Journal of the Medical Research Institute

JMRI, 2025; Vol. 46 No.2: (1-9)

Journal of the Medical Research Institute

Evaluating the Effectiveness of Tocilizumab in Severe and Critically Ill COVID-19 Patients: A Retrospective Cohort Study.

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ABSTRACT:
Tocilizumab, an interleukin-6 receptor antagonist, has been utilized as a treatment for severe COVID-19 cases due to its anti-inflammatory properties. However, its effectiveness in critically ill patients remains controversial. This retrospective cohort study aimed to evaluate the effectiveness of tocilizumab in reducing mortality and improving clinical outcomes in severe or critically ill COVID-19 patients. Data from 320 patients were reviewed, with 105 meeting the inclusion criteria. Patients were divided into two groups: 72 received the standard COVID-19 treatment protocol, and 33 received tocilizumab. The tocilizumab group had a lower mortality rate (63.6%) compared to the standard protocol group (79.2%), although this difference was not statistically significant (risk difference: 15.6%; 95% CI: –4.3 to 35.5; p = 0.091). The length of hospital stay was significantly longer in the tocilizumab group (median: 11 days, IQR: 7–17) compared to the standard treatment group (median: 7.5 days, IQR: 5–12; 95% CI: 0.014–0.019; p = 0.016). Kaplan–Meier survival analysis demonstrated a statistically significant trend in favor of the tocilizumab group (p = 0.021), despite the non-significant difference in overall mortality rates. These findings suggest that tocilizumab may offer a potential survival advantage in severe COVID-19 patients, although further studies are needed to confirm its effectiveness.

Keywords: Tocilizumab, interleukin-6, COVID-19, and cytokine release syndrome.

1. INTRODUCTION

The World Health Organization (WHO) declared COVID-19 a pandemic due to rising global morbidity and mortality rates (1). To date, over 60 million people have been infected, and more than 6 million deaths have occurred due to COVID-19. The hospital mortality rate is 13.6%, with a median length of stay (LOS) of 5 days (2). Older age, ICU admission, and/or the use of invasive mechanical ventilation (IMV) are linked with longer hospital length of stay (LOS) and higher in-hospital mortality. Patients requiring both ICU and IMV had the longest median hospital LOS (15 days) and the highest in-hospital mortality rate (53.8%) (3).

Egypt, the first country in Africa to confirm a COVID-19 case, reported 94,078 cases and 4,805 deaths by the 1st of August 2020, ranking as the second most affected African nation after South Africa. This highlighting the need for increased clinical capacity to improve case detection and management (4). Globally, the WHO reported 17,396,943 cases and 675,060 deaths at the same time, and like many other countries, Egypt's health system faced significant challenges in rapidly expanding capacity to manage the pandemic (5).

In severe COVID-19 conditions, there was a significantly increased prevalence of common clinical symptoms such as fever, cough, lethargy, chest tightness, hemoptysis, diarrhea, and abdominal discomfort, all of which are linked to the severity of the disease (6). In COVID-19, the virus attaches to alveolar epithelial cells, exaggerating innate and adaptive immunity, releasing a tremendous number of cytokines, including interleukin-6 (IL-6), and increasing vascular permeability (7).

Patients infected with COVID-19 may

Received: 15-4-2025 Accepted: 25-5-2025
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experience worsening symptoms, including acute respiratory distress syndrome, elevated C-reactive protein (CRP), and increased levels of IL-6; an inflammatory cytokine that causes cytokine release syndrome (CRS) which is a systemic hyperinflammatory state (8, 9). Additionally, they may develop other systemic illnesses that present with varying degrees of pulmonary symptoms and cardiac conduction abnormalities (10).

Anti-cytokine therapy has been proposed as a treatment for COVID-19; however, its effectiveness and safety in this population remain unknown (11). On August 30, 2017, the U.S. Food and Drug Administration approved tocilizumab (Actemra®) for the treatment of severe or life-threatening chimeric antigen receptor (CAR) T-cell-induced CRS in adults and pediatric patients two years of age and older (12).

Tocilizumab, a recombinant humanized monoclonal antibody targeting the human IL-6 receptor of the IgG1 subtype, has been utilized in the treatment of rheumatoid arthritis, systemic juvenile idiopathic arthritis, and various autoimmune conditions (13). Additionally, as an IL-6 receptor inhibitor, tocilizumab effectively blocks cytokine release triggered by IL-6 receptor activation, thus preventing CRS (7). It is specifically employed for treating CRS secondary to CAR T-cell therapy and CRS that may arise in COVID-19 patients [(14).]

