



AN OBSERVATIONAL, RETROSPECTIVE STUDY ON THE IMPACT OF CORTICOSTEROIDS AND THEIR OUTCOMES IN COVID-19 PATIENTS

Pulmonary Medicine

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ABSTRACT

Background: Corticosteroids were a topic of controversy during the ongoing pandemic. Safety and effectiveness of corticosteroids still remains questionable in COVID-19.

Aims and objectives: To determine the reduction of morbidity and mortality, to assess the length of hospital stay, secondary infections and adverse events in COVID-19 patients receiving corticosteroids.

Settings and Design: A retrospective, observational study was performed at Krishna Institute of Medical Sciences (KIMS) hospital, Secunderabad.

Materials and Methods : A total of hundred RT-PCR positive patients aged >18 years were included in the study, of which, 75 patients received corticosteroids and 25 patients did not. All the necessary information was collected for a period of 6 months from January, 2021-June, 2021 through the subjects' medical records.

Statistical analysis used: Statistical SPSS version 2.0 software by carrying out chi-square test and independent t-test.

Results: Patients in the corticosteroids group showed 80% recovery and 20% mortality, while corticosteroid-free patients showed 100% recovery. From the overall sample, 15% (15) fatality cases were reported in corticosteroid group out of which 80% were male, 67% aged 61-80 years, and 40% and 33% had HTN and HTN + DMII as co-morbidities respectively. No significant difference was observed in mean hospital LOS between corticosteroid (10.76 ± 5.26) and corticosteroid-free (9.92 ± 6.04) patients. 13% of secondary infections and 12% of adverse events were observed in the corticosteroids group.

Conclusions: The study concludes that COVID-19 patients who received corticosteroids showed no survival benefit. It reveals that corticosteroids have no impact on hospital LOS. Secondary infections and adverse events were more pronounced in the corticosteroids group.

KEYWORDS

COVID-19, corticosteroids, mortality

INTRODUCTION

The life-threatening outbreak in human history was observed in the form of COVID-19 caused by SARS-CoV-2. Since the initial instances in Wuhan, China towards the end of December 2019, the pandemic exploded. [1] COVID-19 was designated by the WHO as a Public Health Emergency of International Concern (PHEIC) because of its rapid spread capacity. [2] Overall, 203,295,170 confirmation of cases of COVID-19 have been recorded by the WHO as of 10th August 2021, including 4,303,515 deaths.

SARS-CoV-2 is single stranded RNA virus that targets the respiratory system. The spectrum of disease associated with this infection ranges from asymptomatic or mild self-limiting infection to rapidly progressing life threatening conditions known as acute respiratory failure and acute respiratory distress syndrome (ARDS). [3],[4],[5] Fever, cough, and high viral loads characterise the early stage of the disease. The following stage is marked by continuous inflammation of the lungs with diffuse alveolar destruction, inflammatory infiltrations, and microvascular thrombosis. [6] The uncontrolled hyperinflammatory reaction in the latter stage leads to multi-order dystrophy with a substantial probability of fatality. [7],[8]

Although several treatment strategies have been examined, there is no substantial proof of profit. [9] Corticosteroids are one type of agents that received significant attention. [10] It has been proposed that the potent anti-inflammatory properties of corticosteroids have primarily been thought about in COVID-19 as a means to stave off the "cytokine storm" which often occurs in the first 5-7 days. [7]

The corticosteroid proposal is mainly based on the results of the RECOVERY trial, which showed that the results of corticosteroids are promising in severe and critically ill COVID-19 patients. [11] In other investigations, however, the effects of corticosteroids in COVID-19 have been inconsistent. Some even determined that the risk of death

may increase with corticosteroids. One of the published meta-analysis reviewed 5270 patients from 15 observational studies on corona virus disease which concluded that patients receiving corticosteroids were more likely to be critically ill, had a longer length of hospital stay, higher mortality and more bacterial infections. [12],[13],[14] Since corticosteroids promote immunological suppression, their use has been mainly discouraged by fear of deteriorating virus multiplication. [15]

Corticosteroids thus seem to be double-edged sword in the fight against COVID-19 and need to be used judiciously considering the risk benefit ratio. These findings revived our desire to explore the role of corticosteroids and their influence on clinical outcomes in confirmed COVID-19 patients.

We aimed to investigate the impact of corticosteroids and their outcome in COVID-19 patients. This observational retrospective study was conducted with the objective to determine the reduction of morbidity and mortality, the hospital length of stay and to assess adverse events and secondary infections in COVID-19 patients receiving corticosteroids.

