Scientific Research Publishing

Open Journal of Epidemiology, 2023, 13, 128-143
https://www.scirp.org/journal/ojepi
ISSN Online: 2165-7467
ISSN Print: 2165-7459

Diabetes Risk Factor and Its Relationship to Increasing Coronavirus (COVID-19) Mortality Rate in United States in 2019-2022: An Epidemiological Study

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How to cite this paper: Zeidan, H., Zeidan, I. and Scholer-Bland, L. (2023) Diabetes Risk Factor and Its Relationship to Increasing Coronavirus (COVID-19) Mortality Rate in United States in 2019-2022: An Epidemiological Study. *Open Journal of Epidemiology*, **13**, 128-143.
https://doi.org/10.4236/ojepi.2023.132010

Received: January 18, 2022
Accepted: March 13, 2023
Published: March 16, 2023

Abstract

As an effort to understand the effect of diabetes on the increasing rate of COVID-19 infection, we embarked upon a detailed statistical analysis of various datasets that include COVID-19 infection and mortality rate, diabetes and diseases that may contribute to the severity and risk factor of diabetes in individuals and this impact on COVID-19 and the mortality rate. These diseases include respiratory diseases, cardiovascular diseases, and obesity. Equally significant is the statistical analysis on ethnicity, age, and sex on COVID-19 infection as well as mortality rate. Their possible contributions to increasing the severity and risk factor of diabetes as a risk to mortality to individuals who have COVID-19. **Objectives:** The ultimate objectives of this investigation are as follow: 1) Is there a risk factor of diabetes on COVID-19 infection and increasing mortality rate? 2) To what extent do other disease conditions that include, obesity, heart failure, and respiratory diseases influence the severity and risk factor of diabetes on increasing COVID-19 infection and mortality rate? 3) To what extent does age, race, and gender increase the mortality of COVID-19 and increase the severity and risk factor of diabetes on COVID-19 mortality rate? 4) How and why COVID-19 virus increases the risk of diabetes in children? 5) Diabetes and COVID-19: Who is most at Risk? Lastly, understanding the misconception of COVID-19 and diabetes.

Keywords

Middle East Respiratory Syndrome Coronavirus (MERS-COVID) Infection, Risk Factors, Omicron Virus, COVID-19 Risk on Children, Interactions of Independent Variables, Poisson Regression, Linear Regression

1. Introduction

More than 425 million people across the globe have diabetes, which can be further classified into type$_1$ (T_1D) and type$_2$ (T_2D). T_2D is the most prevalent form of diabetes, constituting more than 85% - 95% of all diabetes cases [1] [2]. The etiology of T2D is closely intertwined with obesity and results from chronic inflammation induced by excess adipose tissue. Stressed adipocytes and adipose tissue macrophages secrete numerous proinflammatory mediators that result in chronic low-grade inflammation, which alters homeostatic glucose regulation by decreasing cellular responsiveness to insulin [3].

In a recent investigation by Emory University School of Medicine investigators reported that death rates are four times higher among people with diabetes and hyperglycemia who are infected with COVID-19. The investigators used health data from 1225 individuals who were admitted to Emory University hospital with COVID-19 between March 1 and April 6, 2020. This new research has found that people with diabetes and poorly managed hyperglycemia who are hospitalized with COVID-19 have a much higher death rate and longer length of hospital stay that is four times higher than people without these conditions. Forty-two percent of those without a prior diagnosis of diabetes before being admitted, and who developed hyperglycemia during their time in the hospital died [4].

In another recent study, reported by Robert, A, *et al.* in 2021 showed that epidemiological studies identified diabetes as the primary comorbidity associated with severe or lethal Middle East respiratory syndrome coronavirus (MERS-COVID) [5].

In a very insightful investigation led by John Hopkins researchers in a collaborative effort with the University of Maryland, investigators identified diabetes as the primary comorbidity associated with the lethal Middle East respiratory syndrome coronavirus (MERS-COVID). In 2012 MERS-COVID has caused over than 2400 cases and more than 800 deaths in Saudi Arabia [6] [7]. Understanding how diabetes affects COVID-19 and MERS is highly crucial and significant because of the global burden of diabetes (Type I and 2) and pandemic potential of COVID-19 and MERS-COVID. The researchers concluded from their outstanding investigation that upon infection with COVID-19 or MERS-COVID, diabetic patients had a prolonged phase of severe disease and delayed recovery that was independent of virus titer. Detailed histological analysis concluded that diabetic patients had delayed inflammation, which was prolonged through 21 days after infection [8] [**Figure 10**].

A recent detailed study reported in 2020 that 17 million identified Crucial Factors for Coronavirus Deaths. The largest study yet confirms that race, ethnicity, age, and sex raise an individual's chances of dying from COVID-19 [9].

Risk factors that are associated with the development of more severe disease or death following COVID-19 and MERS-COVID infection include gender. This is specifically seen in males, who are older age, and have comorbid illnesses [9]. Diabetes, obesity, heart, and kidney diseases, underlying respiratory disease, and hypertension have all been shown to predispose a patient to more severe or le-

thal disease after COVID-19 and MERS-COVID infection [6] [7].

