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Dimensions of Pathophysiology of COVID 19 on the Body Systems and Its Implication for Investigations, Treatment and Further Studies

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Authors' contributions

This work was carried out in collaboration among all authors. Author AO designed the study and did the literature review with authors JSA, JOD, ONM and KBS. Authors AKBY and NAO wrote the protocol and the first draft of the manuscript. Authors PT and RSM edited the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: The 2019–20 coronavirus pandemic is a continuing pandemic of coronavirus disease 2019 (COVID-19), result in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). By May 27th, 2020, over 5.61 million people have been infected with COVID 19 across the globe in over 200 countries with more than 350,000 deaths. So far more than 2.3 million people have recovered from the COVID 19 pandemic.
Objective: To review literatures associated with various pathophysiology on the body systems identified and published so as to guide effective management of patient with COVID 19. To highlight some pathological dimensions of the systems significantly affected by COVID 19 to identify gaps for the enhancement of further studies.

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Methodology: The LILACS-BIREME, SCIELO, PUBMED, ACADEMIA, SCIENCE DOMAIN databases and some textbooks were accessed for the study. Scientific papers published in English between January and May, 2020 on the pathophysiology of COVID 19 were reviewed. A total of 89 reports published between 1st January 2020 to 29th May 2020 were identified and reviewed. Sixty-seven publications meeting the inclusion criterion on COVID 19 pathophysiology were selected for this review. Finally, an analysis was conducted and the papers were assessed in agreement with the study objectives.

Results and Discussion: The review has discovered different pathophysiological changes on about seven body systems namely respiratory, cardiovascular, hematological, nervous, urinary, digestive and reproductive systems.

Conclusion: There are a lot of pathophysiological dimensions that have devastating effect on the body systems which may need immediate investigations, treatment and further studies.

Keywords: Dimensions; pathophysiology; COVID 19; body systems and treatment.

1. INTRODUCTION

The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has been found to be the cause of this current pandemic of corona virus infection (COVID 19), (World Health Organization [1]. It is of interest to note that Wuhan, which is located in the Hubei province of China, was the first community within which this outbreak was first identified in December 2019. However, it was not until 30th January, 2020 that the World Health Organization (WHO) declared the outbreak to be a Public Health Emergency of International Concern. Later, on 11th March, 2020, the WHO described COVID 19 as a pandemic condition of international concerned. By May 27th 2020, over 5.61 million have been infected with COVID 19 across the world in over 200 countries, resulting in more than 350,000 deaths. So far more than 2.3 million people have recovered from the COVID 19 pandemic [2].

The time from development of symptoms to death has been between 6 and 41 days, with the most common being 14 days [3]. The 3 main symptoms that are normally exhibited by COVID 19 patients are fever, dry cough, and tiredness. Additional symptoms that are less common and may affect some patients comprise aches and pains, nasal congestion, headache, conjunctivitis, sore throat, diarrhea, loss of taste or smell or a rash on skin or discoloration of fingers or toes. These symptoms are generally mild and begin slowly [4]. Some people become infected but experience mild symptoms. Large number of people (around 80%) improve and recover from the disease without requiring hospital treatment [5]. About 1 out of every 5 patients of COVID-19 becomes seriously ill and progresses to get difficulty breathing. Patients with COVID 19 and having other medical condition such as hypertension, heart and lung diseases, diabetes mellitus and cancer, are more likely to develop serious illness [4]. That notwithstanding, anyone could be infected with COVID-19 and become seriously sick. People of all ages who experience fever and/or cough associated with difficulty breathing/shortness of breath, chest pain/pressure, or loss of speech or movement should seek medical attention immediately. Furthermore development of the COVID 19 could result in complications such as pneumonia, Acute Respiratory Disease Syndrome (ARDS), sepsis, septic shock, and kidney failure [3].

