

The clinical outcome of Tocilizumab in treatment of elderly patient with severe COVID-19 pneumonia

Alaa Wagih Husseiny, Walaa Wessam Aly, Mohamed Mortada.

Geriatrics and Gerontology Department, Faculty of Medicine, Ain Shams University

ABSTRACT

Background: Since the COVID-19 epidemic has caused serious public health problems and is connected to the viral aggravation, steroids, which have anti-inflammatory effects, initially were used to manage severe cases marked by the cytokine storm. Tocilizumab may be able to reduce the hyperinflammatory reaction connected to the progressive respiratory failure brought on by SARS-CoV-2 by inhibiting the interleukin 6 receptor (IL-6R), one of the main cytokines involved in infection-induced cytokine storm.

Objective: to evaluate the efficiency of tocilizumab regarding clinical outcomes in elderly cases suffering from severe COVID-19 infection who have received standard of care treatment and tocilizumab in comparison with similar patients who have received standard of care treatment only.

Methods: A retrospective cohort study was done involving sixty patients enrolled to Ain Shams Geriatrics University Quarantine hospital with severe coronavirus infection from 1st of June 2020 to 31st of August 2020. Retrospective interpretation of medical reports was applied to gather data. The trial involved 60 patients older than 60 years with proof of SAR-CoV2 by nasopharyngeal swab classified into 2 groups: 30 patients received the standard of care and tocilizumab (8mg/kg/dose) as a single dose and when clinical improvement does not occur, another dose was given >8hours following the initial dose and control group consisting of 30 patients who received standard of care treatment as recommended by WHO guidelines on treatment of COVID-19 2020, CDC recommendations of 2020, and Ain Shams University Guidelines 2020. Clinical outcomes were detected through assessment of symptoms, oxygenation, need for noninvasive and invasive ventilation, period of ICU stay, and rate of mortality.

Results: Studying the documents gathered from Ain Shams Geriatrics University hospital, a total of 60 patients with severe coronavirus pneumonia were included in this trial between 1st of June 2020 to 31st of August 2020, which revealed that tocilizumab reduced inflammatory markers, enhanced blood oxygen levels of cases ($p<0.001$), and recede the demand for mechanical ventilator ($p<0.001$), but there was no direct significance on mortality rate and period of hospital stay.

Conclusion: Tocilizumab treatment at a dose of 8mg/kg/dose for senior patients with severe coronavirus pneumonia improved some clinical outcomes.

Key words: Tocilizumab; COVID-19; elderly; Coronavirus

INTRODUCTION

An unprecedented coronavirus disease (COVID-19) in December 2019, resulted from SARSCoV2 infection, rapidly spread in between continents. The initial evidence of the pathogenic features of patients who died from acute infection with SARSCoV2

showed an increased concentration of pro-inflammatory cytokines (18). The clinical course of coronavirus disease is variable, ranging from asymptomatic pneumonia to severe respiratory failure with the potential for invasive ventilation or death. The illness is

Alaa Wagih et al., EJGG.2023; 10(1): 13-22

distinguished by a viral replication-driven first phase, which may be followed by an inflammatory host response-driven secondary phase. According to usual radiological findings, infection with the SARS-CoV-2 coronavirus may activate an overactive immune response that results in acute respiratory distress syndrome. The most vulnerable patients may experience a condition known as a "cytokine storm," which is defined by an increase in the release of many cytokines that cause lung tissue fibrosis and long-term damage. (5)

When manifested by interstitial lung pneumonia along with respiratory failure, coronavirus infection has a very high mortality rate. Previous research demonstrated that immune hyper-activation, or "cytokine storm," may contribute to interstitial lung damage in coronavirus patients and result in a more severe clinical outcome. In the stage of hyper-activation of the immune system, peripheral CD-4 and CD-8 T-cell counts were significantly reduced while their status was hyper-activated. Furthermore, CD-4 T-cells from deceased patients had higher numbers of pro-inflammatory CCR-6+T-helper-17 (Th-17) and cytotoxic granules in CD-8 lymphocytes. (4)