Recently, Vakharia, Jin 2020 reported the misconception of diabetes and COVID-19 Risk factor by stating that "We do not believe that people with diabetes are more likely to get COVID-19 than the general population," [10]. They are, however, at risk for more severe outcomes, based on what we have been learning so far from research studies. We know from our experiences with other viral illnesses that patients with diabetes also tend to have more severe reactions to those illnesses [10]. Although the exact cause of severe outcomes in patients with diabetes and COVID-19 is not clearly understood, research over the years has suggested that people who have diabetes may have impaired immune systems, which would affect their ability to heal from an illness or disease quickly. Furthermore, diabetes, especially if uncontrolled for a long period of time, may cause inflammation, which also affects the immune system [10]. Studies have reported that patients with well-controlled diabetes who have been hospitalized for COVID-19 have a higher rate of survival. Better controlled diabetes is also associated with lower markers of inflammation, which may explain this better rate [10]. Equally significant, within the diabetic population for those most at risk for severe COVID-19 outcomes are elderly patients, though we are increasingly seeing younger patients coming in, and men. Hispanic and Black patients seem to be disproportionately affected, which could be related to social determinants of health or differences in job type (essential workers), extended-family home structure (making it more difficult to physically distance) or reliance on public transportation [10].

Fink J recently reported that with a soaring rate of hospitalizations and deaths among children, caused by the new Omicron variant, as well as a likely increase in long COVID infection, the Centers for Disease Control and Prevention now has added diabetes to the list of conditions produced by COVID-19 among children [11] [12]. According to IQVIA's data, children with COVID were 2.66 times more likely to be diagnosed with diabetes than non-infected cohorts during the pandemic and 2.16 times more likely than the pre-pandemic cohort that had an acute respiratory illness (non-COVID infection) [12]. For the COVID group, the incidence of diabetes was 316 per 100,000 person-years, while for the non-COVID group, it was around 118 per 100,000 [13]. Health Verity's data found that children who had been infected with SARS-CoV-2 were 1.31 times more likely to be diagnosed with diabetes. In absolute terms, the difference was 399 vs. 304 per 100,000 person-years, and the difference was statistically significant for both medical data records [13]. The CDC reported that a recent European study found an increase in type 1 diabetes among children during the pandemic. Pre-existing diabetes is a risk factor for severe COVID, but so was having very high blood sugar levels at the time of infection [12] [13]. 44% of Black children and 26% of Hispanic children experienced severe disease, compared with 22% of White children, but the association between severe COVID-19 and race or Hispanic ethnicity was not statistically significant [14].

The exact pathophysiologic mechanism behind developing diabetes after

COVID-19 remains to be investigated. It is believed that the coronavirus can infect the pancreas cells that make insulin. Furthermore, other research points to the virus' impact on fat cells that lead to errors in metabolic signaling that leads to diabetes.

The diabetes report only adds to the frightful impact of the Omicron variant on children. According to the CDC, the hospitalization rates among children are soaring across the United States. As of last week, the number of children admitted to hospitals has climbed to 800 each day, more than twice the figures from two weeks ago. In the week ending December 31, 2021, the American Academy of Pediatrics reported more than 325,000 children had been infected. This high will be surpassed by all accounts when they publish their report today [12] [15].

2. Methods/Analysis

2.1. Methods

We performed a comprehensive search of MEDLINE via PubMed, Google Scholar, and EMBASE, CDC and NCHS data sets and to identify corresponding peer reviewed publications between January 1, 2019, and December 2021, that had data on diabetes in patients with COVID-19. The data collection form used in this study was created by the study authors and designed to gather information on statistical methods described in each randomly selected article. The results presented in the following tables in this article are framed to correspond to the data collection form. In reviewing each article, the selection of any variable on the review form indicated that variable had been explicitly or implicitly reported within the text of the paper.

2.2. Analysis

We conducted statistical analyses using Stata software. We performed statistical analysis that include descriptive and inferential statistics to characterize data, frequency data for COVID and various diseases, Poisson and linear regression analysis to characterize the nature of the variable's interaction, and meta-analysis. We deemed p values of 0.05 statistically significant, with tests being two-sided. Independent variables include, age, diabetes, obesity, respiratory, cardiovascular, kidney failure diseases, ethnicity, gender. Interaction variables, diabetes*obesity, diabetes*respiratory diseases. Dependent variables include COVID-19 mortality rate. Data were counts, discrete, counts, and categorial.

3. Results

1) Coronavirus Mortality Rate and Age: Groups at Higher Risk

a) Interpretation of **Figures 1-10** and **Tables 1-9**: The results shown clearly in all figures and tables support that age plays a significant risk factor for Coronavirus-19 infection. Furthermore, Asians have the lowest mortality rate at all ages and, Hispanic/Latino have the highest mortality rate among ages of 18 - 45 years (**Figure 3**) and pneumonia, influenza and respiratory disease increased the risk for COVID-19 mortality rate (**Table 1**).

COVID Data in the US by Age		
	Count Cases	Count Deaths
0 - 29	1732614	897
30 - 64	2810447	30454
65 - 85+	804145.00	119758.00
Chi	P	
1281793941339	<0.00001	<0.05

