Review Article

Review of COVID-19 Management Guidelines

ABSTRACT

The COVID-19 pandemic has adversely affected many countries across the globe both socially and economically and continues to be a major concern to the healthcare system. The majority of the patient group that was affected were elderly patients and patients with existing co-morbidities such as diabetes, hypertension, cardiovascular disease, etc. who were highly vulnerable and susceptible to the infection. Although various protective measures such as quarantine from confirmed and suspected cases, nationwide lockdowns, etc., have been implemented in all the affected countries, to contain the spread of the virus, there is a dire need to develop effective therapeutic strategies to stop the spread of the disease and minimize its high rates of morbidity and mortality especially considering the rapid evolution of the virus giving rise to different variants. Several COVID-19 management guidelines have been eventually published by various well-known Indian organizations such as the Indian Council of Medical Research (ICMR) and the Ministry of Health (MoH) India and International organizations such as the Infectious Diseases Society of America (IDSA), National Institute of Health (NIH), and WHO. Other countries such as China, South Korea, Brazil, and Haiti, etc., have also published their own general public guidelines and healthcare professionals' (medical institutions) guidelines for the management of COVID-19. The main aim of this article is to review guidelines for the management of COVID-19 published by ICMR, Ministry of Health (MoH) India, IDSA, WHO, and NIH and provide a side-by-side comparison of various important aspects of these guidelines.

KEYWORDS – COVID-19, Management guidelines, IDSA, WHO, ICMR, NIH

INTRODUCTION

The COVID-19 disease which was declared as a global pandemic by the World Health Organization (WHO) in 2020 due to its high transmissibility causing widespread across the globe in less than three (3) months was first discovered in the capital city of Hubei province, Wuhan city, China in December 2019. It was caused by a severe acute respiratory syndrome coronavirus (SARS-CoV-2) and the source of origin of the virus is still unknown. However, it is known to have pathogenic similarities with SARS-CoV and MERS-CoV viruses and was named SARS-CoV-2 due to its novel enveloped RNA betacoronavirus structure. Many countries have been adversely affected due to the pandemic both economically and socially. High rates of mortality and morbidity have been reported in elderly patients and patients with existing co-morbidities such as diabetes, hypertension, cardiovascular disease, etc.[1]

Although protective measures such as quarantine from confirmed and suspected cases, nationwide lockdowns, etc., have been implemented in all the affected countries, to contain the spread of the virus, there is a dire need to develop effective therapeutic strategies to stop the spread of the disease and minimize its high rates of morbidity and mortality.

Many researchers and scientists have proposed and studied the role of several antiviral and antimicrobial agents as potential therapeutic options for the management of COVID-19. However, no definitive therapeutic cure is yet available for COVID-19. Management of COVID-19 patients mainly involves individualized supportive care and symptomatic treatment such as antipyretics for fever, oxygen therapy for Acute Respiratory Distress (ARDS) for cases with

moderate symptoms and empiric antimicrobial therapy, and implementation of mechanical ventilation for cases with severe symptoms.

During the initial phases of the COVID-19 pandemic, dealing with the increased positive cases and managing the critically ill atients with no proper management guidelines or protocols proved to a challenge to the front-line treating physicians and health care providers [2]. Several national and international organizations have later developed their own COVID-19 treatment guidelines to address the rapidly increasing global burden of COVID-19 disease and to help the overburdened front-line workers and health care providers stay updated on the management protocols. However, the guidelines developed by the World Health Organization (WHO) remain standard and widely accepted around the world.

These COVID-19 management guidelines have provided good information on management strategies to help front-line health care providers improve clinical outcomes. However, there are certain limitations to these guidelines as well and very little is known about the quality and variability of the recommendations among different guidelines. For ex: these guidelines provide very less information on other management strategies related to the clinical management of acute COVID-19 and use of noninvasive ventilation (NIV), a high-flow nasal cannula (HFNC), use of corticosteroids or other supportive treatments, and other antiviral medications etc [3]. Furthermore, the significant differences in management strategies that exist across the countries and hospitals depending on their individual health care capacities must also be considered. Therefore, it is imperative that the health care providers and clinicians understand the limitations of these guidelines as well for better clinical outcomes.

