



# **Biological and Comorbidity as Risk Factors for COVID 19 High Morbidity and Mortality among the Aged Population and Its Implications for Public Health Education and Research in Ghana**

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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 searches. Authors JSA and AKBY wrote the protocol and the first draft of the Manuscript. Authors JOD and PT edited the Manuscript. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**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 (WHO) 2020). 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. There is high morbidity and mortality among the elderly patients with COVID-19 than the young and middle-aged patients. Again, most of the morbidity and mortality have comorbid conditions (presence of more than one disease in one person) from 1 to 3 in addition to COVID 19 and most of these conditions are age related.

**Objective:** The aim of this work is to describe changes in biological processes in aged population in relation to the presence of a possible comorbidity vis-à-vis COVID 19. To review publications

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and other studies associated with biological changes in the ageing process as well as identifying some specific comorbidity among the aged. To develop an appropriate health educational programs to protect the aged population on COVID 19. To develop an educational strategy on COVID 19 for the aged and the general public.

**Methodology:** The LILACS-BIREME, SCIELO, PUBMED, ACADEMIA, SCIENCE DOMAIN databases and some textbooks were consulted for the study. Scientific papers published English between January and March, 2020 on the subject of COVID 19 among the aged were selected for inclusion. A total 65 of studies published between January 1st, 2020 to March 30th, 2020 and some textbooks on Anatomy and Physiology were identified and evaluated. Twenty-seven (27) articles meeting the inclusion criterion (COVID 19 among the aged) 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 studies reviewed discovered a high prevalence and mortality of COVID 19 among the aged with comorbidity due to deterioration in ageing process in Respiratory and the Immune systems.

**Conclusion:** It is recommended that some further research be done locally on COVID 19 to increase the knowledge on this subject in Ghana. It is also recommended that an appropriate health educational strategy be developed to create awareness among the aged.

*Keywords: Biological; comorbidity; COVID 19; aged; morbidity.*

## 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. Wuhan, Hubei province of China, in December 2019. However, it was not until 30<sup>th</sup> January, 2020 that the World Health Organization (WHO) declared the outbreak to be a Public Health Emergency of International Concern. Later on, in 11<sup>th</sup> March, 2020, the WHO described COVID 19 as a pandemic condition of international concerned. More than 803,000 cases of COVID 19 have been reported in 200 countries and territories, resulting in approximately 39,000 deaths. More than 172,500 people have since recovered [2].

The time from development of symptoms to death has been between 6 and 41 days, with the most common being 14 days [3]. As of 31st March, 2020, approximately 39,000 deaths had been attributed to COVID-19 [3]. In China, as of 5th February about 80% of deaths were in those over 60 years, and 75% had pre-existing health conditions including cardiovascular diseases and diabetes [4]. Liu and his colleagues in their study concluded that, the mortality of elderly patients with COVID-19 is higher than that of young and middle-aged patients, and the proportion of patients with Patient Safety

Indicators (PSIs) PSI grade IV and V is significantly higher than that of young and middle-aged patients [5]. Elderly patients with COVID-19 are more likely to progress to severe disease. In one study "Italy has an older population than China but only has 60 million people while China has 1.4 billion people [6].

Medical experts say the new virus is killing people over 65years at a much higher rate than younger age groups. The mortality rate in Italy has been reported to be far higher due to her peculiar demographics as having the second oldest population globally, according to Prof. Walter Ricciardi, who is a scientific adviser to the Minister of Health in Italy [7]. Additionally, it has been established that the mortality rate of COVID 19 in Italy can be associated with comorbidity of 1 to 3 disease conditions as well as age related. These conditions were said to range from cardiovascular, diabetes, respiratory disorders and cancers. All these conditions were identified in some studies in Italy and China. In Italy for example 48.5% had 3 conditions in addition to Covid 19, 25.6% had 2 conditions, and 25.1% had 1 condition and 0.8% died from only Covid 19. In another study conducted by the CDC, the first 4,200 cases of COVID 19 patients examined in the US, it was found out that 508 representing 12% were admitted to the various hospitals; and 121 out of the total had to be put in the intensive care unit with 44 deaths [7]. Relating the US to China, increasing age was seen to be having a direct association with hospitalization and mortality rates, although this data showed that

about 20% of hospitalized patients and 12% of patients admitted to an ICU had their ages between 20-44. The number of patients that died of the ages 20-44 were nine (9) whilst most of the deaths were among the adults with age 65 and above in the entire group. It is clear from the above that COVID 19 has devastating effect on the aged and patients with comorbidity [7].