MATERIALS AND METHODS

An observational, retrospective study was conducted in the department of Pulmonology at Krishna Institute of Medical Sciences (KIMS), Secunderabad, Telangana, India. It is a multispecialty, tertiary care private hospital approved by National Accreditation Board for Hospitals and Healthcare (NABH) & National Accreditation Board for Testing and Calibration Laboratories (NABL). The study was carried out for a period of 6 months from January, 2021-June, 2021 after obtaining the approval from KIMS ethics committee. A total of 100 RT-PCR confirmed COVID-19 patients of either sex, aged >18 years and with co morbidities (hypertension, diabetes mellitus-2, CVA, CKD) were included in the study as per the inclusion criteria. From the

overall population (n=100), 75 patients received corticosteroids and 25 patients did not. All the necessary information was taken down on specially designed data collection form from the subject's medical records that are maintained electronically. The collected data was analysed using a statistical SPSS version 2.0 software by carrying out chi-square test and independent t-test.

RESULTS

The study population accounts a total of 100 subjects diagnosed with COVID-19, out of which 75 patients received corticosteroids and 25 patients did not. It contains both male and female participants, with the majority being male and with a mean age of 53.97 ± 13.63 years. Co morbidities existed in the study population include hypertension, diabetes mellitus-2, CVA and CKD.

Outcomes of treatment:

The outcomes of treatment in the study population are presented in (Figure 1). 85% of the population showed recovery and 15% showed mortality. In the subjects who received corticosteroids, there is 80% recovery and 20% mortality, whereas in the subjects who did not receive corticosteroids, there is 100% recovery rate. P value was calculated by chi-square test ($p=0.0153$) which indicates that statistically significant relationship exists between outcome and treatment provided.

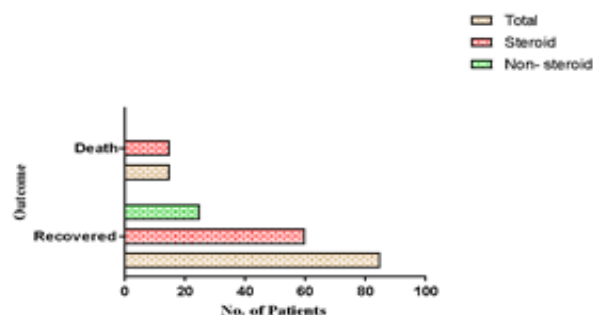


Figure 1: Outcome of Treatment

Analysis of mortality

The mortality in corticosteroids group is demonstrated in (Figure 2) (Figure 3) and (Figure 4). Among 15 fatality cases that were reported, 80% were male, 67% aged 61-80 years, and 40% and 33% had HTN and HTN + DM II as co-morbidities respectively.

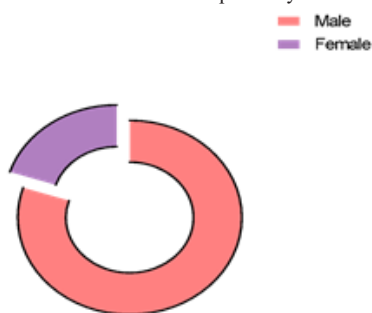


Figure 2: Gender Wise Mortality

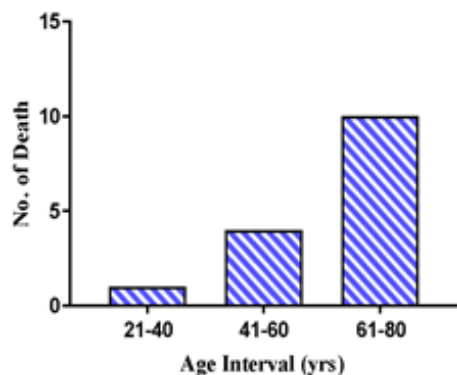


Figure 3: Age Wise Mortality

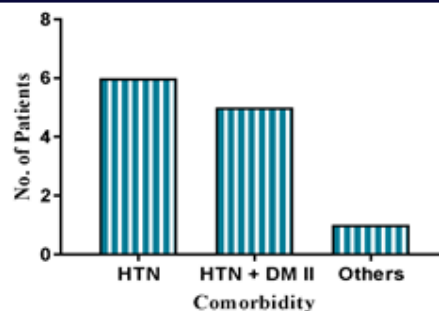


Figure 4: Comorbid conditions in mortality patients

Determination of Hospital length of stay (LOS)

The impact of corticosteroids on hospital length of stay is depicted in (Table 1). The findings show that there is no significant difference in the mean hospital LOS between the subjects who received corticosteroids and those who did not receive corticosteroids. P value was calculated by independent t-test.

Table 1: Determination of Hospital Length of Stay

Days	Total Patients	Steroid Patients	Non-steroid Patients	P value
Minimum	3	3	5	0.5073
Maximum	30	29	30	
Median	9	9	8	
Mean±SD	10.55±5.45	10.76±5.26	9.92±6.04	

Determination of Adverse events

The development of adverse events in the overall population is demonstrated in (Figure 5). 12% of patients in the corticosteroids group reported adverse events, whereas none were reported in corticosteroid free group. P value was calculated by chi-square test ($p=0.0694$).