AVAILABLE GUIDELINES FOR MANAGEMENT OF COVID-19 IN ADULT PATIENTS

Several COVID-19 management guidelines have been eventually published by various well-known Indian organizations such as the Indian Council of Medical Research (ICMR) and the Ministry of Health (MoH) India and International organizations such as the Infectious Diseases Society of America (IDSA), National Institute of Health (NIH), and WHO. Other countries such as China, South Korea, Brazil, and Haiti, etc., have also published their own general public guidelines and healthcare professionals' (medical institutions) guidelines for the management of COVID-19. This article will focus on reviewing guidelines for the management of COVID-19 published by ICMR, Ministry of Health (MoH) India, IDSA, WHO, and NIH. Despite minor differences in the severity classification, SpO_2 levels, quarantine period, and criteria of severity classification these guidelines were mostly similar pertaining to the clinical signs and symptoms of COVID-19, criteria for severity classification, preliminary advice, risk factors, isolation, and methods of prevention of spread – criteria for home quarantine, use of face mask, social distancing, etc. (See Table 1 below).

Table 1: Comparison of guidelines for the management of COVID-19 in adults – severity classification, criteria for classification, initial treatment advice, risk factors, and quarantine guidelines

Category	Recommendations				
Organization	**ICMR [4]**	**IDSA [5]**	**MoH India [6]**	**WHO [7,8]**	**NIH [9]**
Severity classification	Mild Moderate Severe	Mild to moderate, non-hospitalized Mild to moderate, hospitalized Severe Critical	Mild Moderate Severe	Mild Moderate Severe Critical	Asymptomatic or pre-symptomatic Mild Moderate Severe Critical
Criteria for severity classification	Mild – Upper respiratory tract symptoms and/or fever WITHOUT shortness of breath or hypoxia. Moderate – Any one of the following: 1. Respiratory rate ≥ 24/min, breathlessness 3. SpO_2: 90% to ≤ 93% on room air. Severe – Any one of the following: 1. Respiratory rate >30/min, breathlessness 2.SpO_2 < 90% on room air.	Mild to moderate, non-hospitalized – Patients without the need for supplemental oxygen, no signs of upper respiratory tract infection, but may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, and headache. Mild to Moderate, hospitalized – Pneumonia with no signs of severe disease and no need for supplemental oxygen. Severe – Severe Pneumonia, severe respiratory distress, SpO_2 <94% on room air. Critical – acute respiratory distress	Mild – Patients with uncomplicated upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, and headache. Without shortness of breath or Hypoxia (normal saturation). Moderate – Pneumonia with no signs of severe disease. Adults with the presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO_2 90 to ≤93% on room air, Respiratory Rate more or equal to 24 per minute. Severe – Severe Pneumonia, respiratory rate >30 breaths/min, severe respiratory	Mild – Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia. Moderate – Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including SpO_2 ≥ 90% on room air. A child with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 Severe – SpO_2 < 90% on room air; in adults, signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, respiratory rate >	Asymptomatic or pre-symptomatic – Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19. Mild illness – Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging. Moderate illness –

Category	Recommendations				
Organization	**ICMR [4]**	**IDSA [5]**	**MoH India [6]**	**WHO [7,8]**	**NIH [9]**
		syndrome (ARDS), sepsis, septic shock, acute venous thromboembolism (i.e., pulmonary embolism), acute coronary syndrome, acute stroke, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or ECMO.	distress, SpO_2 <90% on room air, acute ARDS, sepsis, septic shock.	30 breaths per minute), and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs (inability to breastfeed or drink, lethargy or reduced level of consciousness, convulsions) in addition to the signs of severe pneumonia. Critical – acute respiratory distress syndrome (ARDS), sepsis, septic shock, acute venous thromboembolism (i.e. pulmonary embolism), acute coronary syndrome, acute stroke, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy. In children and adolescents 0–19 years of age with fever > 3 days AND two of the following: rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP); evidence of coagulopathy (by PT, PTT, elevated D-dimers), acute	Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO_2) ≥94% on room air at sea level. Severe illness – Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%. Critical illness – Individuals who have respiratory failure, septic shock, and/or multiple organs dysfunction.

