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COMPARISON OF EPIDEMIOLOGICAL AND CLINICAL PARAMETERS IN PATIENTS WITH SEVERE COVID-19 TREATED WITH AND WITHOUT TOCILIZUMAB

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Abstract

Cytokine storm is an uncontrolled immune response in the immunopathogenic mechanism of COVID 19, similar to that of severe influenza. Inflammatory cytokines including: TNF-α, IL-6, IL-8, IL-12, are released in large amounts during of disease progression, causing potential Acute Respiratory Distress Syndrome (ARDS), Hemophagocytic Lymphohistiocytosis (HLH) and Multi-Organ Dysfunction (MOFS).

Tocilizumab is an immunosuppressive drug that is used in the treatment of Rheumatoid Arthritis and Systemic Juvenile Idiopathic Arthritis in children. As a human monoclonal antibody targeting Interleukin 6 receptors (IL-6R), it interrupts its action in the cytokine storm and thereby reduces vascular permeability and increased passage of fluid and blood elements into the alveoli that would lead to severe respiratory distress (ARDS).

Objectives: To evaluate the effect of Tocilizumab treatment in patients with severe form of COVID-19

Materials and methods: This retrospective study included 213 patients with a severe form of COVID-19 divided into 2 groups: Group 1 of 131 male and female patients who received Tocilizumab and Group 2 of 82 male and female patients who did not receive tocilizumab.

Results: Patients who received tocilizumab had a significantly shorter stay in the intensive care unit compared to patients who did not received tocilizumab (p=0.021).
A significantly lower mortality was registered in patients who were treated with Tocilizumab .

Conclusion: This retrospective case control study showed that treatment with Tocilizumab as a human monoclonal antibody in patients with severe form of COVID-19 can lead to shorter hospital stay and reduced mortality compared to patients who did not receive Tocilizumab.

Keywords: Cytokine storm, Tocilizumab, COVID 19, Interleukin 6, ARDS.

Introduction

The beginnings of COVID-19 was in December 2019, with the appearance of the first infected people in the city of Wuhan, Hubei District in N.R. China. The disease gets a pandemic character and quickly leads to 48,539,872 infected people and causes 1,232,791 deaths in 215 countries of the world, leading to a global health and economic collapse of the world population. [1].

On March 11, 2020, the World Health Organization declared COVID-19 as a pandemic disease. Cytokine storm is an uncontrolled immune response in the immunopathogenic mechanism of COVID 19, similar to that of severe influenza. Inflammatory cytokines including: TNF-α, IL-6, IL-8, IL-12, are released in large amounts during disease progression, causing potential Acute Respiratory Distress Syndrome (ARDS), Hemophagocytic Lymphohistiocytosis (HLH) and Multiorganic Failure Syndrome (MOFS). Elevated IL-6 values are associated with severe prognosis in patients with COVID-19.

Moderately elevated IL-6 levels above 80 pg/ml have been confirmed to be adequate to identify COVID-19 patients at high risk of respiratory failure [2].

Tocilizumab is a human IgG 1 monoclonal antibody capable of interfering with interleukin 6 (IL-6) and binding to the soluble membrane receptor (IL-6R), thereby blocking the formation of an activated complex with the transmembrane protein (gp130- IL-6-sILr). Tocilizumab also has the ability to block

IL-6 trans-signalisation, which is associated with the pro-inflammatory effects of IL-6 (such as the release of acute phase proteins). As a drug, it is primarily used in the treatment of Rheumatoid Arthritis, Systemic Juvenile Idiopathic Arthritis and polyarticular juvenile idiopathic arthritis[3].

Considering the role of IL-6 in the pathogenesis of COVID-19, the mechanism of the cytokine storm and its role as a prognostic factor for the severity of the disease and survival of patients with COVID-19, tocilizumab as a blocker of IL-6 receptors provides hope for preventing or controlling the cytokine storm and the complications that arise from it.

Objective*:* To evaluate the effect of Tocilizumab treatment in patients with severe form of COVID-19.

Materials and methods

This is a case-control study, who was conducted in the infectious disease (Covid) department at the Acibadem Sistina clinical hospital in the period from November 2020 to February 2022.

The study includes 213 patients with severe form of COVID-19 aged from 34 to 86 years , divided into 2 groups:

- A case group of 131 patients with severe COVID-19 who received Tocilizumab during hospitalization in intensive care unit.
- Control group of 82 patients with severe form of COVID-19 who did not receive Tocilizumab during hospitalization in intensive care unit.