A cytokine called Interleukin-6 (IL-6) is essential for immune system response and inflammation. According to the most recent clinical research in China, IL-6 is one of the most important cytokines involved in COVID-19-induced cytokine storm. According to the latest edition of the National Health Commission of China's Diagnosis and Treatment of Pneumonia Infected by Novel Coronavirus, tocilizumab (TCZ), a humanized monoclonal antibody aims to block the interleukin-6-receptor (IL-6R), is advised in critical patients with increased IL-6 levels. (10)

OBJECTIVE

To evaluate the effectiveness of tocilizumab in terms of clinical outcome in elderly patients suffering from severe coronavirus pneumonia who were treated with the standard of care regimen and tocilizumab

Till 2020, there was no definite management course approved for coronavirus pneumonia, but the recommended treatment regimens considered combining antivirals and immune active therapies, such as tocilizumab. During May 2020, PubMed, Embase, Cochrane Review, ISI Web of Science, and SCOPUS were used to perform literature researches on the benefit of using TCZ in coronavirus infection treatment. Since then TCZ use in coronavirus pneumonia has become common, according to some studies. Furthermore, the findings of a single-site trial from Wuhan, China, which included 15 patients with COVID-19 pneumonia who were going to develop a cytokine storm, demonstrated that TCZ management proved to have a therapeutic advantage, even if the doses varied and ranged from (80 mg to 600 mg). (5)

Similarly, a case-control trial done retrospectively in France revealed that patients who did not have TCZ had a higher rate of mortality, intensive care unit enrollment, or both. Tocilizumab is expected to have positive effects when compared to standard of care treatment administered solely, according to randomized clinical trial CORIMUNO (Cohort Multiple Randomized Controlled Trials Open-label of Immune Modulatory Drugs and Other Treatments in COVID-19 Patients). Patients with coronavirus treated with TCZ in small clinical case series, many of whom also received glucocorticoids, typically showed improvements in oxygen blood levels and inflammatory markers levels, as well as high rates of discharge from hospitals. These results imply that TCZ may be an effective therapy option for hospitalized patients. (5,16)

compared to similar cases who were treated with only the standard of care regimen.

METHODS

A cohort study was performed retrospectively gathering medical documents from the Ain Shams Geriatrics University hospital from the 1st of June 2020 till 31st of August 2020. Sixty

Alaa Wagih et al., EJGG.2023; 10(1): 13-22

(60) patients over the age of 60, both males and females, with SAR-CoV2 confirmed by nasopharyngeal swab in the intensive care unit (ICU) were included according to the following inclusion criteria for severe COVID-19 pneumonias: a computerized tomography scan detecting multifocal interstitial lung pneumonia, respiratory distress with respiratory rate (RR) >30 breaths/min while resting, demand of oxygen supply to keep $SO_2 > 93\%$ at rest, lungs' condition deterioration interpreted as arterial blood oxygen partial pressure (PaO_2)/fraction of inspired oxygen concentration (FiO_2) ≤ 300 mmHg, need for mechanical ventilator, and extension of consolidations in the pulmonary areas or developing sepsis in the last 24h.(7)

Data collected in this study were demographic information, co-morbidities, oxygen saturation at the time of admission, inflammatory markers, and liver enzymes, APACHE2 (Acute Physiology and Chronic Health Evaluation) score upon hospital admission and the clinical outcomes of cases as symptoms, oxygen demand, period of hospital stay, and rate of mortality.

After the study approach was authorized by MASRI committee, the faculty ethics board, and the committee of research analysis of the department of Geriatrics and Gerontology medicine at the Faculty of Medicine at Ain Shams University, data were acquired retrospectively by reviewing medical records. Participants' anonymity and confidentiality were guaranteed.

