



## UNDERLYING FACTORS INCREASING THE RISK OF HOSPITALIZATIONS IN COVID-19 PATIENTS

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### ABSTRACT

COVID-19 has been confirmed a public health emergency across countries globally. Following the increasing incidences of the COVID-19 pandemic, healthcare professionals and healthcare systems are challenged by the surge of COVID-19 patients seeking medical assistance. Hospitalization for COVID-19 patients is increasing, which is associated with the severity of the disease. Hospitalization is needed for viral clearance and good prognostic outcomes. Understanding the underlying factors of hospitalization among COVID-19 patients informs medical opportunities to recognize at-risk people and develop clinical strategies to reduce adverse events and reduce the healthcare burden. This article highlights that age and inflammatory responses, gender, and preexisting medical conditions are the underlying factors of hospitalization. It is well-described that these factors increase the severity of COVID-19 illnesses, which requires further hospitalization of the affected people to provide the needed care and reduce mortality. Thus, taking into consideration such factors is crucial towards taking appropriate measures to reduce hospitalization rates of COVID-19 patients that pose an economic burden to the health care system and the country at large.

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### INTRODUCTION

In late 2019, a new variant of coronavirus, classified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first witnessed in China, and it has spread widely across countries. The SARS-CoV-2 has caused an outbreak of a viral infection globally, which is termed the coronavirus disease 2019 (COVID-19) [1]. The infection is a highly transmittable viral infection and is now considered a global pandemic, which has contributed to a dramatic loss of human lives across nations. Since the emergence of the disease, several cases have been reported worldwide following the increased transmission from one person to another. More recent data on the prevalence of COVID-19 cases globally showed that since the beginning of 2021, approximately 103 million COVID-19 cases have been reported worldwide, with a recovery of more than 75 million people [2]. In terms of mortality rates, it is found that as of January 2021, nearly 2.3 million deaths have been reported globally, which indicates a significant loss of human lives [2]. Following the increasing prevalence of COVID-19 globally, the disease has been confirmed as a public health emergency. The pandemic has challenged the healthcare system due to an acute increase in the need or demand for medical care services. It is established that there is

a surge in capacity in the health care system in response to the high demand for health services for COVID-19 patients [3]. The disease is acknowledged as an acute respiratory infection that has placed high demands on the health system, especially in screening and testing the suspected cases. Such demands require hospitalization, which has resulted in many healthcare organizations experiencing a lack of space and clinical equipment to support the COVID-19 patients [3, 4]. Hospitalization of COVID-19 patients occurs mainly in intensive care units, which has posed an economic burden to the health care system and the patient. It is evident that in countries like the United States, many COVID-19 patients are admitted to the intensive care units with a hospital length of stay of approximately five days. The healthcare costs for such admission increase with the usage of intensive care units, posing an economic burden to the country [5].

COVID-19 and related complications vary between nations owing to differences in hospitalization. Existing published articles on hospitalization or admission to intensive care units because of COVID-19 infections show that hospitalization has resulted in a limited number or availability of beds in healthcare organizations due to the surge capacity of COVID-19 patients [3, 6]. Despite that several published articles or reports described the increasing number of hospitalized

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COVID-19 patients, there is limited evidence on the underlying factors of hospitalization. Therefore, understanding these factors may provide an in-depth understanding of the surge capacity of COVID-19 patients in hospitals.

### ***Underlying Factors of Hospitalization among COVID-19 Patients***

Even though strict social confinement measures have been implemented and seem effective in reducing the prevalence and mortality of COVID-19 infections, the risks and incidence of COVID-19 infections remain a public health concern globally, which poses a significant threat to the healthcare systems due to the increasing number of patients being hospitalized [7]. Hospitalization of COVID-19 patients could be associated with the severity of the disease. Existing clinical evidence illustrates that patients diagnosed with COVID-19 infection present mild to moderate symptoms, which become severe and critical if not treated well [8]. Thus, the healthcare system aims to ensure COVID-19 patients get the needed care, which is overburdening the healthcare system, especially the intensive care units. It is well established that the influx of critically ill COVID-19 patients is overburdening the emergency units. The surge of COVID-19 patients poses challenges in the capacity of health systems in response to the health care needs of both severe and non-severe patients seeking the necessary medical examinations and treatment [7]. Therefore, understanding the factors that lead to hospitalization of COVID-19 patients is important to predict health care demand and plan resource allocation, especially in resource constraint centers. The key factors that influence hospitalization of COVID-19 patients include age and inflammatory response, gender or sex, and preexisting health conditions, as discussed in the subsequent sub-sections.

