Review

DOI: 10.5582/ddt.2021.01054

India and management of COVID-19: A case study on published guidelines

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SUMMARY In the face of the ongoing pandemic, the primary care physicians in India are dealing not only with an increased number of patients but are also facing difficulties in the management of complex critically ill patients. To guide the management plans of primary care physicians, several guidelines have been published by the central and state health bodies. In such a situation, an updated and unifying state, national and international guidelines based on critical analysis and appraisal of evolving data is the need of the hour. In this review, we critically analysed the current existing guidelines that have been formulated within India in light of recent evidence.

Keywords Coronavirus disease 2019, SARS-CoV-2, antiviral

1. Introduction

India's healthcare sector was on its knees during the second wave due to the high number of Coronavirus disease-2019 (COVID-19) cases. Besides the shortage of hospital beds, oxygen supply, and medications highlighted in the news reports, primary care physicians all over the country were dealing with increasingly complex and critically ill patients. With new research papers getting published every day, it is incredibly challenging for physicians to keep abreast with the latest evidence. As a result, most physicians resort to the clinical management guidelines published by competent authorities. The problem lies with the number of different guidelines (state, national, international) that differ on the critical aspects of management. For this commentary, the websites of the Infectious disease Society of America (IDSA), World Health Organisation (WHO), and health bodies of central/state governments of India were searched for the last available guidelines on the management of COVID-19 as of 31.05.2021. Apart from the national guidelines, the guidelines from various states were available. While most of the states endorsed the national management protocol; the states of Goa (GA), Jharkhand (JH), Karnataka (KA), Kerala (KL), Madhya Pradesh (MP), Maharashtra (MH), Meghalaya (MG), Tamil Nadu (TN), and West Bengal (WB) had their management guidelines. Last year, we published a comprehensive review pointing to the lack of congruency between these guidelines (*1*). Since then, the guidelines have been revised, but the lack of congruency continue to exist. This review aims to examine the existing guidelines for congruence and critically analyse them in light of current evidence.

The definitions for categorising the severity of COVID-19 varied with guidelines. For uniformity, the spectrum of COVID-19 has been categorised into mild, moderate and severe in this review. The multiple definitions for these categories used in the guidelines have been summarised in Table 1. The recommendations of the guidelines have been tabulated in Table 2. The current evidence on the utility of drugs and therapeutics of COVID-19 has been summarised in Table 3.

2. Hydroxychloroquine (HCQ)

HCQ was initially recommended based on small non-randomised studies, but later studies showed no effect of HCQ on mortality (*2,3*). However, it was evident from the results of the SOLIDARITY trial that the use of HCQ is not associated with any decrease in mortality, the requirement of ventilation and hospital stay (*4,5*). The drug was also suggested for post-exposure prophylaxis by some guidelines, but a randomised trial found that HCQ did not prevent illness when initiated within four days of exposure (*6*). HCQ also failed to show any reduction in symptom severity in patients of COVID-19 when given early in the course (*7*). Therefore, the WHO and IDSA have recommended

Table 1. Classification scheme of COVID-19 and definitions used by various guidelines

Guidelines	Mild	Moderate	Severe
WHO	Symptoms without evidence of viral pneumonia or hypoxia.	Pneumonia + no signs of severe pneumonia + SpO2 ≥ 90%	Pneumonia + RR > 30 per minute; severe respiratory distress; or SpO2 < 90%
IDSA	Non-severe illness - patient with SpO2 > 94%; not requiring supplemental oxygen		SpO2 ≤ 94%
India	No dyspnoea and Spo2 > 94%	Pneumonia + SpO2 90 to ≤ 93%, RR > 24 per minute	Pneumonia + RR >30 per minute, severe respiratory distress, SpO2 < 90%
Jharkhand	Non critically ill + hemodynamically stable	RR > 30 per minute, SpO2 < 90%, altered sensorium, oliguria, high lactate, bilateral radiograph opacities	
Kerala	No breathlessness or Hypoxia, RR < 24 per minute, SpO2 > 94%	RR - 24-29 per minute, SpO2 - 91-94%	RR > 30 per minute, SpO2 < 90 %
Madhya Pradesh	No dyspnoea, SpO2 > 94%, RR < 16/min	Pneumonia + SpO2 90 - 94%	Pneumonia + severe respiratory distress, SpO2 < 90%
Maharashtra	A - asymptomatic, B - Symptomatic without comorbidity, C - Symptomatic with comorbidity - obesity, age > 60 years, DM, hypertension/IHD, chronic lung disease, immunosuppressed, CKD	Pneumonia + SpO2: 90-94%, RR > 24 per minute.	Pneumonia + RR > 30 per minute, severe respiratory distress, SpO2 < 90%
Meghalaya	Category A - asymptomatic Category B - Symptomatic with no signs of severe pneumonia; RR - 16-24 per minute, Spo2 > 94%	Category C (Severe) - RR > 24 per minute, SpO2 < 94% Category D (Critical) - RR > 30 per minute, SpO2 < 90%	
Tamil Nadu	RR < 24 per minute, Spo2 > 94%	RR- 24-30 per minute, SpO2 - 90 - 94%	RR > 30 per minute, SpO2 < 90%
Goa	No dyspnoea, SpO2 > 93%	Pneumonia + SpO2 90 to ≤ 93%, RR > 24 per minute	Pneumonia + RR > 30 per minute, severe respiratory distress, SpO2 < 90%
West Bengal	Symptoms without shortness of breath	RR > 24 per minute; SpO2 < 94%; altered sensorium drowsiness/confusion/ stupor; infiltrates on Chest X-ray; altered liver and renal function tests	Moderate Disease + ARDS, sepsis, septic shock