The above clinical features suggest that COVID 19 may have some pathologic and physiologic effect on the body systems. It is therefore important to compile pathophysiological changes on the body systems to serve as a guide for investigations, treatment and further studies for COVID 19 patients.

2. RESPIRATORY SYSTEM CHANGES WITH COVID 19

The respiratory system has been described as the main system with severe devastating effect from COVID 19 as indicated by several reports. The World Health Organization (WHO), described COVID 19 as life threatening condition that cause severe pneumonia with associated symptoms in the lungs [5]. According to the Center for Disease Control and Prevention (CDC), COVID 19 could be described as a respiratory illness. A patient with COVID 19 might exhibit a dry cough, fever, muscle aches, and fatigue. The virus can move through the respiratory tract and into individual's lungs to cause inflammation in the air sacs, or alveoli and can be filled with fluid and pus. This development then restricts a person's ability to take in oxygen. People with severe cases of pneumonia may

have lungs that are so inflamed, they cannot take in enough oxygen or expel enough carbon dioxide. Continuous oxygen deprivation can damage many of the body's organs, causing kidney failure, heart failure, and other life threatening conditions [6]. Another report also suggests that the whole lung tissue displayed diffuse congestive appearance or partly haemorrhagic necrosis on gross examination. The haemorrhagic necrosis was prominently present in the outer edge of the right lobe of the right lung. It continued that the key pathological lung changes presented bronchiolitis and alveolitis with proliferation, atrophy, desquamation and squamous metaplasia of epithelial cells. Great pulmonary interstitial fibrosis, and partly hyaline degeneration, variable degrees of hemorrhagic pulmonary infarction. Small vessels hyperplasia, vessel wall thickening, lumen stenosis, occlusion and microthrombosis formation were also identified. In addition to that, focal monocytes, lymphocytes and plasma cells infiltrating into pulmonary interstitium were also seen. Furthermore, exhibition of atrophy, vacuolar degeneration, proliferation, desquamation and squamous metaplasia in alveolar epithelial cells were also discovered. Alveolar cavity congestion was noticeable, and contained mucus, edema fluid, desquamated epithelial cells, and inflammatory cells. The report further identified several multinucleate giant cells and intracytoplasmic viral inclusion bodies. It finally revealed massive pulmonary interstitial fibrosis as evidence by Masson staining investigations [7]. In another study concerning the effect of COVID 19 on the respiratory system, some clinicians suspected that, the driving force in many seriously ill patients' declining course, is a disastrous overreaction of the immune system known as a "cytokine storm," which similar viral infections are famous to activate. Cytokines are chemical signaling molecules that guide a healthy immune response; but in a cytokine storm, levels of certain cytokines increase far above what's needed, and immune cells start to attack healthy tissues. Blood vessels leak, blood pressure drops, clots form, and catastrophic organ failure can ensue [8].

3. CARDIOVASCULAR SYSTEM CHANGES WITH COVID 19

There have been some reports of several effects of COVID 19 on the cardiovascular system as some medical scientists have revealed. COVID 19 may result in some complications of the cardiovascular system. Nevertheless, there are no conclusive studies to clearly indicate the effects of COVID 19 on the cardiovascular system except for circumstantial reports that showed the risk of myocardial infarction or heart attacks and acute coronary syndrome [8]. In one study of 75 patients with COVID 19, out of the 5 cases of deaths, two were as a result of heart attacks. Thromboembolism and subendocardial infarction have also been reported in patients with COVID 19 [9]. In one study among 45 patients and reported by Maria Cohut and Rita Ponce, the investigators identified an association between COVID 19 and myocardial injury, heart attacks, acute heart failure, abnormal heartbeats, and venous thromboembolism or blood clotting. Another report from the initial days of the epidemic pronounced the extent of cardiac injury among 41 patients hospitalized with COVID 19 in China: Five or 12%, had signs of cardiovascular damage which was associated with elevated levels of cardiac troponin (a protein released in the blood by the injured heart muscle) and abnormalities on electrocardiograms and heart ultrasounds [10]. Subsequently, other reports have admitted that cardiac injury could be part of COVID 19 - induced harm. Besides that, certain reports point to certain clinical situations in which patients' initial symptoms were primarily cardiovascular rather than respiratory in nature. According to Ridker and Libby, the cardiac association in COVID-19 is additional example of the general effects of inflammation on multiple organs systems. They further indicated that Inflammation is a serious defense reaction during infection, but it has a side effect. They then concluded that Infections could set off a cascade of immune reactions that affect various organs [11]. There has been documented reports that suggest Cardiac injury due to viral infections, but COVID 19 appears to be particularly harmful, according to several studies [12]. Further findings revealed patients with known underlying heart conditions to be at the highest risk for cardiovascular and respiratory-related COVID 19 complications, followed by those with formerly undiagnosed conditions that are unmasked by the virus. Some patients with asymptomatic fatty plaques inside the heart vessels may find those plaques destabilized by fever and inflammation [13].

