

Relationship between Underlying Diseases with Morbidity and Mortality in Patients with COVID-19

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Background: This study aims to investigate the clinical and demographic features of underlying medical conditions and the potential relationship between underlying diseases and the increased rate of morbidity and mortality due to COVID-19.

Materials and Methods: This study was conducted on 350 COVID-19 patients hospitalized at the Masih Daneshvari Hospital from February-July 2021. All participants had confirmed COVID-19 diagnosis based on symptoms and/or positive PCR test or chest X-ray results. Data was collected from medical records on demographics, disease severity, symptoms, underlying conditions like diabetes, hypertension, coronary heart disease, obesity, renal disease/transplantation, and outcomes like hospital stay, ICU admission, and mortality. Relationships between age, underlying diseases, and mortality were analyzed using chi-square and Fisher's exact tests."

Results: A total of 350 patients diagnosed with COVID-19 were included in the study, with an average estimated age of (60.8±15.4). The age group of 56 and above had the highest morbidity rate, which accounted for 50% of the total participants. Among the COVID-19 patients, diabetes was the most common underlying medical condition, accounting for 31.4% of the cases. High blood pressure was present in 27.1% of the patients, and 17.1% of the total participants had coronary heart disease (CHD). Additionally, 10.9% of the participants were overweight, and 30 of them had previously experienced kidney failure or transplantation. Moreover, the study found that 40% of patients with diabetes died, while the mortality rate was 38.3% in patients with CHD and 47.4% in overweight participants. High blood pressure patients had a mortality rate of 43.2%, and patients with renal failure or kidney transplantation had a significantly increased risk of mortality at 83.3%. The research also revealed a significant and direct relationship between mortality rate, age group, and underlying disease among the patients (P<0.05).

Conclusion: The findings of the present study hold significant implications for preventive interventions and policy adoption, particularly in relation to the use of calendar age as the key criterion for risk evaluation. These results underscore the need for a more precise and focused approach to prioritizing patients with identified risk factors.

Keywords: COVID-19; Diabetes; Hypertension; Chronic renal failure

INTRODUCTION

The primary source of acute respiratory syndrome or coronavirus (COVID-19), initially appeared in December 2019 in the city of Wuhan, China. This contagious disease rapidly spread and infected individuals around the world and was eventually declared a pandemic by the World Health Organization (WHO) (1). Countless lives are globally lost every day due to this lethal virus. It is also worth noting that various studies have shown that risk factors can directly be associated with the severity and lethality of COVID-19 (2). Furthermore, the complete acknowledgment of various factors affecting the severity of the disease and its lethality requires further researches. Besides, different factors such as the availability of medical services and their overall quality, hospital facilities and equipment, old age, immunodeficiency, low efficiency of various organs, and simultaneous infection of other potential diseases are the effective factors in increasing the severity of the disease and its mortality rate (3).

Based on a paper published in the Journal of the American Medical Association (JAMA), researchers also aim to discover more findings on hospitalized patients after the development of the new coronavirus (COVID-19) in their system, which essentially included the evaluation and review of the e-medical records obtained from 5,700 COVID-19 patients who were hospitalized by the Northwell Health System in New York during March-April. The obtained results indicated that 94% of these patients had at least one underlying health condition, which essentially means that they were also suffering from another disease before COVID-19. It is also essential to add that the most common underlying diseases found in these patients include high blood pressure (with approximately 53% of the total COVID-19 patients), overweight (42%), and diabetes (32%) (4).

Various studies have also shown that patients with multiple chronic diseases have a more severe prognosis in comparison to patients with a single disease; however, the relationship between the disease type and the number of concomitant diseases with prognosis in COVID-19 patients

is neither definitive nor transparent (5). Furthermore, the prevention of disease exacerbation, triage, and prioritization of patients, as well as lowering the overall COVID-19 mortality rate is considered a significant challenge, due to the high mortality rate and nature of the disease (6). Therefore, this investigation was conducted to explore the clinical and demographical characteristics of the diseases, in addition to evaluate the relationship between the severity and mortality rate of COVID-19 patients and other underlying medical conditions, which primarily include diabetes, high blood pressure, coronary heart disease (CHD), obesity, renal failure, and kidney transplantation..