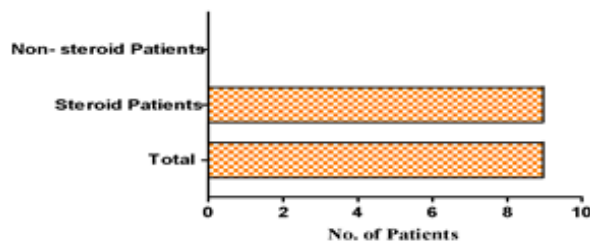


Figure 5: Determination of Adverse Events

Incidence of secondary infections

The development of secondary infections is depicted in (Figure 6). 13% and 4% of patients in the corticosteroid and corticosteroid-free group respectively, experienced secondary infections. P value was calculated by chi-square test ($p=0.1965$).

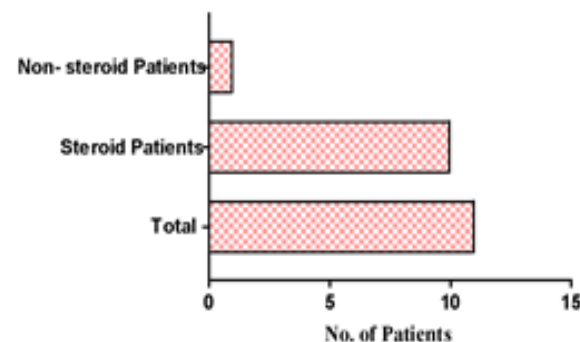


Figure 6: Incidence of Secondary Infections

DISCUSSION

COVID-19 primarily affects the respiratory system of the patient, in particular, the lungs, presenting with either acute respiratory failure or acute respiratory distress syndrome. [16] Management of this disease is based on the limited data and keeps changing rapidly as new clinical data emerge as per the Corona virus disease 2019 treatment guidelines,

NIH.^[17] After the RECOVERY trial, corticosteroids were soon accepted as the standard therapy for severe and critical COVID-19 patients including recent WHO living guidance.^[18] Even though the earlier results of corticosteroids in corona virus disease 2019 are encouraging; the role of corticosteroids is still controversial.

This observational, retrospective study investigated the impact of corticosteroids and their outcomes in COVID-19 patients. A total of 100 RT-PCR confirmed, hospitalized COVID-19 patients were involved in the study, of which 75 (75%) patients received corticosteroids therapy and 25 (25%) patients did not. The study contains both male and female participants, with the majority being male, with a mean age of 53.97 ± 13.63 years and a few co-morbidities (age ≥ 65 , hypertension, diabetes mellitus-II, CVA, CKD, smoking and obesity).

It is observed that, patients who received corticosteroids showed no survival benefit when compared with those who did not receive corticosteroids (Figure 1). Contrary to the hypothesized association between corticosteroids and their outcome in COVID-19 patients, the study showed that there is increased mortality in the corticosteroids group. These results build on existing evidence that corticosteroids use in COVID-19 patients may not be associated with in-hospital mortality stated by Liu Z et al,^[19] in which patients with corticosteroid treatment had greater mortality rate when compared to those who did not receive any corticosteroid treatment. The fatality cases were high among the males, advanced age (61-80 years) and with comorbidities (HTN, HTN+DM-II).

Our findings show that there is no significant difference in the mean hospital length of stay between corticosteroid (10.76 ± 5.26) and corticosteroid-free (9.92 ± 6.04) patients (Table 1), contradicting the claims of Fadel R et al,^[20] who stated that corticosteroids reduced hospital LOS by 3 days.

In this study, 12 % of patients with corticosteroids reported adverse events (Figure 5). According to The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group (2020), 64 adverse events varied across trials but there was no suggestion that the risk of serious adverse events was higher in patients assigned to corticosteroids except for the 2 smallest trials, in which the total number of serious adverse events was 1 and 3.^[21]

13% of patients who received corticosteroids experienced secondary infections (Figure 6). According to Judith van P et al., (2020) *Corticosteroid use in COVID-19 patients: a systematic review and meta-analysis on clinical outcomes*,^[22] more secondary infections or sepsis episodes were described in the patients receiving corticosteroids.

CONCLUSION:

The present study has been focused on the impact of corticosteroids and their outcome in COVID-19 patients. It is concluded that, COVID-19 patients did not show survival benefit when treated with corticosteroids. Our study revealed that there is no impact of corticosteroids on hospital LOS. Secondary infections and adverse events were more pronounced in the corticosteroids group. However, it is difficult to ascertain the causal relationship between adverse events and corticosteroids due to lack of evidence. Patients aged 61-80 years, male sex and with co-morbid conditions such as HTN and HTN+DM-II were high in number among the deceased in the corticosteroid group. The present study has some limitations such as the lack of larger control group, side effects of corticosteroids such as hypertension and hyperglycemia were missed and data on the imbalances in baseline characteristics is lacking as this is a retrospective study. Despite these limitations, our study provides early findings in the context of a rapidly evolving situation. Conduct of further studies is recommended for the evaluation of impact of corticosteroids in different subtypes of COVID-19 that are in association with ARDS, risk of super infections and long-term outcomes.

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