

# Is There a Role for the Early Use of Tocilizumab and Interleukin-6 Levels in the Management of SARS-CoV-2 Patients with Early Respiratory Failure?

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## INTRODUCTION

Respiratory failure in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection appears related to cytokine release syndrome (CRS) that often results in mechanical ventilation (MV). We investigated the role of tocilizumab (TCZ) on interleukin-6 (IL-6) trends and MV in SARS-CoV-2 patients

## METHODS

In this longitudinal observational study, 112 patients were evaluated from 2/1/2020 - 5/31/2020. TCZ was administered followed by methylprednisolone to patients with > 3L oxygen (O2) requirement and pneumonia severity index (PSI) score ≤ 130 with CT scan changes. IL-6, C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), D-dimer, and procalcitonin were monitored on days 0, 3, and 6 of therapy. Statistical analyses were performed with significance ≤ 0.05.

## RESULT

80/112 SARS-CoV-2-positive patients (45 males, 56.96%; 34 females, 43.04%) were included in this study. Seven patients expired (8.75%) and nine patients required MV (11.25%). Median IL-6 levels pre-administration of TCZ was 342.50 (78.25 - 666.25) pg/mL compared to post-administration on day 3 (563; 162 - 783) pg/mL ( $P < 0.00001$ ). On day 6, the median dropped to 545 (333.50 - 678.50) pg/mL compared to day 3 ( $P = 0.709$ ). CRP, ferritin, LDH, and D-dimer levels were reduced following TCZ therapy.

# The sequential use of methylprednisolone for 72 hours following tocilizumab seems to potentiate the effect and prolong the suppression of the cytokine storm in SARS-CoV-2.

## IL-6 levels may be helpful as a prognostic tool.



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**TABLE 1: Clinical outcomes among SARS-CoV-2 patients treated with TCZ**

Clinical outcomes	Frequency (n = 80)	Percentage (%)
Mortality		
Yes	7	8.75
No	73	91.25
Use of mechanical ventilation		
Yes	9	11.25
No	71	88.75

Abbreviations: n, number of patients; %, percentage of patients; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TCZ, tocilizumab.

**TABLE 2: Interleukin-6 (IL-6) levels of SARS-CoV-2 patients before and after TCZ treatment**

Variables	Days	Median (IQR)	Wilcoxon signed rank	P value
IL-6	IL-6 d 0 (pre)	342.50 (78.25-666.25)	5.022	<.00001*
	IL-6 d 3 (post)	563.00 (162-783)		
	IL-6 d 0 (pre)	342.50 (78.25-666.25)	2.750	
	IL-6 d 6 (post)	545 (333.50-678.50)		
	IL-6 d 3 (post)	563.00 (162-783)	0.374	
	IL-6 d 6 (post)	545 (333.50-678.50)		

Note: IL-6, normal 0.0-12.2 (pg/mL)  
Abbreviations: IQR, interquartile range; (pre), before TCZ use; (post), after TCZ use; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TCZ, tocilizumab.  
\*Statistically significant ( $P \leq .05$ ).

**TABLE 3: Laboratory findings of SARS-CoV-2 patients at before and after TCZ treatment**

Variables	Days	Median (IQR)	Wilcoxon signed rank	P value
C-reactive protein (CRP)	CRP day 0 (pre)	11 (6-18.75)	5.720	<.00001*
	CRP day 3 (post)	5 (2-13)		
	CRP day 0 (pre)	11 (6-18.75)	6.744	
	CRP day 6 (post)	2 (1-4)		
	CRP day 3 (post)	5 (2-13)	6.362	
	CRP day 6 (post)	2 (1-4)		
Ferritin	Ferritin day 0 (pre)	595 (311.25-1022.50)	0.003	.998
	Ferritin day 3 (post)	558 (368-1009)		
	Ferritin day 0 (pre)	595 (311.25-1022.50)	3.225	
	Ferritin day 6 (post)	432.50 (234-676)		
	Ferritin day 3 (post)	558 (368-1009)	4.536	
	Ferritin day 6 (post)	432.50 (234-676)		
Lactate dehydrogenase (LDH)	LDH day 0 (pre)	364 (278-543)	0.969	.333
	LDH day 3 (post)	366 (265-502)		
	LDH day 0 (pre)	364 (278-543)	2.645	
	LDH day 6 (post)	328 (234-432)		
	LDH day 3 (post)	366 (265-502)	3.280	
	LDH day 6 (post)	328 (234-432)		
D-dimer	D-dimer day 0 (pre)	1.065 (0.65-2.3)	0.321	.748
	D-dimer day 3 (post)	1.2 (0.92-2.05)		
	D-dimer day 0 (pre)	1.065 (0.65-2.3)	1.426	
	D-dimer day 6 (post)	1.2 (0.66-1.84)		
	D-dimer day 3 (post)	1.2 (0.92-2.05)	2.080	
	D-dimer day 6 (post)	1.2 (0.66-1.84)		

Note: CRP, normal <8.0 (mg/L); ferritin, normal 12 to 300 for males, 12-150 for females (ng/mL); LDH, normal 109 to 245 (U/L); D-dimer, normal <0.5 (mcg/mL).  
Abbreviations: (pre), before TCZ use; (post), after TCZ use; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TCZ, tocilizumab.  
\*Statistically significant ( $P \leq .05$ ).