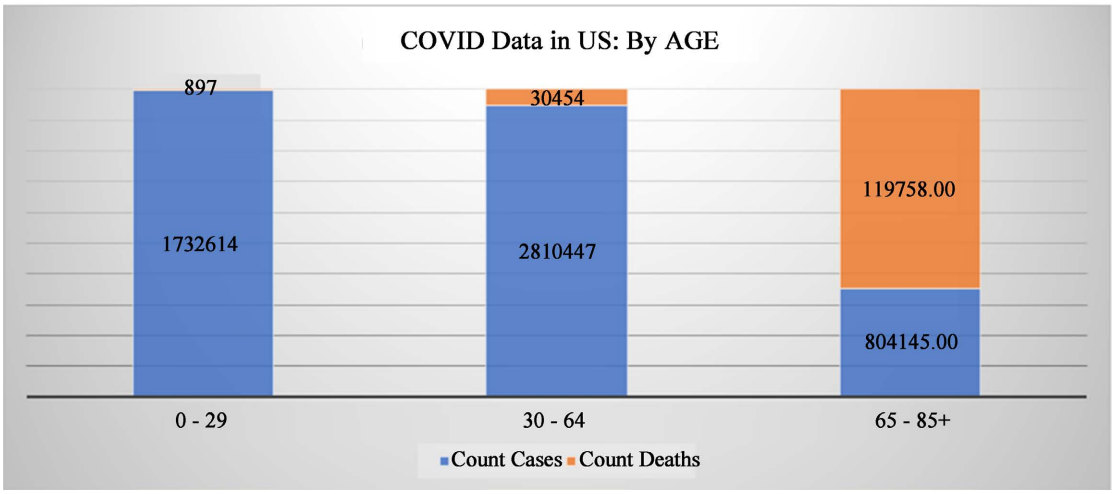

Figure 1. COVID-19 data by age.

Age Group	% Case	% Deaths
0 - 4	1.8	<0.1
5 - 17	6.8	<0.1
18 - 29	23.7	0.5
30 - 39	16.7	1.3
75 - 84	4.3	26.4
85+	3.2	31.7

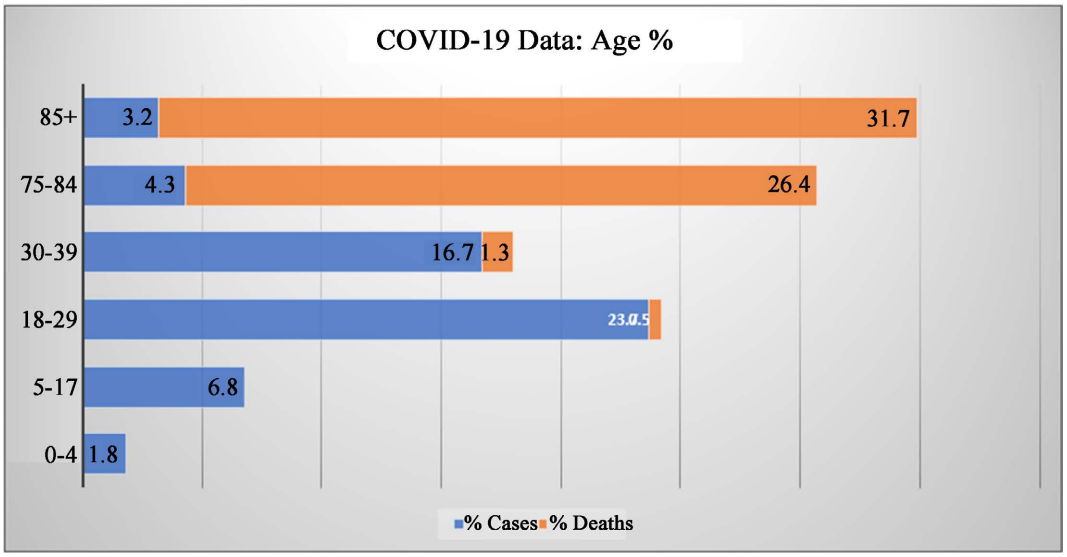

Figure 2. COVID-19 cases/deaths by age.

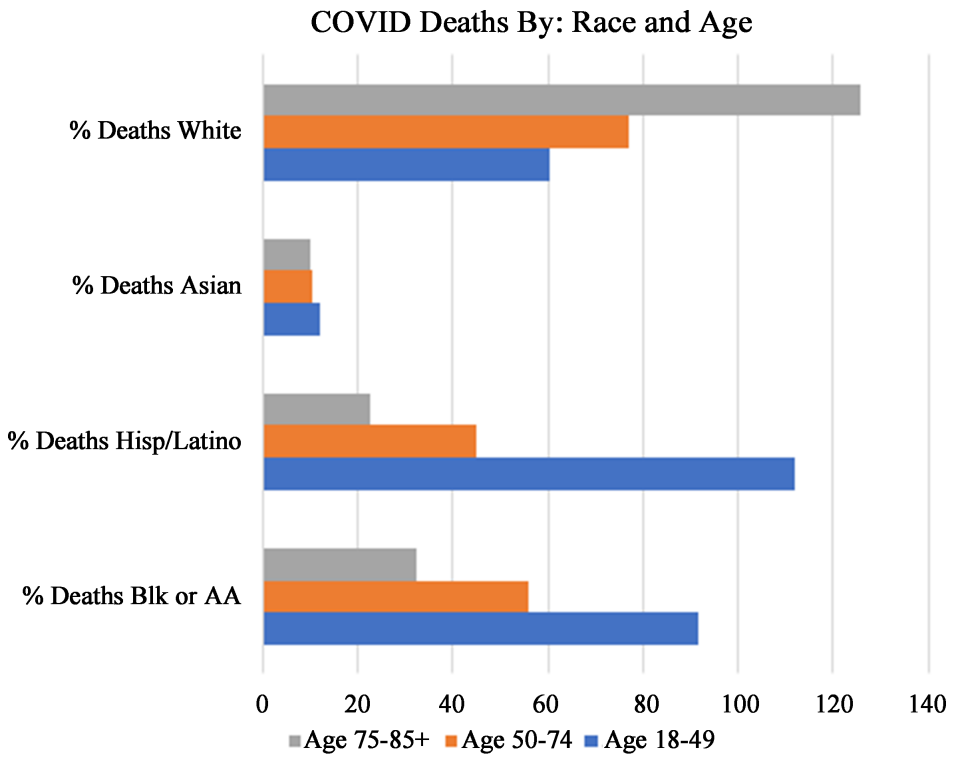

Figure 3. COVID-19 deaths by age and race. Asians have the lowest mortality rate at all ages and, Hispanic/Latino have the highest mortality rate among ages of 18 - 45 years.