Statistical Package for Social Science (SPSS) usage on a personal computer facilitated data entry and statistical analysis (version 26) Means and standard deviation were used to present quantitative variables. Frequency tables were used to depict qualitative characteristics (number and percent). Comparative analysis of quantitative variables was done. Using Pearson's 2 test, qualitative variables were compared to one another. Using the Spearman correlation coefficient, two quantitative variables were correlated. When $P < 0.05$ and $P < 0.001$ are regarded as extremely significant, the statistical difference was accepted.

RESULTS:

Table (1) shows a sample of 60 patients with critical coronavirus infection who were enrolled at the Ain Shams Geriatrics University Quarantine hospital between June 1st and August 31, 2020. The mean age of these cases was 68.5 years old. Males made up 58% of the study population, while females made up 41.6%. Additionally, 55% of the study population were nonsmokers compared to 45% of smokers.

Table (2) shows that dyspnea was the most prevalent presenting symptom in severe cases (90–100%), while vomiting and diarrhea were the least common (10% and 16%), however other symptoms were equally prevalent, as cough (56%) and fever (56%).

Table (3) shows the recurrence of comorbidities among the study population with no statistical significance between both groups as HTN (29 patients) and DM (31 patients) were the commonly encountered disorders while liver cirrhosis (8 patients) and heart failure (6 patients) were the least encountered disorders. Also, table 3 reveals that there was no statistical significance regarding Charlson co-morbidity index between both groups of the study population (P-value 0.625).

Table(4) shows that no statistical significance was found among the study population regarding laboratory findings on admission preceding treatment.

Table (5) shows that on admission most patients were on either non rebreathing mask (20 patients) or venturi mask (17 patients) while fewer patients were on nasal (12 patients) or noninvasive ventilation (6 patients) , and only 5 patients were mechanically ventilated prior treatment. This table shows that there was no statistical significance regarding oxygen demand before treatment between both groups of study population with unremarkable P-value(0.625).

Table (6) shows the difference in serum levels of ferritin, lactate dehydrogenase(LDH), alanine transaminase(ALT), and aspartate aminotransferase(AST) before and after administering tocilizumab within 48-72 hours

Alaa Wagih et al., EJGG.2023; 10(1): 13-22

revealed that cases who were administered the medication displayed differences statistically significant in their body's ability to fight inflammation as measured by serum levels of those two proteins. However, there was no differences statistically significant in AST levels either prior to or following tocilizumab treatment (P-value 0.122).

Table (7) shows a comparison between symptoms before and after treatment with Tocilizumab with a statistical significance in regression of dyspnea with P-value (0.001) and fever(0.024) , while other symptoms including cough, vomiting , and diarrhea showed no statistical significance before and after treatment.

Table (8) shows that treatment with tocilizumab resulted in statistical significance with P value (<0.002) on oxygen demand and modes of oxygen support: 10 patients have become on room air after either being on non-rebreather mask or noninvasive ventilation or venturi mask, while none of the patients needed either nonrebreather mask or noninvasive ventilation, and of the 30 patients

only 6 required mechanical ventilation as displayed in this table.

Table (9) shows a statistical significance in the methods of ventilation before and after the administration of standard of care treatment only with a P-value (<0.001); however, 15 patients did not respond to treatment and were mechanically ventilated while 9 patients became on room air after being on either nonrebreather masks, noninvasive modes of ventilation, or venturi masks.

Table(10) shows that there was no statistical significance of both treatment regimens on length of hospital stay in both groups of the study population (P value 0.317).

Table (11) shows that there was higher mortality rate in the control group (53 %) and lower discharged rate (46 %) compared to the case group whose mortality rate was (40%) and discharge rate was (60%). But unfortunately, no statistical significance was found between the outcome in terms of mortality and discharge in both groups of the population being studied (P value 0.301).