4. HEMATOLOGICAL CHANGES WITH COVID 19

The hematological changes normally affect complete blood count, biochemistry and

hemostasis as several studies have shown some changes in these parameters.

4.1 Biochemistry of Blood and Complete Blood Count

There is a rush in the clinical manifestations of the disease with a pronounced systemic increase of inflammatory mediators and cytokines, which may even be characterized as a "cytokine storm" nearly 7 to 14 days from the start of the early symptoms [14]. At this point, significant lymphopenia becomes evident. Even though further thorough study on the causal etiology is necessary, several factors may contribute to COVID 19 related lymphopenia. It has been shown that lymphocytes express the ACE2 receptor on their surface [15]; thus COVID 19 may directly infect those cells and ultimately lead to their lysis. Furthermore, the cytokine storm is characterized by evidently increased levels of interleukins (mostly IL-6, IL-2, IL-7, granulocyte colony stimulating factor, interferon-γ inducible protein 10, MCP-1, MIP1-a) and tumor necrosis factor (TNF)-alpha, which may stimulate lymphocyte apoptosis [16]. Significant cytokine activation may be also related with atrophy of lymphoid organs like the spleen, and further impairs lymphocyte production [17]. A study by Guan et al during the first two months of the epidemic in China provided data on the clinical characteristics of 1,099 COVID 19 cases with laboratory confirmation [18], the vast majority of patients presented with lymphocytopenia (83.2%), whereas 36.2% had thrombocytopenia, and 33.7% revealed leukopenia. These hematological anomalies were more conspicuous among severe as opposed to non-severe cases representing 96.1% against 80.4% for lymphocytopenia, 57.7% as opposed to 31.6% for thrombocytopenia and 61.1% against 28.1% for leukopenia [19]. These results were consistent in four other descriptive studies that were carried out during the same period in China and included 41, 99, 138 and 201 confirmed cases with COVID 19, respectively [20]. Huang et al and Wang et al stressed a relationship between lymphopenia and the need for ICU care for COVID 19 patients [21]; whereas Wu et al showed an association between lymphopenia and ARDS development. Precisely, Wu et al in their retrospective study, analysed probable risk factors for developing ARDS and death among 201 patients with COVID 19 pneumonia in Wuhan, China [22]. Increased risk of ARDS during the disease course was significantly associated with increased neutrophils, decreased lymphocytes in a bivariate Cox regression analysis. Increased neutrophils were associated with increased risk of death [20]. Furthermore, lymphopenia was also documented in approximately 40% of the first 18 hospitalized patients with COVID-19 in Singapore [21]. A more current study on 69 patients proved that 80% of the study population had lymphocytopenia, whereas 20% had mild thrombocytopenia [22]. Interestingly, 69% of patients with a low lymphocyte count showed a reactive lymphocyte population including a lymphoplasmacytoid [23] subset, which was not common in the peripheral blood of patients with SARS infection in 2003 [24]. Flow cytometry did not reveal any inversion in the CD4+/CD8+ lymphocyte ratio. However, functional studies have suggested that SARS-CoV-2 may impair the function of CD4+ helper and regulatory T-cells [25] and promote the initial hyperactivation which is followed by rapid exhaustion of cytotoxic CD8+ T-cells [26]. In Singapore, Fan et al also found that patients requiring ICU support had significantly lower lymphocyte levels at baseline [27]. Lymphopenia was also prominent among critically ill patients with COVID 19 in Washington USA [28]. In another retrospective study including 52 critically ill patients from Wuhan, China, lymphopenia was reported in 85% of patients [29]. During hospitalization, non-survivors demonstrated a more significant deterioration in lymphopenia compared with those who survived. It has also been reported that patients with severe disease and fatal outcomes present with a decreased lymphocyte/white blood cell ratio both in admission and during hospitalization compared with those who survived [30]. Recent studies have shown that myocardial injury among inpatients with COVID 19 is associated with increased mortality [31]. In a prospective study in China among 416 consecutive patients, 82 (19.7%) had documented myocardial injury. Compared with the others, these patients with myocardial injury had higher leukocyte, lower lymphocyte and lower platelet counts [32]. A retrospective study including 187 patients with COVID 19 from another hospital in Wuhan showed that patients with high troponin-T levels had leukocytosis, increased neutrophils and decreased lymphocytes. A meta-analysis of nine studies has suggested that thrombocytopenia is significantly associated with the severity of COVID 19 disease, with a very high heterogeneity between studies though; a more sizeable drop in platelet counts was noted especially in no survivors [33].

