Why obesity, hypertension, diabetes, and ethnicities are common risk factors for COVID-19 and H1N1 influenza infections

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Abstract

Obesity, hypertension, diabetes, and specific ethnicities (Black and Hispanic) have been reported to be common comorbidities and possible risk factors for the severity of both COVID-19 and H1N1 influenza infections. Thus, it is important to understand why these four risk factors are common to both COVID-19 and H1N1 influenza infections, and whether a common mechanism exists. Respiratory failure is the most important pathology that contributes to the severity of both COVID-19 and H1N1 influenza infections. Additionally, obesity has been reported to be a risk factor for the development of acute respiratory distress syndrome (ARDS), which is a serious clinical manifestation of both COVID-19 and H1N1 infections. Obesity is a risk factor for hypertension. All studies found in the search showing hypertension as a risk factor for the severity of COVID-19 and H1N1 infections were either not based on multiple logistic regression analyses or did not include obesity or BMI as an explanatory variable in their multiple logistic regression models Moreover, similar attention is needed when specifying patients with diabetes or of specific ethnicities (Black and Hispanic) as potentially more vulnerable to either infection, because obesity also correlates with diabetes, and is more prevalent in these ethnicities. Notably, a retrospective cohort study has shown that obesity or high BMI are predictive risk factors for severe COVID-19 outcomes, independent of age, diabetes, and hypertension. Associations between hypertension, diabetes, ethnicities and severity of COVID-19 and H1N1 infections may be confounded by obesity to a considerable extent.

Obesity, hypertension, diabetes, and specific ethnicities (Black and Hispanic) have been reported to be common comorbidities and possible risk factors for the severity of both COVID-19 and H1N1 influenza infections [1,2]. Thus, it is important to understand why these four risk factors are common to both COVID-19 and H1N1 influenza infections, and whether a common mechanism exists.

Respiratory failure is the most important pathology that contributes to the severity of both COVID-19 and H1N1 influenza infections. Patients with obesity show a restrictive breathing pattern and reduced lung volumes. In severe cases, this obesity-hypoventilation syndrome can lead to respiratory failure. Additionally, obesity has been reported to be a risk factor for the development of acute respiratory distress syndrome (ARDS) [3], which is a serious clinical manifestation of both COVID-19 and H1N1 infections. Among patients admitted for ARDS, the PaO_2-to-FiO_2 ratio has been found to significantly increase in the prone position in patients with obesity compared to patients without obesity [4]. Critical care clinicians treating COVID-19 patients have reported that patients with ARDS appear to respond well to invasive ventilation in the prone position, and hence, prone ventilation has been recommended by the international guidelines for the management of COVID-19[5].

Although patients with obesity have a higher risk of developing ARDS, they appear to have lower mortality rates compared to patients without obesity [6]. Obesity is associated with lower mortality in patients with sepsis [7], the most common cause of ARDS, and also with lower mortality in patients with community-acquired bacterial pneumonia [8]. These phenomena are examples of the 'obesity paradox' and may reflect

stronger immunity in patients with obesity [9] since bacterial infections are the most common causes of sepsis and community-acquired pneumonia. Heightened immune responses, however, could be harmful to patients with COVID-19 because of excessive cytokine production, known as the cytokine storm, which can contribute to ARDS or multi-organ dysfunction in some infected individuals. Therefore, the obesity paradox might not apply to COVID-19 infections.

Obesity is a risk factor for hypertension, but importantly, no published study has presented a convincing mechanism explaining how hypertension could contribute to the severity of COVID-19 and H1N1 infections. We searched PubMed on May 24, 2020 for the terms 'hypertension' combined with 'COVID', 'coronavirus', 'SARS-CoV-2', or 'H1N1'. All studies found in the search showing hypertension as a risk factor for the severity of COVID-19 and H1N1 infections were either not based on multiple logistic regression analyses or did not include obesity or BMI as an explanatory variable in their multiple logistic regression models. Therefore, there might be a statistical artefact resulting from the confounding influence of the association between hypertension and obesity. Additionally, it is important to mention that the accuracy of the patient height and weight measurements is unreliable in emergency and critical care admissions, where pre-admission measurements are not taken.

Moreover, similar attention is needed when specifying patients with diabetes or of specific ethnicities (Black and Hispanic) as potentially more vulnerable to either infection, because obesity also correlates with diabetes, and is more prevalent in these ethnicities[1]. Similarly, attention is needed when dealing with COVID-19 death rates as a result of people belonging to different ethnicities and the obesity rates in each country. Notably, a retrospective cohort study has shown that obesity or high BMI are predictive risk factors for severe COVID-19 outcomes, independent of age, diabetes, and hypertension [3].

Taking all the above-mentioned points into consideration, it can be concluded that associations between hypertension, diabetes, ethnicities and severity of COVID-19 and H1N1 infections may be confounded by obesity to a considerable extent.

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