

Does Colchicine Prevent Progression to Artificial Ventilation in Covid-19 Positive Patients? A Study from Lahore, Pakistan

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Abstract

Objective: To find out the effect of colchicine in prevention of progression to artificial ventilation in Covid-19 patients including young and elderly patients.

Material and Methods: Study was conducted from 1st April 2020 till 30th September 2020 in a private, tertiary care hospital of Lahore. A retrospective cohort study was conducted on conveniently selected 179 PCR or radiologically confirmed Covid-19 positive adult and elderly, male and female patients admitted in Covid ward and Intensive care Unit (ICU) using the electronic as well as paper-based record. Amongst these patients, 33 patients were given colchicine, 137 recovered and 20 progressed to invasive ventilation.

Result: Total 179 patients were included in the study and 96 (53.6%) were males and 83 (46.4%) were females. 52.5% had Diabetes mellitus, 58.7% had hypertension, 27.9% had ischemic heart disease, 8.4% had renal disease, 6.7% had lung disease/smoker. The average length of stay in hospital was 6.569 ± 6.355 days. The outcome and progression to artificial ventilation in the patients who were given colchicine as compared to those who were not given colchicine were not statistically significant with a p value of 0.053 and 0.619, respectively.

Conclusion: Colchicine has not shown a significant improvement in the outcome of Covid-19 and does not help in prevention of progression to invasive ventilation irrespective of age, gender, and co-morbidities.

Keywords: Colchicine, invasive ventilation, outcome, Covid-19

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Introduction

Covid-19 is caused by a novel coronavirus also known as SARS-CoV-2 was first reported in December 2019 in Wuhan, Hubei Province, China.¹ The Coronaviruses (CoVs) are a group of viruses that can be found

in birds as well as mammals causing respiratory and intestinal disease.²

According to the World Health Organization (WHO) on 28th June 2023, 6,947,192 deaths have been reported globally.³ World health organization (WHO) on 27th May 2020, defined the severity of the disease as, adults with clinical signs of pneumonia accompanied by one of the following: respiratory rate of more than 30 breaths/min, severe respiratory distress, or oxygen saturation (SpO₂) of less than or equal to 90% on room air.⁴ WHO also provided a clinical progression scale to measure the disease severity including the scores from 0 (non-infected) to 10 (death) for Covid-19 clinical status assessment.⁵ Patients with intense disease have airway failure and they usually need endotracheal intubation and mechanical ventilation.⁶ The Viral load can be a marker to assess the severity of disease and prognosis. Early

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viral clearances and a negative RT-PCR test by 10th day of onset was found in patients having mild disease as compared to those having severe disease.⁷ Another factor associated with the disease severity is inflammation. Thus, the use of corticosteroids and interleukin-6 (IL-6) inhibitors reduce the mortality in severe Covid-19.⁸ The infection caused in Covid-19 diseases can be divided into phase of initiation, pulmonary and hyper-inflammatory with treatment varying from antivirals and corticosteroids to anti-inflammatory drugs depending on the intensity of disease. The hyper-inflammatory stage has increased C-reactive protein, d-dimers, pro-inflammatory cytokines, and chemokines and all these indicate towards the disease severity.⁹ The inflammatory effect is more eminent in the lungs and the vascular endothelium. Inflammasomes play an important role in innate immunity of Covid-19 infection. The degree of inflammasomes activation particularly the nucleotide binding domain (NOD)-like pyrin domain 3 (NLRP 3) has shown relation with the disease severity.¹⁰ After the emergence of Covid-19, lots of treatment options were considered for its treatment including antivirals, lopinavir, remdesivir and corticosteroids.¹¹

Colchicine has been in use for over 2000 years. Colchicine has anti-inflammatory and antiviral properties, and it acts via the tubulin-colchicine complex. Currently, the Food and Drug Administration (FDA) has approved the use of oral Colchicine for the treatment of gout, Familial Mediterranean fever, off-label uses include arthritis and pericarditis.¹² The use of colchicine has shown beneficial results due to its anti-inflammatory effect including the inactivation of NLRP 3 inflammasome. However, only a few randomized control trials support this.¹⁰ Colchicine was found to be beneficial in reducing Covid-19 disease severity and mortality particularly giving it early in the course of disease. Giving colchicine in outpatient settings can also have the same effect.¹³