Category	Recommendations				
Organization	**ICMR [4]**	**IDSA [5]**	**MoH India [6]**	**WHO [7,8]**	**NIH [9]**
				gastrointestinal problems (diarrhea, vomiting, or abdominal pain); AND elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin. AND no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.	
Treatment advice	Mild – Home isolation and care Moderate – Admit to the ward Severe – Admit to intensive care unit (ICU)	Mild to moderate, non-hospitalized – Home isolation and care. Mild to moderate, hospitalized – isolated at the designated COVID-19 health facility, community facility. Severe – Managed health facilities, including emergency units and critical care units. Critical – Managed health facilities, including emergency units and critical care units, and/or admit to ICU.	Mild – Home isolation or COVID care center. Moderate – Managed in Dedicated Covid Health Centre (DCHC). Severe – Managed in DCHC and/or admit to ICU.	Mild – isolated at the designated COVID-19 health facility, community facility, or at home (self-isolation). Moderate – isolated at the designated COVID-19 health facility, community facility, or at home (self-isolation). The decision is to be made on a case-by-case basis. Severe – Managed in DCHC, health facilities, including emergency units, critical care units, primary care/outpatient clinics, as well as pre-hospital settings and ad hoc community facilities. Critical – Managed in DCHC and/or admit to ICU.	Asymptomatic or pre-symptomatic – Home isolation and care. Mild – managed in an ambulatory setting or at home through telemedicine or telephone visits. Moderate – isolated at designated COVID-19, community facility, or at home (self-isolation). The decision is to be made on a case-by-case basis. Severe – Managed in DCHC, health facilities, including emergency units, critical care units, primary care/outpatient clinics, as well as pre-hospital settings and ad hoc community facilities. Critical – Managed in

Category	Recommendations				
Organization	**ICMR [4]**	**IDSA [5]**	**MoH India [6]**	**WHO [7,8]**	**NIH [9]**
					DCHC, and health facilities, including emergency units and critical care units/ICU.
Risk factors identified	• Age > 60 years • Cardiovascular disease, hypertension, and CAD • Diabetes mellitus and other immunocompromised states (such as HIV) • Active tuberculosis • Chronic lung/kidney/liver disease • Cerebrovascular disease • Obesity	• Age ≥65 years • Obesity or being overweight (for example, adults with BMI >25 kg/m^2 • Pregnancy • Chronic kidney disease • Diabetes • Immunosuppressive disease or immunosuppressive treatment • Cardiovascular disease (including congenital heart disease) or hypertension • Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate to severe], interstitial lung disease, cystic fibrosis, and pulmonary hypertension) • Sickle cell disease • Neurodevelopmental disorders (for example, cerebral	• Age more than 60 years • Underlying non-Communicable diseases like cardiovascular disease, hypertension, CAD, DM (Diabetes Mellitus) and other immunocompromised states, Chronic lung/kidney/liver disease, cerebrovascular diseases, and obesity	• Age > 60 years • Cardiovascular disease, hypertension, and CAD • Diabetes • HIV • Active tuberculosis • Chronic lung/kidney/liver disease • Cerebrovascular disease • Obesity • Cancer • Chronic Obstructive Pulmonary Disease (COPD) • Pollution • Alcohol and Smoking	• Age > 60 years • Cardiovascular disease, hypertension, and CAD • Diabetes • HIV • Active tuberculosis • Chronic lung/kidney/liver disease • Cerebrovascular disease • Obesity

Category	Recommendations				
Organization	**ICMR [4]**	**IDSA [5]**	**MoH India [6]**	**WHO [7,8]**	**NIH [9]**
		palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies) • Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])			
Quarantine guidelines	• As per the recent updated guidelines for isolation of COVID-19 positive patients, the home quarantine period is14 days (ICMR, MoH India, WHO and NIH) and 5 days (IDSA) from contact with a confirmed case or earlier if a suspect case (of whom the index person is a contact) turns out negative on laboratory testing. • Asymptomatic family members exposed to symptomatic individuals should monitor their health. • Testing is NOT mandatory for asymptomatic contacts • Physical distancing, indoor mask use, strict hand hygiene. • Symptomatic management (hydration, antipyretics – paracetamol every 6 hourly, anti- tussive). • Stay in contact with the treating physician. • Monitor temperature and oxygen saturation (by applying a SpO_2 probe to fingers) every 6 hours. • Seek immediate medical attention if: - Difficulty in breathing or dizziness or High-grade fever/severe cough, particularly if lasting for >5 days. - If fever $\geq 100^{\circ}F$ persists for >3 days. - A low threshold is to be kept for those with any of the high-risk features. • Therapies are based on low certainty of the evidence, especially for those with a high risk of progression. Inhalational Budesonide (given via Metered dose inhaler/ Dry powder inhaler) at a dose of 800 mcg BD for 5 days) to be given if symptoms (fever and/or cough) are persistent beyond 5 days of disease onset.				

