



Review of Pathogenesis of COVID-19: Considerations

C. N. Stanley¹, O. A. Ayodeji² and P. C. Stanley^{2*}

¹*Department of Pharmaceutical Microbiology and Biotechnology, Faculty of Pharmaceutical Sciences,
University of Port Harcourt, Nigeria.*

²*Department of Neuropsychiatry, University of Port Harcourt Teaching Hospital (UPTH),
Port Harcourt, Nigeria.*

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.

Article Information

DOI: 10.9734/JAMMR/2020/v32i730446

Editor(s):

(1) Dr. Thomas I. Nathaniel, University of South Carolina, USA.

Reviewers:

(1) Pichon Maxime, University Hospital of Poitiers, France.

(2) Oseni, Tijani Idris Ahmad, Ambrose Alli University, Nigeria.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/57151>

Review Article

Received 30 April 2020

Accepted 14 May 2020

Published 22 May 2020

ABSTRACT

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with a primary target on the human respiratory system. Coronavirus disease was first discovered in Wuhan, China in December 2019 and has currently become a global pandemic. A lot is still unknown about COVID -19 pathogenesis. Prompt assessment, adequate follow up, test and retest of recovered cases to corroborate immune related considerations will go a long way to understand the pathogenesis.

Keywords: COVID -19; SARS-CoV-2; DIC; pathogenesis; Centre for Disease Control (CDC).

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a novel type of coronavirus, the severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) that mainly targets the human respiratory system. It was first reported in Wuhan, China in December 2019 and has currently become a global pandemic [1,2]. Globally, the number of

*Corresponding author: E-mail: stanleypc2001@yahoo.com;

confirmed cases as at 24th April 2020 was over 2.7 million with a mortality of about 181,000. Nigeria had up to 1,095 confirmed cases and a mortality of 32 (WHO, CDC).

The name "Coronavirus" was coined from the word "corona" that is, a crown depicting its crown-like morphology as seen under the electron microscope in 1968 [3]. It belongs to the family of coronaviridae [4,5]. Coronavirus causes acute and chronic inflammatory changes in the respiratory, enteric and central nervous system (CNS) in various kinds of animals, including humans [6]. Prior to the discovery of the severe acute respiratory syndrome coronavirus SARS-CoV in 2003, two prototypes of the coronaviruses were identified namely OC43 and 229E, both of which are the main etiology of common cold [6,7].

2. PATHOGENESIS

The biological vector of coronavirus is not known, but serological and genetic studies point to a zoonotic origin [8].

Being a novel virus, relatively little is known about the exact pathogenesis of COVID-19 but there has been a previous, and ongoing research that implicates the immune system. For instance, it is well established that immune changes occur in patients with SARS, Middle East Respiratory Syndrome (MERS) and influenza (H1N1). Also previous studies on peripheral blood T-cell lymphocytes improved the understanding of diagnosis, monitoring, treatment and prevention of COVID-19 [9-11].

The incubation period of COVID-19 is about 2-14 days, which is referred to as the acute phase of the illness. In the acute phase, there is a marked rapid reduction in peripheral blood lymphocytes, mainly CD3+, CD4+ and CD8+ and this may lead to abnormal changes seen as ground glass appearance in chest X-rays of patients with the disease.

Pathological findings of COVID-19 reveal an overactivation of T cells following an increase in T-helper -17 (Th17) and cytotoxicity of CD8 T probably accounting for the severe immune injury [12]. Cell recovery takes about three to twelve months and follow up of recovered patients should be for at least twelve to eighteen months. It should be noted that even after the follow up period, the cell counts would still be lower compared to healthy controls [9-11,13].

SARS –specific IgG antibodies are produced towards the end of acute phase (about 2 weeks). The level of IgG is considerably higher in mild compared to severely ill patients. This is the rationale for the use of low dose glucocorticoids in acute phase of illness although relatively high doses have been documented in some studies [14-17].

The time from the onset of symptoms of COVID-19 to death ranges from 6 to 41 days [18]. This depends on several factors: Age of patient, immune status, co-morbid medical conditions such as respiratory infections, hypertension, diabetes, and viral load amongst others [18]. It is shorter in those with advanced age \geq 70years and the immune compromised [18]. Age is an independent and non-modifiable risk factor for death [19].

Older people are not as effective as the young at mounting an immune response to micro-organisms to which they are naive, a situation that has been referred to as "the twilight of immunity" [20]. With advancing age the number of T cells in the body, which are responsible for the production of virus-fighting cytokines, decreases. For example, by the age of puberty, the thymus is producing tenfold fewer T cells than it did in childhood, and by age 40 or 50 years, there is another tenfold drop [20,21]. With advancing age, therefore, the body has fewer immature T cells to defend against a specific microbe. Fewer of such "naïve T cells" means fewer T cells are available to be deployed against a never-before-seen microbe [20,22].

