COVID-19 MANAGEMENT, CURRENT CONCEPTS

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BACKGROUND

COVID-19 also known as SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) is a novel Corona-virus affecting primarily the respiratory system. It is transmitted by exposure to virus-containing respiratory droplets and airborne particles exhaled by an infected person[1] or by direct contact with infected persons or by contact with contaminated objects and surfaces[2]. COVID-19 infections range from being completely asymptomatic to having mild to moderate symptoms and then to becoming completely overwhelmed and coming down with a critical illness which may often lead to death.

The incubation period for COVID-19 which is the time between exposure to the virus (becoming infected) and symptoms onset, is, on the average, 5-7 days, but can be up to 14 days[2]. One study reported that 97.5% of people with COVID-19 who have symptoms will do so within 11.5 days of SARS-CoV-2 infection.[3]

In the majority of the cases, 80% will exhibit mild symptoms, 14% will have pneumonia, 5% will suffer from septic shock and organ failure (mostly respiratory failure) and in 2% cases, it will be fatal [4].

BRIEF HISTORY

COVID-19 was first identified in a pneumonia patient in Wuhan, Hubei province, China. First discovered as a disease from the Wuhan seafood market, its ease of spread by human to human contact took it beyond Chinese borders and made it a global disease [5].

The novel human coronavirus disease COVID-19 has thus become the fifth documented pandemic since the 1918 flu pandemic6. While 1,813,188 COVID-19 deaths were reported in 2020, recent WHO estimates suggest excess mortality of at least 3,000,000[7]. In Nigeria, there are 166,918 confirmed cases, out of which were 163,259 recovered cases and 2,117 deaths[8].

VIRUS CHARACTERISTICS

SARS-CoV-2 is identical to some of the β coronaviruses generally found in bats which are located in the SARS / SARS-like CoV groups. The COVID-19 S-protein strongly interacts with human ACE-2 molecules despite the dissimilarity of its sequence with that of SARS-CoV[9]. The SARS CoV-2 has, like other beta coronaviruses, an untranslated region (UTR), a replicase complex encoding non-structural proteins (NSPs), a spike protein (S), an envelope protein (E), a membrane protein (M), a nucleocapsid protein(N) gene and many other proteins.[10]

CLINICAL FEATURES/PRESENTATION[11,12]

Fever 43-98%

- Often high and sustained for 10 days but may be intermittent
- Absence of fever does not rule out diagnosis

Cough 68-82%

- Sputum 14-56%

Breathlessness 3-64%

- Onset around day 6
- May be silent hypoxia (especially elderly)
- No increased work of breathing but severe hypoxia

Less common

- GI (diarrhoea, nausea, may precede fever) - up to 10%
- Runny nose-4-24%
- Sore throat -14%
- Myalgia -11-15%
- Headache - 6-34%

Anosmia:

- Up to 2/3rd of patients with covid-19 have anosmia
- Significant amounts of patients present with anosmia with no other symptoms

CLASSIFICATION:-

MILD DISEASE

- Patients with a mild clinical presentation (absence of

viral pneumonia and hypoxia) may not initially require hospitalization, and most patients will be able to manage their illness at home. [13]

- It is recommended that patients with mild COVID-19 be given symptomatic treatment such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration[2]. At present, there is no evidence to indicate that there are severe adverse events in patients with COVID-19 as a result of the use of non-steroidal anti-inflammatory drug[14]. Counsel patients about the reason for isolation, signs and symptoms of complications. Antibiotic therapy or prophylaxis should not be used in patients with mild COVID-19[2] as their use may lead to higher bacterial resistance rates, which will impact the burden of disease and deaths in a population[15,16,17].

MODERATE DISEASE

- For patients with suspected or confirmed moderate cases i.e Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air[18] or 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 19; It is recommended that they be isolated to contain virus transmission as they may not require emergency interventions or hospitalization.

It is also recommended for patients with suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection[2].

- A recent systematic review of patients hospitalized with COVID-19 reported only 8% were reported as experiencing bacterial/fungal co-infection during hospital admission [20].

SEVERE DISEASE

Some patients with COVID-19 will have severe disease requiring hospitalization for management[21]. Provision of supplemental oxygen therapy is the hallmark of treatment in this situation. As much as possible, all areas where severely ill patients are being cared for should be equipped with a pulse oximeter, functioning oxygen system and disposable, single-use oxygen delivery interfaces (nasal cannula, simple face mask, and mask with reservoir bag).
Commence oxygen therapy at 5L/min and titrate flow rate to reach target SpO2 >90% in non-pregnant adults and SpO2 >92-95% in pregnant adults. Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and convulsion) should receive oxygen therapy during resuscitation to target SpO2 >94%.
Empiric antibiotics treatment should be given where necessary. Monitor patients closely for signs of clinical deterioration such as progressive respiratory failure and sepsis and apply supportive care interventions immediately.[22]
Glucocorticoids probably reduce mortality and the need for ventilatory support in a patient with severe COVID-19 compare with other medication[23].