These guidelines also have significant similarities in diagnosis, and testing criteria as well. While the majority of the differences noted were mainly in the COVID-19 management strategies and/or treatment recommendations (See Table 2).

Table 2: Comparison of guidelines for the management of COVID-19 in adult patients

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
ICMR [4]	• Recommended in patients with moderate disease. • Conventional dose prophylactic unfractionated heparin or Low Molecular Weight Heparin (weight based e.g., enoxaparin 0.5mg/kg per day SC). • There should be no contraindication or high risk of bleeding.	• Remdesivir (EUA) may be considered ONLY in patients with mild to moderate disease and in whom the onset of sympltoms was seen within 10 days of infection. Remdesivir can also be considered in patients with moderate disease requiring supplemental oxygen), but who are NOT on IMV or ECMO. • Consider remdesivir for 5 days to treat hospitalized patients with COVID-19 (No evidence of benefit for treatment more than 5 days) • Not to be used in patients who are NOT on oxygen support or in the home setting • Monitor for RFT and LFT (remdesivir not recommended if eGFR <30 ml/min/m2; AST/ALT >5 times UNL) (not an absolute contraindication) • Recommended dose: 200	• Injection Methylprednisolone 0.5 to 1 mg/kg in 2 divided doses (or an equivalent dose of dexamethasone) for moderate cases and 1 to 2 mg/kg in 2 divided doses (or an equivalent dose of dexamethasone) for severe cases, usually for a duration of 5 to 10 days is recommended. • Patients may be initiated or switched to the oral route if stable and/or improving. • There is no evidence for the benefit of injectable steroids in those NOT requiring oxygen supplementation, or the continuation after discharge. • Anti-inflammatory or immunomodulatory therapy (such as steroids) can have the risk of secondary	Not recommended in general except in severe cases of sepsis.	• Indiscriminate use of CPT is not advisable. • CPT therefore should only be used when the potential recipient is in the early stage of COVID-19 disease, 3-7 days from onset of symptoms, but not later than 10 days, and no IgG Antibody against COVID-19.

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
		mg IV on day 1 followed by 100 mg IV OD for the next 4 days. • Use of Chloroquine or hydroxychloroquine and ivermectin is not recommended.	infection such as invasive mucormycosis when used too early, at a higher dose, or for longer than required. • Tocilizumab may be considered when ALL OF THE BELOW CRITERIA ARE MET - Rapidly progressing COVID-19 needing oxygen supplementation or IMV and not responding adequately to steroids (preferably within 24-48 hours of the onset of severe disease/ ICU admission). - Preferably to be given with steroids. - No active TB, fungal, systemic bacterial infection. - Long-term follow-up for secondary infections (such as reactivation of TB, flaring of Herpes, etc.) - Significantly raised inflammatory markers (CRP and/or IL-6). - Recommended single dose: 4 to 6 mg/kg (400 mg in 60 kg adult) in 100 ml NS over 1 hour.		