Table 1. COVID-19 cases by comorbidities.

State	State	Age group	COVID-19 Deaths	Pneumonia Deaths	Pneumonia and COVID-19 Deaths	Influenza Deaths	Pneumonia, influenza, or COVID-19 Deaths	Total Deaths
United States	Male	0 - 24 years	276	167	11	64	274	15,397
United States	Male	24 - 64 years	48,559	6061	3129	395	10,109	588,526
United States	Male	65 - 85+ years	70,545	23,890	11,130	807	36,626	676,401

As shown in Figure 4, diabetes (Type 1 and 2) and obesity contribute the highest increase in COVID-19 mortality rate, followed by respiratory disease. Figure 5, on the other hand, shows obesity risk factor is higher than diabetes, however, it must be clearly stated that obesity increases the risk of type 2 diabetes and therefore, collectively diabetes is considered the highest risk factor for increasing COVID-19 mortality rate.

Poisson graph is shown below in Figure 6(a) and Figure 6(b), with only 10 obs about 85% of COVID-19 mortality rate for all groups are 5000 cases. Data do not show a normal distribution, it follows Poisson distribution. Figure 6(b) includes more obs, this counts for more spread and better analysis for a larger group. The data appears to be more diverse with 25 obs. The data skewed positively and is more pronounced with 25 observations and shows an apparent Kurtosis.

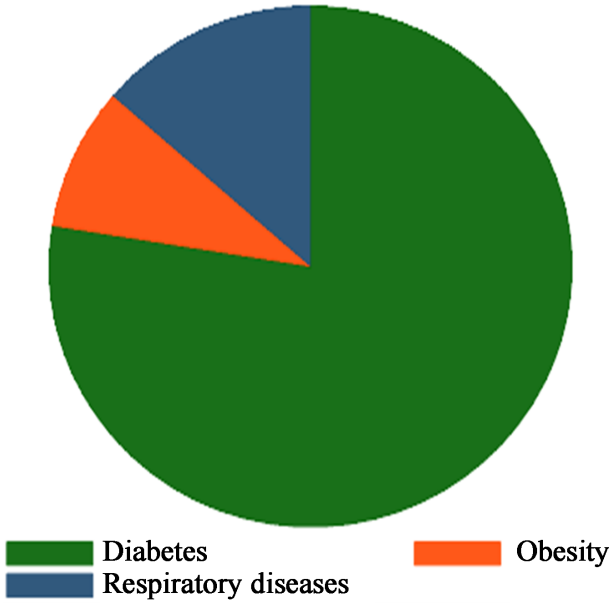

Figure 4. COVID-19 cases by comorbidities. Diabetes is the major risk factor for increasing COVID-19 mortality rate.

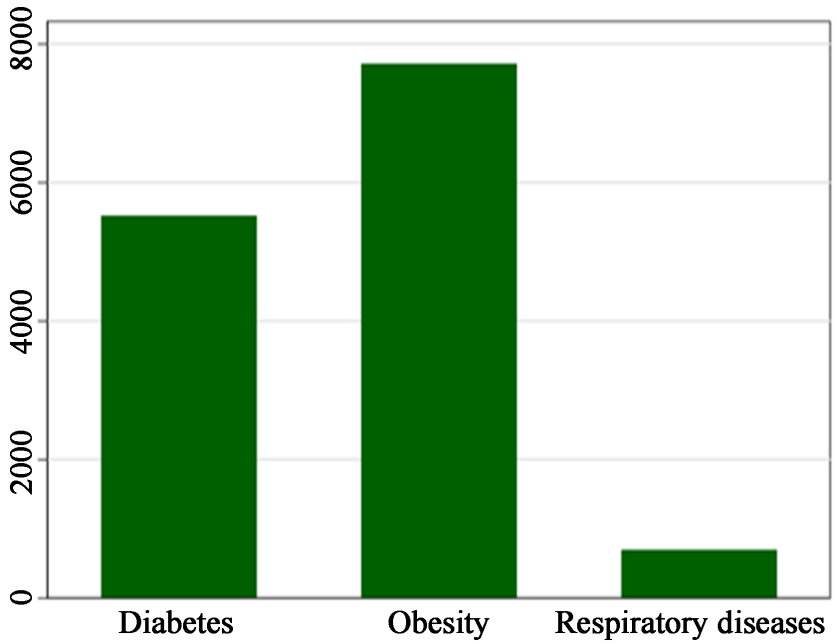

Figure 5. Mean number of COVID-19 deaths/comorbidities. Obesity, a major contributor to Type 2 diabetes is the highest risk for increasing COVID-19 mortality rate. Diabetes (Type 1 and 2) are the highest risk for COVID-19 mortality rate.

COVID-19 mortality cases by age, and regions are shown in **Figure 7(a)** and **Figure 7(b)**.