Criteria for severe form of COVID-19 [4]

• Severe pneumonia

• Signs of severe respiratory distress (Use of accessory respiratory muscles, inability to pronounce a complete sentence, respiratory rate >30/min.)

• Spo2 < 90% on ambient air.

1. Patient data are obtained from:

• Questionnaires filled in by the patients or their families, data from the medical documentation for stay in another COVID center and the therapy received there.

• From the electronic system CEREBRAL+ of the Acibadem Sistina Hospital, which contains all the medical data for the treated patients.

Patient follow-up is up to 40 days, whichever occurs first, such as discharge or death.

Treatment

All patients from this study were treated with antibiotic, antiviral, antifungal, corticosteroid therapy with a gradual reduction of doses according to the protocol.

Oxygen therapy such as: OM- Oxygen mask with a flow of 10-15 l/min, HFO-High flow oxygenation with a flow of 50-75 l/min, NIV-Non-invasive mechanical ventilation and MV-Mechanical ventilation. Anticoagulant therapy with low molecular weight heparin or Heparin continuously on a perfusor , depending on the D Dimer values and consultation with a Transfusiologist. Gastroprotective, hepatoprotective therapy, diuretics, inhalations, intravenous fluids and other supportive and symptomatic therapy. 131 patients were treated with the human monoclonal antibody Tocilizumab (Actemra).

Results

213 respondents participated in the research, patients from the Acibadem Sistina Clinical Hospital with a severe form of COVID 19.

The gender structure of the patients consisted of 142 (66.67%) male and 71 (33.33%) female patients. The age of the patients ranged from 34 to 86 years, the average age was 62.8±11.4 years. **(Table 1)**

Table 1 Patient characteristics

variable	**n (%)**
Gender	
male	142 (66.67)
female	71 (33.33)
Age/years (mean±SD) (min – max)	(62.82 ± 11.4) (34 – 86)

In this series of patients with severe form of COVID 19, 131 (61.5%) patients received tocilizumab.

92(64.79%) male and 39(54.93%) female patients received tocilizumab, 50(35.21%) male and 32(39.02%) female patients did not.

The gender structure of patients receiving and not receiving tocilizumab was homogeneous, so the tested difference in the distribution of male and female patients between the groups with and without prescribed tocilizumab was statistically insignificant (p=0.16) **(Table 2).**

Table 2. Gender distribution of patients / group with and without tocilizumab

Gender	**tocilizumab**			**p-level**
	n	received n(%)(131)	not received n (%) (82)	
male	142	92 (70.23)	50 (60.98)	X^2=1.9 p=0.16
female	71	39 (29.77)	32 (39.02)	

X^2 (Pearson Chi-square)

Patients who received tocilizumab had a mean age of 62.1 ± 10.9 years, the mean age of patients who did not receive tocilizumab was 63.9 ± 12.1 years.

The age of patients from the groups with and without tocilizumab was statistically insignificantly different (p=0.27), **(Table 3).**

Table 3. Mean values of age / group with and without tocilizumab

Age years	**tocilizumab**		**p-level**
	received	not received	
mean ±SD	62.1 ± 10.9	63.9 ± 12.1	t=1.1
min- max	34 – 83	35 – 86	p=0.27

t(Student t-test)

Patients with a severe form of COVID 19 admitted from home were treated with tocilizumab more often than patients admitted from another hospital – 78 (66.10%) versus 53 (55.79%). No statistically significant difference was found in the distribution of patients admitted from home or from another hospital depending on whether they received/did not receive tocilizumab (p=0.12). **(Table 4).**

Table 4. Distribution by place of admission / group with and without tocilizumab

Admission from :	**tocilizumab**			**p-level**
	n	received n (%) (131)	not received n (%) (82)	
Home	118	78 (59.54)	40 (48.78)	X^2=2.4 p=0.12
Another hospital	95	53 (40.46)	42 (51.22)	

X^2 (Pearson Chi-square)

Tocilizumab received 116 (64.81%) unvaccinated patients against COVID-19 and 15 (44.12%) vaccinated patients. 63 (35.19%) unvaccinated and 19 (55.88%) vaccinated patients did not receive tocilizumab. For p=0.023, a statistically significant difference was confirmed in the distribution of vaccinated and unvaccinated patients between the groups that received/did not receive tocilizumab. Unvaccinated patients were significantly more likely to receive this type of therapy. **(Table 5).**