4.2 Changes in Hemostasis (Coagulation) in COVID 19

Hemostasis and Coagulation conditions are somewhat frequently encountered among COVID 19 patients, especially among those with severe disease as indicated in some studies [32]. In a multicenter retrospective study, during the first two months of the epidemic in China, 260 out of 560 patients (46.4%) with laboratory confirmed COVID 19 infection had elevated D-dimer, whereas the elevation was more pronounced among severe cases (59.6% versus 43.2% for non-severe ones). D-dimer (or D dimer) on the other hand, is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two D fragments of the fibrin protein joined by a cross-link. D-dimer dynamics can reflect the severity of a disease condition and their increased levels are associated with adverse outcomes among patients with community-acquired pneumonia [34]. Accordingly, elevated D-dimer was detected in 36% of patients in a descriptive study of 99 COVID 19 cases in Wuhan, China. Another retrospective study in China including 41 patients showed that D-dimer and prothrombin time (PT) levels were higher on admission among patients requiring intensive care unit (ICU) support. In the study by Wang et al, which was previously described, patients requiring ICU treatment had significantly higher D-dimers compared with less severe cases [35]. Patients presenting with cardiac injury in the context of COVID 19 infection are more prone to coagulation disorders compared with those without cardiac involvement [36]. Patients with high troponin-T levels may present more frequently with elevated PT, activated partial thromboplastin time (APTT), and D-dimer [37]. Among 201 COVID 19 patients with pneumonia, increased PT was associated with increased risk of ARDS, whereas increased levels of D-dimer were significantly associated with increased risk of ARDS and death [38]. The difference in median levels of D-dimer between survivors and non-survivors was larger than that between the ARDS and non-ARDS groups, which might also suggest a disseminated intravascular coagulation (DIC) related complication to be a probable factor to have led a subset of patients to death independently of ARDS. In a multicenter retrospective cohort study from China, increased D-dimer levels were significantly associated with in-hospital death in the multivariable analysis [39]. Interestingly, D-dimer levels showed a sequential increase in time among non-survivors compared with those who survived. In another retrospective study by Tang et al. encompassing data from 183 consecutive patients with COVID 19, non-survivors had significantly higher D-dimer and fibrin degradation products (FDP) levels compared with survivors at the initial evaluation. By the late hospitalization, the fibrinogen and AT levels were also significantly lower in non-survivors. Interestingly, 71.4% of non-survivors versus 0.6% of survivors fulfilled the clinical criteria for DIC during the disease course. The median time from admission to DIC manifestation was 4 days (range: 1-12 days) [40]. In a prospective study evaluating the coagulation profile of patients with COVID 19, D-dimer, FDP, and fibrinogen levels were markedly higher among patients compared with healthy clients used as controls. Patients with severe disease showed higher values of D-dimer and FDP than those with milder manifestation [41]. All the above indicated that D-dimer elevation and DIC may be common in patients with severe form of COVID 19 infection, a fact despite methodological limitations, became evident in a meta-analysis of four published studies. Immune deregulation and endothelial dysfunction may be actively implicated in the underlying pathophysiology [42], which remains to be elucidated in future studies. The scoring system for compensated and overt DIC endorsed by the International Society on Thrombosis and Hemostasis [43] should be followed for early DIC identification [44].