Age plays a severe negative impact on individuals. Age of 75 and above and the state of New York had the highest number of cases reported. **Figure 8(a)** shown below highlights US COVID cases and mortality rate by gender, while **Figure 8(b)** focuses on selected states and their COVID mortality rate by gender. Overall

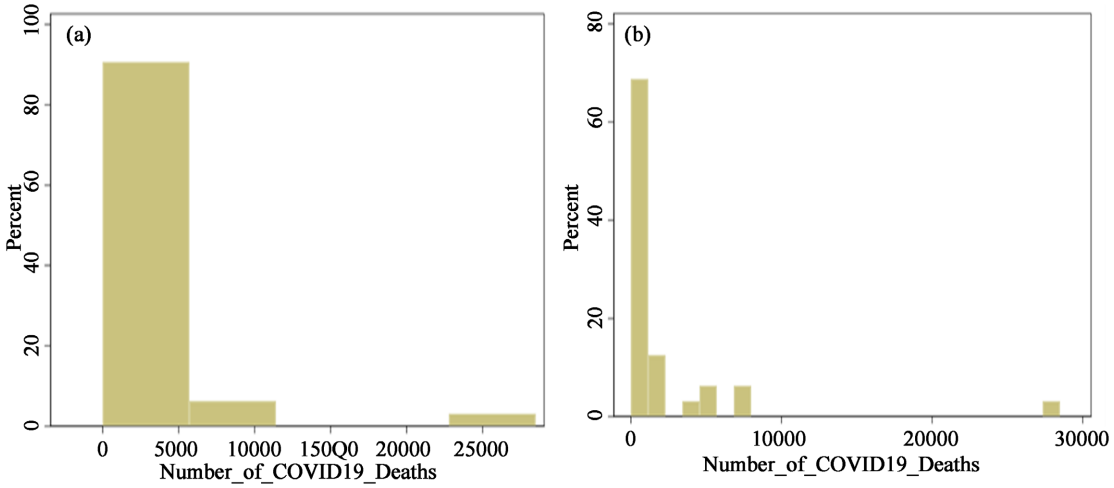

Figure 6. Poisson distribution for COVID mortality rate for 10 observations (22) 25 observations (23).

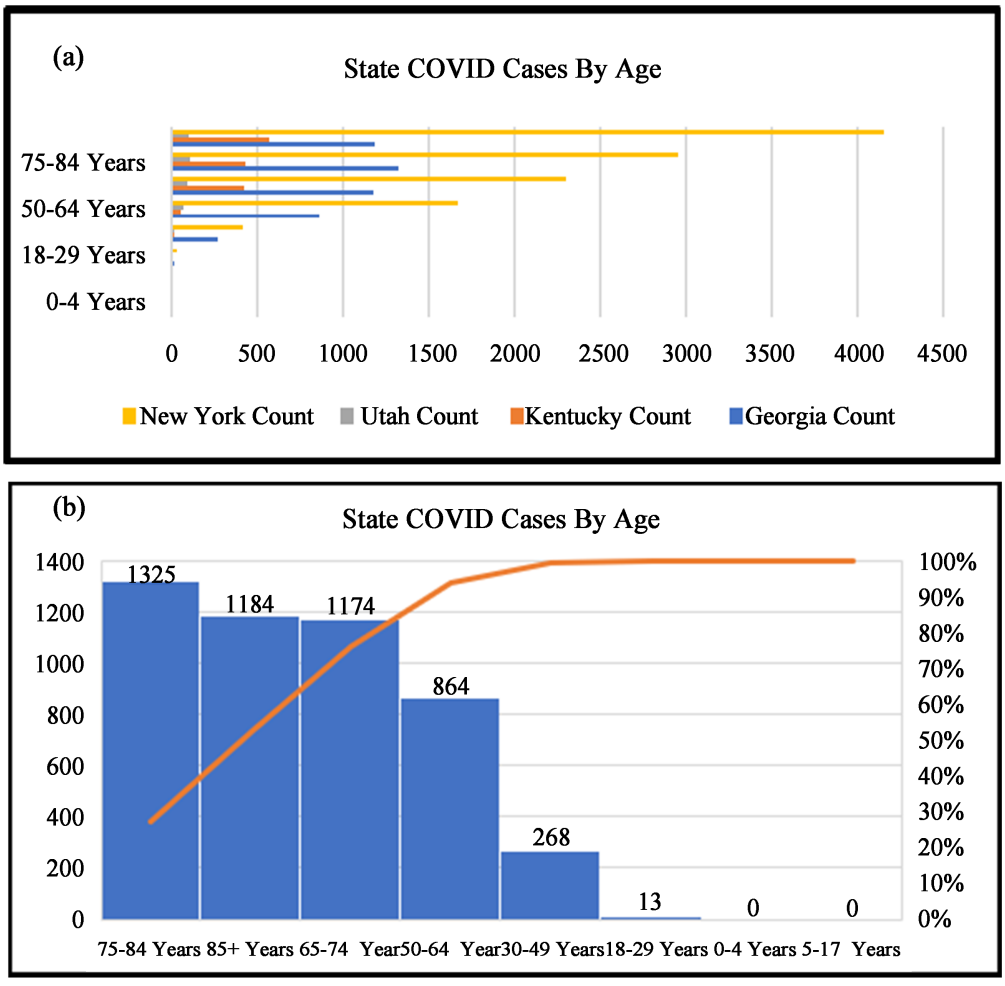

Figure 7. Risk COVID-19 mortality rate by age and states.

US COVID data shown in a, it appears that the number of COVID cases for female is higher comparing male, however, the mortality rate for male is much higher comparing to female. For the selected states chosen in **Figure 7** and **Fig-**

ure 8, it appears that COVID-19 cases for female are higher than male and the mortality rate for male is higher.