Table 5. Distribution according to vaccination status / group with and without tocilizumab

Vaccine	**tocilizumab**			**p-level**
	n	received n (%) (131)	not received n (%) (82)	
no	179	116 (88.55)	63 (76.19)	X^2=5.2 *p=0.023
yes	34	15(11.45)	19(23.17)	
Sputnik	2	1	1	
Sinopharm	15	7	8	
Astrazeneca	4	2	2	
Pfizer	9	4	5	
Johnson&Johnson	1	1	0	
Moderna	1	0	1	
Sinovac	2	0	2	

X^2 (Pearson Chi-square); *p<0.05

Patients who received tocilizumab had a significantly shorter stay in the intensive care unit compared to patients who did not (p=0.021).

Patients who received tocilizumab stayed in the intensive care unit on average 11.5±6.6 days, patients who did not receive stayed on average 13.0±6.6 days.

Half of the patients who received tocilizumab were in the intensive care unit for more than 10 days (median=10), half of the patients who did not received tocilizumab therapy were in the intensive care unit for more than 12 days (median=12). **(Table 6).**

Table 6. Length of ICU stay / group with and without tocilizumab

Days of ICU stay	**tocilizumab**		**p-level**
	received	not received	
n	131	82	Z=2.3
mean ±SD	11.46 ± 6.6	13.01 ± 6.6	*p=0.021
min- max	2 – 40	2 – 37	
median (IQR)	10 (7 – 13)	12 (8 – 16)	

Z(Mann-Whitney U Test);*p<0.05

The average length of hospitalization was 13.0 ± 7.3 days in the group of patients who received tocilizumab, 14.5 ± 7.2 days in the group of patients without tocilizumab therapy. The median length of hospitalization was 11 days and 13 days, respectively, in the groups of patients receiving and not receiving tocilizumab. Days of hospital stay were non-significantly shorter for patients who received tocilizumab compared to patients who did not (p=0.069)**.(Table 7).**

Table 7. Length of hospitalization / group with and without tocilizumab

Days of hospital stay	**tocilizumab**		**p-level**
	received	not received	
mean ±SD	13.0 ± 7.3	14.5 ± 7.2	Z=1.8
min- max	4 – 42	4 – 37	p=0.069
median (IQR)	11 (8 – 16)	13 (10 – 18)	

Z(Mann-Whitney U Test)

Tocilizumab was received by 50 (48.08%) surviving and 81 (74.31%) deceased patients with a severe form of COVID-19. 54 (51.92%) surviving and 28 (25.69%) deceased patients were not treated with tocilizumab.

The tested difference in the distribution of surviving and deceased patients with a severe form of COVID-19 between the groups receiving/not receiving tocilizumab was statistically significant (p=0.00008).

A significantly lower mortality was registered in patients who were placed on tocilizumab therapy. – 50(38.17%) versus 54(65.85%). **(Table 8).**

Table 8. Distribution by deceased / group with and without tocilizumab

Exitus letalis	**tocilizumab**			**p-level**
	n	received n (%) (131)	not received n (%) (82)	
yes	104	50 (38.17)	54 (65.85)	X^2=15.5
no	109	81 (61.83)	28 (34.15)	***p=0.00008

X^2 (Pearson Chi-square); ***p<0.0001

Patients on oxygen mask significantly more often than patients without an oxygen mask received tocilizumab (p=0.00059).

In the oxygen mask group, 71 (73.96%) patients received tocilizumab, 25 (26.04%) patients did not; in the group without oxygen mask 59(50.86%) patients received tocilizumab, 57(49.14%) patients did not. **(Table 9).**

Table 9. Distribution according to frequency of Oxygen mask use / group with and without tocilizumab

OM	**tocilizumab**			**p-level**
	n	received n (%) (130)	not received n (%) (82)	
yes	116	59 (50.86)	57 (49.14)	X^2=11.81 **p=0.00059
everyone else	96	71 (73.96)	25 (26.04)	

X^2 (Pearson Chi-square); **p<0.001

Patients who received and patients who did not receive tocilizumab did not differ significantly in terms of length of oxygen mask use (p=0.57).The mean number of days on an oxygen mask was 5.5 ± 3.9 and 4.7 ± 2.9, respectively, in the tocilizumab and non-tocilizumab groups; 50% of patients from both groups were on an oxygen mask for longer than 5 days (median=5). **(Table 10).**

