

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Retrospective Case Cohort Study of 3,219 Hospitalized Patients with COVID-19 in Southeast Michigan
AUTHORS	Mulhem, Elie; Oleszkowicz, Andrew; Lick, David

VERSION 1 – REVIEW

REVIEWER	Eleftheria Vasileiou The University of Edinburgh, Scotland, UK
REVIEW RETURNED	02-Aug-2020

GENERAL COMMENTS	<p>This retrospective cohort study investigated characteristics and outcomes among COVID-19 positive hospitalised patients. Characteristics and outcomes under investigation included demographic, clinical conditions, medications and hospital discharge or death. The timely study design and data analysis of this study is a first but important step towards improving our understanding of the demographic and clinical profile of hospitalised patients and their subsequent outcomes.</p> <p>METHODS No information on the deprivation level of this population was included. Is it possible that deprivation rather than race explains some of the increased risk of hospital admissions seen in some ethnic groups in this study?</p> <p>RESULTS Asthma was not significantly associated with the study's outcomes of interest. No significant association of asthma with COVID-19 related outcomes is also seen in other studies. Do authors have a theory of why asthma seems to have a protective effect based on their data?</p> <p>DISCUSSION The strengths and implications of this study were not discussed. Could authors include a few lines on these?</p>
-------------------------	---

REVIEWER	Conor McAloon University College Dublin Ireland
REVIEW RETURNED	23-Sep-2020

GENERAL COMMENTS	<p>This is an interesting study. I just have a few comments that I think should be addressed in a revised manuscript.</p> <p>Introduction</p>
-------------------------	---

	<p>As a general comment it would be useful to have an additional paragraph that articulates the motivation for the study, how might these findings be useful?</p> <p>Line 12-14 - The number of cases in Michigan is reported but for the purpose of the international reader, it would be useful to quote the population of the state to put these figures in context.</p> <p>Methods Were reporting guidelines used for this study? If so it should be stated which were used.</p> <p>As general comment, what is presented in the methods section is clearly written, however there are a lot of gaps. For example, the results describe 3 different models - but there is no mention of these in the methods section. The methods behind the three different models should be described here.</p> <p>Patients still in hospital were not included in the study. This seems reasonable, but it will bias your summary (median) of the duration of hospital stay downwards for both those who died and those who did not (by excluding those with exceptionally long hospital stays). This step needs to be discussed as a limitation.</p> <p>The modelling section is not adequately described. Each model and the variables offered to the model should be described separately. Furthermore the model building process is not described adequately to allow reproduction: Were all of the variables in each model added to the multivariable model together, or were they evaluated first based on the bivariate to only add some terms to the model? If so, what were the criteria for adding the multivariable model? What were the criteria for retaining variables in the model? Did you look for interactions between all of the variables or only those that were significant? What were the criteria for retaining interaction terms within the model. If you dropped variables from the model, did you try adding them to the final model? How did you deal with correlated variables when adding them to the model? Did you assess for any non-linear associations between the odds of death and continuous variables? Also could you please check your use of the term "multivariate" (as opposed to multivariable) -Many would assume this to mean you are assessing multiple outcomes.</p> <p>Results I think you should present the results of the three models - If space does not allow then I would advise adding the tables of additional models as supplementary materials.</p> <p>The structure of the results section is a little confusing. First you describe descriptive statistics, then model results, then summarise mortality, and then into interactions.</p> <p>However, I would suggest that this section would flow better if the mortality section was moved to after or within the descriptive statistics section, then the model outcomes description (including the interaction terms since these are part of the model).</p> <p>In explaining your results you suggest the reason that mortality was lower than NY might be due to reduced number of cases being admitted at peak resulting in less strain on your hospitals.</p>
--	--

	<p>But this obviously depends on the capacity of the two hospital systems as well as the number of cases. Therefore it might be useful if the numbers presenting at peak in both areas could be compared using a consistent denominator (e.g. per 100,000 population).</p> <p>Re redirecting some patients to other hospitals - have you any information on the criteria for redirecting these patients - are they likely to be lower risk patients for example?</p> <p>"This difference in age and possibly the fact that our hospital system drew more suburban than urban patients could probably explain the lower rate of mortality in Blacks compared to the State reported rates." It would be useful to know how the estimate for Race changed when age was added to the model.</p> <p>Table 1- it would be useful to note in the caption what the P-values here represent</p>
--	--

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
 Reviewer Name
 Eleftheria Vasileiou

Institution and Country
 The University of Edinburgh, Scotland, UK

Please state any competing interests or state 'None declared':
 None

Please leave your comments for the authors below This retrospective cohort study investigated characteristics and outcomes among COVID-19 positive hospitalised patients. Characteristics and outcomes under investigation included demographic, clinical conditions, medications and hospital discharge or death. The timely study design and data analysis of this study is a first but important step towards improving our understanding of the demographic and clinical profile of hospitalised patients and their subsequent outcomes.

METHODS

-No information on the deprivation level of this population was included. Is it possible that deprivation rather than race explains some of the increased risk of hospital admissions seen in some ethnic groups in this study?

Added to the method section: White patients tend to live in suburban communities while Black patients tend to live in urban and poorer community

RESULTS

-Asthma was not significantly associated with the study's outcomes of interest. No significant association of asthma with COVID-19 related outcomes is also seen in other studies. Do authors have a theory of why asthma seems to have a protective effect based on their data?