- Conclusion: Males are at a higher risk factor comparing to female. It will be interesting to correlate these findings with the physiological and clinical interpretation and determine whether this variation is statistically significant and if it is not, why it is clinically significant.

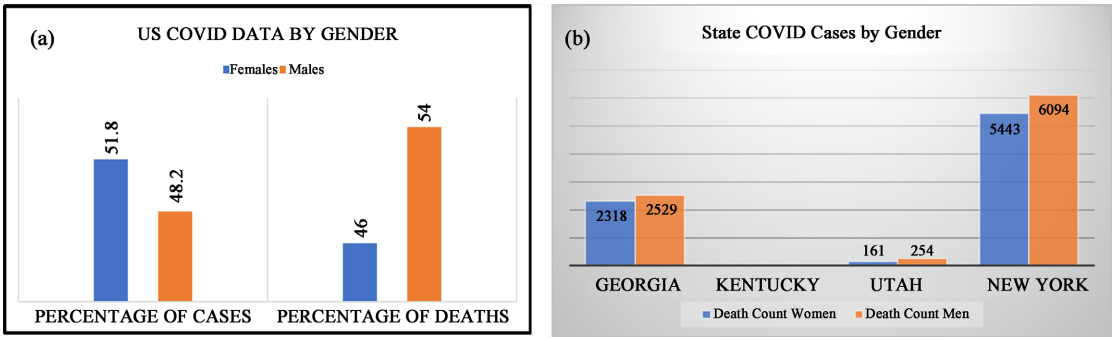

Figure 8. Effect of gender on COVID-19 on mortality rates.

Minority populations COVID-19 mortality rate is highlighted in Figure 3, Figure 9 and Table 2. Hispanic Latinos population are the highest followed by black population.

Table 2. Coronavirus mortality rate: Groups at higher risk.

Race	Percent	Count
Hispanic Latino	27.8	931,979
Amer Indian	1.2	39,736
Asian	3.2	107,367
Black	16.9	567,461
Native Hawaiian	0.4	13,861
White	45.9	1,539,741
Others	4.6	152,978

Summary Statistics analysis for the mean of selected groups of COVID-19 patients with diabetes, obesity and respiratory diseases is shown in Table 3. The mean value is for 10 obs for diabetes risk factor on Coronavirus mortality rate is 5528. The mean values are 789 for 8 obs for obesity risk factor on Coronavirus mortality rate and mean of 693 for 14 obs for respiratory disease. Frequency tables follow for the three categories by all ages.

Results of descriptive and interferential analysis and frequency condition group/tabulation condition group are shown in Table 4 and Table 5 respectively.

b) Interpretation of Table 4 & Table 5: The total mean for the COVID-19 mortality rate is 4072. The mean value for diabetes is 0.466, obesity is 0.4523, and for respiratory disease 0.424. Obesity is consistent which indicates no miss-

ing observations, and all are considered in the mean value.

c) Linear Regression Model:

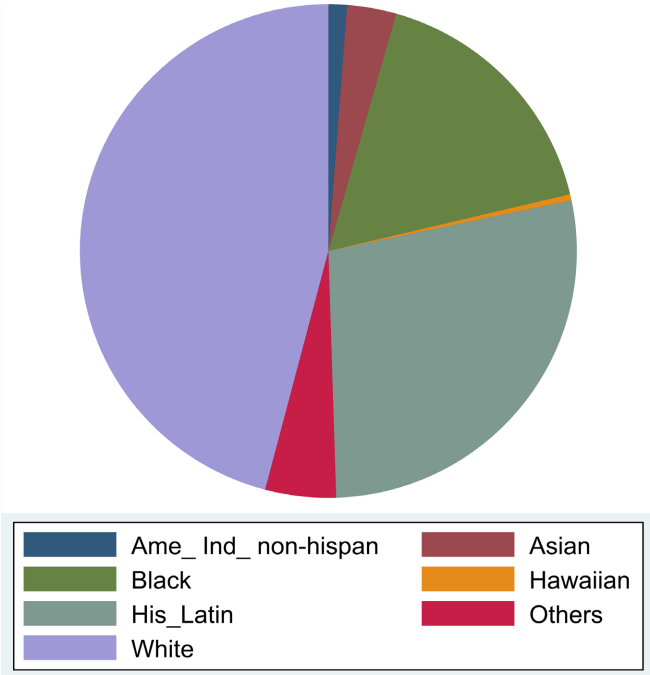

Figure 9. Effect of race on COVID-19 mortality rate. Asian population has the least mortality rate, white have the highest, followed by His-Latin, Black populations.

Table 3. Summary statistics analysis for the mean of selected groups with diabetes, obesity and respiratory diseases.

Variable	Observations	Mean	Std Dev	Min	Max
	Condition Group = Diabetes				
# of ~S	10	5528	8679	2	2848
	Condition Group = Obesity				
# of ~S	8	789	572	89	1579
	Condition Group = Respiratory Disease				
# of ~S	14	693	937	0	3550

Table 4. Frequency condition group/tabulation condition group.

Condition/Group	Frequency	Percent	Cumulative
Diabetes	10	31.25	31.25
Obesity	8	25	56.25
Respiratory Disease			
	14	43.75	100
	32	100	

Table 5. Results of descriptive and interferential analysis.

