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Steroid Prescribing Practices for Mildly Symptomatic and Asymptomatic COVID-19 Patients, among Doctors of Selected Sri Lankan Hospitals

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ABSTRACT

Introduction: Effects of infection by SARS-COV-2 virus (COVID-19) range from asymptomatic infection to respiratory failure with multi-organ dysfunction. Steroids are indicated in patients with severe pneumonia, who require oxygen supplementation. There is evidence of harm if steroids are given for asymptomatic or mildly symptomatic patients.
Objectives: This study assesses the steroid prescribing practices among Sri Lankan doctors for mildly symptomatic and asymptomatic COVID-19 patients.
Methodology: This clinical survey was conducted during 20/11/2021 to 15/03/2022 using an electronic questionnaire, sent to doctors in 16 hospitals, representing all provinces of Sri Lanka. Doctors who have not treated nor advised patients with COVID-19 were excluded.
Results: Hundred and thirty-five participants were incorporated into the study. The mean age was 33.7 years (SD=7.82). The majority did not prescribe steroids routinely for asymptomatic (n=132, 97.8%) and mildly symptomatic (n=124, 91.9%) COVID-19. Dexamethasone was the most prescribed steroid. Doctors who treated COVID-19 patients in the private sector were more likely to prescribe steroids for mild symptoms (p=0.016). The majority (n=101, 81.5%) identified a decrease of oxygen saturation to below 94% on room air as an indication to start steroids.
Conclusions: Most of the study participants adhered to the recommended guidelines and refrained from prescribing steroids in mildly symptomatic and asymptomatic COVID-19 patients.

Keywords: COVID-19, SARS COV-2, Steroid, Prescribing Practices, mildly symptomatic, Asymptomatic

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INTRODUCTION

By June 2022, COVID-19, caused by the SARS-COV-2 virus has been responsible for more than 6 million deaths worldwide [1]. Identified in 2019 in Wuhan – China, COVID-19 caused a global pandemic lasting for 2 years with major geo-political implications including nationwide lockdowns.

Infection by the SARS-COV-2 virus can be asymptomatic, have mild symptoms like fever, sore throat, and other upper respiratory tract inflammatory symptoms, or have severe pneumonia with or without multi-organ involvement [2]. The driving pathology of the severe disease is thought to be a systemic hyperinflammatory state due to dysregulated immune response against the viral infection [2,3].

With the discovery of the role of aberrant immune hyper-activation in the pathogenesis of severe COVID-19, therapeutic trials with immunosuppressants were initiated and steroids and interleukin-6 antagonists became the mainstay of treatment in severe COVID.

The efficacy of steroids in improving clinical outcomes and mortality in hospitalised patients with COVID-19 who require oxygen supplementation has been established by several randomised clinical trials [4,5]. However, the use of steroids in hospitalised patients who do not require supplemental oxygen has no benefit and may be harmful [6,7]. There is no data on the effect of steroids in non-hospitalized patients with COVID-19 [8].

The National Institute of Health guidelines (NIH) for 'therapeutic management of non hospitalised adults with COVID-19' [9] state "there is currently a lack of safety and efficacy data on the use of systemic steroids agent in outpatients with COVID-19; using systemic glucocorticoids in this setting may cause harm." The NIH guidelines for 'therapeutic management of hospitalised adults with COVID-19' recommends against the use of dexamethasone or other corticosteroids for the treatment of patients who do not require supplemental oxygen and dexamethasone with or without remdesivir for hospitalised patients who require supplemental oxygen. [10]

In Sri Lanka, doctors of many specialties with varying levels of experience and training were called to treat COVID-19 patients due to the high caseload. Although there are no proper studies, it is the experience of the authors that many patients who are in home quarantine informally seek medical advice from a doctor known to them, due to restricted access to medical care. This study assesses the steroid prescribing practices for asymptomatic and mildly symptomatic COVID-19 among Sri Lankan doctors who have treated patients with COVID-19.

MATERIALS AND METHODS

This clinical survey was carried out through an electronic questionnaire developed using 'Google Forms from 20th November 2020 to 15th March 2021. The questionnaire and the electronic consent form were sent to doctors in 16 hospitals, representing all provinces of Sri Lanka through social media platforms. Doctors registered in the Sri Lanka Medical Council and who were practicing (government or private sector) and residing in Sri Lanka at the time when the study was initiated were included in the study. Doctors who had never advised nor treated a patient with COVID-19 were excluded from this study.

The algorithm of the questionnaire is given as supplementary material.