Table 10. Length of Oxygen mask use / group with and without tocilizumab

OM total days	**tocilizumab**		**p-level**
	received	not received	
n	71	25	Z=0.56 p=0.57
mean ±SD	5.5 ± 3.9	4.7 ± 2.9	
min- max	1 – 24	1 – 12	
median (IQR)	5 (3 – 7)	5 (2 – 7)	

Z(Mann-Whitney U Test)

Tocilizumab was received by 96 (60%) patients in whom high-flow oxygenation was used and 34 (65.38%) patients who were not placed on high-flow oxygenation. No statistically significant difference was found in the distribution of patients with and without high-flow oxygenation between the groups receiving/not receiving tocilizumab (p=0.49). **(Table 11).**

Table 11. Distribution according to frequency of use of HFO / group with and without tocilizumab

HFO	**tocilizumab**			**p-level**
	n	received n (%) (130)	not received n (%) (82)	
yes	52	34 (26.15)	18 (21.95)	X^2=0.5 p=0.49
everyone else	160	96 (73.85)	64 (78.05)	

X^2 (Pearson Chi-square)

Patients who received tocilizumab were on high-flow oxygenation for a nonsignificantly shorter time compared to patients who did not (p=0.2). Patients who received and did not receive tocilizumab, on high-flow oxygenation averaged 5.5 ± 4.2 and 6.1 ± 4.1 days, respectively; 50% of patients from both groups were on high-flow oxygenation for longer than 5 days (median=5). **(Table 12).**

Table 12. Length of HFO use / group with and without tocilizumab

HFO total days	**tocilizumab**		**p-level**
	received	not received	
n	96	64	Z=1.3
mean ±SD	5.5 ± 4.2	6.1 ± 4.1	p=0.2
min- max	1 – 21	1 – 19	
median (IQR)	5 (2 – 7)	5 (4 – 8)	

Z(Mann-Whitney U Test)

The difference in the distribution of patients with and without non-invasive mechanical ventilation between the groups receiving/not receiving tocilizumab was statistically insignificant (p=0.57). Patients placed on non-invasive mechanical ventilation were treated with tocilizumab insignificantly less frequently compared to patients in whom this method was not used. – 63(59.43%) versus 67(63.21%). **(Table 13)**

Table 13. Distribution according to frequency of use of NIV / group with and without tocilizumab

NIV	**tocilizumab**			**p-level**
	n	received n (%) (130)	not received n (%) (82)	
yes	106	67 (63.21)	39 (36.79)	X^2=0.32 p=0.57
everyone else	106	63 (59.43)	43 (40.57)	

X^2 (Pearson Chi-square)

Patients who received and patients who did not received tocilizumab did not differ significantly in terms of length of use of non-invasive mechanical ventilation (p=0.52).

The mean number of days on an oxygen mask was 4.3 ± 3.4 and 3.6 ± 2.4, respectively, in the tocilizumab-treated and non-treated groups; 50% of patients from both groups were on non-invasive mechanical ventilation for longer than 3 days (median=3). **(Table 14)**

Table 14. Length of NIV use / group with and without tocilizumab

NIV total days	**tocilizumab**		**p-level**
	received	not received	
n	63	43	Z=0.65
mean ±SD	4.3 ± 3.4	3.6± 2.4	p=0.52
min- max	1 – 16	1 – 11	
median (IQR)	3 (2 – 6)	3 (1 – 5)	

Z(Mann-Whitney U Test)

Patients on mechanical ventilation received tocilizumab significantly less often than patients in which mechanical ventilation was not indicated (p=0.021).

Tocilizumab was received by 57 (53.77%) patients on mechanical ventilation and 72 (69.23%) patients in which mechanical ventilation was not used; 49(46.23%) intubated and 32(30.77%) non-intubated patients did not receive tocilizumab. **(Table 15)**

Table 15. Distribution according to frequency of use of MV / group with and without tocilizumab

MV	tocilizumab			p-level
	n	received n (%) (130)	not received n (%) (82)	
yes	104	72 (69.23)	32 (30.77)	X^2=5.29 p=0.021
everyone else	106	57 (53.77)	49 (46.23)	

X^2 (Pearson Chi-square)

Patients who received tocilizumab were on mechanical ventilation for a non-significantly shorter time compared to patients who did not (p=0.0091). Patients who received tocilizumab on mechanical ventilation were on average 3.8 ± 3.5 days, half of them longer than 3 days (median=3); patients not receiving tocilizumab on mechanical ventilation were on average 6.6 ± 6.7 days, half of them longer than 5 days (median=3);**(Table 16).**