### ***Age and Inflammatory Responses***

Hospitalization among COVID-19 patients is associated with age. Older adults are more likely to be hospitalized than young adults, which could be associated with changes in their body functioning, including the functions of the immune system and the need for more care than the general population. This is supported in a cohort study that investigated the risk factors of hospitalization and mortality in Brazil due to COVID-19 [9]. The study revealed that older people aged 60 years and older are more likely to be hospitalized. The hospitalization of the aging population is associated with poor functioning of the immune system and an increase in protein expression of angiotensin-converting enzyme-2 [9]. The impaired functioning of immune systems among older people is supported in other research studies, which showed that the immune response of older individuals is weak, hence facilitates viral infections because of poor antibody-dependent enhancement [10, 11]. It is also evident that the angiotensin-converting enzyme-2 is the essential surface receptor responsible for the entry of SARS-CoV-2 into the weak immune cells among older people [12]. Thus, the entry of the virus into these cells leads to decrease inflammatory and immunological responses. This increases the vulnerability of older adults to have more contact with viral infections from SARS-CoV-2, which increases hospitalization risks [10, 11].

Further, severe pneumonia is common among COVID-19 patients, especially in older individuals that require appropriate oxygenation. Consequently, these patients require hospitalization to receive oxygen therapy. A review on

pathogenesis and clinical management of severe COVID-19 pneumonia shows that COVID-19 patients have diffuse alveolar damage that requires invasive and non-invasive mechanical ventilation. These patients require interdisciplinary approaches for critical disease recovery [13]. As such, hospitalization is needed to optimize the recommended oxygenation to prevent mortality among COVID-19 patients. The health care need for invasive or non-invasive mechanical ventilation requires a longer length of hospital stay to ensure a quality of life among COVID-19 patients [13]. Age and inflammatory responses are also associated with recurrent pneumonia, which causes hospitalization and rehospitalization of COVID-19 patients. Older adults discharged from the hospital after COVID-19 infections are more likely to develop recurrent pneumonia that requires readmission. This is supported in a case report that investigated recurrent pneumonia in a 40-year-old patient with COVID-19 infections and insufficient antibody production and discharged from the hospital [14]. The study revealed that the COVID-19 patient had recurrent pneumonia, which could be associated with immunodeficiency, weak humoral immune response, and deficient production of protective antibodies. The study indicated that the recurrence of pneumonia requires further hospitalization for good recovery from the disease [14].

### ***Gender***

Gender plays a significant role in the hospitalization of COVID-19 patients. Sex differences are assumed to increase hospitalization in COVID-19 patients. It is well established that the male sex is at higher risks for serious COVID-19 infections than women, which increases hospitalization. Increased hospitalization among men is attributed to immune activation. The existing body of knowledge showed that women have a more robust immune activation than men, leading to reduced severity of diseases and decreased hospitalization [15]. Also, male sex is associated with hospitalization due to inflammatory activation. Soares and other researchers established that hospitalization rates are higher among male sex than women because of differences in the immune response to viral infections [9]. The immune system and immune response to viruses are stronger in women than in the male sex, and a possible explanation is because of the protection of genes expressed in the X chromosome and sex hormones in women [9]. As such, men have a lower innate and adaptive immune response to SARS-CoV-2 infection than women that facilitates their infection severity for COVID-19 [9].

Further, the information presented by the Center for Disease Control and Prevention supported the role of sex differences in COVID-19-associated hospitalizations. The research indicated higher hospitalization rates for males (5.1% per 100 000 population) than for females (4.1% per 100 000 population) [16]. The increased hospitalization rates among men are attributed to immune and inflammatory responses. Similarly, the severity of COVID-19 infections among men explains higher hospitalization rates than women due to underlying factors, including elevated expressions of angiotensin-converting enzyme 2, immunological differences, behavioral and social differences, and hormonal differences [17]. However, there is a lack of enough evidence on how these differences are associated with higher hospitalization rates. Other researchers proposed health behaviors, such as tobacco and alcohol use, elevated body mass index, and complicated

hypertension as the underlying factors of hospitalization among males than women. This is evident in a retrospective cohort study that examined the relationship between sex and gender differences and hospital admission among male and female patients with COVID-19 [21]. The study revealed that males were at higher risks for severe COVID-19 due to poor inflammatory responses. The researchers proposed that the increased severity of disease among males could be associated with increased use of alcohol and tobacco, elevated body mass index, asthma, and complicated hypertension, which place male patients at higher risk for hospitalization than female patients [21]. Other researchers proposed that alcohol and tobacco use increase the risk of men acquiring respiratory infections and impaired cardiovascular functions. These individuals experience breathing difficulties and decreased diaphragm excursion that restricts ventilation [8]. Such infections could be associated with the impaired immune response; hence, the body cannot fight any pathogens, therefore facilitating the entry of SARS-CoV-2 more in men than women[8].