Many countries have developed specific protocols to manage illness symptoms, which have contributed to reduced hospitalizations and improved healthcare systems (15). The Egyptian Ministry of Health's protocol includes the use of tocilizumab for COVID-19 treatment, alongside steroids like methylprednisolone at a dose of 1-2 mg/kg/day in cases of therapeutic failure or oxygen desaturation upon admission [(16)]. The aim of the current study is to evaluate the effectiveness of tocilizumab in reducing mortality and improving outcomes in severe or critically ill COVID-19 patients.

2. Methods:

2.1. Study Design:

Our study employed a retrospective cohort design to evaluate the effectiveness of tocilizumab in reducing mortality and improving outcomes in severe or critically ill COVID-19 patients.

Settings: The study was conducted at Kafer Eldwar General Hospital, Egypt, a designated COVID-19 treatment facility – at the time of the epidemic - equipped with intensive care units and specialized care for severe and critically ill patients.

Duration of Recruitment: The recruitment period spanned from the 1st of January 2021 to the 31st of August 2021. During this period, the medical records of 320 patients admitted with severe or critical COVID-19 were screened for eligibility based on predefined inclusion and exclusion criteria.

2.2. Ethical Considerations:

The study was conducted in accordance with the Declaration of Helsinki and its later amendments (17), and was approved by the Ethics Committee of the Central Directorate of Research and Health Development, Egyptian Ministry of Health and Population (approval number: 18-2021/18). All participants were treated according to the Egyptian COVID-19 management protocol issued by the Ministry of Health and Population, November 2020 version, for critically ill COVID-19 cases (16, 18). Their medical records were screened following approval from the hospital administration, ensuring data confidentiality. The authors declared no conflicts of interest.

2.3. Eligibility Criteria:

A retrospective cohort study was conducted using the medical records of 320 patients diagnosed with COVID-19.

Inclusion Criteria:

1. Patients diagnosed with confirmed COVID-19.
2. Patients classified as severe or critically ill based on the following criteria:
   - **Severe cases**:
     - Respiratory rate (RR) > 30 breaths/min.
     - Oxygen saturation (SaO_2) < 92% at room air.
     - Partial pressure of oxygen (PaO_2) to fractional inspired oxygen (FiO_2) ratio < 300.
     - Chest radiological findings of ≥50% lesions or progressive lesions within 24–48 hours.
   - **Critically ill cases**:
     - RR > 30 breaths/min.
     - SaO_2 < 92% at room air.
     - PaO_2/FiO_2 ratio < 200 despite oxygen therapy.

Exclusion Criteria:

1. Patients classified as mild or moderate COVID-19 cases.
2. Severe or critically ill patients with any contraindications to anti-interleukin-6 (IL-6) therapy, including:
   - Presence of bacterial infection.
   - Absolute neutrophil count (ANC) < 500 cells/mm³.
   - Platelet count (Plat) < 50,000 cells/mm³.
   - Alanine transaminase (ALT) > 5× the upper limit of normal (ULN).

Based on the aforementioned criteria, the total sample of 320 patients was classified into four severity groups: critically ill, severe, moderate, and mild, using clinical and laboratory data. A total of 215 patients were excluded due to being classified as mild or moderate cases, while 105 patients, classified as critically ill or severe, were included in the study. These 105 patients were further evaluated to determine eligibility for anti-interleukin-6 (IL-6) therapy. Patients without contraindications (n = 33) received tocilizumab, whereas those with contraindications (n = 72) followed the standard treatment protocol (16, 18). The treatment assignment was strictly based on predefined eligibility criteria, specifically the presence or absence of contraindications to IL-6 therapy. (Figure 1)

Figure 1. A total of 320 COVID-19 patient records were reviewed. Patients were categorized into four groups based on disease severity: critically ill, severe, moderate, and mild, using established criteria. Criteria for severe patients included respiratory rate (RR) > 30, oxygen saturation (SaO2) < 92% at room air, partial pressure of oxygen (PaO2) to fractional inspired oxygen (FiO2) ratio < 300, and significant chest radiological findings (≥50% lesions or progressive lesions within 24–48 hours). Critically ill patients met similar criteria with a PaO2/FiO2 ratio < 200 despite oxygen therapy. Mild and moderate cases (n=215) were excluded. Among the remaining 105 critically ill or severe cases, further

stratification was performed based on contraindications for anti-interleukin-6 (IL-6) therapy. Patients without contraindications (n=33) received tocilizumab, while those with contraindications (e.g., bacterial infection, absolute neutrophil count [ANC] < 500 cells/mm³, platelet count [Plat] < 50,000 cells/mm³, or alanine transaminase [ALT] > 5× upper limit of normal [ULN]) followed the standard treatment protocol.