MATERIALS AND METHODS

This study was conducted particularly on those COVID-19 patients who were hospitalized in the Masih Daneshvari Hospital from February to July 2021. The participants were considered to be COVID-19 positive, considering either having severe symptoms or a positive radiological or laboratory report that officially indicates COVID-19. These clinical tests often include a positive PCR test or common COVID-19 radiography (x-ray).

Data Collection

The medical records of patients was used to provide contextual and demographical information about participants including age, gender, body mass index, disease severity, oxygen levels, symptoms (fever, chills, myalgia, respiratory dyspnea, chest pain, coughs, anorexia, nausea, vomiting, diarrhea, syncope), in addition to the co-occurrence of underlying diseases such as (diabetes, high blood pressure, CHD, overweight, renal failure and kidney transplantation) as independent variables and potential consequences including the duration of hospital stay, prior history of ICU hospitalization and the aftermath of the disease (dead/recovered patients).

Statistical Analysis

The standard and average deviations were used to further describe the quantitative data as well as the frequency and its percentage which were used to describe

qualitative data. Also, several tables and graphs were used to describe the obtained data. The Chi-Square test and Exact Fisher Test used to examine the potential relationship between qualitative variables such as age group and underlying diseases with the mortality rate in patients. The SPSS software version 26 was used for data analysis, and the significance threshold in all analyses was considered less than 0.05.

RESULTS

A total number of 350 patients with a definitive diagnosis of COVID-19 who were hospitalized in the Iran Coronavirus Center were included in this study. The average age of the participants was estimated between (60.8 ± 15.4) years of age, including 229 male subjects (65.4%) (Table 1). Additionally, the highest morbidity rate among the participants was directly associated with the age group of 56-66 years, which included 97 individuals in this particular age group (27.7%). On the other hand, the lowest COVID-19 incidences were related to the age group of 16-26 years old, in which 8 patients were in this group (2.3%). Results also indicated that the morbidity rate is higher amongst male participants in comparison with their female counterparts.

Table 1. Demographic and baseline characteristics of patients infected with COVID-19

| Variables | N (%) / Mean \pm SD |
|------------------------------|-----------------------|
| Age | 60.8 \pm 15.4 |
| Gender (Male) | 229(65.4) |
| Co-diseases | |
| Diabetes Mellitus | 110 (31.4) |
| IHD | 60 (17.1) |
| Obesity | 38 (10.9) |
| CRF & Kidney Transplantation | 30 (8.6) |
| HTN | 95 (27.1) |
| Without Any Disease | 17 (4.9) |

The obtained results of regarding the relationship between mortality rate and participants age group are described below in Table 2: it indicates a higher and significant mortality rate for patients at older ages in comparison with the rest (P-Value = 0.0017).

Table 2. Distribution of patients by the age group

| Age Group | Death/ n (%) | P-value |
|-----------|--------------|---------|
| 16-26 | 8 (2.3) | 0.0017 |
| 26-36 | 19 (5.4) | |
| 36-46 | 30 (8.6) | |
| 46-56 | 55 (15.7) | |
| 56-66 | 97 (27.7) | |
| 66-76 | 79 (22.6) | |
| 76+ | 62 (17.7) | |