## 2. BIOLOGICAL FACTORS

The biological factors describe structural and functional changes in both the respiratory and the immune systems as they occur in the ageing process.

### 2.1 Structure and Functions of the Respiratory System

The carrying in of oxygen and carrying out of carbon dioxide in the human body is the responsibility of organs of the respiratory system. These organs from outward to within include: nose, pharynx, larynx, trachea, bronchi (primary, secondary, and tertiary), bronchioles, (terminal and respiratory), alveolar ducts, alveolus, and respiratory muscles such as the diaphragm and inter costal muscles. The lungs however are the primary organs of the respiratory system which perform the exchange of gases during breathing. The respiratory system together with the circulatory system work to send blood that is rich with oxygen to the general cells of the body. This oxygen-rich blood after circulating to the cells of the body for the various cellular metabolic activities then returns to the lungs with more carbon dioxide and other waste products, where they are carried out of the body during exhalation [8].

The five primary functions of the respiratory system, in order of significance as mentioned by are: [9].

1. **Breathing:** Taking in oxygen (inhalation) and bringing out carbon dioxide (exhalation). The organs needed for breathing include the cavities of the nose and mouth, the pharynx, the larynx, the trachea and the lungs. Other important organs that perform breathing mechanism in addition to those listed above include the muscles of respiration (diaphragm, intercostal muscles), and the entire rib cage to draw in air for inhalation and send air out for exhalation.

2. **External Respiration:** Exchange of gases that go on between the two lungs and the bloodstream. This is the movement of oxygen from the air in the alveoli (tiny sacs at the end of the bronchioles in the lungs) through the alveolar and capillary walls to the blood in the capillaries, as well as the movement of carbon dioxide from the bloodstream to the alveoli.
3. **Internal Respiration:** The exchange of gas between the blood and the tissues of body. This involves the transport of oxygenated blood from the heart to all parts of the body, where the oxygen is delivered to tissues and cells for energy and metabolism, while carbon dioxide, as a waste product, is absorbed by the blood.
4. **Sound Production:** Vibration of the vocal cords in the larynx to produce sound. This is a more specialised function in which air passing over the vocal cords is modulated by laryngeal muscles pushing the vocal cords together so that they vibrate when air passes over them, creating sound.
5. **Olfaction:** The sense of Smell. Olfaction, or the sense of smell, occurs when air passes over olfactory fibres in the nasal cavities that sense certain chemicals in the inhaled air that bind to them and transmit a signal to the brain which is then identified.

### 2.1 Defense Mechanisms of the Respiratory System

Dezube in his work described the respiratory defense mechanism as follows; It is said that a person in his/her active period would moderately breathe 20,000 liters (5,000 gallons or more) of air within the 24-hour period. The totality of this air that is breathed in is believed to harbour possible elements and gases which are considered very harmful. The weight of this amount of air can be estimated as 20 kilograms or 44 pounds. Non-living harmful particles, like soot and dust; as well as other harmful pathogens such as mold, fungi, bacteria, and viruses deposit on airway and alveolar surfaces. Importantly, there is a defense mechanism that serve to clean and protect the respiratory system [10]. This is because only particles with extremely smaller sizes especially those less than 3 to 5 microns (0.000118 to 0.000196 inches) in diameter, will infiltrate to the deep parts of the lung tissue. One of the defense mechanisms for the respiratory system is the tiny muscular, hair-like projections on the cell surfaces that line the airway called the cilia. The

mucus layer that protects the airways is made of cilia which function to move in one direction the liquid mucus. This mucus layer, which serve as a trap to these potentially infectious microorganisms as well as other particles, prevent these pathogens from reaching the lungs. Within 24 hours, it is believed that the cilia can about 1,000 times or more to move the mucus that lines the wind-pipe (trachea) upwards about 0.5 to 1 centimeter per minute (0.197 to 0.4 inch per minute) [10]. These entrapped pathogens and other particles within the airway tube are then brought out through coughing and sneezing or moved to the mouth and swallowed [10].