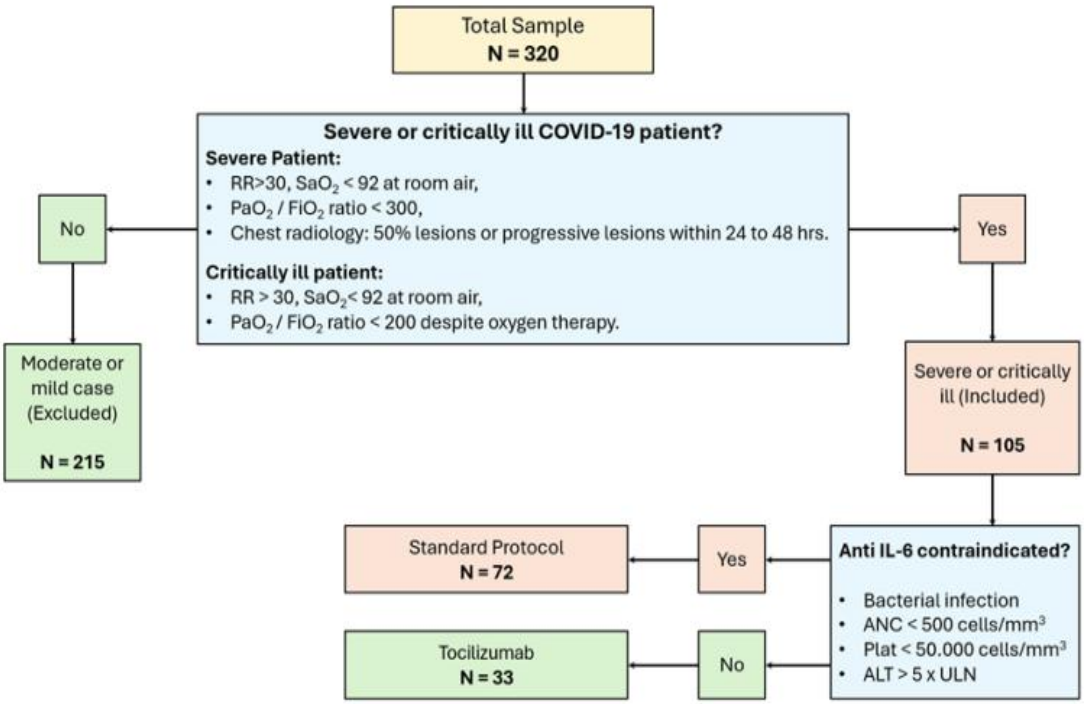

Figure 1: Workflow of the study design.

2.4. Sample Size Calculations:

The required sample size was calculated using Epi Info™ (version 7.2.6, CDC, Atlanta, GA, USA) based on $\alpha = 0.05$, power = 80%, and an assumed hazard ratio of 1.6 for patients receiving tocilizumab. A minimum sample size of 268 was determined, with a 20% dropout rate yielding a total required enrollment of 320 patients.

2.5. Outcomes:

Primary Outcome:

- The mortality rate during the hospital stay was assessed, with a follow-up period extending until the patient either died in the hospital or was discharged.

Secondary Outcomes:

- Length of hospital stay (in days).
- Survival rate (evaluated using Kaplan-Meier survival analysis).
- Changes in laboratory markers (e.g., CRP, TLC, ferritin).

2.6. Data Collection:

Data was extracted from medical records. Collected information included demographic characteristics, comorbidities, clinical parameters, and laboratory findings. Any laboratory marker not reported in the results section was excluded from the final analysis.

2.7. Statistical Analysis:

Statistical analysis was conducted via SPSS® version 22. Categorical variables were compared using the chi-square test, while continuous variables were analyzed using the Mann-Whitney U test. Kaplan-Meier survival analysis with the log-rank test ($p < 0.021$) was used to compare mortality rates between study groups, and Cox proportional hazards regression models were employed to assess the association between tocilizumab use and survival, adjusting for potential confounders. Subgroup analysis was conducted to evaluate risk factors affecting therapeutic outcomes, with a p-value of <0.05 considered statistically significant.

