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Letter

Tocilizumab improves survival in patients with persistent hypoxia in severe COVID-19 pneumonia

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Kewan et al. [1] have shown that using single dose 400 mg tocilizumab reduces the duration of critical resource use in severe Coronavirus disease 2019 (COVID-19) pneumonia. They had included patients with hypoxia, lung infiltrates and elevated inflammatory markers. We work at a government-funded tertiary care center in India. We had compassionate use access to tocilizumab from 13th May 2020. In view of resource-limitation, we decided to use it in patients with severe COVID-19 pneumonia with lung infiltrates, elevated inflammatory markers and persistent hypoxia (oxygen saturation of 94% or less despite giving supplemental oxygen of 15 L/min via non-rebreathing mask or PaO_2/FiO_2 ratio of less than 200).

We present data from a retrospective cohort study performed at our center over a 6 week period from 20th April 2020 to 5th June 2020. A total of 1370 patients with COVID-19 were admitted in the department of medicine during this period. Of these, 985 (72%) had hypoxia, defined as oxygen saturation 94% or less, at presentation. Of these, 210 patients met the inclusion criteria of oxygen saturation of 94% or less despite giving supplemental oxygen of 15 L/min via non-rebreathing mask or PaO_2/FiO_2 ratio of less than 200. Of these, 49 patients died within 24 h of admission and were excluded from the analysis. The remaining 161 patients were considered for analysis. Of the 161 patients, 70 received a single intravenous dose of 400 mg tocilizumab while 91 did not. All patients received antibiotics, hydroxychloroquine 400 mg once daily, ivermectin 12 mg once daily, oseltamivir 75 mg twice daily, low molecular weight heparin 1 mg/kg subcutaneously once daily (twice daily if D-dimer >3000 ng/mL), methylprednisolone 125–500 mg intravenously once daily, and other supportive care as needed.

Tocilizumab group had younger patients than control group (median 52 years versus 55 years; p value 0·001) (Table 1). Eight (8·8%) patients in the control group while 2 (2·9%) patients in the tocilizumab group received invasive ventilation (p value 0·122). One (1·1%) patient in the control group and 17 (24·3%) patients in the tocilizumab group received non-invasive ventilation (p value 0·001). The median days of hospitalization were 11 (interquartile range (IQR): 4·5 to 21). The median days of follow up was 16 (IQR: 4·5 to 50). At last follow up, 94 (58·4%) patients died, 56 (34·8%) have been discharged from the hospital and 11 (6·8%) are still admitted. On multivariable Cox regression analysis with age, hypertension, tocilizumab use, use of invasive ventilation and use of non-invasive ventilation, the independent predictors of death were age (Hazards ratio (HR) 1·022; 95% CI: 1·001 to 1·044) and tocilizumab use (HR 0·616; 95% CI: 0·382 to 0·992).

Thus, we conclude that tocilizumab use is associated with survival benefit in patients with persistent hypoxia in severe COVID-19 pneumonia.

Table 1
Comparison between patients who received tocilizumab versus those who did not. The data are expressed as either median (interquartile range) or number (percentage). Category E was defined as pneumonia with respiratory failure while Category F was defined as pneumonia with respiratory failure and multi-organ dysfunction [2]. Chi-square test was used for categorical data while Mann Whitney U test was used for continuous data.

	Tocilizumab group	Control group	P value
Number of patients	70	91	
Age	52 (44–57)	55 (48–65)	**0·001**
Male Sex	47 (67·1)	53 (58·2)	0·248
Diabetes	33 (47·1)	49 (53·8)	0·399
Hypertension	16 (22·9)	39 (42·9)	**0·008**
Any comorbidity	43 (61·4)	68 (74·7)	0·071
CRP	115·5 (56–178·7)	97 (88–104)	0·314
Respiratory Rate	34(30–38)	31(25–40)	0·281
Category			0·753
E	62 (88·6)	82 (90·1)	
F	8 (11·4)	9 (9·9)	
Noninvasive ventilation	17 (24·3)	1 (1·1)	**0·001**
Invasive ventilation	2 (2·9)	8 (8·8)	0·122
Days of hospitalization	14 (9–25·5)	6(3–14)	**0·001**
Days of follow up	31 (11·75–48)	7(3–50)	0·072
Discharged patients	26 (37·1)	30 (33)	
Ongoing hospitalization	11 (15·7)	0 (0)	
Deaths	33 (47·1)	61 (67)	**0·011**

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Declaration of Competing Interest

Dr Gokhale has nothing to disclose. Dr Mehta has nothing to disclose. Dr Karnik has nothing to disclose. Dr Kulkarni has nothing to disclose. Mr Gokhale has nothing to disclose.

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Data sharing statement

The raw data will accessible on contacting the corresponding author.

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