Table1: Demography data of the whole study population:

Age	Range	60	-	88
	Mean ±SD	68.567	±	8.168
		N	%	
Gender	Male	35	58.33	
	Female	25	41.67	
Smoking	Yes	27	45.00	
	No	33	55.00	

Table 2: An overall comparison between both study groups in regard of demography data along with clinical symptoms on admission :

		Group				T-Test			
		Non-Tocilizumab		Tocilizumab		T	P-value		
Age	Range	60	-	88	60	-	86	1.141	0.259
	Mean ±SD	69.767	±	8.637	67.367	±	7.627		
Chi-Square		N	%		N	%		X ²	P-value
Gender	Male	20	66.67		15	50.00		1.714	0.190
	Female	10	33.33		15	50.00			
Clinical symptoms	Dyspnea	27	90.00		30	100.00		3.158	0.076
	Fever	7	23.33		10	33.33		0.739	0.390
	Cough	7	23.33		10	33.33		0.739	0.390
	Vomiting	1	3.33		2	6.67		0.351	0.554
	Diarrhea	2	6.67		3	10.00		0.218	0.640

Table 3: The Frequency and significance of comorbidities and Charlson co-morbidity index in both study groups:

Co- morbidities	Non-Tocilizumab		%	Tocilizumab		%	t	P-value
	DM	14	46.67	17	56.67	0.601	0.438	
	HTN	14	46.67	15	50.00	0.067	0.796	
	ISHD	9	30.00	4	13.33	2.455	0.117	
	CKD	9	30.00	9	30.00	0.000	1.000	
	HF	2	6.67	4	13.33	0.741	0.389	
	Liver cirrhosis	4	13.33	4	13.33	0.000	1.000	
	Malignancy	3	10.00	1	3.33	1.071	0.301	
T-Test							t	P-value
CCI	Range		3	-	8	2	-	9
	Mean ±SD		5.300 ±	1.579	5.067 ±	2.067	0.491	0.625

DM (Diabetes mellitus), HTN(Hypertension), HF (Heart Failure), ISHD(ischemic heart disease), CKD (chronic kidney disease), CCI (Charlson co-morbidity index)

Table 4 : An overall comparison between both study groups as regard laboratory findings on admission :

		Group				T-Test			
		Non- Tocilizumab		Tocilizumab		t	P-value		
TLC	Range	3	-	32	3.4	-	18	1.836	0.072
	Mean ±SD	11.910 ±	6.438	9.397 ±	3.847				
Lymphocytes	Range	0.2	-	7	0.2	-	10	-1.104	0.274
	Mean ±SD	1.797 ±	1.761	2.407 ±	2.462				
CRP	Range	2.8	-	400	6	-	320	0.250	0.804
	Mean ±SD	118.080 ±	102.329	112.333 ±	73.522				
D. Dimer	Range	0.2	-	9.7	0.2	-	5	0.443	0.660
	Mean ±SD	1.857 ±	1.947	1.671 ±	1.219				
BUN	Range	6	-	127	13	-	114	1.617	0.111
	Mean ±SD	46.467 ±	34.028	34.367 ±	22.831				
Creatine	Range	0.5	-	11	0.2	-	7.8	1.319	0.192
	Mean ±SD	2.537 ±	2.752	1.747 ±	1.785				
Ferritin	Range	54	-	2600	265	-	5600	-1.819	0.074
	Mean ±SD	1035.567 ±	664.414	1502.367 ±	1238.223				
LDH	Range	211	-	1071	200	-	987	-0.332	0.741
	Mean ±SD	463.600 ±	205.615	479.467 ±	162.402				
AST	Range	8	-	155	12	-	514	-0.920	0.361
	Mean ±SD	48.467 ±	37.516	64.600 ±	88.420				
ALT	Range	6	-	534	10	-	444	-0.266	0.791
	Mean ±SD	58.333 ±	104.897	64.867 ±	83.892				

TLC(total leukocyte count), CRP(C - reactive protein), AST(aspartate aminotransferase), ALT(alanine transaminase), BUN (blood urea nitrogen), LDH(lactic acid dehydrogenase)

Table5: Modes of oxygen support on admission of the two study groups:

Saturation	Group				Chi-Square	
	Non- Tocilizumab		Tocilizumab		X ²	P-value
	N	%	N	%		
MV	1	3.33	4	13.33	6.071	0.194
Nasal	8	26.67	4	13.33		
Venturi	11	36.67	6	20.00		
NRM	8	26.67	12	40.00		
NIV	2	6.67	4	13.33		
Total	30	100.00	30	100.00		