3. Results:

Between January and August 2021, 105 patients met the eligibility criteria and were included in the study. Of these, 72 patients received the standard COVID-19 protocol (remdesivir, dexamethasone, and enoxaparin), while 33 received tocilizumab in addition to the standard protocol. The tocilizumab group had a median age of 58 years, while the standard treatment group had a median age of 63 years, with no statistically significant difference ($p = 0.092$). Female patients constituted 51.5% (17/33) of the tocilizumab group and 59.7% (43/72) of the standard protocol group ($p = 0.622$). (Table 1)

Table 1: Baseline characteristics of the study population:

	Total (n=105)	Standard Care (n=72)	Received Tocilizumab (n=33)	*p* value
Demographics				
Age	64 (57,74%)	63 (57,73%)	58 (53,69%)	0.092 U
Male	45 (42.9%)	29 (40.3%)	16 (48.5%)	0.622 χ^2
Female	60 (57.1%)	43 (59.7%)	17 (51.5%)	
No PMH	20 (19%)	13 (18.1 %)	7 (21.2%)	0.702 χ^2
Comorbidities				
DM	51 (48.6%)	34 (47.2 %)	17 (51.5%)	0.683 χ^2
HTN	60 (57.1%)	39 (54.2 %)	21 (63.6%)	0.363 χ^2
IHD	12 (11.4%)	10 (13.9 %)	2 (6.1%)	0.332 MC
Hepatic disorders	4 (3.8%)	4 (5.6%)	0 (0%)	0.306 MC
COPD	4 (3.8%)	3 (4.2%)	1 (3%)	1.000 MC
Splenectomy	1 (1%)	1 (1.4%)	0 (0%)	1.000 MC
Asthma	1 (1%)	1 (1.4%)	0 (0%)	1.000 MC
CKD	5 (4.8%)	5 (6.9%)	0 (0%)	0.322 MC
CVD	1 (1%)	1 (1.4%)	0 (0%)	1.000 MC
Malignancy	2 (1.9%)	2 (2.8 %)	0 (0%)	1.000 MC
Asthmatic	1 (1%)	0 (0%)	1 (3%)	0.314 MC
2^{ry} bacterial infection	1 (1%)	1 (1.4%)	0 (0%)	1.000 MC

U: Mann Whitney test, χ^2: Chi square test, MC: Monte Carlo, PMH: past medical history, DM: diabetes mellitus, HTN: hypertension, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, CVD: cardiovascular disease.

3.1. Primary Outcome: Mortality:

The mortality rate was lower in the tocilizumab group (63.6%) compared to the standard protocol group (79.2%), although the difference was not statistically significant (95% CI: –4.3 to 35.5; p = 0.091). Mortality follow-up duration extended until death occurred in the hospital or the patient was discharged. (Table 2)

Table 2: Clinical outcomes evaluation among study groups:

	Standard Care (n=72) [(1)]	Received Tocilizumab (n=33) [(1)]	*p* value
Primary Outcome			
Death rate (Mortality)	57 (79.2%)	21 (63.6%)	χ^2
Improved	15 (20.8%)	12 (36.4%)	0.091
Secondary Outcome			
Length of stay (Days)	7.5 (5,12)	11 (7,17)	U 0.016 *

[(1)] n (%), Median (IQR), χ^2: Chi square test, U: Mann Whitney, *Statistically significant at $p \leq 0.05$

3.2. Secondary Outcomes:

The length of hospital stay (LOS) was significantly longer in the tocilizumab group, with a median LOS of 11 days compared to 7.5 days in the standard treatment group **(**95% CI: 0.014–0.019; p = 0.016**).** This trend, favoring prolonged hospitalization for the tocilizumab group, was further confirmed using Kaplan–Meier survival analysis and a log-rank test, which showed a statistically significant difference (p = 0.021). (Figure 2)

Figure 2. Kaplan–Meier survival curve comparing mortality rates between patients treated with the standard COVID-19 protocol and those receiving tocilizumab in addition to the standard protocol. The analysis demonstrates a significant survival benefit in the tocilizumab group (log-rank test, p = 0.021).