5. NERVOUS SYSTEM CHANGES WITH COVID 19

The effect of the COVID 19 has been identified by several studies as there has been significant set of symptoms in COVID 19 patients on the nervous system. Frontera, a neurologists after assessing 5% to 10% of coronavirus patients at her hospital, identified brain inflammation (encephalitis), seizures, and with a “sympathetic storm,” a hyperreaction of the sympathetic nervous system that causes seizure like symptoms and is most common after a traumatic brain injury among patients with COVID 19. She further mentioned brief loss of consciousness stroke and loss of sense of smell among COVID 19 patients. Wadman et al in their work which made reference to Frontera and her friend’s research article, indicated that Frontera and her friends were surprised whether in

some cases, COVID 19 infection depresses the brain stem reflex that senses oxygen starvation. This could be another explanation for anecdotal reasons that some patients may not be gasping for air, regardless of dangerously decrease blood oxygen levels. According to Robert Stevens, an intensive care physician at Johns Hopkins Medicine, ACE2 receptors are present in the neural cortex and brain stem, not known under what conditions the virus penetrates the brain and interacts with these receptors. He continued, the coronavirus, the 2003 severe acute respiratory syndrome (SARS) epidemic, which is similar to COVID 19 could also infiltrate neurons and sometimes caused encephalitis [45]. A Case Study on 3rd April in the International Journal of Infectious Diseases, from a team of medical scientist in Japan, reported some traces of new COVID 19 in the cerebrospinal fluid of a COVID 19 patients who developed meningitis and encephalitis, suggesting that COVID 19 could penetrate the central nervous system. They however suggested that other factors like cytokine storm could cause brain swelling and the blood's blown up tendency to clot and strokes. Sherry Chou, a neurologist at the University of Pittsburgh Medical Center, organized neurological data from different cares patients received and mentioned that, the possible invasion route of COVID 19 is: through the nose, then upward and through the olfactory bulb, explaining reports of a loss of smell, which then connects to the brain [8]. Ling Mao et al, mentioned in their study that COVID 19 may infect nervous system and skeletal muscle as well as the respiratory tract. Their study further revealed that those with severe infection of COVID 19 have greater neurologic involvement which includes acute cerebrovascular diseases, impaired consciousness, and skeletal muscle injury. Their study offers important new clinical information on COVID 19 that would help clinicians raise awareness of its involvement of neurologic manifestations. It is especially meaningful to learn that for those with severe COVID 19, rapid clinical deterioration or worsening could be associated with a neurologic event such as stroke, which would contribute to its high mortality rate. Ling Mao et al. then concluded that during the epidemic period of COVID 19, when seeing patients with these neurologic manifestations, clinicians should consider COVID 19 infection as a differential diagnosis to avoid delayed diagnosis or misdiagnosis and prevention of transmission [9].