### **Preexisting Health Conditions**

Preexisting medical conditions have a significant impact on hospitalization among COVID-19 patients. People with preexisting medical conditions, such as diabetes mellitus, cardiovascular diseases, cancer, hypertension, chronic kidney diseases, and obstructive pulmonary diseases, are highly susceptible to COVID-19 infections [22]. The severity of COVID-19 among these people increases their hospitalization rates. Clinical research that has been conducted on the association between preexisting health conditions and COVID-19 infections supported that higher hospitalization rates are reported among COVID-19 patients with preexisting medical comorbidities because of the severity of the disease [23]. It is well-described that people with preexisting cardiovascular diseases, particularly coronary heart disease and hypertension, are at higher risks of acquiring severe COVID-19 infections, requiring hospitalization for emergency care, especially in intensive care units [23]. Hospitalization in COVID-19 patients with preexisting medical conditions is attributed to impairment in body functions, especially immune systems and body cells involved in fighting pathogens. For instance, a retrospective study that investigated the underlying factors of length of hospital stay among non-severe COVID-19 patients revealed that preexisting health conditions, such as diabetes, has an impact on duration of hospital stay[7]. The study presented an example of diabetes as the most prevalent morbidity among COVID-19 patients and revealed that hospitalization among these patients is high with a prolonged hospital stay. This is because of the impaired functions of lymphocytes and macrophages that adversely affect the growth of T-cells and the production of signaling proteins, such as interferon that acts as anti-viral defenses [7]. Thus, impaired T-cell growth and poor production of interferon result in suppressed immunological functions, which facilitate viral infections. This also contributes to fluctuations in levels of blood glucose among COVID-19 patients, which exacerbate diabetes complications and prolonged recovery process [7].

Similarly, COVID-19 patients with cardiovascular comorbidities are at higher risks for hospitalization due to poor prognosis and the need for improved functioning of cardiovascular systems. Existing clinical evidence

demonstrates that the preexisting comorbidities of heart diseases and hypertension are prevalent among COVID-19 patients, leading to acute cardiac injury and uncontrolled release of pro-inflammatory cytokines [24, 25]. This, in turn, causes poor acute systematic inflammatory responses that affect the cardiovascular systems. Thus, the COVID-19 patients are hospitalized for a longer period of time for the recovery process [24]. Further, hospitalization among COVID-19 patients is associated with the presence of underlying obesity that decreases thrombogenesis, hyper-immune reactivity, and cardiorespiratory reserve. Based on the impairment of such activities, the functional receptor of SARS-CoV-2 and expression of angiotensin-converting enzyme 2 are upregulated in the COVID-19 patients' adipocytes, which makes the adipose tissue a potential reservoir of viruses [26]. This leads to severe COVID-19 diseases, which require proper management and treatment through hospitalization [26].

To further expand on the contribution of underlying medical conditions to hospitalization among covid-19 patients, obese people with elevated body mass index are at higher risks of poor prognostic outcomes that require readmission and prolonged hospital stay. The findings in a retrospective cohort study showed that among obese people with a body mass index of over 40 kg/m<sup>2</sup>, the hospitalization rate is high because of poorer prognostic outcomes that require further admission to the hospital [17]. The study showed that such patients show severe illness of COVID-19 that requires hospitalization [17]. Despite the viral clearance, underlying conditions lead to health complications that require further clinical management and treatment. It is well-established that despite viral clearance in hospitalized COVID-19 patients with other underlying health conditions, the patients are more likely to have post-SARS-CoV-2 infections due to the onset of other health complications [22]. For instance, these patients develop chronic fatigue, insomnia, mental illnesses, and breathlessness. These COVID-19-associated complications and poor health outcomes require hospitalization for post-clearance of SARS-CoV-2 and to achieve good clinical outcomes [22].

### **CONCLUSION**

The COVID-19 confirmed cases globally have led to higher hospitalization rates among the infected people. The disease's severity facilitates hospitalization, which is based on underlying factors, such as age and inflammatory responses, gender, and underlying or preexisting health conditions.

Older adults have poor immunological responses due to impaired immune system, which facilitates viral infections because the body cannot fight against pathogens. Hospitalization among COVID-19 patients is also attributed to sex differences, with more men being admitted to the healthcare facility than women. Further, preexisting health conditions, including cardiovascular diseases, diabetes, and obesity, leads to the severe illness of COVID-19, which indicates the need for hospitalization. Thus, understanding these underlying factors provide the basis to improve early recognition of people at risk of mortalities and may encourage the implementation of medical strategies to prevent additional adverse events.

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