After obtaining the consent, the socio-demographic details and the work exposure in a designated COVID-19 treatment unit were recorded. Whether patients with COVID-19 reached out to the participants to get advice on treatment for COVID was asked. If so, the average number of such inquiries per week was recorded.

The questionnaire assessed the prescribing practices for steroids as well as antibiotics. This article will focus on steroid prescription practices only. All participants were asked whether they routinely prescribe steroids for asymptomatic and mildly symptomatic COVID-19 in two separate questions. Mild symptoms were defined as the presence of fever and/or cough and/or sore throat and/or rhinorrhoea with no evidence of pneumonia and do not require supplemental O2

treatment. The participants who opted to routinely prescribe steroids in the above instances were questioned on the steroid regimen they usually prescribe (drug, dose, frequency, duration, and co-prescription of a proton pump inhibitor). Those who did not prescribe steroids for asymptomatic and mildly symptomatic COVID-19 were given a list of scenarios and were asked to select the instances where they would prescribe steroids.

Details that would direct towards personal identification of the respondents were not collected. The participants were not allowed to view the responses made by others.

The socio-demographic details and work experience of the participants were described using descriptive statistics. Frequencies were calculated for the practice of prescribing or not prescribing steroids for a particular scenario. Participants were grouped based on whether they did or did not prescribe steroids and the associations were sought with socio-demographic factors using the chi-square statistic.

Statistical Analysis

The socio-demographic parameters of the participants were described by calculating the mean, standard deviations, percentages, and frequencies. Frequencies of different steroid prescribing practices were calculated and were expressed as percentages. Associations between different steroid prescribing practices and the socio-demographic and educational qualifications of the prescribers were calculated using Pearson's chi-square test.

RESULTS

A total of 138 doctors responded to the questionnaire. Only 135 met the inclusion and exclusion criteria. The mean age of participants was 33.7 years (±15.64) and ranged from 27 to 72 years. The majority of the participants were medical officers without post-graduate qualifications (n=92, 68.1%) while 18 were relief house officers (13.3%) and 16 (11.9%) were registrars. There were only 4 senior registrars (3%) and one (0.7%) consultant among the participants. There was representation from all 9 provinces. The highest participation was from Colombo district (n=52, 38.5%) followed by Galle (n=10, 7.4%). Thirty-nine (28%) participants worked at base hospitals and teaching hospitals respectively while 27 (20%) worked at a national hospital. Only two (1.5%) doctors worked full-time in the private sector. The rest of the participants were equally distributed between district hospitals (n=14,10.4%) and district general hospitals (n=14,10.4%). Doctors working in all specialties (clinical and non-clinical) participated, while the majority worked in either a medical (n=48, 35.6%), surgical (n=15, 11.1%), or a paediatric (n=11, 8.1%) specialty unit. Dedicated units to treat COVID-19-infected patients (COVID-19 units) were considered a medical specialty.

Twenty-nine (21.5%) participants were working in a COVID-19 unit at the time of the study, while another 56 (n=41.5%) had worked in such a unit but were working in a non-COVID unit at the time of the study. Fifty (37.0%) had never worked in a dedicated COVID-19 unit. Most participants were not involved (n=110, 81.5%) in treating COVID-19-infected patients in the private sector. A majority (n=102, 75.6%) of participants declared that they receive telephone calls from an average of 9 patients with COVID-19 per week, to get treatment advice.

The practice of routine prescription of steroids for asymptomatic and mild COVID-19 among the participants is given in Table 1.

Associations were sought for the practice of routine prescription of steroids for asymptomatic and mild COVID-19, with the workplace, designation, and work experience in a designated COVID unit of the study participants, using the Pearson Chi-Square test. The only statistically significant association was that the study participants who were involved in managing COVID-19 patients in the private sector were more likely to prescribe steroids for mild COVID ($\chi2=5.76$, df =1, p=0.016) compared to participants who did not. This was not seen with prescribing steroids for asymptomatic COVID-19 ($\chi2=0.131$, df=1, p=0.717).

Characteristics of the participants who prescribed steroids for asymptomatic and mild COVID-19 are given in Table 3. The significance given in the table is the p-value of the Chi-Square statistic when compared to participants who did not prescribe steroids for the given occasion.

Table 1: Practice of prescribing steroids routinely for patients with asymptomatic and mild COVID-19

	Does not prescribe steroids routinely	**Prescribes steroids routinely**	**Total**
Asymptomatic COVID-19	132 (97.8%)	3 (2.2%)	135
Mildly symptomatic COVID-19	124 (91.9%)	11 (8.1%)	135

Table 2: Steroid prescription regimens used by prescribers.

