

Uncontrolled Blood Sugar Contributes to COVID-19 Mortality in Type 2 Diabetics

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Type 2 diabetes has been strongly associated with increased risk of mortality among COVID-19 patients, and our findings support this strong association. In a population of 185,600 COVID-19 positive patients, diabetic patients were 86% more likely to die after controlling for age, sex, and race/ethnicity.

Some researchers have suggested factors associated with diabetes, such as high blood sugar, high insulin levels, and impaired immune response, are responsible for the increase risk.¹ Focusing on high blood sugar, we found that high blood sugar explained 75% of the increased risk of mortality in type 2 diabetics.

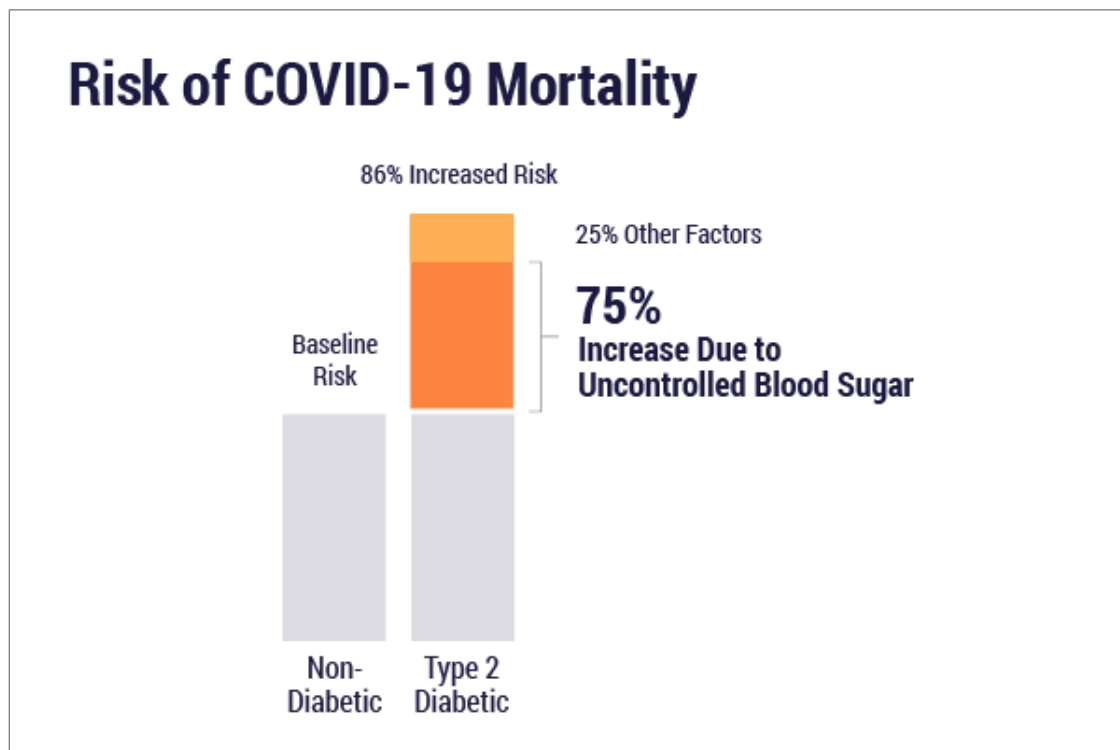


Figure 1. Type 2 diabetics experience a higher COVID-19 mortality rate compared to the general population. Our analysis found that 75% of this increased risk is explained by high blood sugar, while the remaining 25% is the result of other factors.

33,060 COVID-19 positive patients with type 2 diabetes were studied. A hemoglobin A1c (HbA1c) result was used as a measure of blood glucose control with a value greater than 7% an indicator of uncontrolled blood sugar. An HbA1c was resulted in the past one year for 43% of patients. We used a statistical technique to account for the patients without HbA1c data. This and other methods are addressed in the attached PDF.

Data are pooled from 41 healthcare organizations representing 412 hospitals that span 21 states and cover 167 million patients.

NOTES ON OUR METHODS

We used a natural effects model to evaluate whether HbA1c mediates the relationship between type 2 diabetes and COVID-19 mortality (using an imputation-based approach²). This model adjusted for age group, sex, race/ethnicity, and metabolic comorbidities that frequently co-occur with diabetes, including hypertension, obesity, stroke, and vascular disease. All patients were included in our sample regardless of time since COVID-19 diagnosis.

Of type 2 diabetic patients, 56.2% did not have HbA1c documented. Examining trends at specific health systems revealed that many of these patients were admitted at a health system where they had not previously been seen. However, patients with missing HbA1c may not be receiving routine care, which may suggest they are more likely to have uncontrolled blood sugar. If higher HbA1c were associated with mortality, as our analysis has suggested, excluding these patients would minimize the association between HbA1c and COVID-19 mortality. To account for this high rate of missing HbA1c, multiple imputation was used to estimate the impact of HbA1c values for these patients based on data on comorbidities, age group, sex, and race/ethnicity. We also performed a sensitivity analysis excluding these patients.

NOTES ON OUR FINDINGS

Diabetes was associated with a 63% increase in mortality through the mechanism of uncontrolled blood sugar. Diabetes was directly associated with a 21% increase in mortality after accounting for hyperglycemia, which suggests that other mechanisms are involved.^{1,3,4} The ratio of the indirect effect to the total effect is 0.75.

When we excluded patients with missing HbA1c rather than using multiple imputation, uncontrolled blood sugar explained a smaller percentage of the association between diabetes and COVID-19 mortality. The ratio of the indirect effect to the total effect fell from 0.75 to 0.43.

Several characteristics of our dataset may impact the findings. We controlled for age group rather than exact age, so the independent association between type 2 diabetes and COVID-19 mortality could be the result of imprecision in our age measurement (i.e., residual confounding). In addition, we classified HbA1c as a binary (high vs. low) rather than continuous variable, meaning that our results may not accurately reflect the impact of HbA1c. Future research may confirm these findings using more precise clinical indicators of diabetic control and investigate additional mechanisms that could help explain the high mortality rate among type 2 diabetics with COVID-19.

DATA DEFINITIONS

Term	Definition
Type 2 Diabetes	SNOMED (422014003 or 44054006) AND NOT (199223000)
COVID-19 Positive Patient	Patient with a positive SARS-CoV-2 lab result or a COVID-19 diagnosis.
COVID-19 Related Death	A COVID-19 patient with a death date or discharge date with discharge disposition of deceased within 6 weeks of their COVID-19 “start date.”

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Document Date: August 11, 2020

Data Date: June 12, 2020

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