Abbreviation: WHO, World Health Organisation; IDSA, Infectious disease Society of America; RR, respiratory rate; SpO2, oxygen saturation; DM, diabetes mellitus; IHD, ischaemic heart disease; CKD, chronic kidney disease; ARDS, acute respiratory distress syndrome.

against the use of HCQ in COVID-19 in their latest guidelines. While HCQ is no more recommended in national guidelines and state guidelines of KL, TN & WB, several state guidelines (JH, MG, MH, MP, KA) continue to recommend it.

3. Ivermectin

Ivermectin, an anti-parasitic drug, has also found a place in the treatment of COVID-19 since the start of the pandemic. A pilot randomised trial reported a reduction in self-reported symptoms using ivermectin within 72 hours of the onset of symptoms (*8*). Another study found reduced time to negativity with ivermectin (*9*). However, in two randomised, double-blind placebo-controlled trials, on mild (Lopez Medina *et al.*) and severe (Galan *et al.*) patients, there was no improvement in clinical outcomes with ivermectin (*10,11*). Ivermectin use has been incorporated in some guidelines based on a meta-analysis of 18 studies showing decreased mortality with ivermectin (*12*). However, most of these studies had a very high risk of bias and one of the study from the meta-analysis has been retracted. In the absence of new studies demonstrating absolute benefit, ivermectin has been removed from the national guidelines, but some states still recommend it (JH, KL, MH, TN, GA, WB).

4. Favipiravir

Favipiravir is a selective and potent inhibitor of influenza RNA polymerase. An initial, before-after, comparative study found a shorter median time to viral clearance and significant improvement in radiological findings (*13*). It was initially postulated that early administration of favipiravir might be more useful. Still, a study showed no difference in early *vs.* late administration of favipiravir in asymptomatic or mild COVID19 illness (*14*). In the open labelled trial from India, the viral clearance time was not significant, but the subjective clinical cure was faster in those who received favipiravir (*15*). However, subsequent studies by Dabbous *et al.*, Solaymani-Dodaran *et al.*, and Khamis *et al.* did not show any significant clinical benefit with favipiravir (*16-18*). The WHO and IDSA do not make any recommendation on the use of favipiravir in COVID-19. However, based on small studies showing limited benefit, favipiravir is recommended in some state guidelines (KL and MH).

Table 2. Comparison of recommendations by various guidelines on key drugs used in management of COVID-19