The mechanism of the damage caused by SARS –CoV infection has not been completely elucidated. However, the SARS model which consists of three phases namely viral replication, immune hyperactivity and pulmonary destruction [23] has been proposed. A little insight appears to clear any doubt with a lung pathology which shows diffuse alveolar damage, epithelial cell proliferation and increased macrophages [24].

The SARS-CoV-2 is predominantly transmitted through contact with respiratory droplets from infected persons. SARS-CoV 2 has a large molecular size, total length of the genome is about 30 Kb, consisting of a 5'-terminal noncoding region, an open reading frame (ORF) 1a/b-coding region, a spike glycoprotein (S protein), envelope protein (E protein), membrane protein (M protein), nucleocapsid protein (N

protein) and a -3'-terminal noncoding region [25]. The interplay between these proteins guides the formation, replication, transcription, and translation of the virus genome [26]. Coronaviridae family can be divided into four genera based on genome structure: α , β , γ , and δ . The coronaviruses of the α and β genera commonly infect mammals and humans, while the coronaviruses of the γ and δ genera mainly infect birds. SARS-CoV-2 is a novel coronavirus of the β genus; it is round or oval, with a diameter of approximately 60–140 nm and could travel up to a length of more than 2 meters in air, hence the need for social distancing [27]. The similarity between the SARS-CoV-2 genome and the bat SARS-like coronavirus (Bat-CoV (RaTG13)) genome is 96% [28]. Coronaviruses are highly sensitive to heat and ultraviolet rays. They can be stored for several years at -80°C and inactivated at 56°C for 30 min (the most commonly used method to inactivate SARS-CoV-2 in the laboratory). In addition, 75% ethanol, peracetic acid, and chlorine containing disinfectants can effectively inactivate SARS-CoV-2. Hence the need for frequent hand washing with soap and water, or application of hand sanitizers containing about 75% alcohol for prevention [26-28].

Viral replication is presumed to start from the epithelium of the upper respiratory tract and as the disease progresses, further multiplication occurs at the lower respiratory tract, and in the gastrointestinal mucosa leading to mild level of viremia. At this point, the common symptoms of infections are fever and cough, though a few persons might be asymptomatic [29].

The virus would eventually attack all organs that express Angiotensin Converting Enzyme 2 (ACE 2) like the lungs, heart, kidneys and gastrointestinal tract [30,31]. ACE 2 has been shown to be a co-receptor for viral entry for SARS-CoV-2 with a developing evidence that it has an extended role in the pathogenesis of COVID-19 [32]. Recently, a study showed that SARS-CoV-2 nucleic acid can be detected in the feces and urine of patients with COVID-19, suggesting that SARS-CoV-2 may also be transmitted from the digestive tract through the fecal–oral route.

The main symptoms of COVID-19 are fever, dry cough, and fatigue. A few patients may have runny nose, sore throat, and diarrhea [33]. In severe cases, they may present with dyspnea which rapidly progresses to acute respiratory

distress syndrome, coagulation dysfunction, and septic shock [33,34].

3. HYPOTHETICAL PATHOGENESIS

On arrival of the virus to the lungs, there appears to be worsening of breathlessness. Increasing breathlessness is associated with a possible release of toxins which in turn could trigger anaphylactic reactions, edema and copious plug formation. The narrowed bronchioles and swollen alveoli and mucous plug lead to severely impaired gas exchange resulting in respiratory distress [35].

Anaphylactic reactions have been reported in some patients. This could possibly lead to impaired functioning of the components involved in the blood coagulation cascade. Multiple organ involvement, possibly multi organ failure, could result from Disseminated Intravascular Coagulopathy (DIC) [35-37]. These are areas to be looked at for further consideration in deepening our knowledge of pathogenicity in order to gain insights to improve interventions. Also, careful post mortem studies could help to lay a strong credence to the hypothesis of DIC.

4. CONCLUSION

A lot is yet to be understood about the pathogenesis of COVID -19. Prompt assessment and treatment, adequate follow up, test and re-test of recovered cases to corroborate immune related processes will go a long way to help elucidate the pathogenesis and guide the treatment as well as improve the prognosis of the disease [1,27].

AVAILABILITY OF DATA

Internet, Electronic and print media, WHO and CDC documentation.

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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The peer review history for this paper can be accessed here:
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