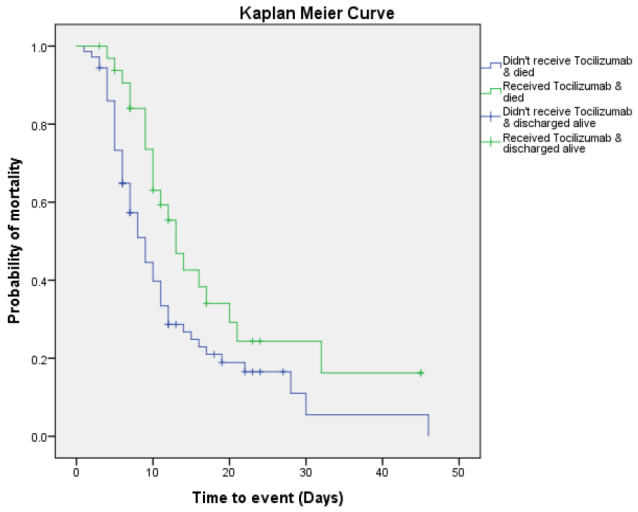

Figure 2: Kaplan–Meier survival analysis.

3.3. Risk Factors and Associated Outcomes:

Risk factors such as diabetes, hypertension, chronic kidney disease, and cardiovascular diseases were assessed for their association with mortality and LOS. However, no statistically significant causal relationships were observed.

3.4. Laboratory and Clinical Observations:

All laboratory tests, listed in Table 3, showed no statistically significant differences between the two groups except for total leukocyte count (TLC) and blood urea nitrogen (BUN), which were lower and higher, respectively, in the tocilizumab group ($p < 0.001$ for TLC; $p = 0.018$ for BUN).

Table 3: Baseline of laboratory tests at administration of the study population:

	Standard Care (n=72) Median (IQR)	Received Tocilizumab (n=33) Median (IQR)	*p* value for Mann Whitney test
TLC	14.6 (12,20.35)	11.4 (10.6,12.2)	<0.001*
Hemoglobin	12.7 (11.85,14.5)	12.7 (12.5,12.9)	0.486
Platelets	136 (113,227)	233 (116,350)	0.411
Creatinine	0.9 (0.7,1.25)	0.9 (0.8,1.3)	0.216
BUN	35 (27,50)	46 (32,60)	0.018*
SGOT	31(20,40)	46 (28,64)	0.829
SGPT	46 (34,68)	32 (25,40)	0.150
INR	1.27 (1.13,1.43)	1.48 (1.45,1.5)	0.328
CRP	54 (27,81)	60 (24,96)	0.768
Ferritin	1103 (496,1955)	498 (272,1049)	0.222
IL-6	76 (59,249)	54.5 (52,57)	0.285
D dimer	825 (240,2002)	710 (400,1300)	0.505
Procalcitonin	0.23 (0.1,0.45)	0.15 (0.1,0.29)	0.073

*Statistically significant at $p \leq 0.05$. TLC: total leukocyte count, BUN: blood urea nitrogen, SGOT: serum glutamic oxaloacetic transaminase, SGPT: serum glutamic pyruvic transaminase, INR: international normalized ratio, CRP: C-reactive protein, IL-6: interleukin-6.

Both groups underwent chest computed tomography (CT) scans at admission to assess pulmonary involvement. Clinical symptoms, including fever, dyspnea, and cough, were also recorded at admission but showed no significant differences between groups. (Table 4).

Table 4: Baseline of clinical variables at administration of the study population:

	Standard Care (n=72)		Received Tocilizumab (n=33)		p value
	n	%	n	%	
CT/CXR Finding					
Nothing	1	1.4	0	0.0	MC p = 0.125
GGO	21	29.2	15	45.5	
Bilateral GGO	37	51.4	10	30.3	
Scattered patches	1	1.4	0	0.0	
Massive GGO	0	0.0	1	3.0	
NA	0	0.0	1	3.0	
Bilateral GGO, 50% consolidation	2	2.8	2	6.1	
Bilateral GGO, consolidation	8	11.1	3	9.1	
Bilateral	1	1.4	0	0.0	
GGO multiple	0	0.0	1	3.0	
GGP	1	1.4	0	0.0	
Dyspnea					
No	1	1.4	0	0.0	FE p = 1.000
Yes	71	98.6	33	100.0	
Fever					
No	47	65.3	19	57.6	0.448 $\chi 2$
Yes	25	34.7	14	42.4	
Cough					
No	26	36.1	10	30.3	0.561 $\chi 2$
Yes	46	63.9	23	69.7	

$\chi 2$: Chi square test, MC: Monte Carlo, FE: Fisher Exact, CT: computed tomography, CXR: chest x ray, GGO: ground glass opacity, GGP: ground glass pattern.