*: Significant at 0.05 level

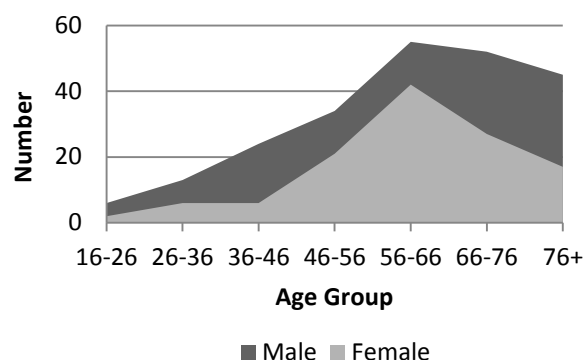
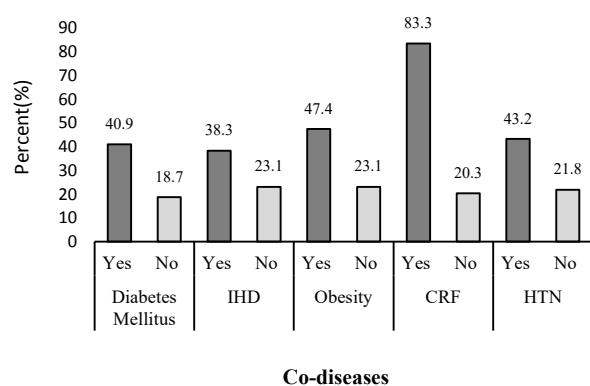
According to Table 1, the most influential underlying disease in COVID-19 patients who were hospitalized at the center was diabetes, which included 110 patients (31.4%). Besides, 95 of patients were diagnosed with high blood pressure (27.1%), 60 patients had coronary heart disease (17.1%), 38 of them were considered overweight (10.9%), and 30 patients had previously experienced renal failure or kidney transplantation. It is also essential to add that 17 of the patients had no previous underlying medical condition (4.9%). Figure 1 shows the distribution of the number of death by gender and age group. In general, the trend of the distribution of the number of deaths for both genders is similar in all age groups. Only in age group, 36-46, the percentage of deaths in men is twice as high as in women, 10.5% compared to 5%.

The obtained results regarding the mortality rate and its relationship with underlying diseases showed that amongst the total 110 patients diagnosed with diabetes, 45 lost their lives (40.9%), while the mortality rate in patients with coronary heart disease (CHD) was estimated at 38.3%, and 47.4% in overweight patients. Patients with kidney transplants and renal failure had a mortality rate of 83.3%. Additionally, patients with high blood pressure had an estimated mortality rate of 43.2% (Table 3 and Figure2). Additionally, the relationship between the mortality rate and underlying health conditions was considered significant and direct (P-Value=0.033).

Table 3. Mortality of patients according to the type of disease

| Mortality Status | Co-diseases Type | n (%) |
|------------------|------------------------------|-----------------|
| Yes | Diabetes Mellitus | 45/110 (40.9%) |
| | IHD | 23 / 60 (38.3%) |
| | Obesity | 18 /38 (47.4%) |
| | CRF & Kidney Transplantation | 25 / 30 (83.3%) |
| | HTN | 41/95 (43.2) |
| No | Diabetes Mellitus | 45/240 (18.7%) |
| | IHD | 67/290 (23.1%) |
| | Obesity | 72/312 (23.1%) |
| | CRF & Kidney Transplantation | 65/320 (20.3%) |
| | HTN | 49/255 (21.8) |
| P-value | | 0.033* |

*: Significant at 0.05 level

**Figure 1.** Distribution of the number of deaths by gender and age group**Figure 2.** Mortality of patients according to the type of disease

DISCUSSION

The COVID-19 pandemic is a global health crisis that poses a significant threat to people of all ages (7). Although COVID-19 has a high mortality rate, there is limited

documentation on simultaneous incidence of multiple diseases and their severity. The main goal of this study was to provide a detailed description of the clinical and demographic features of various diseases, along with conducting a comprehensive investigation on the correlation between these underlying diseases and the severity and mortality rate of COVID-19.

Various studies have indicated that the morbidity and mortality rate can directly be associated with the age of the patient. Additionally, the obtained results of this study showed that approximately half of the morbidity and mortality cases are amongst the age group of 60 or above, which is slightly higher than the mortality rate in the elderly found in Korea (8,9).

On the other hand, chronic diseases have become a significant financial burden globally. This burden is causing financial toxicity for individuals and healthcare systems (11). Current research found that at least one underlying medical condition was present in 95% of participants. According to a study conducted by Atkins et al, the most common underlying health conditions found among COVID-19 patients were high blood pressure (44.4%) and diabetes (17.1%) (12). However, current research suggests that the most prevalent underlying diseases among patients are diabetes (31.4%) and high blood pressure (27.1%).