Table 6: Comparison between systemic inflammatory markers and liver enzymes of cases group before and after treatment with Tocilizumab:

		Time				Differences		Paired Test			
		Pre		Post		Mean	SD	t	P-value		
Ferritin	Range	265	-	5600	256	-	2300	591.267	1067.397	3.034	0.005*
	Mean ±SD	1502.367	±	1238.223	911.100	±	512.687				
LDH	Range	200	-	987	90	-	655	187.367	114.045	8.999	<0.001*
	Mean ±SD	479.467	±	162.402	292.100	±	116.458				
AST	Range	12	-	514	10	-	140	19.767	67.949	1.593	0.122
	Mean ±SD	64.600	±	88.420	44.833	±	26.730				
ALT	Range	10	-	444	9	-	116	24.800	62.693	2.167	0.039*
	Mean ±SD	64.867	±	83.892	40.067	±	25.336				

LDH (Lactate dehydrogenase) , ALT (Alanine transaminase) ,AST (Aspartate aminotransferase)

Table7: A comparison between symptoms of cases group before and after treatment with Tocilizumab:

	Before		After		Chi-Square	
	N	%	N	%	X ²	P-value
Dyspnea	30	100.00	19	63.33	11.132	0.001*
Fever	10	33.33	2	6.67	5.104	0.024*
Cough	10	33.33	5	16.67	1.422	0.233
Vomiting	2	6.67	0	0.00	0.517	0.472
Diarrhea	3	10.00	0	0.00	1.404	0.236

Table 8: A comparison in modes of oxygen support of cases group before and after treatment with Tocilizumab:

	Before		After		Chi-Square	
	N	%	N	%	X ²	P-value
MV	4	13.33	10	33.33	18.454	0.002*
Nasal	4	13.33	8	13.33		
Venturi	6	20.00	2	10.00		
NRM	12	40.00	0	16.67		
Room air	0	0.00	10	26.67		
NIV	4	13.33	0	0.00		

MV : mechanical ventilation, NRM : nonrebreather mask , NIV: noninvasive ventilation

Table 9: A comparison in modes of oxygen support of control group before and after receiving standard of care treatment only :

Non- Tocilizumab	Pre		Post		Chi-Square	
	N	%	N	%	X ²	P-value
MV	1	3.33	16	53.33	49.835	<0.001*
Nasal	8	26.67	4	13.34		
Venturi	11	36.67	1	0.00		
NRM	8	26.67	0	0.00		
Room air	0	0.00	9	33.33		
NIV	2	6.67	0	0.00		

MV : mechanical ventilation, NRM : nonrebreather mask , NIV: noninvasive ventilation

Table 10: Comparison between both study groups as regard the length of hospital stay :

Length of hospital stay (Weeks)	Group				T-Test	
	Non- Tocilizumab		Tocilizumab		t	P-value
	Range	1 - 4	1 - 4			
	Mean ±SD	2.167 ± 0.834	2.383 ± 0.827	-1.010	0.317	

Table 11: A relation between outcome (in terms of mortality and discharge) and treatment regimens among both study groups:

Outcome		Group				Chi-Square	
		Non- Tocilizumab		Tocilizumab		X ²	P-value
		N	%	N	%		
Died		16	53.33	12	40.00	1.071	0.301
Discharge		14	46.67	18	60.00		

DISCUSSION

The study constituted 60 patients enrolled in Ain Sham Geriatrics University Quarantine hospital in Cairo, Egypt. It was rendered from 1st of June in 2020 to 31st of August in 2020 where retrospective information acquisition from medical records was done.