The use of low dose colchicine as an adjuvant to supportive therapy can help decrease morbidity and mortality.¹⁴ However, according to a study there is minimal role of colchicine in improving the disease outcomes while comparing the effect of colchicine plus standard treatment with standard treatment alone.¹⁵ This study is being carried out to find out the effect of colchicine in prevention of progression to artificial ventilation in Covid-19 patients including young and elderly patients. A lot of research work is being done internationally and nationally on SARS-CoV-2 virus however there are many

loopholes that need to be investigated further. This study can be a fruitful addition to the current available literature on Covid-19.

Materials and Method

All in-patients with either laboratory confirmed Covid-19 via Polymerase Chain Reaction test or radiologically reported Covid-19 on CT chest by a consultant radiologist during the study period were included. A total of conveniently selected 179 patients were retrospectively studied by using the electronic as well as paper-based record from 1st April 2020 till 30th September 2020 at a well-known private hospital in Lahore with dedicated Covid ward and Intensive Care Unit. Patients having known thromboembolic condition were not included in the study. The hospital was selected based on administrative convenience and availability of complete electronic medical records after discharge. Patients records and investigations from the first presentation at the hospital till their discharge/death were examined after obtaining consent from the patient or next of kin in case of deceased patients. The ethical review was done by the hospital ethical review committee and the anonymity of the patients was maintained by de-identification of the record. The patients who received colchicine, progressed to invasive or non-invasive ventilation and those who expired and recovered from Covid-19 were included in the study. Data was entered, cleaned and analyzed using SPSS version 24.0. Frequency tables were generated for all possible variables. Means and other parameters of central tendency were calculated for continuous data. Chi Square was applied to find out association between categorical variables. P value of 0.05 was taken as significant.

Results

This study had an objective to find out the role, if any, of colchicine in prevention of progression to artificial ventilation in adult Covid-19 patients. Total 179 patients were included in the study and 96(53.6%) were males and 83(46.4%) were females, 2 out of 83(1.1%) had Covid-19 during pregnancy. The mean age of the patients was 58.266 ± 14.07 with mean stay in hospital of 6.569 ± 6.355 days, mean Oxygen requirement of 7.04 ± 2.89 liters. There were 33 out of 179 (18.4%) patients who were given colchicine. The non-invasive ventilation was received by 5 out of 179 (2.8%) patients while 20 out of 179 (11.2%) received invasive ventilation. (Table-1) 52.5% had Diabetes mellitus, 58.7% had hypertension,

27.9% had ischemic heart disease, 8.4% had renal disease, and 6.7% had lung disease/smoker. The average length of stay in hospital was 6.569±6.355 days. The outcome of patients who received colchicine was that 12 out of 33 (36.4%) expired and 21 out of 33(63.6%) recovered in comparison to the patients who did not receive colchicine, 30 out of 146(20.5%) expired and 116 out of 146(79.5%) recovered and this difference is statistically insignificant with the p-value of 0.053 using the Chi-square test and taking a statistically significant value of <0.05. The relative risk (RR) of death was 1.7(1.018-3.075) in the colchicine group compared to the group not given colchicine. (Table-2)

The progression to artificial ventilation in patients who received colchicine showed that 5 out of 33 (15.2%) progressed to invasive ventilation and 28 out of 33 (84.8%) did not progress to invasive ventilation as compared to those who did not receive colchicine only 15 out of 146 (10.3%) progressed to invasive ventilation and 131 out of 146 (89.7%) did not progress to invasive ventilation and this difference is statistically not significant with a p-value of 0.619. The relative Risk (RR) of progression to invasive ventilation was found to be 1.47, however, the Confidence Intervals (CI) of 0.57-3.77 indicates that this difference is unlikely to be significantly (Table-3)

Table 1: Frequency of various variables

Variable	n=179	Percentage %
Male	96	53.6
Female	83	46.4
Covid-19 and pregnancy	2	1.1
Non- invasive	5	2.79
Invasive	20	11.17
Colchicine received	33	18.4
Expired	42	23.46
Recovered	137	76.53