Variable	Observations	Mean	Std Dev	Min	Max
Condition_~p	0				
Age_Group	0				
Number_of_~s	33	4072	11,791	0	63,150
C2	33	2.12	857,233	1	3
A2	28	4.5	2.03	1	8
Diabetes	33	0.303	0.466	0	1
Obesity	33	0.272	0.452	0	1
Respiratory	33	0.424	0.501	0	1

Table 6 shown below represents Linear Regression statical data and analysis for the risk of diseases on COVID-19 mortality rate. This data is a continuation to the statical data presented in Table one for the same populations who are at risk with diabetes, obesity, and respiratory diseases and with the same mean group ranges presented in Table 3 and Table 4.

$$\beta_0 = -1585.43,\ \beta_1 = 743.67.$$

- Linear Regression Model:

$$Y = B_o + B_1\left(X_1\right) + e$$

Number of COVID death = −1585.43 + 743.67 (age group) + e

- Interpretation: A change of one unit of age group will increase COVID death by 743 unit. All other variables are kept constant. This is statistically significant ($p = 0.033$, $p < 0.05$). R-squared= 0.149 (14.9% variations in the data predictors in this data set.

Table 6. Linear regression model of data and analysis (1 set).

Regression Number_COVID Deaths_Age			
Source	**SS**	**df**	**MS**
Model	12,139,786	1	12,139,786
Residual	728,238,464	30	24,274,615
Total:	849,635,850	31	27,407,608
Number Observations	32		
F(1, 30)	5		
Prob > F	0.0329		

Number of S	Coeff	St. Err	t	P > [t}	[95% Conf. interval]	
Age group	743.668	322.5155	2.24	0.033	64.214	1422.843
Cons	−1585.38	1913.978	−8.3	0.44	−594.98	233.43

- Risk of Diseases on COVID-19) Mortality Rate Graphical Presentation.

3) Poisson Regression statistical data

Table 7 shown below represent data of Poisson Regression analysis for the Risk of Diseases on COVID-19 Mortality Rate (Cont'd).

- Poisson Regression Model $\log(\lambda) = \beta_0 + \beta_1 x_1 + e$

Analyzing Table 7, β_1 = 0.3556 and β_0 value = 5.460

○ Interpretation:

If we increase age by one unit, the log-count coronavirus deaths would increase by 0.3556 units. Alternatively: an increase in age by 1 year leads to 33.56% more coronavirus death; [exp (0.3556) − 1] × 100 = 39%.

$$\log(\lambda) = \beta_0 + \beta_1 x_1 + e$$

Log Number of Coronavirus Deaths = 5.460 + 0.3556(age) + e

Log Number of Coronavirus Death = 5.460 + 0.3556 × *5520 = 1968.514

Number of COVID-19 Death = 1968.514

*mean for diabetes is taken from Table 3.

Table 7. Risk of diseases on COVID-19 mortality rate. Poisson regression.

Poisson Number of COVID-19 Death age group		
Interaction: 0	log likelihood = 60882.587	
Interaction: 1	log likelihood = 60882.508	
Interaction: 2	log likelihood = 60882.508	
Poisson regression		Number of obs = 32
		LR Chi^2 (1) = 5502.01
		Pr > Chi^2 = 0.000
log likelihood = 60882.508		Pseduo R^2 = 0.3131

Number of COVID-19 deaths	Coef.	St.Err	Z	P > [Z]	[95%] Conf.	Interval
age_ group	0.3555714	0.001602	217.85	0	0.352373	0.3587704
_cons	5.460362	0.0126722	430.89	0	5.43525	5.485199

- Linear Regression Model (Cont'd, 2nd set).
- Statistical Analysis for Interaction of Independent variables.

*Interaction of variables (Diabetes*obesity) reg Number of_COVID19_Deaths diabetes, obesity. note: 1.diabetes#1.obesity identifies no observations in the sample.

Table 8 and Table 9 shown below represent descriptive and interferential analysis mainly to address the interactions of independent variable.

- Interpretation: Regression Model for independent Variable Interaction Y = $B_o + B_1 (x_1) + B_2 (x_2) + B_3$ (diabetes*obesity) + e.

Analyzing the data shown below in Table 8 and Table 9.

Number of Coronavirus mortality rate = 693.643 + 4826.757 (diabetes)

Table 8. Results of descriptive and interferential analysis.

Variable	Observations	Mean	Std Dev	Min	Max
Condition_~p	0				
Age_Group	0				
Number_of_~s	33	4072	11,791	0	63,150
C2	33	2.12	857,233	1	3
A2	28	4.5	2.03	1	8
Diabetes	33	0.303	0.466	0	1
Obesity	33	0.272	0.452	0	1
Respiratory	33	0.424	0.501	0	1

Table 9. Linear Regression (Cont'd)/Statistical variables data.

Model	300,426,504	2	150,213,252	Prob > F	0.3504	
Residual	4.1485e+09	30	138,282,458	R Squared	0.0675	
Total:	4.4489e+09	32	139,028,132	Adj R-Squared	0.0054	
				Root MSE	11,759	
Number of COVID	**Coefficient**	**Std. Error**	**T**	**P > {t}**	**95% Confidence Interval**	
01	7025	5024	1.40	0.172	−3235	17,285
10	4826	4868	0.99	0.329	−5116	14,770
Cons.	693	3142	0.22	0.827	−5724	7112

(diabetes# obesity, 0, 1), Diabetes # obesity (diabetes*obesity (1, 0).

- Number of Coronavirus mortality rate = 693.64 + 4826.76*0.303 + 7024.68* 0.452.
- Number of Coronavirus mortality rate = 693.643 + 4826.757*0.303 +e.
- Interaction of independent variables (Diabetes*obesity) (Cont'd) Number of COVID Mortality rate = 693.64 + 4826.76*0.303 + 7024.68*0.452 + 0 (diabetes*obesity) + e = 5331.303 + 0 = 5331.303.