Our study was done on elderly patients with severe coronavirus pneumonia with mean age 68.5 years as we intended to study the optimum treatment and management plan for this group of frail patients with high risk of mortality. Our findings were consistent with those published in 2021 by *Afriyie-Mensah et al.*, who conducted a retrospective trial for coronavirus cases with severe to critical disease admitted to the intensive care unit (ICU) at Korle-Bu Teaching Hospital from

April 13 to June 28, 2020, in Ghana. Severe coronavirus infection was distinguished as having oxygen saturation (SpO₂) less than 93% on room air with rising oxygen need, respiratory rate over 30/min, more than 50% pulmonary changes on computerized tomography scans and multiple organ failure along with proof of sepsis; the mean age of the cases who were enrolled in the ICU was sixty-two (62) years old.(1)

In present study, 45% of the study sample were smokers while 55 % were nonsmokers and smoking did not significantly affect the outcome of patients in both groups of the study population. A meta-analysis study conducted by *Gülsen* and his colleagues in 2020 (5) on 11322 coronavirus patients revealed a connection between the history of

Alaa Wagih et al., EJGG.2023; 10(1): 13-22

smoking and severity of coronavirus infection. COVID-19 was found to be serious in 10.7% (978/9067) of non-smokers, whereas it was found to be serious in 21.2% (65/305) of smokers (6). The sample size of the study population differs from that in *Gülksen et al.* study, which may contribute to divergent results.

In current study, dyspnea is the most common presenting symptom among both groups of the study population who have severe COVID-19 pneumonia, followed in prevalence by fever and cough. That proves that dyspnea was linked to the severity and mortality of coronavirus pneumonia. However, just few patients complained of vomiting and diarrhea. These findings were comparable to those published by *Shi et al., (2020)*, who conducted a meta-analysis according the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline on 2851 coronavirus cases (2114 survived and 737 did not survive) of varying age and severity. The majority of the articles were created in China. They revealed that shortness of breath (dyspnea) was closely accompanied with higher death rates in coronavirus cases on account of eleven studies with 2091 cases.

Nevertheless, based on 15 studies with 2818 cases, it was established that there was no significant association between high grades of fever and the occurrence of death in patients with coronavirus, implying that it could actually protect coronavirus cases from developing severe and critical disease outcomes, which could explain why fever was not common among our study population who suffered from severe pneumonia. (16)

The study done by *Perotte et al.(2021)*, that was a retrospective computational analysis of all coronavirus patients (confirmed and suspected) presenting to the adult American emergency rooms (patients aged 22 and older) with varying severity, showed that in the COVID-positive group, dyspnea occurred in 49% of cases, whereas "fever" occurred in 44% of cases.

In current study, most cases had diabetes mellitus and hypertension, with less

prevalence ischemic heart disease, heart failure, liver cirrhosis, malignancy and chronic kidney disease, which revealed no statistical significance among both groups of the study population. Also, overall there was no statistical significance regarding Charlson co-morbidity index between both groups of the study population (P-value 0.625). Our reports agreed with data published by *Alattar et al (2020)* who performed a review retrospectively of patients who received tocilizumab with confirmed severe coronavirus infection by laboratory. Twenty-five individuals were involved, with a mean age of 58 years and a male predominance (92%). DM (48%), CKD (16%), and cardiovascular disease (12%) were among the comorbidities. (2)

On the contrary, these results disagree with *Petrilli et al. (2020)*'s study, which is a cohort study done prospectively in one academic medical center in New York City and Long Island on 5279 patients with severe acute respiratory syndrome caused by coronavirus (SARS-Cov-2) between 1st of March 2020 and 8th of April 2020 for different groups of age. It found that the most associated comorbidities were cardiovascular disease (70.6%), DM (34.7%), and CKD (21.2%).