Table 2: Outcome and Colchicine

Variable	Outcome		p value	Relative Risk	
	Expired	Recovered			
Colchicine	Given	n=33 12 36.4	21 63.6	0.053	1.7 (1.018-3.075)
	Not given	n=146 30 20.5	116 79.5		

Discussion

Colchicine is an anti-inflammatory drug that has shown to be beneficial in the treatment of Covid-19 disease. Colchicine helps in reducing mortality and hospitali-

Table 3: Progression to Invasive Ventilation and Colchicine

Variable	Progression to Invasive Ventilation		P value	RR	
	Yes	No			
Colchicine	Given	n=33 5 15.2	28 84.8	0.619	1.47 (0.57 – 3.77)
	Not given	n=146 15 10.3	131 89.7		

zation. It has shown an advantage in decreasing the level of neutrophils in blood and ultimately decreasing the risk of disease severity.¹⁶ Colchicine decreases inflammation through inhibition of microtubule polarization thus decreasing the viral load.¹² A study conducted in China shows that elevated levels of neutrophils or neutrophil to lymphocyte ratio (NLR) play a role in formation of cytokine storm leading towards the inflammatory process in Covid-19, which is associated with the severe disease and mortality.¹⁷

Our study proved that Colchicine does not decrease the mortality and progression to invasive ventilation. This relationship could also be found in RCTs and meta-analysis done in China, UK, Indonesia and Nepal that efficacy of colchicine for the treatment of Covid-19 and in preventing the progression to severe disease is relatively low.^{10,11,18,19}

A meta-analysis conducted in 2022 included 6 RCTs, and amongst these only one trial included hospitalized patients and had showed that colchicine did not cause any significant reduction in mechanical ventilation.²⁰

A study done in Mexico in 2021, showed that 56 patients were given Colchicine and 60 patients received placebo, however, Colchicine had no effect decreasing the symptoms of Covid-19 nor in the days of ICU and hospitalization instead it raised the level of BUN and decreased the level of IL-8, IL-12p70 and IL-17A thus concluding that Colchicine is safe but not effective for the treatment of Covid-19.²¹

A meta-analysis done in 2021 showed that there was no association of colchicine with mortality, duration of hospitalization, risk of ventilation or dying of those not ventilated at baseline. There was no benefit of giving colchicine with corticosteroid.¹⁰

Substantial number of studies done in Pakistan have shown the benefit of Colchicine in decreasing the mortality related to Covid-19. A meta-analysis done in April 2022 in Pakistan showed that Colchicine helped in decreasing the level of CRP, d-dimers and mechanical ventilation.⁹

A meta-analysis conducted in 2021 in Pakistan showed

that 4 out of 6 studies showed the decreasing trend of CRP in comparison between the patients who were given Colchicine and the control group, thus stating the benefit of Colchicine in decreasing the biomarkers of inflammation in moderate to severe Covid-19 patients.¹⁴ Our study was conducted in a single institute so we would recommend randomized controlled trials at a larger scale might help to evaluate the effect of colchicine on progression to invasive ventilation and outcomes. The results in our study did not support the role of colchicine in Covid-19 treatment, however, the sample size was small and the colchicine group was much smaller than the usual care group.

Conclusion

Colchicine does not play a significant role in prevention of progression to invasive ventilation and improving the outcomes irrespective of age, gender, and co-morbidities.

