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Overview of the Management of COVID-19 Efficacy and Doubts

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Authors' contributions

This work was carried out in collaboration among all authors. Author PCS designed the study and wrote the protocol. Authors CNS and OAA wrote the first draft of the manuscript and performed statistical analysis searches. All authors managed the literature searches, read and approved the final manuscript.

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is defined as an illness caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2. It was first identified during an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China. Management of COVID-19 is still unspecific as there are no vaccine or specific antiviral drugs are available for its treatment. This paper reviews the management efficacy and doubt of COVID-19.

Methods: A comprehensive search from relevant literatures, World Health Organization (W.H.O), Centre for Disease Control and prevention (CDC) official websites and announcements was performed between 1 March 2020 to 10:30 am 22 April 2020 (Nigerian time). A latest summary of 2019- nCoV and the current outbreak was drawn.

Conclusion: The covid-19 pandemic is spreading rapidly and several researchers are making efforts to discover drugs for its treatment. Chloroquine phosphate, vaccines and other forms of management strategies have been employed. However, preventive measures like social distancing, washing of hands with soap and water, wearing of face masks and psychosocial treatment should be adopted while waiting for pharmacological treatments.

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1. INTRODUCTION

Coronavirus disease (COVID-19) is caused by SARS-CoV2 [1,2]. Since the outbreak in Wuhan City, China, in December 2019, it has been an epidemic until recently, the World Health Organization (WHO) referred to it as a global pandemic [1]. The primary target is the respiratory system. Coronavirus disease (COVID-19) symptoms appear after an incubation period of 2-14 days, an average of about 5-7 days [1]. It is not an airborne nor a free living organism but a protein bound virus [3]. Globally, the number of confirmed cases as at 14th May 2020 was 4,348,246 with a mortality of 297,226. Nigeria had 4,787 number of confirmed cases and Mortality of 158 [4].

The structural proteins of SARS-CoV-2 comprise the spike (S), membrane (M), envelope (E) and nucleic capsid (N) proteins [5]. Amongst these receptors, S protein has been studied widely with respect to human beings. The role of S protein, among others includes; initiation of cell fusion on the host cell surface, direct interaction of the subtype S1 within the receptor-binding domain (RBD) with host receptors [6], binding site at the Angiotensin-converting enzyme 2 (ACE2) receptor on human alveolar epithelial cells [7-9] suggesting SARS-CoV-2 uses the same receptor, ACE2, as SARS-CoV [10]. The high affinity of the S protein for human ACE2 may lead to the great human-to-human transmission of SARS-CoV-2. Due to the key role of the S protein, it is the core target for antibody-mediated neutralization. The spike protein is a type 1 glycoprotein which form the peplomers on coronavirus particles. Corona spike protein plays a major role in viral entry through endosomal portal [2,11,12].

2. DIAGNOSIS

Clinical diagnosis of COVID-19 is mainly based on clinical history and ancillary examinations, such as viral nucleic acid detection, CT scan of the chest, immune identification technology (Point-of-care Testing (POCT) of IgM/IgG, enzyme-linked immunosorbent assay (ELISA)) and blood culture. The clinical symptoms and signs of patients infected with SARS-CoV-2 including respiratory symptoms, fever, dyspnea, viral pneumonia, headache and testicular pain are non-specific and may even be even be atypical such as malaise, GIT symptoms and anosmia. Hence, the aforementioned ancillary examinations are essential for the diagnosis of COVID-19 [13]. Rapid diagnosis of viral pneumonia with computed tomography (CT) scans can potentially lead to early identification and control of transmission especially where there is scarcity of the testing kits. Patients with suspected disease can be isolated and early so that the management of patients will be optimized, especially for the hospitals or communities lacking nucleic acid testing kit [14].