Another defense mechanism for the lungs are the aveolar macrophages, which are a type of white blood cells on the surface of the aveoli. Due to the demands of the body in exchanging gases at the aveolar end of the respiratory system, which is also not protected by mucus and cilia, it makes the mucus at this end very thick and therefore slow movement of oxygen and carbon dioxide. As a result of this, the alveolar macrophages almost always search for the entrapped microorganisms and other particles, bind to them, engulfed them, kill any that are living, and digest them. In the event that the lungs become exposed to hazardous particles, additional leukocytes like the neutrophils which are in circulation, can be sent to the appropriate site to help fight the said pathogens. For instance, when an individual inhale dust potentially dangerous to his/her health or is battling with a respiratory infection,

then more macrophages are produced and neutrophils are recruited to defend the body from the effects of these harmful agents [10].

### 2.3 Respiratory System Changes with Ageing

On the changes in the respiratory system, the respiratory muscles, like all skeletal muscles, weaken with age. Lung tissue loses its elasticity and alveoli are lost as their walls deteriorate. All of this results in decreased ventilation and lung capacity, but the remaining capacity is usually sufficient for ordinary activities [11]. The cilia of the respiratory mucosa deteriorate with age, and the alveolar macrophages are not as efficient, which make elderly people more prone to pneumonia, a serious pulmonary infection [12]. Chronic alveolar hypoxia from diseases such as emphysema or chronic bronchitis may lead to pulmonary hypertension, which in turn overworks the right ventricle of the heart. Congestive heart failure and pulmonary edema is said to be associated with systemic hypertension which often leads to the weakening of the left ventricle of the heart. This also creates an accumulation of excess tissue fluid which collects in the alveoli and decreases gas exchange. Though true at any age, the interdependence of the respiratory and circulatory systems is particularly apparent in elderly people. Scanlon and Sanders then suggested that the most important way to help your respiratory system age gracefully is not to smoke [11]. In the absence of chemical assault, respiratory function does diminish but

## Respiratory System

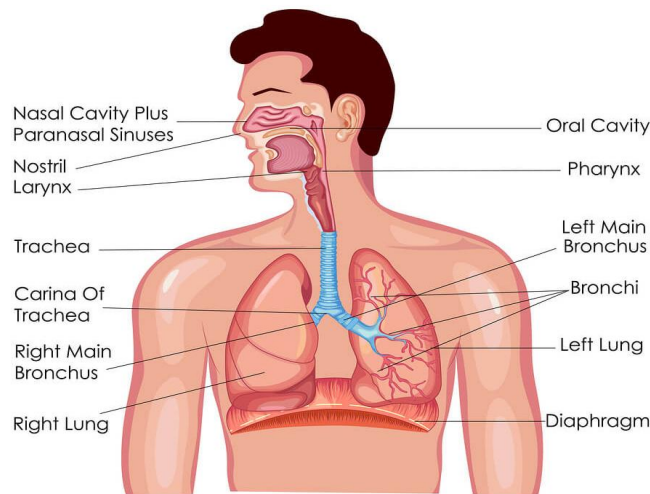


Fig. 1. Anatomical view of human respiratory system

usually remains adequate. With these structural and functional changes in the respiratory system of the aged, it is evidence that, the gradual deterioration could be aggravated by COVID 19 which also has devastating effect on the respiration system as it could cause severe pneumonia with associated complication and death among the aged.

## **2.4 Structure and Functions of Immune System**

Our existence as humans depends on efficient immune system. The human body would be exposed to microorganisms such as bacteria, viruses, parasites, and others without robust immune system. The immune system of our body keeps us very healthy as we swim through large range of pathogens. The extensive network of cells and tissues are always on surveillance for attackers of body tissues to destroy them. The immune system is made of cells, tissues, organs and proteins that are spread all over the body. Critically, it can differentiate the body tissues from foreign tissues and self from non- self. Our immune system can identify dead and damaged cells so that it could clear them from the body [13]. The immune system consists of white blood cells, antibodies, complement system, lymphatic system, spleen, bone marrow and thymus gland.