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
IDSA [5]	No specific recommendations except in patients treated with Janus Kinase Inhibitors (JAK) inhibitors such as Tofacitinib and baricitinib (4 mg/day for 14 days) due to the increased risk of Venous thromboembolism (VTE).	• Not recommended for use in COVID-19 patients as the use of antivirals is still being investigated in clinical trials except for remdesivir 200 mg on day 1 followed by 100 mg on days 2 and 3. However, routine initiation of remdesivir is not recommended. • Use of chloroquine/hydroxychloroquine and azithromycin, lopinavir/ritonavir are suggested against use. • While the use of nirmatrelvir/ritonavir and molnupiravir is recommended in mild to moderate cases with a high risk of progression to severe disease. • Use of nirmatrelvir/ritonavir should be avoided in combination with rivaroxaban and salmeterol due to increased risk of bleeding and cardiac effects, respectively.	• Usually, not recommended due to the risk of developing immunologic complications. • However, use of dexamethasone is recommended among hospitalized critically ill patients with COVID-19. If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used. Dexamethasone 6 mg IV or PO for 10 days (or until discharge) or equivalent glucocorticoid dose may be substituted if dexamethasone is unavailable. Equivalent total daily doses of alternative glucocorticoids to dexamethasone 6 mg daily are methylprednisolone 32 mg and prednisone 40 mg. • The use of inhaled corticosteroids is not recommended. • Use of tocilizumab and sarilumab is	Not recommended due to risk of superinfection that is antibiotic resistant.	Among ambulatory patients with mild to moderate COVID-19 at high risk for progression to severe disease who have no other treatment options, the IDSA guideline panel suggests FDA-qualified high-titer COVID-19 convalescent plasma within 8 days of symptom onset rather than no high-titer COVID-19 convalescent plasma.

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
			recommended among hospitalized adults with progressive severe or critical COVID-19 who have elevated markers of systemic inflammation. Pre-exposure of tixagevimab 300 mg and cilgavimab 300 mg as two separate intramuscular injections is recommended in cases with activity against regional predominant variants within 7 days of onset.		
MoH India [6]	Recommended for use in moderate and severe cases. A prophylactic dose of Un-Fractionated Heparin (UFH) or Low Molecular Weight Heparin (LMWH) (e.g., enoxaparin 0.5 mg / Kg body wt per day SC) There should be no contraindication or high risk of bleeding [Contraindications: End Stage Renal Disease (ESRD), active bleeding, emergency surgery]. Consider unfractionated heparin	• Remdesivir (EUA) may be considered ONLY in patients with mild to moderate disease and in whom the onset of sympltoms was seen within 10 days of infection. Remdesivir can also be considered in patients with moderate disease requiring supplemental oxygen), but who are NOT on IMV or ECMO. • Consider remdesivir for 5 days to treat hospitalized patients with COVID-19 (No evidence of benefit for treatment more than 5 days) • Not to be used in patients	In moderate cases - consider IV methylprednisolone 0.5 to 1 mg/kg OR IV Dexamethasone 0.1 to 0.2 mg/kg usually for a duration of 5 to 10 days. Review the duration of administration as per clinical response. Patients may be initiated or switched to the oral route if stable and/or improving. In severe cases - Inj Methylprednisolone 1 to 2mg/kg IV in 2 divided doses (or 0.2-0.4 mg/kg of dexamethasone) usually for the duration of 5 to 10 days is recommended.	Antibiotics should not be prescribed routinely unless there is clinical suspicion of a bacterial infection. Few patients with COVID-19 develop a secondary bacterial infection, consider empiric antibiotic therapy as per local antibiogram.	No specific recommendations.

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
	in ESRD.	who are NOT on oxygen support or in the home setting • Monitor for RFT and LFT (remdesivir not recommended if eGFR <30 ml/min/m^2; AST/ALT >5 times UNL) (not an absolute contraindication) • Recommended dose: 200 mg IV on day 1 followed by 100 mg IV OD for the next 4 days.			
WHO [7,8]	• Therapeutic dosing of anticoagulation refers to the dose used for the treatment of acute venous thromboembolism; intermediate dosing is commonly interpreted as twice the standard thromboprophylax is dose. • The suggested dosing of standard thromboprophylax is is as follows: • Enoxaparin 40 mg by subcutaneous injection every 24h: -Prophylactic dosages (non-	• Conditional use of molnupiravir among patients with non-severe COVID-19 at the highest risk of hospitalization is recommended. • Use of lopinavir/ritonavir is suggested against use. • Use of Chloroquine or hydroxychloroquine and ivermectin is not recommended. • The use of nirmatrelvir-ritonavir is strongly recommended in non-severe cases at the highest risk of hospitalization.	• Systemic corticosteroids are strongly recommended for patients with severe or critical COVID-19. The use of baricitinib as an alternative to IL-6 receptor blockers, in combination with corticosteroids, is strongly recommended among patients with severe or critical COVID-19. • Use of ruxolitinib and tofacitinib is not recommended unless necessary in severe cases. • The use of interleukin-6 (IL-6) receptor blockers (tocilizumab or sarilumab) in	No specific recommendations.	Not recommended except in the context of a clinical trial.