6. RENAL SYSTEM CHANGES WITH COVID 19

The COVID 19 infection in the body has also been found to be having pathophysiological effect on the renal system as indicated by some reports across the world. In one such report by Jennifer Frontera of New York University's Langone Medical Center, she said that "The worldwide fears of ventilator shortages for failing lungs have received plenty of attention. Not so a scramble for another type of equipment: dialysis machines "If these folks are not dying of lung failure, they're dying of renal failure," In her view, she anticipated that COVID 19 could have devastating effect on the renal system of COVID 19 patients. This according to her might lead to kidney damage and the need for dialysis, which might be because the kidneys that are abundantly endowed with ACE2 receptors could be the target of other viruses. According to one report, 27% of 85 hospitalized patients in Wuhan, China exhibited kidney failure as a result of COVID 19 infection. Another study reported that 59% of nearly 200 hospitalized COVID 19 patients in Hubei and Sichuan Provinces of China had proteinuria, and 44% had hematuria of which both suggest kidney impairment. Those with acute kidney injury (AKI), were more than five times as likely to die as COVID 19 patients than those without it. In addition to liver injuries, some articles have also reported an increased incidence of acute renal injury following COVID 19 infection cause by inflammation induced by the disease, or a synergistic effect of both on kidneys. Furthermore, they reported that patients with acute renal injury have a higher mortality rate compared to other patients [46]. Hongbo Jia, a neuroscientist at the Chinese Academy of Sciences, Suzhou Institute of Biomedical Engineering and Technology; and a colleague author of a study quoted as saying: - "The lung is the primary battle zone but a fraction of the virus possibly attacks the kidney [47]. And as on the real battlefield, if two places are being attacked at the same time, each place gets worse," [8].

7. DIGESTIVE SYSTEM CHANGES WITH COVID 19

The digestive system is also not spared with the onslaught of COVID 19 effect as reported by many studies. In one of such reports by Carvalho et al. a 71-year-old Michigan woman who returned from a Nile River cruise with bloody diarrhea, vomiting, and abdominal pain of which doctors suspected she initially had a common

stomach infection, such as Salmonella. Nevertheless, she started coughing later and the doctors took a nasal swab for investigations and she tested positive for the novel COVID 19 [48]. Her stool sample tested positive for viral RNA, as well as signs of colon injury seen in an endoscopy report, an indication for a gastrointestinal (GI) infection with COVID 19. Her condition had therefore added up to the evidence suggesting that the novel COVID 19, like other similar viruses such as SARS, could infect the lining of the lower digestive tract, where the crucial ACE2 receptors are profuse. Viral RNA has been found in as many as 53% of patients' stool samples. A press statement by Chinese Gastroenterology team reported biopsies result from a COVID 19 patient and discovered protein shell in cells of stomach duodenum and rectum of the GIT. Mary Estes, a virologist then suggested, probably the virus could replicate in the GIT [49].

Another report suggests up to half of patients, close to about 20% across studies, experience diarrhea, as put forward by Brennan Spiegel of Cedars-Sinai Medical Center in Los Angeles, co–editor-in-chief of American Journal of Gastroenterology (AJG) [50]. The presence of virus in the GI tract raises the unsettling possibility that it could be passed on through feces. Nevertheless, it's not yet clear whether stool contains intact, infectious virus, or only RNA and proteins. There is therefore no evidence that COVID 19 could be transmitted through feces, says coronavirus expert, Stanley Perlman of the University of Iowa [51]. According to CDC, based on experiences with SARS and with the virus that causes Middle East respiratory syndrome, another dangerous counterpart of the new coronavirus in relation to the risk from fecal transmission is possibly low [8].