DIAGNOSIS

Criteria for diagnostic suspicion

Consider the diagnosis in patient requiring admission to hospital (for at least 1 night) with:

- Clinical or radiological evidence of pneumonia OR
- ARDS OR
- Influenza like illness

Consider discharge for home management/self isolation if:

- NEWS 0-4
- SaO2 >94%
- RR<20
- With no underlying lung disease

The WHO has put forward case definitions[24].

Suspected cases of COVID-19 are persons (a) with severe acute respiratory infections (history of fever and cough requiring admission to hospital) and with no other aetiology that fully explains the clinical presentation and a history of travel to or residence in China during the 14 days prior to symptom onset; or (b) a patient with any acute respiratory illness and at least one of the following during the 14 days prior to symptom onset: contact with a confirmed or probable case of SARS-CoV-2 infection or worked in or attended a health care facility where patients with confirmed or probable SARS-CoV-2 acute respiratory disease patients were being treated.

Probable cases are those for whom testing for SARS-CoV-2 is inconclusive or who test positive using a pan-coronavirus assay and without laboratory evidence of other respiratory pathogens.

Confirmed cases is one with a laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs and symptoms. For patients who meet diagnostic criteria for SARS-CoV-2 testing, the CDC recommends collection of specimens from the upper respiratory tract (nasopharyngeal and oropharyngeal swab) and, if possible, the lower respiratory tract (sputum, tracheal aspirate, or bronchoalveolar lavage[25]. In each country, the tests are performed

by laboratories designated by the government.

EVALUATION

In patients with clinical evidence of COVID-19 infection, laboratory tests may reveal lymphocytopenia, thrombocytopenia, elevated liver transaminases, elevated C-reactive protein and erythrocyte sedimentation rate, elevated serum lactate dehydrogenase and decreased or normal serum albumin. Elevated serum troponin-T may be present, indicating myocardial injury. The following tests are used in patients with symptoms suggestive of COVID-19 infection.

Viral testing

Viral testing is performed by the RT-qPCR test, used for qualitative detection of the nucleic acid for SARS-CoV-2. Swabs are usually taken from nasal, nasopharyngeal, oropharyngeal, sputum or lower respiratory tract aspirates or wash. Positive tests indicate the presence of SARS-CoV-2 RNA, and together with the clinical picture support the diagnosis. Negative test results do not preclude SARS-CoV-2 infection, and shall be interpreted in light of the clinical picture and epidemiologic information[26].

Serology

Serology testing for SARS CoV-2 is now available. The test can assess prior exposure to virus and cannot be used in the diagnosis of current infection. Cross-reactivity with other human coronaviruses may occur. The serology test is particularly useful (i) When the viral test is not available. Using the serology test together with the clinical picture could guide in decision making. (ii) Patients with late disease complications and their physicians need to make immediate decisions (the viral test takes more time to get the results) (iii) In some patients, virus shedding is reduced, making RT-qPCR results falsely negative. The serology test can detect IgM and IgG antibodies against SARS-CoV-2 in serum, plasma and whole blood[27].

Rapid antigen testing;

Rapid antigen testing is a monoclonal antibody test against the SARS-CoV-2 nucleocapsid protein (N). This protein is abnormally expressed in infected cells. Monoclonal antibodies are specifically directed against nucleocapsid protein, and by using enzyme-linked immunosorbent assay, it is possible to detect SARS-CoV-2. The test has a reported sensitivity of 84.1% and a specificity of 98.5%. No cross-reaction with human and animal coronaviruses in the assay were reported. There are no reports yet about applying this test to SARS-CoV-2 [28,29].

MANAGEMENT OF COVID-19 - SEVERE

Clinical management of COVID-19 includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated [13].

INFECTION PREVENTION AND CONTROL MEASURES

These two approaches usually should go hand-in-hand and may be difficult to delineate. It involves wearing a mask that covers the nose and mouth; social and physical distancing; getting vaccinated for COVID-19; avoiding crowds and poorly ventilated indoor spaces; and washing hands often, with soap and water.[21] In areas with other endemic infections that cause fever, such as malaria, dengue, tuberculosis (TB) etc., as part of the screening, febrile patients should be tested as per routine protocols. [30,31,32,33,34]

SUPPORTIVE CARE

The aim of providing support to patients with COVID-19 is to supply timely intervention essential to halting the progress of symptoms into fatal complications and ultimately saving lives. Persons with symptoms that meet the definition for suspected COVID-19 enter into the COVID-19 care pathway and should immediately be given a medical mask and directed to a single room. If a single room is not possible, then group patients with a similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation of at least 1m between patients. Suspected cases should not be nursed together with confirmed cases.[2]