Asthma in our data did not increase the risk of in-hospital mortality, but did not have a protective effect, odd ratio: 1.14 (0.84 to 1.55) P value: 0.398. we reported about 13% prevalence of asthma in our patient population similar to other studies [1, 2]. Some studies have suggested that type 2 immune response may provide protection against COVID-19 [3].

1. Grasselli, G., et al., Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA, 2020. 323(16): p. 1574-1581.
2. Richardson, S., et al., Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA, 2020.
3. Liu, S., Y. Zhi, and S. Ying, COVID-19 and Asthma: Reflection During the Pandemic. Clin Rev Allergy Immunol, 2020. 59(1): p. 78-88.

DISCUSSION

-The strengths and implications of this study were not discussed. Could authors include a few lines on these?

Added strength in the discussion section before limitations "Strength of the study includes that it is the largest report of hospitalized COVID-19 patients in Southeast Michigan, and we included diverse population from a largest health system in Detroit metropolitan area"

Revised the conclusion and added study implications

Reviewer: 2

Reviewer Name

Conor McAloon

Institution and Country

University College Dublin

Ireland

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below This is an interesting study. I just have a few comments that I think should be addressed in a revised manuscript.

Introduction

-As a general comment it would be useful to have an additional paragraph that articulates the motivation for the study, how might these findings be useful?

Added to Introduction "Understanding the clinical characteristics of hospitalized COVID-19 patients in the Midwest region of the United States will help to provide a more complete description of this population on a national level."

-Line 12-14 - The number of cases in Michigan is reported but for the purpose of the international reader, it would be useful to quote the population of the state to put these figures in context.

Added in the methods section: Southeast Michigan is the Metro area of Detroit and is home for 4.5 Million people, almost half of the population of the State of Michigan.

Methods

-Were reporting guidelines used for this study? If so it should be stated which were used.

See STROBE checklist

-As general comment, what is presented in the methods section is clearly written, however there are a lot of gaps. For example, the results describe 3 different models - but there is no mention of these in the methods section. The methods behind the three different models should be described here.

Described the models in the supplement section we added

-Patients still in hospital were not included in the study. This seems reasonable, but it will bias your summary (median) of the duration of hospital stay downwards for both those who died and those who did not (by excluding those with exceptionally long hospital stays). This step needs to be discussed as a limitation.

We did discuss this point in the limitation section.

-The modelling section is not adequately described. Each model and the variables offered to the model should be described separately. Furthermore the model building process is not described adequately to allow reproduction: Were all of the variables in each model added to the multivariable model together, or were they evaluated first based on the bivariate to only add some terms to the model? If so, what were the criteria for adding the multivariable model? What were the criteria for retaining variables in the model? Did you look for interactions between all of the variables or only those that were significant? What were the criteria for retaining interaction terms within the model. If you dropped variables from the model, did you try adding them to the final model? How did you deal with correlated variables when adding them to the model? Did you assess for any non-linear associations between the odds of death and continuous variables?

We described the modeling in the supplement section added to the manuscript

-Also could you please check your use of the term "multivariate" (as opposed to multivariable) -Many would assume this to mean you are assessing multiple outcomes.

We checked and "multivariate" is the term

Results

-I think you should present the results of the three models - If space does not allow then I would advise adding the tables of additional models as supplementary materials.

Added in the supplement section

-The structure of the results section is a little confusing. First you describe descriptive statistics, then model results, then summarise mortality, and then into interactions. However, I would suggest that this section would flow better if the mortality section was moved to after or within the descriptive statistics section, then the model outcomes description (including the interaction terms since these are part of the model).

We moved mortality section to after descriptive stats and renumbered table 3 and 4

-In explaining your results you suggest the reason that mortality was lower than NY might be due to reduced number of cases being admitted at peak resulting in less strain on your hospitals. But this obviously depends on the capacity of the two hospital systems as well as the number of cases.

Therefore it might be useful if the numbers presenting at peak in both areas could be compared using a consistent denominator (e.g. per 100,000 population).

The report from NY, like ours did not include all the hospitalized patients in the area. For that reason, we cannot report a denominator or calculate the number of cases per 100,000 during the peak period.

-Re redirecting some patients to other hospitals - have you any information on the criteria for redirecting these patients - are they likely to be lower risk patients for example?

Since Southeast Michigan is most densely populated part of the State, the local health officials gave permission to Southeast Michigan hospitals to transfer patients to other hospitals in the state which did not have many COVID-19 admissions during the peak of the pandemic.

-"This difference in age and possibly the fact that our hospital system drew more suburban than urban patients could probably explain the lower rate of mortality in Blacks compared to the State reported rates."

It would be useful to know how the estimate for Race changed when age was added to the model.

Added to discussion "Further evaluation of the data showed 26.7% of Blacks in the study were 50 years of age or younger compared to 12.5% of whites while only 11.6% of Blacks were over the age of 80 years compared to 30.4% of whites. This difference in age distribution probably contributed to the lower rate of mortality in Blacks."

-Table 1- it would be useful to note in the caption what the P-values here represent

Added in the caption of table 1 "P value for the difference between discharged alive and died in the hospital groups"

VERSION 2 – REVIEW

REVIEWER	Eleftheria Vasileiou The University of Edinburgh, UK
REVIEW RETURNED	13-Dec-2020
GENERAL COMMENTS	Authors have addressed all suggested revisions and manuscript has now improved.