According to Zhang et al, the incidence of hepatic abnormalities significantly increased after infection with COVID 19 and during the course of the disease, which may indicate the effect of COVID 19 infection on the liver or side effects of the medications used by patients [52]. Additionally, Xu et al reported steatosis and liver injury in the liver biopsy of a patient with COVID 19 [53]. COVID 19 is allegedly causing diarrhea, vomiting, and other GIT clinical features in about half of all patients. Patients with GI symptoms may also develop a cough and vice-versa, but one symptom typically appears days before the other. Acute viral hepatitis has also been found in some patients battling COVID 19. A team of researchers documented the case of one 59-year-old woman in Long Island, NY, who presented with dark urine that was later diagnosed as acute viral hepatitis. After developing a cough, physicians connected it with COVID 19.

8. REPRODUCTIVE SYSTEM CHANGES WITH COVID 19

The reproductive system has also been implicated with the effect of COVID 19 as indicated by some study reports. In Wuhan, China a team of medical experts embark on a long-term study of the effects of the COVID 19 on the male reproductive system and reported that the pathogen could affect sex hormone levels in men [54]. Even though preliminary and not peer reviewed, the study is the first clinical observation on the male reproductive system especially among the younger group in relation to the potential impact of COVID 19. In another study conducted at Zhongnan Hospital of Wuhan University and the Hubei Clinical Research Centre for Prenatal Diagnosis and Birth Health, also revealed that analyses of blood samples from 81 men aged 20 to 54 who tested positive for the coronavirus and with the median age of 38, approximately 90 per cent of them had only mild symptoms. The team looked at the ratio of testosterone to luteinising hormone (T/LH). A low T/LH ratio can be a sign of hypogonadism, which in men is a malfunction of the testicles that could lead to lower sex hormone production. The average ratio for the COVID 19 patients was 0.74, about half of the normal level [55]. Testosterone is the main male sex hormone critical for the development of primary and secondary sexual characteristics including testes, muscle, bone mass and body hair. Luteinising hormone is found in both men and women, and best known for its ability to trigger ovulation. Since more than half of the people with COVID 19 were reproductive-aged, more attention should be paid to the effect of COVID 19 on the reproductive system. The study thus concluded that there was the need for more research in the area of COVID 19 and reproductive system.

Earlier studies have indicated that the new COVID 19 could bind with ACE2, a receptor protein cell, a large number of which are concentrated in the testicles. Li Yufeng, a professor of reproductive medicine at Tongji Hospital in Wuhan, had predicted in a study that the testicles could become a major target of the

coronavirus attack and need further studies [56].

A cohort study by other researchers, found that COVID 19 could be present in the semen of patients with COVID 19, and may still be detected in the semen of recovering patients. It further explained that, because of ineffective blood and the testes vas deferens/epididymis barriers, the virus may cross from the blood to the male reproductive tract, especially in the presence of systemic local inflammation [57].

9. CONCLUSION

From the above literature review, it has been established that COVID 19 has different systemic dimensions of pathophysiological effects on the general body. People of all ages who experience signs and symptoms of COVID 19 should seek medical attention immediately and conduct various investigations possibly within all the systems of the body. This is because COVID 19 infection could cause severe complications on all the body systems as it has been revealed in this study. The study has further revealed that there are not much research studies on the COVID 19 pathophysiology especially in Sub-Saharan African and for that matter Ghana. Hence, most of the non-documented reports on COVID 19 clinical manifestations and/or presentations and their claims of treatment should be critically studied to improve the scientific way of treating people who contract this deadly COVID 19. Lastly, we conclude that it will be appropriate for some further works to be done that will help in identifying the gabs in managing COVID 19 especially in our setting as Africans.

10. RECOMMENDATIONS

1. There is the need for health care professionals to conduct thorough investigations to improve our understanding on the pathophysiology of COVID 19 on all the body systems to ensure effective management.
2. We also recommend that, the various clinical treatment as well as management among COVID 19 patients should be broad-based to cover all body systems instead of directing treatment only on COVID 19 infection.
3. Lastly, there is also the need for further studies to improve the knowledge on the pathophysiological changes of all the body systems in relation to COVID 19.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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