



### **Investigation of Inflammatory Serum Parameters in Long-Covid Patients with Neurological Complaints**

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### Symptoms



- Li M, Li L, Zhang Y, Wang X. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infectious Diseases of Poverty. 2020;9(1). - Larsen J, Martin M, Martin J, Kuhn P, Hicks J. Modeling the Onset of Symptoms of COVID-19. Frontiers in Public Health. 2020; 8: 4.



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## Long Covid Syndrome

### Definition



Yong S. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infectious Diseases. 2021;53(10):737-754.





#### Multisystem involvement

#### 3 – 6 months after the acute infection

#### Time and severity of the acute infection

#### Hospitalization, need of ICU and vaccination history

### **Diagnosing the Acute Covid-19**





#### **RT-PCR**

RT-PCR analysis of the swabs taken from Upper **Respiratory Tract** 

TBC, CBC, CRP, Ferritin, D-dimer, LDH...

Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. International Journal of Clinical Practice. 2020;75(3). Kazancioglu S, Bastug A, Ozbay B, Kemirtlek N, Bodur H. The role of haematological parameters in patients with COVID-19 and influenza virus infection. Epidemiology and Infection. 2020;148.





#### **Blood Test**

#### **Chest Imaging**

X-ray or CT scan of the lungs





#### **Previous Covid-19 infection**

Being diagnosed with Covid before Long-Covid symptoms

#### New symptoms

Experiencing previously non-existent findings

#### **Parameters to investigate**

It is not clear to investigate which parameters for Long-Covid patients.



## **Aim of the Research**

- signaling in the brainstem and/or vagus nerve.
- COVID patients.
- routine blood examinations.
- followed up.

Our aim was to analyze the changes in these parameters, which are frequently used in routine examinations in Long-Covid patients



Multiple hypotheses have been proposed for long COVID's pathogenesis, some include persistent reservoirs of SARS-CoV-2 in tissues, immune dysregulation, autoimmunity and molecular mimicry priming of the immune system, microvascular blood coagulation with endothelial dysfunction, and dysfunctional

Multiple studies have found that cytokines like IL-6, interferons, and tumor necrosis factor increases in long

Infection and Inflammation parameters such as total blood count (CBC) and CRP are frequently used during

• The change of these routine parameters, especially in this specific Long-COVID patients are limited and not











### Method of the Research **Selection of the Patients**

- determined.
- Admissioned to the hospital with newly experienced Long-Covid symptoms 3 to 6 months after the acute infection were selected.
- These patients were called via telephone and their symptoms were questioned and checked with their hospital admission records.
- Patients who admissioned to any hospital with another condition that could effect their blood test results between their Covid diagnose and follow-up were excluded from the research.





#### Patients diagnosed with Covid-19 between 1<sup>st</sup> January 2021 – 30<sup>th</sup> June 2021 with RT-PCR were

### **Method of the Research Investigated Patients**

#### **563 Patients**

Investigated retrospectively

Checked their eligibility for the research.

Suitability for the research criteras was considered.



Were eligible for the study.

Admissioned to the hospital with Long-Covid

First and 3-6 month control admission results were compared.





#### **122** Patients

#### **91** Patients

Data were used for the statistical analysis

All of the parameters were completely examined in these patients between the first and follow-up admission















- Aging from **22** to **77**
- Median age: 43
- Average age: 44

• %73.6 of the patients were younger than 50 years.





## Symptoms

Post – Exertional Fatigue – <b>45</b>	Dizzir 6.2 Insomnia 6.9%		
Headache - <b>28</b>			
Myalgia - <b>26</b>			
Insomnia - <b>9</b>			
Dizziness - <b>8</b>			
Anosmia – Ageusia - <b>8</b>			
Weakness - <b>3</b>			
<b>Others: - 3</b> Forgetfulness, Syncope, Epilepsy	Myalgi 20%		





## Symptoms

- 67 % of the patients were monosymptomatic (61 out of 91)
- 33 % admissioned with multiple symptoms (30 out of 91)





- Myalgia
- Anosmia Ageusia



- Post Exertional Fatigue
- Myalgia
- Headache







### **Statistical Analysis**

	First Mean	Follow-up Mean	First Standart Dev.	Follow-up Standart Dev.	P Value
Leukocyte Count (WBC)	5.80	7.07	1.75	1.94	< 0.001
	First Min-Max	Follow-up Min-Max	First Median	Follow-up Median	P Value
CRP	0.20 - 82.71	0.20 - 75.48	3.9	0.35	< 0.001
D-Dimer	83 - 2427	27 - 395	240	118	< 0.001
Ferritin	2 - 6376	1 - 4590	86.435	48.04	< 0.001
Creatinine	0,43 - 0.8	0.54 - 1.45	0.82	0.80	= 0.017
LDH	121 - 516	97 - 325	193	186	< 0.001
Neutrophile/Lymphocyte Ratio	0.4 - 10.97	0.58 - 11	2.07	1.923	= 0.004
<b>Erythrocyte Sedimentation Rate</b>	2 - 42	2 - 33	11	5	<0.001
	First Min-Max	Follow-up Min-Max	First Median	Follow-up Median	P Value
Serum ACE Receptor	3 - 51	4 - 36	21	20.50	= 0,113
Procalcitonin	0.01 - 2.298	0.01 - 2.00	0.177	0.120	= 0.381





## **Limitations and Strenghts**

- We wanted to see if we could find a useful marker which is monitored during the routine check of the infection for Long Covid patients. More specific inflammatory markers like TNF, IL-2 and cytokines could have been beneficial.
- The results of the research are valuable and similar with the literature, but it is recommended to investigate the parameters to be used in the diagnosis and follow-up of the Long-Covid patients in a larger group with multicentre studies.
- This research is one of the few studies conducted since the beginning of the pandemic with this hypothesis and followed the patients' symptoms and blood test results. It's also valuable to reach enough follow-up patients that can be statistically evaluated.





### Discussion

### **Comparison with other Studies**

- The frequency of admission symptoms in our study was consistent with the literature. (Reported as (30%) fatigue, (44%) headache, (8%) myalgia in previous studies.)<sup>1</sup>
- Distribution of age, gender and the number of patients with multiple Long-Covid symptoms was similar with the literature. (Mean age: 39.8, 60% were younger than 40 years, Male/Female Ratio: 1.4:1, Ratio of patients with multiple symptoms: 16% in previous studies.)<sup>2</sup>
- Although the Neutrophile/Lymphocyte Ratio was reported as a predictive marker during the acute infection <sup>3</sup>, it isn't useful in Long-Covid patients' follow-up according to our research.

#### Please scan the QR codes to reach

#### the full texts of the compared studies



















### Conclusion

- Based on the data obtained, a statistically significant decrease and normalisation to the baseline were found in CRP, D-Dimer, Ferritin, Creatinine, LDH, NEU/LYM Ratio, Leukocyte count and ESR compared to the values during the first and follow-up admissions.
- ACE and Procalcitonin remain high for a longer period of time.

As a result, we found that there is no persistently elevated marker that is used during acute infection screening that can be used for the follow-up of the Long-Covid patients with neurological complaints.







# Thank you very much for your interest...

Kerim Ferhatoğlu

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