

# COVID-19 Cytokine Storm Biomarkers. Comorbidities and Outcomes in Hemodialysis Patients

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## Abstract

Markers of inflammation and thrombosis have been well documented in patients with Covid-19. In parallel to it muscle markers of heart muscle can occur concomitantly in the case of kidney injury. The aim of the study was to investigate associations of the markers in Covid-19 patients and find out the connections among them as well as with their other parameters. A total of 536 seriously affected Covid-19 patients were admitted to a tertiary hospital from February to September 2020. Their mean age was 63,4 years, being 61 percent male and on hemodialysis. Their clinical, anthropometric, laboratory values and therapies were the basis for the construction of a data bank with 16700 informations. Statistical analysis was performed on the R system, due to the large size of data and for the sake of correlations being done among all the measurements. Having Creatin Kinase as reference variable, in descending order, the associations were with MB Creatin Kinase, C Reactive Protein, Creatinine, D Dimer, Lactic Dehydrogenase, Diabetes, Body Mass Index, Fibrinogen and Hypertension. When the marked variable was Troponin associations were MB Creatin Kinase, Lactic Dehydrogenase, D Dimer, Creatin Kinase, Diabetes, Fibrinogen, Creatinine, Dyslipidemia, C Reactive Protein, Body Mass Index, Race, Hypertension and Statin use. Associations of muscle markers as Troponin and Creatin Kinase were found with all inflammation and thrombosis markers as well as factors such as Race, Diabetes, Hypertension, Dyslipidemia, Body Mass Index and Statins are interrelated in Covid-19 infection. The large spectrum of concomitant alterations caused by the same disease demonstrates that these factors are not altered independently but by one and the same infectious agent. Patients on dialysis showed the same pattern of biomarkers as the overall of Covid-19 patients in the Intensive Care Unit.

**Keywords:** Covid-19; Cytokine storm biomarkers; Comorbidities; Hemodialytics; Inflammation; Thrombosis; Intensive care; Diabetes; Hypertension

**Abbreviations:** BMI - Body Mass Index; CK - Creatin Kinase; CRP - C Reactive Protein; ICU - Intensive Care Unit; LD - Lactic Dehydrogenase; MBCK - MB Creatin Kinase

## Introduction

Biomarkers of inflammation and thrombosis have been well documented in patients with Covid-19. Recent publications point to studies of the muscle markers Troponin and Creatine Kinase in Covid-19 patients and find out the associations among them as well as with all the available laboratory data that can interfere with them.

## Objective

Evaluation of the association of inflammatory, thrombogenic and cardiac muscle injury parameters in patients with severe Covid-19 and comorbidities evolution hospitalized in Intensive Care Units (ICU) of a tertiary hospital in São Paulo, being a significant proportion of them on hemodialysis [1-5].

## Method

From February 20, 2020 to September 20 of the same year, 536 COVID-positive patients were admitted to the ICU of a tertiary hospital in a private public system. All identification data, clinical, anthropometric, laboratory, therapeutic procedures and discharge conditions

were recorded by the Tasy system. A database was assembled from it, and 63 parameters were recorded for their correlation and association, and in the present study the highlight focused on the inflammatory marker C Reactive Protein (CRP), thrombogenic and its associates D Dimer, Lactic Dehydrogenase (LD) and Fibrinogen, as well as those of general and cardiac muscle injury Creatin Kinase (CK), MB Creatin Kinase (MBCK) and Troponin. Due to the size of the database and the hypotheses to be searched, the R System was used for statistical calculations, using both the data tree and the classifications in bar charts.

**Result**

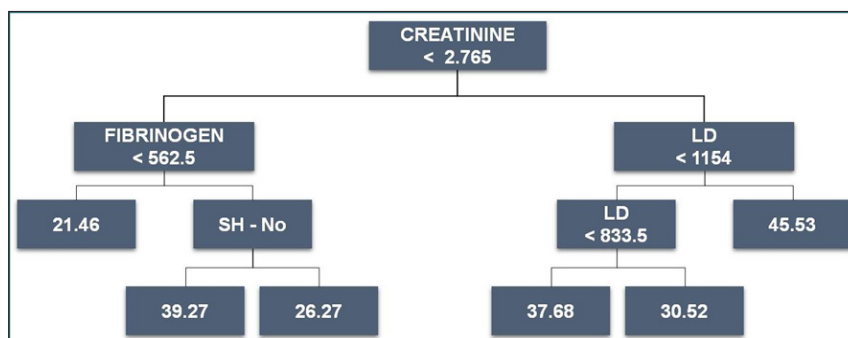
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**Table 1:** Average demographics - first five months\*.