### **2.4.1 White blood cells**

The White blood cells, also known as leukocytes are very important components in the human immune system. White blood cells circulate through blood stream and tissue all over the human body, looking for foreign attackers (microbes) such as bacteria, viruses, parasites and fungi. When they find them, they launch an immune attack to destroy them. White blood cells (WBC) or leukocytes are larger than red blood cells (RBCs). They have nuclei when mature and produced in the red bone marrow, except some lymphocytes which produced in the thymus. Granular WBCs are the neutrophils, eosinophils, and basophils. Agranular WBCs are the lymphocytes and monocytes. Neutrophils and monocytes phagocytize pathogens; monocytes become macrophages, which also phagocytize dead tissue. Eosinophils detoxify foreign proteins during allergic reactions and parasitic infections, they phagocytize anything labeled with antibodies. Basophils contain the anticoagulant heparin and histamine, which contributes to inflammation. Lymphocytes consist of T cells, B cells, and natural killer cells. T cells recognize

foreign antigens and destroy them. B cells become plasma cells, which produce antibodies to foreign antigens. NK cells destroy foreign cell membranes. WBCs carry out their functions in tissue fluid and lymphatic tissue, as well as in the blood.

### **2.4.2 Antibodies**

Antibodies help the body to fight microbes or the toxins (poisons) they produce. They do this by recognising substances called antigens on the surface of the microbe, or in the chemicals they produce, which mark the microbe or toxin as being foreign. The antibodies then mark these antigens for destruction. There are many cells, proteins and chemicals involved in this attack.

### **2.4.3 Complement system**

The complement system is made up of proteins whose actions enhance the work done by antibodies. Complement is a group of more than 20 plasma proteins that circulate in the blood until activated. They are involved in the lysis of cellular antigens and the labeling of non-cellular antigens. Some stimulate the release of histamine in inflammation; others attract WBCs to the site.

### **2.4.4 Immune system changes with ageing**

The immune system protects the body against the invasion of hazardous foreign pathogens such as bacteria, viruses, and fungi, parasites (like worms) and cancer cells and a transplanted organs and tissues [13].

The immune system goes through a series of changes throughout life from childhood to old age like the all the body systems. It becomes less effective as one is ageing in different ways. The aging of the immune system is apparent in the decreased efficiency of immune responses. The T - Cells which active immune response become less active to antigens such as virus. There is reduction in number of white blood cells that are able to response to new antigens. As a result, the aged body cannot remember and defend the body when it encounters new antigen like virus. The Elderly people therefore are more likely than younger ones to develop viral infections like shingles. They are also more susceptible to infections such as influenza and to what are called secondary infections, such as pneumonia following a case of the flu. Delves explained that the elderly people have few numbers of complement proteins and cannot

produce enough of these proteins like the younger once do in reaction to bacterial infection. Generally, the antibodies become less able to attach to the antigen, although the amount of antibody produced in response to an antigen remains almost the same [13]. This variation may somewhat explain why tetanus are more common among older people and result in death more often. These changes may also partially explain why vaccines are less efficacious in older people and therefore it is important for older people to get additional dose of some vaccines. Autoimmune disorders are also more common among older people; the immune system mistakenly perceives a body tissue as foreign and initiates its destruction. Rheumatoid arthritis and myasthenia gravis are examples of autoimmune diseases. Macrophages (which ingest bacteria and other foreign cells) destroy bacteria, cancer cells, and other antigens more slowly. This slowdown may be one reason that cancer is more common among older people. The incidence of cancer is also higher. Malignant cells that once might have been quickly destroyed remain alive and proliferate [13].

The vulnerability among the aged to some infectious agents, cancers and probably the increased mortality as well as COVID 19 mortality rate which seem to be very high among the older population is also believed to be related to the changes in their immune function. A report by Gudrun Heise in 2020, indicated that the average age of a population is a major contributing factor in the death rates of people suffering from COVID 19 in different nations of the affected parts of the world. He further asserted that because the old people usually have pre-existing medical condition, they are usually at a high risk of acquiring corona virus disease after an exposure to this virus. That can make it easier for a virus to overcome a person's immune system - certainly easier than is with otherwise healthy people, who are often also young. He concluded that, our immune defenses weaken as we get older, our immune systems become less effective, and that puts us at risk [14].