3.5. Oxygen Saturation Measurements:

Oxygen saturation levels were measured using pulse oximeters (Mindray uMEC 150 Patient Monitor, China) and recorded at baseline, day 5, and day 10 of hospitalization. The comparison revealed no significant differences between the groups at any time point. (Table 5).

Table 5: Oxygen saturation at administration and during hospitalization evaluation of the study population:

Oxygen saturation	Standard Care (n=72) Median	Received Tocilizumab (n=33) Median	*p* value Mann Whitney test
At administration	87	86	0.104
After 5 days	90	89.5	0.779
After 10 days	90.5	90	0.512

3.6. Treatment Protocols:

Both groups received comparable treatment protocols as per the Egyptian COVID-19 management guidelines. Respiratory aid devices, steroid use, and antiviral administration were distributed similarly across the groups. Specifically, most patients required reservoir masks (81.8% in the tocilizumab group, 72.2% in the standard care group), while mechanical ventilation was less common. Steroid administration was consistent in both groups, and the most frequently used antiviral was remdesivir. (Table 6).

Table 6: Medical interventions during hospitalization among study groups:

	Standard Care (n=72)		Received Tocilizumab (n=33)		p value
	n	%	n	%	
Respiratory aid device					
SM	11	15.3	4	12.1	MC p = 0.495
RM	52	72.2	27	81.8	
MV	3	4.2	1	3.0	
CPAP	4	5.6	0	0.0	
High flow	2	2.8	0	0.0	
Nasal canula	0	0.0	1	3.0	
Steroids					
1	63	87.5	24	3.0	MC p = 0.060
2	9	12.5	7	84.8	
3	0	0.0	2	6.1	
Antiviral					
No	5	6.9	1	3.0	MC p = 0.624
Remdesivir	55	76.4	28	84.8	
Hydroquinone	1	1.4	2	6.1	
Ivermectin	4	5.6	1	3.0	
Ivermectin + Hydroquinone	5	6.9	1	3.0	
Alluvia	2	2.8	0	0.0	

MC: Monte Carlo, SM: simple mask, RM: reservoir mask, MV: mechanical ventilation, CPAP: continuous positive airway pressure.

4- Discussion:

Tocilizumab (Actemra®), an IL-6 receptor antagonist, is controversial in treating critically ill COVID-19 patients due to inconsistent research findings as some studies shows reduced mortality and improved therapeutic outcomes, while others find no significant benefits (19, 20). Early administration may be more effective, yet safety concerns exist due to its immunosuppressive effect (21).

Our study provides a comprehensive analysis of the primary outcome, mortality rate, and secondary outcomes, including length of hospital stay (LOS), oxygen saturation, and survival rates in COVID-19 patients treated with tocilizumab compared to the standard treatment protocol.

In the current study, both groups were well-matched in terms of demographics and comorbidities, ensuring that differences in outcomes could be attributed to treatment rather than baseline differences. There were no significant differences between the two groups in age, gender distribution, or comorbidities such as diabetes, hypertension, and chronic lung diseases, minimizing confounding variables (22).

The primary outcome of interest in our study, the mortality rate, was lower in the tocilizumab group (63.6%) compared to the routine treatment group (79.2%), although this difference did not reach statistical significance ($p = 0.091$). This trend aligns with previous research suggesting that IL-6 inhibitors may improve survival in severe COVID-19 cases.

For instance, a randomized controlled trial demonstrated that tocilizumab reduced all-cause mortality and increased the probability of hospital discharge (23). In another study involving critically ill COVID-19 patients, tocilizumab was linked to nearly a 30% reduction in mortality risk (24). Furthermore, a meta-analysis showed that tocilizumab treatment could reduce mortality rates by approximately 12% (25).

Regarding our secondary outcome, the LOS in our study was significantly longer in the tocilizumab group compared to the routine treatment group (p = 0.016). This finding was confirmed by Kaplan-Meier survival analysis, which indicated a significant survival benefit for the tocilizumab group (p = 0.021). The prolonged LOS could be due to the need for extended care or close monitoring of side effects, such as an increased risk of infections and liver enzyme abnormalities, in the tocilizumab group, consistent with findings from other studies (26, 27).