Conflicts of interest: *None*

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References

1. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. *Clinical immunology*. 2020 Jun 1;215:108427
2. Sun J, He WT, Wang L, Lai A, Ji X, Zhai X, et al COVID-19: epidemiology, evolution, and cross-disciplinary perspectives. *Trends in molecular medicine*. 2020 May 1;26(5):483-95.
3. World Health Organization. WHO Coronavirus (COVID-19) Dashboard [internet].2023 [cited 2023 June 30]. Available from <https://covid19.who.int/>
4. Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al Predictors of COVID-19 severity: a literature review. *Reviews in medical virology*. 2021 Jan;31(1):1-0.
5. Characterisation WHOWGotC, Management of Ci. A minimal common outcome measure set for COVID-19 clinical research. *Lancet Infect Dis*. 2020;20(8): e192-7
6. Lima WG, Brito JC, da Cruz Nizer WS. Ventilator-associated pneumonia (VAP) caused by carbapenem-resistant *Acinetobacter baumannii* in patients with COVID-19: Two problems, one solution?. *Medical hypotheses*. 2020 Nov;144:110139.
7. Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM, et al. Viral dynamics in mild and severe cases of COVID-19. *The Lancet infectious diseases*. 2020 Jun 1; 20(6): 656-7.
8. Group TR. Dexamethasone in hospitalized patients with Covid-19—preliminary report. *The New England journal of medicine*. 2020 Jul 17.
9. Yasmin F, Najeeb H, Moeed A, Hassan W, Khatri M, Asghar MSet al. Safety and efficacy of colchicine in COVID-19 patients: A systematic review and meta-analysis of randomized control trials. *PloS one*. 2022 Apr 5;17(4):e0266245.
10. Group RC. Colchicine in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *The Lancet Respiratory Medicine*. 2021 Dec 1;9(12):1419-26.
11. Stasi C, Fallani S, Voller F, Silvestri C. Treatment for COVID-19: An overview. *European journal of pharmacology*. 2020 Dec 15;889:173644.
12. Schlesinger N, Firestein BL, Brunetti L. Colchicine in COVID-19: an old drug, new use. *Current pharmacology reports*. 2020 Aug;6(4):137-45.
13. Hariyanto TI, Halim DA, Jodhinata C, Yanto TA, Kurniawan A. Colchicine treatment can improve outcomes of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Clinical and Experimental Pharmacology and Physiology*. 2021 Jun;48(6):823-30.
14. Sarwar M, Ali Z, Fatima M, Sarfraz Z, Sarfraz A, Cherez-Ojeda I. Colchicine, COVID-19 and hematological parameters: A meta-analysis. *Journal of clinical laboratory analysis*. 2021 Dec;35(12):e24057.
15. Mikolajewska A, Fischer AL, Piechotta V, Mueller A, Metzendorf MI, Becker M, et al. Colchicine for the treatment of COVID-19. *Cochrane Database of Systematic Reviews*. 2021(10).
16. Hariyanto TI, Halim DA, Jodhinata C, Yanto TA, Kurniawan A. Colchicine treatment can improve outcomes of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Clinical and Experimental Pharmacology and Physiology*. 2021 Jun;48(6):823-30.
17. Li X, Liu C, Mao Z, Xiao M, Wang L, Qi S, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. *Critical Care*. 2020 Dec;24(1):1-0.
18. Lan SH, Hsu CK, Lai CC, Chang SP, Lu LC, Hung SH, et al. Effect of colchicine on the outcomes of patients with COVID-19: a systematic review and meta-analysis of randomised controlled trials. *Annals of Medicine*. 2022 Dec 31;54(1):1956-65.
19. Kow CS, Lee LH, Ramachandram DS, Hasan SS, Ming LC, Goh HP. The effect of colchicine on mortality outcome and duration of hospital stay in patients with COVID-19: A meta-analysis of randomized trials. *Immunity, inflammation and disease*. 2022 Feb;10(2):255-64.

20. Patoulas D, Katsimardou A, Imprialos K, Stavropoulos K, Papadopoulos C, Doumas M. COLCHICINE FOR The Prevention Of COVID-19 “HARD” Out-comes: All That Glitters Is Not Gold. An Updated Analysis Of Randomized Controlled Trials. Journal of Hypertension. 2022 Jun 1;40(Suppl 1):e169.
21. Absalón-Aguilar A, Rull-Gabayet M, Pérez-Fragoso A, Mejía-Domínguez NR, Núñez-Álvarez C, Kershovich-Stalnikowitz D, et al. Colchicine is safe though ineffective in the treatment of severe COVID-19: a randomized clinical trial (COLCHIVID). Journal of General Internal Medicine. 2022 Jan;37(1):4-14.

Authors Contribution

MSR: Conceptualization of Project

MSR, ES: Data Collection

JG: Literature Search

US, MU: Statistical Analysis

HS: Drafting, Revision

JG: Writing of Manuscript