Lung histology shows delayed and unresolved inflammation in male diabetic mice infected with MERS-COVID. Lungs were collected at days 2, 4, 7, 10, 14, and 21 after infection is shown in Figure 10.

- Conclusions and Interpretation of main results related to your research question(s).

*Key results and findings from our statistical data analysis as well as projected future investigations provided evidence that we addressed the objectives listed on page one with the abstract. Furthermore, we fulfilled the following questions:

- Is there a risk factor of Diabetes on COVID-19 infection and increasing the mortality rate?

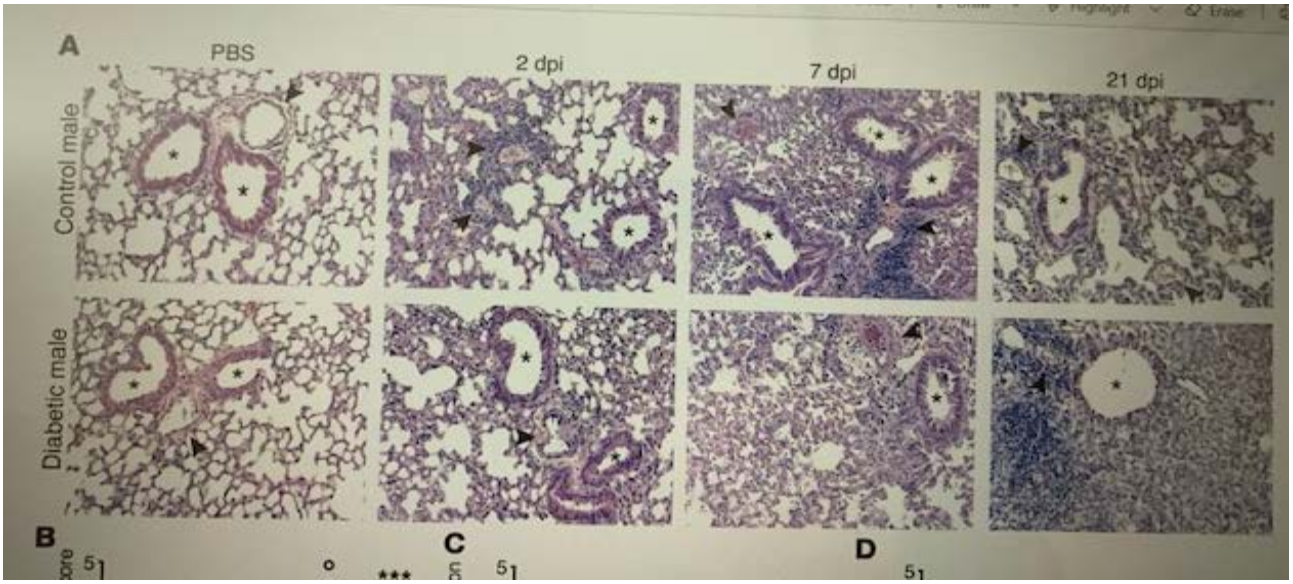

Figure 10. Lung histology shows delayed and unresolved inflammation in male diabetic mice infected with MERS-COVID. Lungs were collected at days 2, 4, 7, 10, 14, and 21 after infection (permission was granted from the publisher, Kulcsar, K, *et al.* [8]).

- We concluded that there is a significant risk factor for diabetes on increasing the mortality rate of Coronavirus infection (please, see the tables presented above that include summary statistics, regression tables, models, charts, and pie graph.

- Is there a risk factor of Age on COVID-19 mortality rate and to what extent, age and diabetes associated disease conditions mainly, obesity, respiratory, heart failure potentiate the risk factor of diabetes on COVID-19 mortality rate?
  - Our statistical data analysis concluded that there is a risk factor of age on COVID-19 mortality rate as well as the risk factor of age on diabetic patients and increasing COVID-19 mortality rate. Populations beyond the age of 60 who are diabetic, or nondiabetic are at risk. Of course, diabetic aged patients at much higher risk.
- To what extent ethnicity, and gender increase the severity and risk factor of diabetes on COVID-19 and the mortality rate due to COVID-19 infection?

- Statistical and graphical presentations on ethnicity, age and gender were analyzed. The findings are included in this presentation and details will be a key focus in future work which will include interaction between variables such as Diabetes*White, Diabetes*black, Hispanic, Latinos., Diabetes*gender.
- We wished sincerely to have statistically significant data on diabetes*obesity interaction and Diabetes*respiratory interaction variables that could support the clinical significance.
- The statistical data analysis concluded that it is statistically insignificant in this data set. All other variables are constant. However, they are clinically significant based on numerous clinical investigations.
- More analysis will follow along with interaction with other disease states such

as kidney failure*diabetes and cardiovascular diseases*diabetes interaction variables and their influence on the severity and risk factor of Diabetes on COVID-19 infection and increasing the mortality rate?

- Detailed regression analysis and models such as logistic regression will be performed on numerous data sets.

Acknowledgements

The authors would like to thank Dr. Yoon-Hoo Professor at the Augusta University for his invaluable assistance, guidance, and mentorship. This project is dedicated to Professor Dr. Ossama El-Husseiny of Cairo University who was among the first group people with the comorbidity diabetes who lost his life due to COVID-19. It is such a sad loss to the research and academic community especially with him having limited to access to the COVID-19 vaccine at the time.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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