

Covid-19 Severity in Patient Comorbidities

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Abstract:

The catastrophic Corona virus disease 2019 (Covid-19) has been an ongoing pandemic. Underlying conditions have been contributed to the severe symptoms of the Covid-19 patients, length of hospital admission, the differences in recovery time, survival outcome, and fatality rate among patients. Several chronic diseases such as cardiovascular diseases, diabetes, and obesity have been discussed. This study highlighted the relationship between chronic comorbidities and the severity of Covid-19 cases. Chronic comorbidities may relate to a severe outcome in patients with COVID-19, as evidenced by the data. According to the current study's reviews, comorbidities significantly adversely impacted COVID-19 treatment outcomes in hospitalised patients.

Keywords: Covid-19, chronic comorbidities, severe Covid-19 symptoms.

I. INTRODUCTION

It is known that the world has faced a devastating outbreak since 2019. Covid-19 is considered to be one of the worst if not the worst infectious disease humanity has ever faced(1). Much information about this Covid-19 virus and its symptoms is yet to be fully discovered and studied. There are some published scientific studies about Covid-19 which claim that the patients with 6 health issues, namely, cardiovascular diseases (CVS), diabetes, obesity, chronic kidney disease, cancer and chronic neurological diseases suffered the most compared to normal patients(2). Although there is not much research that aims for the collocation between these health problems and the severity of Covid-19. Still, most available research related to this topic was done either in European countries or China(3).

The COVID-19 pandemic has resulted in nearly 160 million cases with over 3.21 million deaths as of 12th May 2021(2). Alterations in fatality rates have been recognised worldwide(2). The factors that may have contributed to the

variation of fatality rate and the differences in the clinical management of COVID-19 patients, access to medicines and medical devices, and inconsistencies in healthcare systems.

There is no research about the differences in mortality rate between each of the common health issues(4, 5). It is yet to be fully understood and studied since there are a variety of clinical management of Covid-19 patients, different patients receive different treatments and medicine so it is understandable that they can have different outcomes too(6). Since Covid-19 is a current outbreak that the world is still dealing with, more studies about the virus are expected in order to help medical workers fighting against it. This review aims for the correlation between the patients' underlying health issues and mortality rate with COVID-19 patients.

II. Underlying diseases contributed to severe Covid-19 symptoms

As the mutated capability of the novel coronavirus raises more concern about the severity of the patients, there are still many

impediments to the knowledge of whom specifically this virus would affect critically(6, 7). Elderly people and vulnerable people who have underlying diseases, such as cardiovascular diseases, dyslipidemia, diabetes, and obesity have shown poor prognosis (2, 8).

A. Covid-19 and cardiovascular diseases (CVS)

It is observed that most of the critically ill patients (those admitted to ICU and those who died) had some types of pre-existing health conditions before being infected with COVID-19(9). From the data in a single cohort study, there were 138 cases of COVID-19 patients admitted to hospitals in Wuhan, China, 46% of those had coma, 31% had hypertension, 15% had other cardiovascular disease and 10% had diabetes. Another study in a multicenter cohort also showed similarities,

of all 191 infected patients in Wuhan, 48% had coma, 30%, 19% and 8% had hypertension, diabetes and coronary heart disease respectively(9).

Moreover, according to the Chinese report which involved 1,099 COVID-19 patients, around 24% of which had comorbidity, 15%, 7% and 3% had hypertension, diabetes and coronary heart disease respectively(10). The death rate of COVID-19 patients observed by the Chinese government agency (as so called Chinese Center for Disease Control and Prevention) as of 11 February 2020 was approximately 2.3% (1,023 deaths among 44,672 confirmed COVID-19 cases) (11). Another report based in Italy which involved 1,591 ICU COVID-19 patients, 49% of those had hypertension, 21% of those had CVD and 17% had diabetes before being diagnosed with COVID-19(12).

B. Covid-19 and diabetes

Diabetes and Covid-19 symptoms were reported to have a relationship in two directions(6, 8, 13). Firstly, the risk of getting critical Covid-19 symptoms increased in diabetic patients(8). Another relationship between new-onset diabetes and serious metabolic

complications from pre-existing diabetes e.g. hyperosmolarity and diabetic ketoacidosis and Covid-19 raised more concern about the severity of the symptoms, and therefore, required to have been observed(14-16).

The clinical manifestations of diabetes were suggested to be related to Covid-19 in terms of pathophysiology as there was a clear report about the mechanism of Covid-19 to enter the cell. It is known that SARS-CoV-2 virus enters a human cell by using its spike protein on their cell membrane to bind with angiotensin-converting enzyme 2, as known as, ACE2 receptors. ACE2 is a crucial protein receptor for various organs and tissues, such as the small intestine, pancreatic beta cells, adipose tissue, and also the kidneys as well(17). Hence, it is reasonable that Covid-19 might provoke pleiotropic changes in glucose metabolism, complicating the pathophysiology of preexisting diabetes or resulting in the emergence of novel disease mechanisms(18). Additionally, several precepts for a viral cause of diabetic ketoacidosis, along with other coronaviruses which bind to ACE2 receptors(17). Fasting glycemia and acute-onset diabetes were found to be more prevalent in patients with Covid-19 pneumonia than in patients with non-Covid-19 pneumonia(17, 19). These findings help support the idea and hypothesis that Covid-19 may have a potential diabetogenic effect in addition to the well-known stress response related to severe illness(18). Nevertheless, it is unknown whether the changes in glucose metabolism associated with an abrupt onset of critical Covid-19 infection persist or resolve when the infection resolves(18).