Items	Hydroxy-chloroquine	Ivermectin	Remdesivir	Favipiravir	Tocilizumab	Steroids	Inhaled steroids	Convalescent plasma	Anticoagulation
WHO	Recommends against use	Recommends against use	Recommends against use	No R	No R	Recommended in severe/ critical disease	No R	No R	Prophylactic doses in all hospitalized patients
IDSA	Recommends against use	Recommends against use	Recommended in severe disease	No R	Recommended in severe disease	Recommended if oxygen requirement	No R	Under research setting	Prophylactic doses in all hospitalized patients
National guidelines, India	Not R	Not R	Recommended in moderate-severe disease	No R	Recommended in severe disease	Recommended in moderate-severe disease	Recommended in mild illness	Not R	Prophylactic dose in moderate illness, intermediate dose in severe illness
Jharkhand	Recommended in all categories	Recommended in all categories	No R	No R	No R	Recommended in Moderate-severe disease	No R	No R	Prophylactic doses in critically ill
Kerala	Not R	Recommended in mild illness*	Recommended in moderate-severe disease	Recommended in mild illness*	Recommended in severe disease	Recommended in moderate-severe disease	Recommended in mild illness*	Early moderate disease (< 7 days from onset)	Prophylactic dose: moderate-severe disease; Therapeutic dose: confirmed VTE or high clinical suspicion
Madhya Pradesh	Recommended in moderate disease	No R	Recommended in moderate-severe disease	No R	Recommended in severe disease	Recommended in moderate-severe disease	No R	Under research settings	Therapeutic anticoagulation
Maharashtra	Recommended	Recommended in moderate disease	Recommended in mild disease*, moderate-severe disease	Recommended in mild illness* and moderate illness	Recommended in severe disease	Recommended in moderate-severe disease	No R	Moderate disease with no improvement	Prophylactic dose: Mild disease, Moderate and severe disease: therapeutic dose[#]
Meghalaya	Recommended in mild illness*, moderate-severe illness	No R	Recommended in Moderate-severe disease	No R	Recommended in severe disease	Recommended in moderate-severe disease	No R	Under research settings	Prophylactic dose anticoagulation if risk factors
Tamil Nadu	No R	Recommend	No R	No R	No R	Recommended in mild cases*, moderate and severe cases	No R	No R	Prophylactic doses in moderate-severe cases
Goa	Recommended in mild disease	Recommended in mild disease	Moderate-severe disease	No R	Recommended in severe disease	Recommended in moderate-severe disease	No R	No R	Prophylactic doses in moderate-severe disease
West Bengal	No R	Recommended in mild disease	Recommended in Moderate-severe disease	No R	Recommended in severe disease	Recommended in moderate-severe disease	No R	No R	Prophylactic dose in moderate-severe disease[#]

*mild disease with specific high-risk features, [#]moderate/severe disease with d-dimer cut-offs. Abbreviation: WHO, World Health Organisation; IDSA, Infectious disease Society of America; Not R, Not recommended; No R, No recommendation.

Table 3. Summary of studies of pharmaceuticals used for the treatment of COVID-19

Study	N	Type of study	Severity	Study arms	Results	*Ref.*
Hydroxychloroquine (HCQ) with/without azithromycin (A)						
Geleris *et al.*	1376	Retrospective	All severity	HCQ-59% No HCQ-41%	No association between HCQ use and decrease in intubation or death	(*2*)
Rosenberg *et al.*	1438	Retrospective	All severity	HCQ-51% HCQ+A-19% A-15% Neither-15%	Treatment with either drug not associated with improvement in mortality	(*3*)
RECOVERY	11,197	Open RCT	Hospitalised patients	HCQ-1561 Usual care-3155	Treatment with HCQS was not associated with a reduction in mortality	(*4*)
SOLIDARITY	1860	Open RCT	Hospitalised adults (All severity)	HCQ-954 No HCQ-906	No decrease in mortality, a requirement of ventilation and hospital stay	(*5*)
Boulware *et al.*	821	Double blind placebo RCT	Exposure to case within four days	HCQ-50% Placebo-50%	HCQ did not prevent infection when used as a post-exposure prophylaxis	(*6*)
Skipper *et al.*	491	Double blind placebo RCT	Symptomatic non-hospitalised	HCQ-50% Pacebo-50%	HCQ did not reduce symptom severity	(*7*)
Ivermectin (IVM)						
Chaccour *et al.*	24	Double blind placebo RCT	Mild	IVM-12 Placebo-12	No difference in Day 7 viral load	(*8*)
Babalola et al	62	Double blind placebo RCT	Mild	IVM-6mg-21 IVM-12 mg-21 LPV/r-20	Time to negativity was lesser in IVM (dose-dependant)	(*9*)
Galan *et al.*	168	Double blind RCT	Severe	HCQ-54 CQ-61 IVM-53	No difference in requirement of ICU admission or mortality	(*10*)
Lopez Medina *et al.*	400	Double blind placebo RCT	Mild, less than seven days	IVM-200 Placebo-200	No significant improvement in resolution of symptoms	(*11*)
Favipiravir CT						
Cai *et al.*	80	Open non-RCT	Mild	FPV-35 LPV/r-45	Shorter time to viral clearance with FPV. Significant improvement in radiology more common with FPV.	(*13*)
Doi *et al.*	89	Open RCT	Mild	Early FPV (D1)-44 Late FPV (D6)-45	No significant difference in viral clearance in early *vs* late	(*14*)
Udwadia *et al.*	150	Open RCT	Mild	FPV-75 SOC-75	Time to cessation of viral shedding- not significantly different but faster clinical cure	(*15*)
Dabbous *et al.*	100	Open RCT	Mild and Moderate	FPV-50 HCQ-50	Time to defervescence and time to negativity not different	(*16*)
Solaymani-dodaram *et al.*	380	Open RCT	Moderate/severe	FPV-193 LPV/r-187	Mortality, requirement of intubation, ICU admission, Duration of stay not different	(*17*)
Khamis *et al.*	89	Open RCT	Moderate/severe	FPV-44 HCQ-45	No significant difference in clinical outcomes	(*18*)
Remdesivir (RDV)						
Wang *et al.*	237	Double blind placebo RCT	Moderate/Severe	RDV-67% Placebo-33%	RDV not associated with significant clinical improvement	(*19*)
Beigel *et al.* (ACTT1)	1059	Double blind placebo RCT	Pneumonia	RDV-51% Placebo-49%	RDV shortened the time to recovery	(*20*)
SOLIDARITY	5451	Open RCT	Hospitalised (All severity)	RDV-2743 No RDV-2708	No decrease in mortality, requirement of ventilation and hospital stay	(*5*)