Prescription				**Prescribing a PPI Routinely**	**Frequency**
	Dose	Frequency	Duration		
Dexamethasone	6 mg	Once daily	10 days	Yes	2
Dexamethasone	0.5 mg	Twice daily	3 – 5 days	Yes	1
Dexamethasone	1-6 mg	Twice daily	3 – 7 days	No	1
Dexamethasone	1 mg	Twice daily	Not specified	Yes	1
Dexamethasone	1 mg	Thrice daily	3 days	Yes	1
Dexamethasone	4 mg	Thrice daily	Tailing off regimen	Yes	1
Dexamethasone	10 mg	Once daily	5 days	Yes	1
Prednisolone	10 mg	Once daily	Not specified	Not specified	1
Prednisolone	30 mg	Once daily	3 days	Yes	1
Prednisolone	30 mg	Thrice daily	3 days	Yes	1
Prednisolone	Not specified			Yes	2
Methylprednisolone	Not specified			Not specified	1
Total				9	14

PPI – Proton Pump Inhibitor

Table 3: Characteristics of participants who were prescribed steroids for mild and asymptomatic COVID-19

	Participants who were routinely prescribed steroids for <u>asymptomatic COVID</u> (n=3)			**Participants who were routinely prescribed steroids for <u>mildly symptomatic COVID</u> (n=11)**		
		frequency	P value (vs who did not prescribe steroids) (2-sided)		Frequency	P value (vs) who did not prescribe steroids (2-sided)
Workstation	T Hospital	2		T Hospital	6	
	N Hospital	1		N Hospital	2	
				D Hospital	2	
				B Hospital	1	
	Total	3	0.645	Total	11	0.261
Designation	MO	2		MO	7	
	RHO	1		RHO	3	
				SR	1	
	Total	3	0.914	Total	11	0.396
Work experience in a COVID unit in the government sector	Yes	1		Yes	3	
	No	1		No	5	
	Have worked in a COVID unit, but no longer work there	1		Have worked in a COVID unit, but no longer work there	3	
	Total	3	0.852		11	0.564
Treating COVID patients in the Private Sector	Yes	1		Yes	5 (expected = 2)	
	No	2		No	6 (expected = 9)	
	Total	3	0.504	Total	11	0.016

T Hospital - Teaching Hospital, N Hospital – National Hospital, B Hospital – Base Hospital, D Hospital – District Hospital, MO – Medical Officer, RHO – Relief House Officer, SR – Senior Registrar

Study participants who didn't give steroids for asymptomatic and mildly symptomatic COVID-19(n=124) were given a list of scenarios and were asked to pick instances where they would start steroids in patients with COVID-19. A total of 122 participants had selected scenarios while 2 had not selected any. Each participant could select more than one scenario. Frequencies of the scenarios selected by the participants are given in Table 4.

Table 4 - Scenarios Selected by Participants Where Steroids Would be Started.

Scenario	Frequency	Percentage (out of 124)
SpO2 (Oxygen Saturation) <94% on air	101	81.5 %
A patient with asthma (with exacerbation)	96	77.4 %
CRP (C reactive protein) of 70	31	25.0 %
A patient with asthma (without exacerbation)	17	13.7 %
Severe sore throat	15	12.1 %
Pleuritic type chest pain	14	11.3 %
High spiking fever	11	8.9 %
CRP (C reactive protein) of 30	7	5.6 %

SpO2 – Oxygen saturation in pulse oximetry

Factors that determined the practice of starting steroids when the oxygen saturation falls below 94% while on room air were sought using the Chi-square statistic. The practice of starting steroids in the above instance was not associated with work experience in a COVID unit (p=0.075). All the consultants, senior registrars, and registrars who participated in the study decided to start steroids when the SpO2 fell below 94% although this did not meet statistical significance (p=0.336). Neither was there a significant difference depending on the level of the working hospital (p=0.068) or the involvement of managing COVID-19 patients in the private sector (p=0.15). Details of the associations of starting steroids when SpO2 is <94% while on room air are given in Table 5.

Table 5 - Characteristics of participants depending on the practice of starting steroids when spo2 is <94% on room air.