In the current study, the differences in Ferritin, LDH, and ALT levels were statistically significant, whereas no major difference was found between AST level before and after treatment with Tocilizumab. The previously mentioned results agree with the data reported by *Conrozier et al, (2020)* who made an analysis retrospectively of a series of cases with COVID-19- ARDS who were treated with TCZ (2 infusions of 8 mg/kg). TCZ was used to treat Forty patients. Most of them had chronic conditions. Ten patients died while thirty patients (about 75% of them) benefited from TCZ. Following TCZ administration, CRP in the survivors dramatically declined as early as the fourth day (-86.7%, p0.0001) and stabilized by the sixth day. At the sixth day, the fibrinogen and lymphocyte count were back to baseline levels. Levels of ferritin dramatically dropped as well, while D-dimer's levels (p=0.68) and other analyzed markers levels did not show a

Alaa Wagih et al., EJGG.2023; 10(1): 13-22
significant change (haemoglobin, leucocyte count, AST). (3)

These findings were also consistent with findings published by *Ivan Hariyanto (2021)*, who conducted a meta-analysis research on 577 patients with coronavirus infection. The meta-analysis revealed that treatment with tocilizumab can cause a decline in CRP (C-reactive protein) ($p = .00001$), d-dimer, ferritin ($p = .0002$), procalcitonin ($p = .004$), and a rise in lymphocyte levels ($p = .004$), implying that giving tocilizumab is efficient in reducing the biomarkers of coronavirus infection.

In the trial of *Alattar et al (2020)*, who published an analysis of tocilizumab-treated cases with laboratory-verified severe coronavirus infection., there were 25 patients total, with a mean age of 58 years and a 92% preponderance of males. Three (12%) of the nine patients who were released from the intensive care unit died. Following the start of tocilizumab, the percentage of patients in need of invasive ventilatory methods decreased from 84% to 60% on day 7 ($P = .031$) and 28% on day 14 ($P = .001$). Tocilizumab was linked to a dramatic fall in inflammatory biomarkers, improvement of radiological findings, and a reduction in the need for ventilatory assistance in patients with severe coronavirus infection (2), which is consistent with the findings of our trial.

Our study showed that tocilizumab had a significant impact on decreasing oxygen demand and need for mechanical ventilatory mode in elderly cases known to have severe coronavirus pneumonia, while it proved that

REFERENCE

- 1- Afriyie-Mensah, J., Aboagye, E. T., Ganu, V. J., Bondzi, S., Tetteh, D., Kwarteng, E., ... & Adjei, P. (2021). *Clinical and therapeutic outcomes of COVID-19 intensive care units (ICU) patients: a retrospective study in Ghana. The Pan African Medical Journal*, 38.
- 2- Alattar, R., Ibrahim, T. B., Shaar, S. H., Abdalla, S., Shukri, K., Daghfal, J. N., ... & Omrani, A. S. (2020). *Tocilizumab for the treatment of severe coronavirus disease 2019. Journal of medical virology*, 92(10), 2042-2049.
- 3- Conrozier, T., Lohse, A., Balblanc, J. C., Dussert, P., Royer, P. Y., Bossert, M., ... & Zayet, S. (2020). *Biomarker variation in patients successfully treated with tocilizumab for severe coronavirus disease 2019*

no similar significance on length of hospital stay and mortality was found, we think that tocilizumab did not affect mortality in our patient despite of decreasing oxygen demand and need of mechanical ventilation as most of our patients has long ICU stay (average three weeks) they exposed to the complications of prolonged ICU stay like secondary bacterial infections, pressure ulcers, and metabolic derangement, all these factors make them complicated cases with poor prognosis regardless of COVID-19 state and its impact. A randomized trial published in The New England Journal of Medicine which looked at the effects of tocilizumab on 389 patients agrees with our study findings. This trial established that treatment with tocilizumab lowered progression to the demand for invasive ventilatory methods or death in cases hospitalized with coronavirus pneumonia who were not placed on mechanical ventilators, but it did not increase survival. (15)

Furthermore, preliminary findings from a study in France comparing treatment with tocilizumab in addition to standard of care to treatment with standard of care solely in 129 COVID-19 patients hospitalized with moderate to severe pneumonia revealed that TCZ reduced the rate of non-invasive or mechanical ventilation. (9)

CONCLUSION

Tocilizumab treatment at a dose of 8mg/kg/dose for elderly patients improves some clinical outcomes and prognosis in severe coronavirus pneumonia.