Our findings suggest that tocilizumab may improve long-term survival outcomes, even if it does not lead to immediate discharge from the hospital. The significant finding in the survival analysis suggests that tocilizumab helps to stabilize patients and prevent fatal outcomes over a longer period, which is consistent with previous studies (28, 29).

Baseline laboratory tests were performed at admission, prior to tocilizumab administration. Total leukocyte count (TLC) was significantly lower in the tocilizumab group at baseline (p < 0.001). While low TLC levels have been observed as a common adverse reaction in tocilizumab recipients in other studies (30, 31), our baseline data do not allow attribution of these levels to tocilizumab. Similarly, and in accordance with previous studies (32, 33), the encountered higher blood urea nitrogen (BUN) levels in the tocilizumab group at baseline (p = 0.018) cannot be interpreted as an effect of the drug. Future studies with post-treatment laboratory comparisons are warranted.

In our study, no significant differences were found in CT scan results between both groups, suggesting that tocilizumab does not markedly alter the radiological appearance of COVID-19. This agrees with previous studies that inspected the effects of tocilizumab on lung inflammation and concluded that while tocilizumab can reduce systemic inflammation, which might indirectly improve some radiographic findings, it does not directly cause rapid changes in CT scan results (34, 35). The resolution of ground-glass opacities or consolidation seen on CT scans in COVID-19 patients is usually due to the overall reduction in inflammation and progression of the disease rather than a direct effect of tocilizumab itself (36).

Oxygen saturation levels were measured at admission and during treatment (days 5 and 10). There were no significant differences between groups at any time point, indicating that tocilizumab does not have an immediate effect on respiratory function. These results align with studies showing that IL-6 inhibitors neither lead to significant changes in the need for mechanical ventilation nor immediately impact oxygen saturation levels (37-39), underscoring the complexity of assessing treatment effectiveness solely based on respiratory metrics.

Additionally, the diminished effect on oxygen saturation observed with the routine treatment protocol aligns with previous clinical trials. These trials have concluded that in critically ill patients, delayed initiation of treatment may result in less significant improvements in oxygen saturation (40, 41). Notably, the ACTT-1 trial (Adaptive COVID-19 Treatment Trial) demonstrated that while remdesivir reduced recovery time, its impact on oxygen saturation was not significantly different from placebo in critically ill patients requiring high-flow oxygen or mechanical ventilation (42).

Overall, our findings contribute valuable insights into the role of tocilizumab in managing severe COVID-19 and suggest that while immediate respiratory improvements may be limited, the drug may offer significant benefits in stabilizing patients and enhancing long-term survival. Further studies are warranted to explore these effects in more detail and to refine treatment strategies for optimizing patient therapeutic outcomes.

Strengths and limitations:

The current study's strengths lie in its comprehensive comparative analysis of tocilizumab versus standard COVID-19 treatments where detailed data collection from medical records and laboratory results enhanced the validity of the findings, and the application of statistical methods like Kaplan-Meier curves and Cox proportional hazards models provided a rigorous examination of survival outcomes.

However, our study also has notable limitations. Its non-randomized, retrospective design introduces the risk of selection bias. The observed trends in mortality and survival benefits did not always reach statistical significance, underscoring the need for additional randomized controlled trials to validate their effectiveness and address these concerns.

Future recommendations:

Future studies should focus on larger, randomized controlled trials to better assess the effectiveness and safety of tocilizumab in diverse patient populations. Additionally, investigations into the optimal timing and dosing of tocilizumab, as well as its long-term effects, are crucial for refining treatment protocols and maximizing patient outcomes.

5- Conclusion:

This study suggests that tocilizumab (Actemra®) may reduce mortality and improve long-term survival in severe COVID-19 patients, although the reduction in mortality rate was not statistically significant (63.6% vs. 79.2%, p = 0.091). The tocilizumab group had a significantly longer hospital stay (median of 11 days vs. 7.5 days, p = 0.016), but Kaplan-Meier survival analysis revealed a significant survival benefit (p = 0.021), indicating improved long-term outcomes.

While tocilizumab did not significantly affect immediate survival or clinical/radiological parameters, it may aid in the clinical stabilization of patients and improve overall survival. Further research is required to confirm these findings and investigate the impact of tocilizumab on laboratory and radiological outcomes.

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