Table 16. Length of MV use / group with and without tocilizumab

MV total days	tocilizumab		p-level
	received	not received	
n	57	49	Z=2.6
mean ±SD	3.8 ± 3.5	6.6 ± 6.7	p=0.0091
min- max	1 – 14	1 – 32	
median (IQR)	3 (1 – 5)	5 (2 – 7)	

Z(Mann-Whitney U Test)

The type of end-oxygen and ventilatory support was significantly different between patients receiving and not receiving tocilizumab (p=0.001). Most of the patients that received Tocilizumab were on an oxygen mask - 69 (75%) and didn't require mechanical ventilation, followed by patients that required high flow oxygenation - 5 (62.5%), and the least number of patients that ended on mechanical ventilation - 56 (50%).

Patients on oxygen mask significantly more often than patients on mechanical ventilation were treated with tocilizumab (p=0.0003). **(Table 17).**

Table 17. Distribution of patients by type of completed treatment/group with and without tocilizumab

completed on	tocilizumab			p-level
	n	received n (%) (131)	not received n (%) (82)	
OM-Oxygen mask	92	69 (75)	23 (25)	Fisher's exact **p=0.001
HFO-High flow oxygenation	8	5 (62.5)	3 (37.5)	
MV-Mechanical ventilation	112	56 (50)	56 (50)	OM vs MV X^2=13.3 **p=0.0003

X^2 (Pearson Chi-square); **p<0.001

Extracorporeal membrane oxygenation was indicated in 5 patients, of whom 3 (60%) were treated with tocilizumab. In the group of patients in whom extracorporeal membrane oxygenation was not applied, 128 (61.54%) were treated with tocilizumab.

Tocilizumab therapy had a similar frequency in patients with and without extracorporeal membrane oxygenation, ie non-significantly different (p=0.94). **(Table 18)**

Table 18. Frequency distribution of ECMO use / group with and without tocilizumab

ECMO	**tocilizumab**			**p-level**
	n	received n (%) (130)	not received n (%) (82)	
yes	5	3 (60)	2 (40)	X^2=0.0049
no	208	128 (61.54)	80 (38.46)	p=0.94

X^2 (Pearson Chi-square)

Discussion

The rapid spread of COVID-19 brought severe healthcare and economy strains and substantial morbidity and mortality globally. ARDS and disseminated intravascular coagulation, from uncontrolled inflammatory processes after SARS-CoV-2 infection were the major cause of death. [5].

SARS-CoV-2 invades airway epithelial cells evading the secretion of type I and III interferon as a first line defense to inhibit virus replication [6].

Instead, IL-6 and other pro-inflammatory cytokines are produced from the infected epithelial cells attracting monocytes and cytotoxic T cells to the infection site and macrophages to engulf the apoptotic cells through phagocytosis. In healthy responses, SARS-CoV-2 infections are resolved through this process, the level of inflammatory cytokines recedes, and patients recover [7].

In severely affected COVID-19 patients, however, excessive secretion of IL-6 and other pro-inflammatory cytokines summon T cell aggregation and cause T cell functional exhaustion, and activates signaling pathways that further increase the release of IL-6 and other chemokines, which forms a positive feedback loop that further fuels hyperinflammation , vascular permeability pulmonary edema and ARSD [8].

The cytokine storm also damages the vascular endothelium, which activates coagulation caskade, triggering a hypercoagulable status in COVID-19 patients [9]. It has been well-recognized that COVID-19-induced cytokine storm is a critical contributor to COVID-19 relevant mortality [8].

Given the significance of IL-6 in COVID-19 induced cytokine storm in disease progression and mortality, it is suggested to target hyperinflammation during SARS-CoV-2 infection via the blockage of IL-6. Tocilizumab as a competitive inhibitor of both the membrane-bound and soluble IL-6 receptor, prevents downstream signal transduction of IL-6. Early reports of tocilizumab treatment in COVID-19 patients showed promising results [10, 11].

In this retrospective case control study significantly lower mortality was registered in patients treated with Tocilizumab compared to patients not treated with the same drug. Tocilizumab-treated

patients had a significantly shorter intensive care unit stay compared to patients who did not receive tocilizumab. Patients who were not vaccinated against the SARS CoV 2 virus were significantly more often on treatment with Tocilizumab, compared to vaccinated patients.