Abbreviation: SOC, standard of care; ICU, Intensive Care Unit; Dexa, dexamethasone; MPS, methylprednisolone; hydrocort, hydrocortisone; ECMO, extracorporeal membrane oxygenation; RCT, randomised controlled trial; Open, Open-labelled, placebo- placebo controlled.

5. Remdesivir

Remdesivir is a nucleoside analogue, which acts by inhibiting the ribonucleic acid (RNA) dependent RNA polymerase. In a multi-centric placebo-controlled trial from China, remdesivir use was not associated with a difference in time to clinical improvement (*19*). Two of the most significant studies on the use of remdesivir showed contradictory results. In the ACTT-1 trial, remdesivir showed a faster time to recovery in patients with lung involvement (*20*). However, the results of the SOLIDARITY trial showed no significant benefit

Table 3. Summary of studies of pharmaceuticals used for the treatment of COVID-19 (continued)

Study	N	Type of study	Severity	Study arms	Results	*Ref.*
Steroids						
RECOVERY	6,425	Open RCT	Hospitalised	Dexa-33% SOC-67%	Reduced mortality in those receiving oxygen therapy or mechanical ventilation	(*21*)
Edalatifard *et al.*	68	Single arm	Severe, hospitalised patients	MPS pulse-34 SOC-34	Significant improvement in survival time	(*22*)
Tomazini *et al.*	299	Open RCT	Moderate-severe ARDS	Dexa-151 SOC-148	Significant increase in ventilator-free days	(*23*)
REMAP-CAP trial	384	Open RCT	Severe	Hydrocort-283 SOC-101	No signifcant difference	(*24*)
Tang *et al.*	86	Single-blind, RCT	Hospitalised	MPS-43 Control-43	No significant difference	(*25*)
Gudino *et al.*	64	Open RCT	Moderate-severe disease	MPS-35 SOC-26	No significant difference	(*26*)
Tocilizumab (Tcz)						
Guaraldi *et al.*	544	Retrospective	Severe	SOC-67% Tcz-33%	Tcz associated with reduced mortality and mechanical ventilation	(*30*)
Biran *et al.*	764	Retrospective	ICU patients	SOC-73% Tcz-27%	Tcz was associated with decreased mortality	(*31*)
Salama *et al.*	389	Double blind placebo RCT	Moderate/severe	Tcz-249 Placebo-128	Reduced likelihood of getting mechanically ventilated; no benefit in overall survival	(*32*)
Soin *et al.*	180	Open RCT	Moderate to severe COVID19	Tcz-90 SOC-90	tocilizumab did not provide additional benefit	(*33*)
RECOVERY	1,350	Open RCT	Moderate/severe CRP > 75 mg/L	Tcz-621 SOC-729	Improved survival and other clinical outcomes with tcz	(*34*)
Convalescent Plasma (CP)						
Xia *et al.*	1,568	Retrospective	Severe/critical	CP-9% No CP-91%	Reduction in mortality and improvement of clinical symptoms	(*35*)
Abolghasemi *et al.*	189	Open non-RCT	Moderate/severe	CP-61% No CP-39%	Decreased hospital stay and mortality	(*36*)
Li *et al.*	103	Open RCT	Severe/life-threatening	CP-50% No CP-50%	No significant improvement in time to clinical improvement	(*37*)
PLACID trial	464	Open RCT	Moderate	CP-235 SOC-229	CP not associated with a reduction in progression or reduction of mortality	(*38*)
Libster *et al.*	160	Double blind placebo RCT	Older adults within 72 hours of mild disease	CP with high titre-80 Placebo-80	Early administration of high titre CP reduced disease progression	(*39*)
Abani *et al.* (RECOVERY)	11,558	Open RCT	Hospitalised	CP-5795 SOC-5763	CP does not decrease mortality	(*40*)
Inhaled Steroids						
STOIC trial	146	Open RCT	Mild within 7 days	Budesonide-73 SOC-73	Early administration reduced the requirement of urgent care	(*41*)
PRINCIPLE trial	1,779	Open RCT	Mild within < 14 days	Budesonide-751 SOC-1028	Time to clinical recovery shorter	(*42*)
Anti-coagulation						
INSPIRATION trial	600	Open RCT	ICU patients	Intermediate-276 Standard- 286	No significant difference in the composite outcome of thrombosis, treatment with ECMO, or mortality	(*43*)
ATTACC	1,074	Open RCT	Severe	Therapeutic dose- 529 Standard prophylaxis-545	No significant difference in organ-support free days and survival	(*44*)
ATTACC	2,245	Open RCT	Hospitalized but not critically ill	Therapeutic dose- 1190 Standard prophylaxis-1055	Improved survival with therapeutic dose	(*45*)