### **3. COMORBIDITY**

One important factor that could also increase the morbidity and mortality of the aged to COVID 19 is the issue of comorbidity as confirmed by several studies. In medical practice, comorbidity is the existence of other conditions, either one or more occurring with (concomitant or co-existing

with) the primary disease; in the other sense of the term, a comorbidity is each extra condition. The additional condition may also be an infectious disease like COVID 19.

#### **3.1 Comorbidity in Ageing**

Comorbidity" and "multimorbidity" are terms usually used interchangeably. However, in recent years, comorbidity more often describes the combined effects of additional diseases in reference to an index disease (eg, comorbidity in cancer). Meanwhile, multimorbidity is more often meant to describe simultaneous occurrence of 2 or more diseases that may or may not share a causal link in an individual patient [15]. Elisa Fabbri also explained that aging is associated with increasing predisposition to multiple chronic diseases development and, therefore, contributes to a major risk factor for multimorbidity [16].

Elisa Fabbri's findings continued from the point of gerontology, the increasing buildup of several diseases, which considerably increases at older ages, is a leverage for continuous loss of strength in fighting diseases and age-related multisystem homeostatic dysregulation [16]. It is therefore anticipated that addressing the mechanism which drive ageing may also determine several chronic diseases related to age, hence, managing these mechanisms is also believed to reduce the development of multimorbidity. According to Elisa [16] studying underpinning burden may stimulate innovative connections and dialogues experience, which enhances research into multimorbidity. This may help in understanding the science of aging and at the same time help us to appreciate the underlying processes of aging so as to strategize in preventing or delaying the problem of multimorbidity. In this regards, it is believe that, the time to build networks and try to exchange ideas among the clinical experience of general practitioners, geriatricians and the scientists who study aging. This is to encourage research study in aging, as well as new research works that seek to enhance the management and the treatment of older patients with multiple morbidities. The study concluded that ageing is the risk factor for multimorbidity.

#### **3.2 Comorbidity with COVID 19**

According to Hong-lei Yin et al. [17] comorbid conditions including cardiovascular and cerebrovascular diseases, endocrine and metabolic disorders, psychiatric and neurological

disorders, gastrointestinal diseases, musculoskeletal disorders, non-COPD respiratory conditions, and cancer were significantly higher in patients suffering from COPD than in comparison the non-COPD control patients [17]. Management of comorbidities should be an essential component of COPD control mechanisms that can improve overall outcomes. Yang J et al. [18] assessed the prevalence of comorbidities in the COVID-19 infection patients and found underlying disease, including hypertension, respiratory system disease and cardiovascular, may be a risk factor for severe patients compared with Non-severe patients [18]. In another study, patients with previous cardiovascular metabolic diseases may face a greater risk of developing into the severe condition and the comorbidities can also greatly affect the prognosis of the COVID-19 [19]. On the other hand, COVID-19 can, in turn, aggravate the damage to the heart [19]. COVID-19 can essentially influence the function of the heart which then can lead to myocardial injury. The past medical history of CHD and increased level of cardiac troponin (cTnl) are two independent determinants of clinical disease status in patients with COVID-19 [20]. Myocardial injury is significantly associated with fatal outcome of COVID-19, while the prognosis of patients with underlying CVD but without myocardial injury is relatively favorable. Myocardial injury is again with cardiac dysfunction and arrhythmias. Inflammation may be a potential mechanism for myocardial injury. Aggressive treatment may be considered for patients at high risk of myocardial injury [20].

#### 4. CONCLUSION

In conclusion it is obvious from the above literature review that COVID 19 has devastating effect on the aged due to usual biological deterioration process of the respiratory and the immune system. These biological changes in the ageing process make the aged vulnerable to the COVID 19. Available literatures further review that comorbidity is strong determinant of increase in morbidity and mortality of the aged to COVID 19. Also, the literature reviews suggest that there are not much research studies on the above subject areas especially in sub-Saharan African and for that matter Ghana. Base on the findings from the above literature, it will be appropriate for some further works to be done that will direct some special health educational program targeted at the elderly or the aged.

#### 5. RECOMMENDATIONS

It is recommended that some further research be done locally on COVID 19 to increase the knowledge on this subject in Ghana. It is also recommended that an appropriate health educational strategy be developed to create awareness among the aged.

#### 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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