		General		Acute Kidney Disease		Chronic Kidney Disease		Transplant		No Nephrological Complication	
Total patients		354		132		132		16		188	
Average age		63		66		66		53		60	
Hospital stay		19		26		26		27		14	
Intensive Care Unit stay		12		20		20		13		7	
		N	%	N	%	N	%	N	%	N	%
Group	< 60	150	41	39	30	39	30	10	63	95	51
	61 - 80	159	44	73	55	73	55	6	38	64	34
	> 80	54	15	20	15	20	15	0	0	29	15
Sex	Female	141	39	41	31	41	31	5	31	84	45
	Male	222	61	91	69	91	69	11	69	104	55
Race	Yellow	6	2	2	2	1	4	0	0	3	2
	White	225	62	85	64	19	70	12	75	109	58
	Indigenous	1	0	1	1	0	0	0	0	0	0
	Not informed	37	10	14	11	2	7	0	0	21	11
	Black	18	5	7	5	1	4	1	6	9	5
	Brown	76	21	23	17	4	15	3	19	46	24

\*Both groups studied until July 20 and until September 20 were homogeneous.



**Figure 1:** LD-Lactic Dehydrogenase; SH-Systolic Hypertension. Results in Tree Format: Reference Parameter C Reactive Protein.

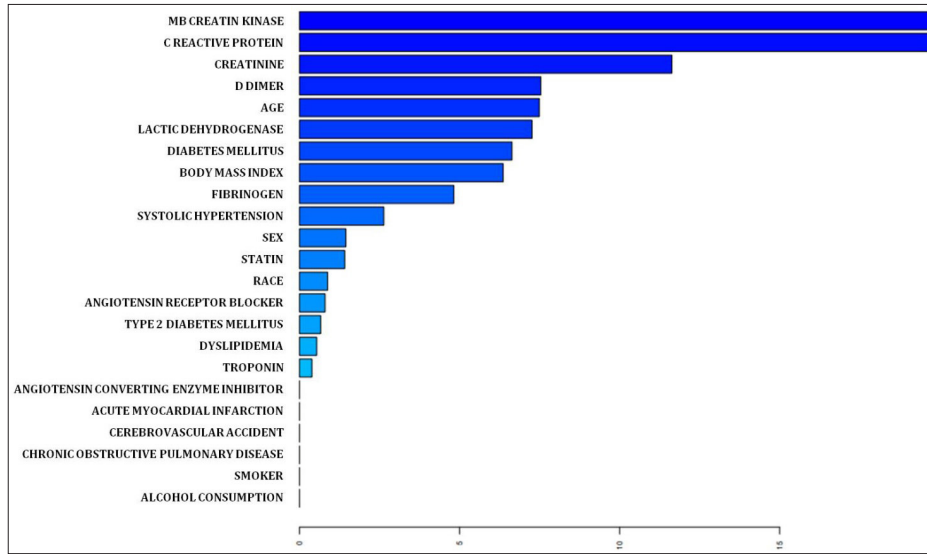


Figure 2: Cytokine Storm-Creatin Kinase parameter reference.

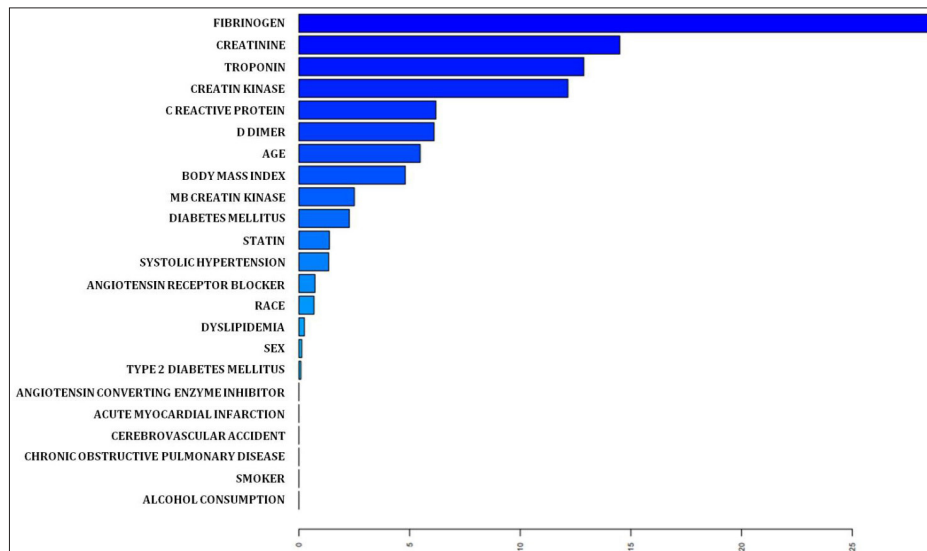


Figure 3: Cytokine Storm-Troponin parameter reference.