A retrospective study conducted in multiple centres in China discovered that elevated fasting levels of glucose (7.0 mmol/l (126 mg/dl)) at admission were a crucial sign of increased mortality in those infected with SARS-CoV-2 who did not have preexisting DM(20, 21). As a result, it is advisable to assess patients' level of glucose and treat hyperglycemia in those who have progressed to critical COVID-19 states(22-24).

Case reports explain patients with newly diagnosed T1DM who developed ketoacidosis shortly after contracting COVID-19 and those patients with newly diagnosed Type 1 Diabetes Mellitus who developed ketoacidosis after recovering from COVID-19(25-27). The observations suggest the risk that SARS-CoV-2 could be the causative agent of this metabolic disorder. In one series, 29 patients with no history of diabetes mellitus developed hyperglycemia while receiving COVID-19 treatment, even though some had a typical HbA1c level on admission(26). Nevertheless, paediatric patients with Type 1 Diabetes Mellitus were sent to specialised Italian diabetes centres at a lower rate than anticipated(28, 29).

Contrasting to the information gathered from specialised hospitals located in the northwestern part of London, UK, there was a significant number of patients diagnosed with critical ketoacidosis, it was even more than what they first expected, implying an increase in the number of people infected with the newly diagnosed Type 1 Diabetes Mellitus(26, 30). These findings which contradict each other could be the result from using just small patient populations: it is likely that they have occurred by chance or due to changes in the availability of medical services in some particular area during the COVID-19 outbreak. A study based on population conducted in Germany discovered no deviation from the expected numbers of newly diagnosed paediatric Type 1 Diabetes Mellitus patients(6, 30-32). Although, the similar research discovered a remarkable increase in diabetic ketoacidosis and critical ketoacidosis in teenagers infected with the newly diagnosed Type 1 Diabetes Mellitus(33, 34). An answer to these findings could be that patients are delaying hospitalisation out of fear for procuring Covid-19. As the current SARS-CoV-2 pandemic continues and more patients are studied. Soon it will be much clearer whether there is a true correlation between Covid-19 and new-onset Type 1 Diabetes Mellitus.

Two population-based analyses conducted in the United Kingdom unequivocally demonstrated that T1DM patients have a higher death rate than the general population(35-37). Patients with T1DM who were at higher death risk were older, had elevated HbA1c levels, arterial hypertension, renal dysfunction, and a history of cardiovascular disease e.g. myocardial infarction and heart failure(38, 39). These findings corroborate the link between Type 1 Diabetes Mellitus and poor Covid-19 outcomes.

Covid-19 and obesity

It is known that Obesity is a risk factor for critical Covid-19 symptoms which can lead to chronic inflammation that disrupts the immune system(40-42). According to the data from the Premier Healthcare Database Special Covid-19 Release (PHD-SR), CDC identified the relationship between BMI and the risk of developing into critical Covid-19 outcomes. The critical Covid-19 outcomes were hospitalization, ICU admission, invasive mechanical ventilation used, and even death(43-45).

There were 148,494 people who were infected with Covid-19 during an emergency department in 238 hospitals in the US from March to December 2020, 50% were obese patients and 28.3% were overweight. The study also showed that obesity and overweight were the 2 significant risk factors for critical COVID-19 in those aged less than 65 years(2, 42, 46). Patients with BMIs of 24.2 kg/m², 25.9 kg/m², and 23.7 kg/m², according to the study, had the lowest risk of developing into critical Covid-19 states when infected with SARS-CoV-2. Patients with BMI \geq 40 kg/m² were associated with increased risk of ICU admission(2).

Obese subjects had a fivefold increased risk of in-hospital mortality.

Andrea P. Rossi et al. evaluated the primary outcome (goal) of obesity infected with Covid19, which is linked with mortality, intensive care unit (ICU) length of stay (LOS), and hospital length of stay (LOS)(47-49). The goal was to determine whether obesity status affects the overall trend of

inflammation as measured by CRP and critically ill-induced myopathy as measured by CPK(50, 51). The findings indicated that those who had BMI of 30 and more were associated with a fivefold increased risk of death and a more extended duration of hospital stay in COVID-19 critically ill subjects(51, 52). During the first week in the ICU, obese subjects had remarkably higher CRP and CPK levels than normal patients. Furthermore, Covid19 patients who were obese were at a higher risk of death than those with average weight(53). Additionally, they demonstrated a more extended hospital stay. Subjects with obesity had elevated CRP levels during their first seven days in the intensive care unit. Subjects with obesity demonstrated elevated CPK levels during their first week in the ICU(41, 52, 53).

Conclusion

To conclude, this study indicates the effect of the possible risk factors and health issues that are likely to be associated with mortality rate and severe clinical outcomes among Covid-19 patients. Chronic comorbidities such as cardiovascular diseases, obesity, and diabetes are risk factors for critical clinical outcomes in those infected with Covid-19, with obesity being the most prevalence and most found among critical COVID-19 patients, respiratory disease being the most predictive. Treatments for diabetic patients, patients' blood glucose become more fluctuated and therefore, more challenging to monitor once they get COVID-19. In addition, BMI is a key predictor of mortality among severe COVID-19 patients. In patients with pre-existing health issues, the presence of ACE2 was found to be upregulated, hence increasing the susceptibility to COVID-19 diagnosis. Patients with critical health issues included obesity, diabetes, hypertension had been linked with poor clinical outcomes. It is reported that angiotensin-converting enzyme 2 (ACE2), which is commonly found in human's respiratory tissues especially in lung tissues and can also be found

in heart tissues, was recognized as a crucial receptor for COVID-19 infection. In patients with pre-existing health issues, the presence of ACE2 was found to be upregulated, hence increasing the susceptibility to COVID-19 diagnosis which can be a clue to the multi-organ dysfunction symptom that can be seen in COVID-19 infection.

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