COMPLICATIONS

Age and sex have been shown to affect the severity of complications of COVID-19. The rates of hospitalization and death are less than 0.1% in children but increase to 10% or more in older patients. Men are more likely to develop severe complications compared to women as a consequence of SARS-CoV-2 infection[35]. Patients with cancer and solid organ transplant recipients are at increased risk of severe COVID-19 complications because of their immunosuppressed status. The main complications reported in patients with SARSCoV-2 may include:

- **Coagulopathy**, mainly disseminated intravascular coagulation, venous thromboembolism, elevated D-dimer and prolonged prothrombin time.
- **Laryngeal oedema and laryngitis** in critically ill patients with COVID-19.
- **Necrotizing pneumonia** due to superinfection caused by Panton-Valentine leukocidin–secreting Staphylococcus aureus infection. This superinfection is usually fatal[36].
- **Cardiovascular complications**; including acute pericarditis, left ventricular dysfunction, acute myocardial injury (associated with increased serum troponin), new or worsening arrhythmias and new or worsening heart
- **Acute respiratory failure;** Approximately 5% of

COVID-19 patients require admittance to an intensive care unit because they develop severe disease complicated by acute respiratory distress syndrome[37].

- **Sepsis, septic shock and multiple organ failure.**
- **Higher risk of death**, particularly in male patients with severe disease, presence of heart injury and cardiac complications, hyperglycaemia and patients receiving high doses of corticosteroids[38].
- **Ventilation-associated pneumonia** in up to 30% of patients requiring intensive mechanical ventilation.
- **Massive pulmonary embolism** complicated by **acute right-sided heart failure**[39].

MORBIDITY AND MORTALITY:

In other settings such as the United States, Europe, and China, morbidity and mortality have been highest in those older than 60 years and with underlying comorbidities such as arterial hypertension, heart disease, diabetes, and chronic lung disease; young adults and children seem to have relatively mild disease and low mortality[14,15]

- Poor prognostic markers

Comorbidities:

- ≥ 60 years
- Medical co-morbidities
- Hypertension, DM
- Chronic lung diseases – COPD, Asthma, PTB, etc
- CKD
- Cardiovascular diseases
- Malignancy

THE CONCEPT OF VACCINATION

Vaccines contain weakened or inactive parts of a particular organism (antigen) that triggers an immune response within the body. Some vaccines require multiple doses, given weeks or months apart. This is sometimes needed to allow for the production of long-lived antibodies and the development of memory cells. In this way, the body is trained to fight the specific disease-causing organism, building up the memory of the pathogen so as to rapidly fight it if and when exposed in the future.[42]

Several safe and effective vaccines are now available to prevent the severe forms of the illness and curb mortality. WHO has evaluated that the following vaccines against COVID-19 have met the necessary criteria for safety and efficacy: Oxford/AstraZeneca vaccine, Johnson and Johnson, Moderna, Pfizer/BionTech, Sinopharm, Sinovac.[43]

PREVENTION OF COMPLICATIONS

Sequalae to COVID-19 infection are complications which may include the following: Hypoxaemic Respiratory Failure (HRF) and Acute Respiratory Distress Syndrome (ARDS); Sepsis and Septic Shock.

WHO guidelines recommend the following interventions to prevent the common complications of COVID-19

ANTICIPATED OUTCOME	INTERVENTIONS
Reduce days of invasive mechanic ventilation	• Use weaning protocols that include daily assessment for readiness to breathe spontaneously • Minimise continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of the continuous sedative infusion
Reduce incidence of ventilator-associated pneumonia	• Oral intubation is preferable to nasal intubation in adults • Keep patient in semi-recumbent position (head of the bed elevation at 300-450 • Use a close suctioning system, periodically drain and discard condensate in tubing • Use a new ventilator circuit for each patient. Once patient is ventilated, change circuit if it is soiled or damaged but not routinely • Change each moisture exchanger when it malfunctions, when soiled, or every 5-7 days

ANTICIPATED OUTCOME	INTERVENTIONS
Reduce incidence of thromboembolism	• Use pharmacological prophylaxis (low molecular weight heparin (preferred if available) or heparin 5,000 units subcutaneously twice daily) in adults without contraindication. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression device).
Reduce incidence of catheter-related bloodstream infection	• Use a checklist, with completion verified by a real-time observer as a reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed
Reduce incidence of stress ulcers and gastrointestinal bleeding	• Give early enteral nutrition (within 24-48 hours of admission) • Administer histamine-2 receptor blocker or proton pump inhibitor in patients with risk factors for GI bleeding. • Risk factors for gastrointestinal bleeding include mechanical ventilation for greater than 48 hours, coagulopathy, renal replacement therapy, liver disease, multiple comorbidities like diabetes and higher organ failure score.

CONCLUSION

COVID-19 is a highly transmissible infection which can be prevented by following the COVID-19 protocols and guidelines of maintaining social distancing, adopting the habit of regular hand washing with soap and water and use of hand sanitizer. Infected individuals should be placed on watch and monitored for any signs and symptoms of disease progression. Prompt interventions and special care are required for patients with critical illness and/or other co-morbidities.

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