However, the use of chest CT scans for COVID-19 diagnosis is controversial. In addition, the detailed CT features of COVID-19 have been reported in only a small number of articles in the literature [15-17]. Quantitative real-time reverse transcriptase-polymerase chain reaction (RT-qPCR) assay and high-throughput sequencing has routinely been used for the detection of causative viruses from respiratory secretions [including bronchoalveolar lavage fluid (BALF)] and final pathogenic diagnostics of COVID-19 [9,18]. More than seven types of SARS-CoV-2 nucleic acid test kit have been developed and approved rapidly. Thus, viral nucleic acid testing is playing a crucial role in helping to reduce the spread of the COVID-19 epidemic (pandemic). However, nucleic acid testing needs rigorous laboratory specifications and requires a relatively long time before results are available. In addition, some patients with suspected COVID-19 may have initial nucleic acid test results that are false-negative for virus infection, which is harmful for the control of infectious diseases [19]. Test specificity may also be an issue for example, Tanzania was said to have locally produced COVID-19 test kits which was seemingly working well until May 6, 2020 when their president raised an alarm after samples taken from a goat and a pawpaw fruit came back with positive results. It is likely that the kits were not subjected to appropriate validity studies .WHO has previously warned against non-approved measure in diagnosis and treatment of COVID-19 [1,3].

Recently, lungs tissues of 38 cases who died for COVID-19 in two hospitals of Northern Italy were systematically analysed. Hematoxylin-eosin staining, immunohistochemistry for the

inflammatory infiltrate and cellular components, electron microscopy were performed. The finding revealed Diffuse Alveolar Disease (DAD): capillary congestion, necrosis of pneumocytes, hyaline membrane, interstitial oedema, pneumocyte hyperplasia and reactive atypia, platelet-fibrin thrombi. This is similar to other two coronaviruses that infect humans, SARS-CoV and MERS-CoV [20].

Treatment of COVID -19 however remains unspecific and has largely followed protocol of SARS-CoV, MERS-CoV and Influenza [21,22]. The following have been used as single or combination therapy with fair clinical response. They include broad spectrum antiviral drugs such as nucleoside analogues, HIV protease inhibitors, hydroxychloroquine, Azithromycin and zinc [1,2,23].

3. CHLOROQUINE /HYDROXY-CHLOROQUINE

Chloroquine/hydroxychloroquine has also been added to the list of drugs that can be used to treat COVID-19. It is a widely used anti-malarial and autoimmune disease drug which also been recently reported to be a potential broad-spectrum antiviral drug [24]. The mechanism of action includes blocking of viral infection by increasing endosomal pH that is required for viral/cell fusion as well as interfering with the glycosylation of cellular receptors of SARS-CoV [25]. According to a study by Jianjun Gao et al. [26], chloroquine phosphate, an old drug for treatment of malaria has efficacy and is accepted for the treatment of covid-19 associated pneumonia.

The FDA cautioned against use of high-dose chloroquine (600 mg twice daily for 10 days) for the treatment of COVID-19, because the high dose carries a higher risk of toxicities than the lower dose. However, recently there has been an uproar following the report of toxicity with the use of both hydroxychloroquine and chloroquine sulfate [27]. Elderly people and persons with comorbid medical conditions such as respiratory infections, diabetes, cardiovascular diseases, and cancer may be more susceptible to SARS-CoV-2 [28,29]. Smoking and obesity are also predisposing factors [30,31]. Cardiac toxicity could be worsened with increased risk of QT interval prolongation, ventricular tachycardia, myocardial infarction (MI), cardiac arrhythmia and sudden death [32,33]. This indeed is a major setback. The promise of a vaccine remains the only solution in sight. However, the thought of the projected time of 18 months creates more anxiety, while we wait [27,34].

4. IMMUNE GLOBULINS

Lin L, et al. [35] recommended that high-dose intravenous immunoglobulins (IVIg) at 0.3-0.5 g per kg weight per day could be given for 5 days, which can interrupt the storm of inflammatory factors at an early stage and enhance immune function. A randomized controlled clinical trial of IVIg in patients with severe SARS-CoV-2 infection has been initiated (NCT 04261426). Although IVIG has shown efficacy in the treatment of patients with influenza [36] and SARS [37], we need more clinical data of COVID-19 patients as evidence.

5. ANTITHROMBOTIC THERAPY

There have been reports of increased incidence of thromboembolic disease associated with COVID-19 in patients in the intensive care unit. Anticoagulation therapy is recommended for COVID-19 patients when the D-Dimer value is 4 times higher than the normal upper limit, except for patients with contraindications to anticoagulant therapy. The recommended dose of LMWH is 100U per kg body weight per 12 hours by subcutaneous injection for 3-5 days. Clinicians should closely monitor the indicators of laboratory examination of patients to be alert for side effects after anticoagulant treatment [35].