Abbreviation: SOC, standard of care; ICU, Intensive Care Unit; Dexa, dexamethasone; MPS, methylprednisolone; hydrocort, hydrocortisone; ECMO, extracorporeal membrane oxygenation; RCT, randomised controlled trial; Open, Open-labelled, placebo- placebo controlled.

with remdesivir (*5*). Based on available data, the WHO gave a conditional recommendation against remdesivir, but the IDSA recommends its use in severe COVID-19 cases. The national and state guidelines (KL, MH, MG and WB) recommend its use in hospitalised, moderate to severe COVID-19 cases. Several parts of the country reported a shortage of remdesivir in the second wave. In addition, there were reports of patient attendants paying an excessive amount of money to procure this drug. It must be therefore emphasised that the drug has limited impact on improvement in mortality outcomes.

6. Systemic steroids (oral/intravenous)

In the RECOVERY trial, dexamethasone was found to help decrease 28-day mortality in patients requiring oxygen (*21*). Other large studies echoed the findings of the RECOVERY trial (*22-24*). The RECOVERY trial showed that the benefit of steroids was in patients who had > 7 days of illness. Early use (< 7 days) of steroids was associated with worse outcomes. A study by Tang *et al.* showed that early use of steroids might prolong viral shedding (*25*). Despite the lack of evidence, national guidelines allow steroids in those without oxygen requirements but with illness (fever and cough) beyond seven days. TN state has also recommended the use of steroids in a sub-category of patients with mild illness. Overall, although the national and state guidelines are consistent with their recommendation on steroid use in moderate-severe cases, there is a lot of heterogeneity in dosing schedules. While some guidelines (IDSA, WHO, MG, MP) mention fixed-dose steroids, others recommend weight-based dosing. MP guidelines recommend the use of 500 mg methylprednisolone pulse therapy in severe disease, which any other guideline has not endorsed. Except for a few studies with small sample size, steroids use in patients requiring oxygen is generally associated with improved outcomes (*26*). Increasing immunosuppression without forethought can be detrimental by increasing secondary infections and sepsis (*27*). This becomes more important as we see an unprecedented rise in COVID-19 associated mucormycosis cases. Steroids not only suppresses the immune system but also causes deranged blood sugar levels, both of which are important risk factors for the development of mucormycosis (*28,29*).