	Starting steroids when SpO2 <94% on room air		**Not starting steroids when SpO2 <94% on room air**	
		Frequency		Frequency
Designation	Consultant	1 (0.9%)	Consultant	0
	Senior Registrar	3 (2.97%)	Senior Registrar	0
	Registrar	16 (15.84%)	Registrar	0
	Medical Officer	67 (66.33%)	Medical Officer	18 (78.26)
	Relief House Officer	11 (10.89%)	Relief House Officer	4 (17.39%)
	Intern House Officer	3 (2.97%)	Intern House Officer	1 (4.35%)
	Total	101 (100%)	Total	23 (100%)
	χ^2=5.708, df=5, p=0.336			
Working Hospital	National Hospital	22	National Hospital	3
	Teaching Hospital	29	Teaching Hospital	4
	Base Hospital	30	Base Hospital	8
	District General Hospital	12	District General Hospital	2
	District Hospital	6	District Hospital	6
	Private Hospital (full time)	2	Private Hospital (full time)	0
	Total	101 (100%)	Total	23 (100%)
	χ^2=10.251, df=5, p=0.068			
Work Experience in a COVID ward	Yes	22 (21.78%)	Yes	4 (17.39%)
	No	32 (31.68%)	No	13 (56.52%)
	Have worked in a COVID unit, but no longer work there	47 (46.53%)	Have worked in a COVID unit, but no longer work there	6 (26.09%)
	Total	101 (100%)	Total	23 (100%)

	χ^2=5.190, df=2, p=0.075			
Treating COVID patients in the Private Sector	Yes	87 (86.14%)	Yes	17 (73.91%)
	No	14 (13.86%)	No	6 (26.09%)
	Total	101 (100%)	Total	23 (100%)
	χ^2=2.070, df=1, p=0.150			

SpO2 – Oxygen Saturation

DISCUSSION

The majority of the study participants (91.9%) adhered to the evidence-based standard practice of not prescribing steroids for asymptomatic and mild COVID-19. However, 8.1% of participants prescribed steroids in the absence of an indication. A nationwide study done in India [11] in January 2021 with 1055 participants (physicians involved in the management of severe COVID-19) indicated that 18.6% prescribed steroids to all patients with COVID-19, irrespective of the severity. In another nationwide Indian study [12] with 384 participants (among critical care physicians) 75.8% indicated that steroids should be prescribed for moderate COVID-19.

Although only a minority prescribed steroids for asymptomatic and mildly symptomatic COVID-19, there is still room for improvement, by increasing awareness about the evidence-based management of COVID-19 given the harm steroids may cause in these categories of patients.

As this practice was higher among the doctors who treated COVID-19 patients in the private sector, it would be imperative to initiate awareness programs from the private hospitals. Interestingly, work experience in a designated COVID unit was not associated with increased practice of guideline recommendations. This was because guideline adherence was observed in a majority, irrespective of the work experience in a COVID-dedicated unit. Except for 1 senior registrar none of the doctors with post-graduate education (including trainees) prescribed steroids without an indication.

The correct practice of starting steroids when a patient requires supplemental oxygen, i.e., when the SpO2 falls below 94%, was observed in a majority (81.5%). In comparison only 70.1% prescribed steroids when the SpO2 was <90% in the above-mentioned Indian study with 1055 participants.[11]

Although it did not meet statistical significance, all participants with postgraduate education did start steroids when it was indicated in the management of COVID-19. It appears that the awareness programs on COVID-19 management should focus more on the doctors who are not involved in post-graduate education. Doctors who were working at COVID-19 units had a tendency towards starting steroids when a patient required supplemental oxygen, although it did not meet statistical significance.

The majority (56.5%) of the doctors who did not start steroids when indicated, had never worked in a dedicated COVID-19 unit. Doctors who were involved in managing COVID-19 patients in the private sector were not different from the doctors who did not, with regards to starting steroids when the patient required supplemental oxygen.

A major limitation of the study is the small sample size. As there is the possibility that the doctors who were not confident about their prescribing practices would have been reluctant to respond to the questionnaire, the study sample might not be an exact representation of the population of doctors who treat COVID-19 in Sri Lanka. As only a small number of doctors prescribed steroids in the

study, the precision of the statistical analysis was low.

CONCLUSIONS

In this study, most practitioners adhered to the guidelines when prescribing steroids to patients with asymptomatic and mildly symptomatic COVID-19 patients, although doctors who treated COVID-19 patients in the private sector were more likely to prescribe steroids for mildly symptomatic COVID-19. However, there is still room for improvement given the nature of harm, steroids could do in COVID-19 infection. Further audits on steroid prescribing practices and interventions to increase awareness are recommended to improve outcomes.

Author declaration

Authors' contributions:
Study concept and design, acquisition of data, analysis and interpretation of data, and drafting of the manuscript: P.R., H.A. and M.A.; Critical revision of the manuscript for important intellectual content and study supervision: S.A.

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The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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