(COVID-19): results of a multidisciplinary collaboration. *Clin Exp Rheumatol*, 38(4), 742-747.

4-De Rossi, N., Scarpazza, C., Filippini, C., Cordioli, C., Rasia, S., Mancinelli, C. R., ... & Montichiari COVID-19 Study Group. (2020). *Early use of low dose tocilizumab in patients with COVID-19: A retrospective cohort study with a complete follow-up. EClinicalMedicine*, 25, 100459.

5-Guaraldi, G., Meschiari, M., Cozzi-Lepri, A., Milic, J., Tonelli, R., Menozzi, M., ... & Mussini, C. (2020). *Tocilizumab in patients with severe COVID-19: a retrospective cohort study. The Lancet Rheumatology*, 2(8), e474-e484.

Alaa Wagih et al., EJGG.2023; 10(1): 13-22

6- Gülsen, A., Yigitbas, B. A., Uslu, B., Drömann, D., & Kilinc, O. (2020). The effect of smoking on COVID-19 symptom severity: systematic review and meta-analysis. *Pulmonary medicine*, 2020.

7-Huang, H., Cai, S., Li, Y., Li, Y., Fan, Y., Li, L., ... & Deng, X. (2020). Prognostic factors for COVID-19 pneumonia progression to severe symptoms based on earlier clinical features: a retrospective analysis. *Frontiers in medicine*, 7, 557453.

8- Ivan Hariyanto, T., & Kurniawan, A. (2021). Tocilizumab administration is associated with the reduction in biomarkers of coronavirus disease 2019 infection. *Journal of Medical Virology*, 93(3), 1832-1836.

9-Kyriakopoulos, C., Ntritsos, G., Gogali, A., Milionis, H., Evangelou, E., & Kostikas, K. (2021). Tocilizumab administration for the treatment of hospitalized patients with COVID-19: a systematic review and meta-analysis. *Respirology*, 26(11), 1027-1040.

10-Luo, P., Liu, Y., Qiu, L., Liu, X., Liu, D., & Li, J. (2020). Tocilizumab treatment in COVID-19: a single center experience. *Journal of medical virology*, 92(7), 814-818.

11-Perotte, R., Sugalski, G., Underwood, J. P., & Ullo, M. (2021). Characterizing COVID-19: a chief complaint based approach. *The American Journal of Emergency Medicine*, 45, 398-403.

12-Petrilli CM, Jones SA, Yang J, et al. (2020): Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease

2019 in New York City: prospective cohort study. *bmj*, 369.

13-Price, C. C., Altice, F. L., Shyr, Y., Koff, A., Pischel, L., Goshua, G., ... & Malinis, M. (2020). Tocilizumab treatment for cytokine release syndrome in hospitalized patients with coronavirus disease 2019: survival and clinical outcomes. *Chest*, 158(4), 1397-1408.

14- Radbel, J., Narayanan, N., & Bhatt, P. J. (2020). Use of tocilizumab for COVID-19-induced cytokine release syndrome: a cautionary case report. *Chest*, 158(1), e15-e19.

15- Salama, C., Han, J., Yau, L., Reiss, W. G., Kramer, B., Neidhart, J. D., ... & Mohan, S. V. (2021). Tocilizumab in patients hospitalized with Covid-19 pneumonia. *New England Journal of Medicine*, 384(1), 20-30.

16- Shi, L., Wang, Y., Wang, Y., Duan, G., & Yang, H. (2020). Dyspnea rather than fever is a risk factor for predicting mortality in patients with COVID-19. *Journal of Infection*, 81(4), 647-679.

17- Xu, X., Han, M., Li, T., Sun, W., Wang, D., Fu, B., ... & Wei, H. (2020). Effective treatment of severe COVID-19 patients with tocilizumab. *Proceedings of the National Academy of Sciences*, 117(20), 10970-10975.-19 patients with tocilizumab. *Proc Natl Acad Sci U S A*. 2020.

18- Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., ... & Wang, F. S. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *The Lancet respiratory medicine*, 8(4), 420-422