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
	weight adjusted) in low body weight (women < 45 kg, men < 57 kg) may lead to a higher risk of bleeding. Careful clinical observation is advised. • If BMI > 40 kg/m^2 or weight > 120 kg: enoxaparin 40 mg by subcutaneous injection every 12h. Unfractionated heparin (UFH) 5000 units by subcutaneous injection every 8 or 12h. • If BMI> 40 kg/m^2 or weight > 120 kg: 7500 units q12h or 5000 units every 8h. Tinzaparin 4500 units/day if BMI < 40 kg/m^2 or weight < 120kg; 9000 units/day if BMI > 40 kg/m^2 or weight > 120 kg. • Dalteparin 5000 units/day BMI <		combination with corticosteroids is strongly recommended among patients with severe or critical COVID-19. • Conditional use of casirivimab-imdevimab (in severe or critical cases) and sotrovimab (in mild or moderate cases) for patients with seronegative status, where rapid viral genotyping is available and confirms infection with a susceptible SARS-CoV-2 variant is recommended.		

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
	40 kg/m2 or weight < 120kg; 5000 units every 12 h if BMI > 40 kg/m2 or weight > 120 kg. Fondaparinux 2.5 mg by subcutaneous injection every 24h.				
NIH [9]	Anticoagulants and antiplatelet therapy should not be initiated in the ED for the prevention of venous thromboembolism (VTE) or arterial thrombosis if the patient is not being admitted to the hospital, unless the patient has other indications for the therapy or is participating in a clinical trial.	• The use of the following antivirals is recommended for use in severe cases: - Ritonavir-boosted nirmatrelvir (Paxlovid). - Remdesivir - Molnupiravir (as an alternative) • Use of Interferons for non-hospitalized patients, interferon alfa or lambda for hospitalized patients, Ivermectin and Nitazoxanide, etc. is not recommended except in clinical trials. • Use of Chloroquine or hydroxychloroquine and/or azithromycin, Lopinavir/ritonavir, and other HIV protease inhibitors is not recommended for hospitalized and non-	The following immunomodulators are recommended for use in hospitalized patients: - Corticosteroids: dexamethasone - Interleukin-6 inhibitors: tocilizumab (or sarilumab) - Janus kinase (JAK) inhibitors: baricitinib (or tofacitinib) - Intravenous immunoglobulin (IVIG) (non-SARS-CoV-2-specific) for the treatment of patients with acute COVID-19.	Use of empiric broad-spectrum antibiotics in adult patients with severe or critical COVID-19 antibiotics in the absence of a proven or suspected bacterial infection is not recommended.	No specific recommendations.

Organization	Recommendations				
	Anticoagulant	**Antivirals**	**Steroids and immunomodulators**	**Antibiotics**	**Convalescent Plasma Therapy (CPT)**
		hospitalized patients, and use of systemic interferon beta is not recommended for hospitalized patients.			