The cause of death in COVID-19 patients can vary and may include multiple organ failure, heart, respiratory, and renal failure, severe shock, and arrhythmias (13). Additionally, it has also previously been declared that having various simultaneous underlying health conditions can potentially lead to defective immune system response to pathogens, organ dysfunction, accelerated inflammation, multiple organ failure, and ultimately death or demise of the patient in the ICU (14). The obtained results from previous studies have revealed that cardiovascular diseases, high blood pressure, obstructive pulmonary disease, and diabetes are the most crucial risk factors for COVID-19 mortality rate and its severity in patients. Similarly, the results of this article showed that

there is a significant and direct relationship between COVID-19 mortality rate and cardiovascular diseases.

According to a study conducted by Ruan et al. on 150 COVID-19 patients, the results showed that patients who had cardiovascular disease and hypertension were more likely to pass away from the disease compared to those who were discharged. The study found that 43% of patients with these conditions passed away, while only 19% of discharged patients had the same conditions ($p < 0.001$) (16). Also, a systematic review and meta-analysis of 16 different studies including 3994 patients indicated that high blood pressure, cardiovascular disease, chronic kidney disease, and diabetes can potentially increase the risk of severe incidence, while solely diabetes had a significantly higher impact on mortality rate among the patients (17).

The relationship between diabetes and severe COVID-19 symptoms has also been previously investigated in a variety of meta-analyses; besides, studies have also shown that diabetes is an influential risk factor and can directly be associated with the severity of COVID-19 patients (18), similar to the obtained results of the current study. Diabetic patients have also a poor prognosis for common infections like SARS-CoV and MERS-CoV (19). Furthermore, the immune system disorders in diabetics caused by chronic hyperglycemia and severe fluctuations in blood glucose levels are considered significantly effective on their rehabilitation and response to treatment.

On the other hand, irregular proinflammatory cytokine responses are also considered to be a crucial cause of the severity of COVID-19 amongst diabetic patients (20). Previous researches have indicated that diabetic patients often have unregulated levels of proinflammatory cytokines, specifically interleukins 1 and 6 (IL-1 & IL-6) as well as tumor necrosis factor (α -TNF). Moreover, various markers including C-reactive protein, D-dimer have also been increased in diabetic patients with COVID-19. Therefore, this particular condition may potentially increase the cytokine storms in COVID-19 patients, which essentially leads to significantly higher disease severity (21).

Cardiovascular disease is a common chronic illness among patients. According to the current study, individuals with cardiovascular disease are at a higher risk of experiencing severe COVID-19 and developing serious outcomes such as admission to the ICU and even death; the result which is consistent with previous studies and meta-analyses (22). Various studies on patients with other coronaviruses, such as acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV), have reported an increased risk of mortality in patients with cardiovascular disease (15).

Inflammation is a possible way that connects lung infection to cardiovascular diseases. Specifically, the inflammatory response that occurs after a lung disease can cause changes in plaque levels and damage blood vessels. Moreover, previous studies have shown signs of increased local inflammation in the coronary arteries and cardiac arrhythmias following acute systemic infections. Furthermore, cardiovascular disease can lead to immune system dysfunction and increased expression of the angiotensin-converting enzyme receptor. This can cause an increased mortality rate and severity of COVID-19 patients (23).

The study thoroughly analyzed the prevalence of chronic renal failure and kidney transplantation in COVID-19 patients. The findings indicated a significantly higher mortality and severity rate in COVID-19 patients with coronary heart disease (CHD) (83.3%). This could be attributed to the use of immunosuppressants after their kidney transplantation. It is important to note that the results of the recent research align with a previous study conducted by Mahalingasivam et al. This study indicated that around 46% of kidney transplant patients who contracted COVID-19 have passed away (24).

CONCLUSION

Chronic underlying diseases can increase the morbidity and mortality of COVID-19 patients. This article aims to prevent this by implementing a more efficient approach for patient prioritization. Patients with underlying health conditions require additional medical care. Regularly

checking blood glucose levels and conducting examinations for cardiovascular factors, BMI, and kidney function is highly recommended to prevent severe exacerbations and mortality rates.

Ethical Considerations

This study followed all ethical codes and principles, and provides patients with the option to withdraw from the study at any point. Participants were fully informed about the research process and their personal information was kept confidential throughout the study. The official code of ethics was obtained from Shahid Beheshti University of Medical Science in Tehran (IR.SBMU.NRITLD.REC.1399.017).

Conflict of Interest

There are no conflicts of interest to be declared.

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