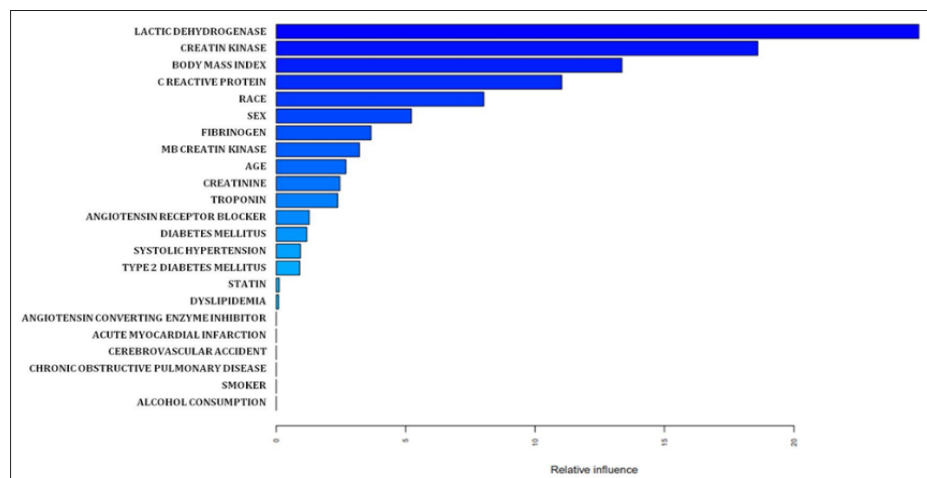
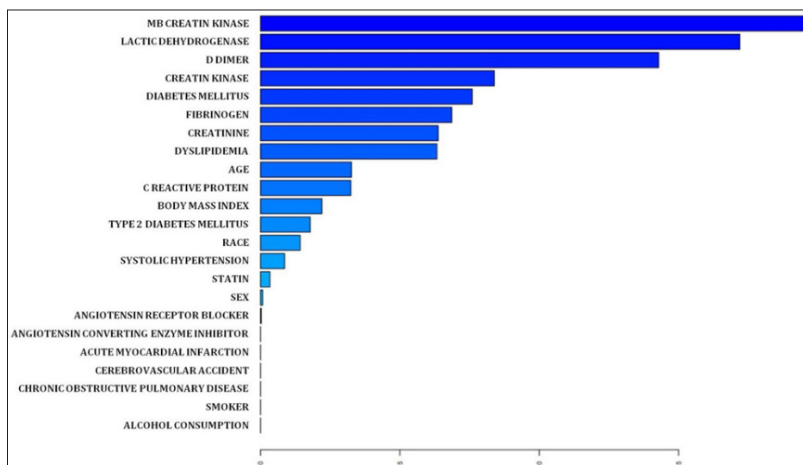


Figure 4: Cytokine Storm-Lactic Dehydrogenase parameter reference.



**Figure 5:** Cytokine Storm-D Dimer Parameter reference.

**Table 2:** Degree of pulmonary area affected and hemodialysis patients.

Dyalysis	Pulmonary Involvement (% area)				Normal
	< 25	25-50	50-75	> 75	
No	69	0	0	0	34
Yes	28	0	0	3	16

**Table 3:** Degree of pulmonary area affected and number of hemodialysis patients in each subgroup.

	Pulmonary Involvement (% area)				Normal
	< 25	25-50	50-75	> 75	
Acute Renal Insufficiency	28	0	0	2	15
Chronic Kidney Failure	10	0	0	1	7
No Kidney Disease	59	0	0	0	28

**Table 4:** Destiny of acute kidney disease patients on hemodialysis after discharges from Intensive Care Unit.

Home	Primary Ward	Origin Clinic	Hospital Ward	Death
204	22	2	30	103
56,2%	6,1%	0,6%	8,3%	28,4%

**Table 5:** Destiny of renal patients not on hemodialysis after discharges from Intensive Care Unit.

Home	Primary Ward	Origin Clinic	Hospital Ward	Death
152	10	2	11	13
80,9%	5,3%	1,1%	5,9%	6,9%

Tables 2 & 3 demonstrate that the outcome raises the hypothesis of association of the pulmonary area affected with pulmonary congestion and not linearly correlated to the area, despite some authors having observed the contrary [6]. It is important to note that although hypertension comorbidity was the more prevalent, diabetes comorbidity that came next had the worst death rate than

hypertension surpassing it in the range of 30%. Although there were no means of estimating by laboratory methods it must be mentioned that the interrelations of alteration of biomarkers induced by the Covid-19 infection is possibly mediated by Covid-19 repression of the anti-aging gene that is critical to programmed cell death [7]. All parameters researched in positive Covid-19 hemodialytic patients [8-11] admitted to the ICU present concomitance of laboratory evaluators of inflammation, thrombotic risk and skeletal and tissue muscle injury, which indicates the need for anti-inflammatory and anti-thrombotic therapies among all others.

**Conclusion**

Associations of muscle markers as Troponin and CK were found with all inflammation and thrombosis markers as well as factors such as, Diabetes, Hypertension, Dyslipidemia, BMI and Race mainly are found in Covid-19 infection. Considering the demographic distribution of severe Covid-19 patients special attention has to be given to the diabetics mortality rate in spite of hypertension being the more prevalent comorbidity in all reports.

The large spectrum of concomitant alterations caused by the same disease demonstrates that these factors are not altered independently but by one and the same infectious agent. Patients on dialysis demonstrated similar patterns of laboratory biomarkers of inflammation, thrombosis and muscle injury as the overall of Covid-19 patients admitted to the Intensive Care Unit.

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