GUIDELINES FOR MANAGING COVID-19 AMONG CHILDREN – MIS-C

Management of COVID-19-related Multisystem inflammatory syndrome in children (MIS-C) among pediatric and adolescent patients during the COVID-19 pandemic proved to be challenging to the general pediatricians, pediatric medical sub-specialists, and pediatric surgical specialists. The current recommended treatment options by IDSA for mild to moderate symptomatic outpatients with COVID-19 who are at risk for progression to severe COVID-19 include paxlovid or remdesivir as primary therapy and bebtelovimab or molnupiravir as alternative therapies along with standard supportive care. While preexposure prophylactic therapy recommendation includes Tixagevimab and cilgavimab (Evusheld) in children and adolescents ≥12 years of age weighing ≥40 kg [5]. While the WHO recommends use of corticosteroids IVIG 2 gm/kg over 12-16 hours (max. 100 g), and IV methylprednisolone 1-2 mg/kg/day) among children of 1-18 years with MIS-C and/or Kawasaki disease in addition to supportive care (instead of IVIG plus supportive care, or supportive care alone) [7]. The NIH recommends the use of both immunomodulatory and antithrombotic as initial therapies in both children and adolescents with MIS-C. Initial immunomodulatory therapy includes IVIG 2 g/kg IBW/dose (up to a maximum total dose of 100 g) IV for 1 dose and divided doses of 1 g/kg IBW/dose IV every 24 hours for 2 doses in the event of cardiac dysfunction or fluid overload. Intensified immunomodulatory therapy includes use of methylprednisolone 1 to 2 mg/kg/dose IV every 12 hours followed by increased dose of 10–30 mg/kg/day (up to maximum of 1,000 mg/day) IV for 1 to 3 days, anakinra 5–10 mg/kg/day IV (preferred) or SUBQ in 1 to 4 divided doses and Infliximab 5–10 mg/kg/dose IV for 1 dose. Initial antithrombotic therapy includes low-dose aspirin 3–5 mg/kg/dose (up to a maximum of 81 mg/dose) PO once daily. Antiviral therapy is not recommended among MIS-C patients with COVID-19 [9]. Reported cases of shock

among MIS-C patients with COVID-19 may include elements of distributive, cardiogenic, or hypovolemic shock. In such patients, management of shock should be as per the usual critical care standards along with IVIG 2 gm/kg over 12-16 hours (max. 100 g), IV methylprednisolone 2 mg/kg/day, and empirical antimicrobials as per hospital antibiogram [10].

INTERNATIONAL GUIDELINES FOR MANAGING NEONATES DURING COVID-19

During the COVID-19 pandemic, several countries have put forward guidelines to manage neonates born to COVID-19-positive women. Managing neonates has become a challenge to health care providers across the world. In a systematic review performed by Anna Lavizzari et al., in 2021; data collected and analysed from 20 countries during March 14 and 21, 2020 on several international guidelines for the management of COVID-19 in neonate patients mainly focusing on components of the central protocol, including triaging, hygiene precautions, delivery management, breastfeeding protocols, and visitor's policy; showed that there was a huge variation on the disease burden between the countries at the time of analysis. In majority of the countries, infants who were asymptomatic were allowed to stay with their mothers and breastfeed with proper hygiene precautions. However, there were a few discrepancies noted between the national guidance regarding triaging, personal protection equipment usage, viral testing, and visitor's policy [11].

DISCUSSION AND CONCLUSION

Management of COVID-19 patients has become a challenging and enriching experience to most of the healthcare practitioners. The various national and international guidelines published on the management of COVID-19 by several scientific bodies and regulatory authorities have been very resourceful and informative to many healthcare providers. These guidelines provide meticulous

details about the use of a specific drug, the timing, dose, and duration of treatment in a very specific manner and deviation from this could lead to unintended adverse treatment outcomes. Some of them are living documents and are updated on a regular and/or periodic basis as well. However, there are certain limitations to these as well. The most important limitation is that these guidelines are based on the knowledge that the issuing bodies had at the time the guidelines were published. The fact that these guidelines need to be updated on a regular basis as new information and/or knowledge about the disease or therapeutic options becomes available is often overlooked which may render the guidelines to become old and invalid if not updated. Hence, it is imperative that the issuing bodies need to be aware that updating the guidelines is a dynamic process and the guideline should be updated on regular basis to maintain their status as current guidelines. Another limitation is the fact that these guidelines are only recommendations and the final decision on the right management of the patient is to be taken by the treating healthcare provider based on the clinical examination of the patient.

During the beginning of the pandemic, several other guidelines were also published on the prevention of COVID-19 and prophylactic treatment options etc. which mainly included use of hydroxychloroquine for prevention and treatment of COVID-19; Vitamin D, Vitamin C, and Zinc to enhance patient immunity; use of antibiotics like doxycycline, azithromycin, an antiviral drug like Oseltamivir and antiparasitic agent Ivermectin in the treatment of COVID-19. However, these guidelines were later withdrawn due to a lack of adequate supporting evidence.

In conclusion, besides the limitations, the various guidelines as discussed in this article can still serve as an important tool to healthcare workers and caregivers by providing adequate guidance on the right management of COVID-19 at that time.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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