Klopfenstein. T et al. [12] in a retrospective Case Control study in which they included 20 patients treated with tocilizumab and 25 with standard therapy, without statistical difference in terms of gender, age and comorbidities.

This study, despite the small number of subjects, showed that deaths and/or admissions in ICUs were higher in patients without tocilizumab than in the tocilizumab group (72% vs. 25%, P=0.002).

In a subsequent observational study Capra, R. et al. [13] included 85 patients of which 23 were treated with standard therapy compared to 62 patients treated with Tocilizumab and standard therapy. Whereas 92% of patients in the tocilizumab group and 42.1% of patients in the standard group were cured.

Respiratory function was improved in 64.8% of patients treated with Tocilizumab, while in 100% of untreated patients respiratory function worsened and they needed mechanical ventilation.

In our study the type of end-oxygen and ventilatory support was significantly different between patients receiving and not receiving tocilizumab (p=0.001). Most of the patients that received Tocilizumab were on an oxygen mask and didn't have the need for NMV, HVO or IMV - 69 (75%), followed by patients that required high flow oxygenation - 5 (62.5%), and the least number of patients that ended on mechanical ventilation - 56 (50%). Patients on oxygen mask significantly more often than patients on mechanical ventilation were treated with tocilizumab (p=0.0003).

Patients receiving tocilizumab were shorter on MV compared to MV patients not receiving tocilizumab. That is 3.8 ± 3.5 days - half of them longer than 3 days compared to 6.6 ± 6.7 days - half of them longer from 5 days.

Similar reports of tozilizumab on reduced need of intubation and mechanical ventilation are reported in other studies. This has significant implication in resources planning given the fact that there was a shortage of ICU beds and respirators during the pandemic. Menzella, F. et all in their study included seventy-nine consecutive patients with severe COVID-19 pneumonia and worsening acute respiratory failure (ARF). All patients were had elevated CRP and IL-6 levels and received NIV at admission according to the presence of a pO_2/FiO_2 ratio ≤ 200 mmHg. The probabilities of dying and being intubated during the follow-up using Kaplan-Meier method were significantly lower in total patients treated with TCZ compared to those of patients not treated with TCZ (log-rank p value = 0.006 and 0.036, respectively)[14].

Giovanni Guaraldi et al. [15], in their retrospective cohort study in which 365 patients received standard therapy compared with 179 patients treated with Tocilizumab.

Tocilizumab treatment was associated with a reduced risk of mechanical ventilation and death compared to patients who received standard therapy alone.

However, 13% of patients treated with Tocilizumab compared to 4% of patients who received standard therapy developed a new infection, which we did not take that analyses in our study.

A cohort study [16] examining the effect of Tocilizumab treatment in patients with a severe form of COVID-19 placed on mechanical ventilation included 154 patients, 78 of whom were treated with Tocilizumab and 76 without Tocilizumab treatment. Although tocilizumab was associated with an increased proportion of patients with superinfections (54% vs. 26%; P < .001), there was no difference in the 28-day mortality rate among tocilizumab-treated patients vs. patients without superinfections (22% vs. 15%, P = .42).

The probability of survival was significantly higher in Tocilizumab-treated compared to untreated patients according to Kaplan-Meier (P= .0189).

A cohort observational retrospective study that also confirms the effectiveness of Tocilizumab [17] covers 13 hospitals in the United States and includes 630 patients, 210 of whom received Tocilizumab and 240 who did not.

In the primary multivariable Cox regression analysis, an association was observed between receiving Tocilizumab and reduced in-hospital mortality (HR 0.64, 95% CI 0.47-0.87; p=0.0040). Similar associations with tocilizumab were observed among subgroups requiring mechanical ventilatory support.

In our study, no significant statistical difference was found in terms of gender structure, age and admission to the COVID center (From home or another health facility), in patients who were or were not treated with tocilizumab. No significant difference was found in terms of length of hospitalization in both groups of patients. No significance was found in terms of length of stay on mechanical ventilation in patients who received tocilizumab compared to those who did not.

Conclusion

This retrospective case control study showed that treatment with tocilizumab as a human monoclonal antibody in patients with severe COVID-19 led to statistically significant lower mortality and shorter stay in intensive care units compared to patients with severe COVID-19 who were not treated with tocilizumab. The results of this study may contribute to the treatment of cytokine storm, reducing mortality and post-hospital complications in patients with a severe form of COVID-19. However, additional studies are needed in order to determine possible side effects and the occurrence of secondary infections during treatment with tocilizumab.

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