6. REMDESIVIR

Remdesivir, an antiviral drug, has also been tried in the US, Italy, Indian and China with favourable outcome [38,39]. The clinical trial by National Institute of Allergy and Infectious Diseases (NIAID) evaluated broad-spectrum antiviral treatment developed by Gilead Sciences, Inc. 1,063 participants were recruited from 47 U.S. and 21 international sites. An independent data and safety monitoring board (DSMB) overseeing the trial met on April 27 and shared their preliminary analysis with the study sponsor, NIAID. Their analysis showed that patients who received remdesivir had a shorter recovery time as compared to patients who received placebo [38]. It is recommended for patients with severe disease, defined as SpO2 ≤94% on ambient air (at sea level), requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation. Despite the above, it is yet to be approved by Food and Drug

Administration (FDA) as the drug of choice for the treatment of COVID-19 [39].

7. TRADITIONAL MEDICINE

Traditional medicine seems to have some effects in supportive treatments for COVID-19. As at February, 2020, the total number of confirmed cases treated by traditional Chinese medicine (TCM) was 60107 [40]. In one study, 102 cases of mild symptoms treated with TCM, the clinical symptom disappearance time was shortened by 2 days, the recovery time of body temperature was shortened by 1.7 days, the average length of stay in hospital was shortened by 2.2 days, the improvement rate of CT image was increased by 22%, the clinical cure rate was increased by 33%, 27.4% reduction in the rate of common to severe cases and 70% increase in lymphocyte count. In addition, in the treatment of severe patients with TCM, the average length of stay in hospital and the time of nucleic acid turning negative has been shortened by more than 2 days [40]. Madagascar has also launched an organic herbal concoction, made from Artemisia and other plants named Covid-organic (CVO) which they claim has been very effective in patient with COVID-19. So far, they have not recorded any mortality in their country due to SARS-CoV-2 infection. Some countries like Chad, Guinea-Bissau, Nigeria and Tanzania have express interest in and/or opted for the use of CVO. However, WHO in a publication on May 4, 2020 reiterated her support for only scientifically sound and clinically tested traditional and alternative medicines for COVID - 19 and seriously warned against use of non-approved medicines. CVO is currently under clinical trials in some places.

8. VACCINE

Vaccine seems to be the future hope of the treatment and cure of COVID 19 as there is no specific treatment for COVID 19 till date (May 14, 2020) [1,3]. Several biotechnology companies are currently in the process of preliminary testing and production of vaccine. The WHO is working with Chinese scientists to launch more than 80 clinical trials of potential treatments for SARS-CoV-2. In order to curtail the outbreak of coronavirus, effective SARS-CoV-2 vaccines are essential with the aim of reducing disease severity, viral shedding and transmission. Various strategies in vaccination against MERS-CoV, SARS-CoV have been tested in animals, including a recombinant DNA (rDNA), inactivated virus, viral vectors, subunit vaccines, and proteins vaccines [32]. However, it has been estimated that it would take about 12 to 18 months for a SARS-CoV -2 vaccine to be readily available for widespread public use [23,39]. More laboratory and clinical evidence should still be explored.

Management option should remain primarily preventive as there is no vaccine or specific anti-viral drug regimen used to treat critically ill patients. It is, therefore necessary to adhere strictly to the outlined prevention protocol by WHO as enumerated below: Maintaining social distancing, frequent washing of hands with soap under a running water or regular sanitization of hands with a sanitizer that is at least 70% alcohol based and use of face masks in open places. However, staying at home remains the best option to curtail its spread.

Early detection with high index of suspicion will go a long way to prevent morbidity and mortality associated with COVID-19 [41]. Continuous monitoring and tracing of suspected cases is the key to avoid widespread of infection within the population. Intervention for those that tested positive has to be quick, professional and continuous until reasonable level of improvement as evidenced by resolution of fever, disappearance of headache and two negative test results [42].

9. CONCLUSION

It is too early to consider the sequelae of this disease for survivors. Hence, the need for a very strong follow-up of all those who have been discharged for about 18 months to determine the course of illness [41]. Moreover, the basic preventive steps such as social distancing, regular hand washing under clean running water, use of face masks at public areas and staying at home orders should still be strongly observed [1,43].

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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