µL)	124.03±66.74	45.89±25.11 *	0.004	676.6±377.78 **	0.0002	29.78±17.66	0.23
% CD4 (out of total T)	60.63±12.34	67.07±12.79	0.26	14.94±4.93 **	<0.0001	15.6±8.92 #	<0.0001
Abs CD4 (µL)	71.55±36.31	31.21±20.6 *	0.009	91.9±32.84 **	0.0005	4.5±4.0 #	0.01
% CD8 (out of total T)	34.12±12.92	24.25±12.28	0.1	77.87±5.15 **	<0.0001	77.48±4.93 #	<0.0001
Abs CD8 (µL)	45.52±40.99	11.08±7.52 *	0.02	524.16±282.67 **	<0.0001	23.3±14.16	0.05
% B cells	12.36±3.57	22.67±8.34 *	0.002	5.05±4.29 **	0.0002	22.4±17.64	0.96
Abs B cells (µL)	21.1±11.18	18.77±15.31	0.7	35.79±25.13	0.1	9.83±7.67	0.25
% NK cells	10.02±6.08	12.03±3.47	0.39	7.5±5.77	0.07	12.34±3.39	0.87
Abs NK cells (µL)	13.86±7.27	9.33±5.59	0.15	50.78±31.96 **	0.001	5.93±2.76	0.23

Table 3: BDNF correlations with other indices in SARS-CoV-2 patients

	All Patients	r	Hospital Admission	r	Mild	r	Moderate	r	Severe	r
BDNF	D-dimer Abs. Lympo	-0.34 0.28	Abs.Lympho	0.43	Ferritin WBCs Abs. Lympho	-0.42 0.24 0.23	Abs. Lympho	0.31	D-dimer PLT Fibrinogen Abs. Lympho Ferritin	-0.69 0.36 0.31 0.27 -0.22

Patients with high serum BDNF levels (i.e. > 10 ng/ml) showed significantly higher abs. lymphocytes and lower D-dimer levels then patients with low serum BDNF levels (i.e.<5 ng/ml)

Figure 1