7. Tocilizumab

Tocilizumab, an interleukin (IL)-6 receptor inhibitor, is an approved treatment for chimeric antigen receptor (CAR) T-cell therapy-related cytokine release syndrome. In severe COVID19, tocilizumab was postulated to decrease the cytokine surge and associated hyper-inflammation, in severe illness, by blocking the site of IL-6. In a case-control study, including 544 patients of severe COVID19 pneumonia (RR > 30/min, Spo2 < 93% on room air) (*30*), the use of tocilizumab was associated with statistically significant benefit in reducing the need for ventilation or death. In another retrospective cohort study of 764 patients, tocilizumab in 210 patients was associated with reduced mortality (*31*). The first prospective data came from a multi-national, multi-centric study of 389 patients, randomised in a 2:1 manner in tocilizumab and placebo groups, respectively (*32*). The use of tocilizumab in 249 patients reduced the likelihood of getting mechanically ventilated, but no benefit in overall survival was noted. In a trial from India including 180 patients (1:1 manner) in tocilizumab and standard of care groups, tocilizumab did not provide additional benefit (*33*). The results of the RECOVERY trial showed improved survival in those with saturation less than 93% and C-reactive protein > 75 mg/L (*34*). Whereas WHO has made no recommendation on its use, IDSA, Indian national guidelines, and certain states (KL, MH, MG and WB) have recommended its use in a select few cases.

8. Convalescent plasma

Convalescent plasma (CP) was postulated to act as a source of neutralising antibodies that can inhibit the replication of the virus. The data from retrospective, observational studies, showing benefit, provided the basis for prospective studies (*35,36*). However, randomised control trials failed to show any benefit with convalescent plasma (*37,38*). Libster *et al.* showed that early use of high-titre CP (within 72 hours) might halt the disease progression in elderly individuals (*39*). However, the use of CP within three days of onset in a high burden resource-limited setting is highly impractical. Besides, the results of the RECOVERY trial show that even high titre CP does not decrease mortality (*40*). Therefore, in accordance with the WHO and IDSA, the national guidelines have changed their stance on 17.05.21 and do not recommend CP in COVID-19. While most states recommend CP only in a trial setting, KL and MH continue to recommend CP as a part of clinical care in COVID-19.

9. Inhaled steroids

Owing to the remarkable success of systemic steroids, it was hypothesised that inhaled steroids might play a role in preventing progression when given early in course in patients with persistent symptoms. The two published, STOIC trial and PRINCIPLE trial showed a reduced time to recovery and reduced need for emergency care (*41,42*). The WHO and IDSA do not make any recommendations on inhaled steroid use in COVID-19. However, inhalational budesonide has been recommended in mild illness with persistent symptoms by the national guidelines and KL state guidelines.

10. Anticoagulation

Anticoagulation has been one of the critical pillars in moderate-severe disease management. Although their use in moderate to severe diseases is uniformly recommended, there is a lack of clarity on the dosing schedule (low-dose *vs*. intermediate/high-dose prophylaxis or therapeutic anticoagulation). INSPIRATION trial in critically ill patients with COVID-19 showed no difference between standard *vs*. intermediate prophylactic dose of anticoagulation in terms of the composite outcome of thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days (*43*). While the WHO and IDSA recommend using low dose anticoagulation for thromboprophylaxis, national and state guidelines have mentioned variable doses. Pooled analysis from three trials (REMAP-CAP, ACTIV-4a and ATTAC trials) show that although the incidence of thrombotic events is lesser in the therapeutic anticoagulation group, there was no difference in major thrombotic events and mortality (*44*). In another analysis, therapeutic doses of anticoagulation decreased the need for oxygen support in non-critically ill hospitalised patients (*45*). Only MP state guidelines mention therapeutic doses of anticoagulation but do not distinguish between critically and non-critically ill patients.

In summary, despite the lack of evidence, some guidelines continue to recommend HCQ, ivermectin, favipiravir and convalescent plasma. With regards to indication, dose and duration of steroids and anti-coagulants, there was wide variability amongst the various guidelines. Many of the recommendations in the guidelines were only expert-based and sometimes even contradictory to the best available evidence. In addition to the massive spurt of cases in the second wave that hampered the access to quality care, the lack of concordance in guidelines might have added to the confusion. Therefore, there is a need to develop a unified living guideline for COVID management that is evidence-informed and beneficial in curbing the proportion of inappropriate prescriptions.

Funding: The views in this article are of the author's personal opinions and do not necessarily indicate the views of their institution.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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Received June 21, 2021; Revised August 16, 2021; Accepted August 22, 2021

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Released online in J-STAGE as advance publication August 26, 2021.