

**Risk factors associated with disease severity in hospitalized COVID-19 patients,
Belize, March 2020 – December 2022**

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Background: Belize has a high burden of chronic non-communicable diseases (NCDs), which may increase vulnerability to severe COVID-19 outcomes. This study identified socio-demographic and clinical risk factors for severe and critical COVID-19 illness among hospitalized patients in Belize.

Methods: A hospital-based case-control study was conducted using secondary data from the Belize Health Information System. Patients admitted with laboratory-confirmed COVID-19 between March 2020 and December 2022 were included. Cases were defined as patients meeting WHO criteria for severe or critical illness; controls were non-severe hospitalized patients. Stratified random sampling by district and laboratory date produced a final sample of 176 cases and 528 controls. Logistic regression was used to estimate adjusted odds ratios (aOR) with 95% confidence intervals (CI).

Results: Severe illness was significantly associated with diabetes (aOR 5.1, 95% CI: 1.2–22.4), obesity (aOR 4.9, 95% CI: 1.5–16.4), and asthma (aOR 8.8, 95% CI: 1.1–72.2). Older age (>45 years) and male sex were associated with severity in univariate analysis but not after adjustment. Other comorbidities, including chronic renal failure, HIV, and cancer, showed no significant associations.

Conclusions: Diabetes, obesity, and asthma independently predicted severe COVID-19 among hospitalized patients in Belize. These findings emphasize the importance of targeted interventions for individuals with chronic conditions and underscore the need to strengthen NCD management as part of pandemic preparedness strategies in Belize and similar settings.

Keywords: COVID-19; risk factors; severe disease; Belize

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, rapidly spread across the globe, impacting countries with varying healthcare capacities and population health profiles. Belize, a small country in Central America, at the time the COVID-19 pandemic started in Belize on March 20, 2020 [1], grappled with a high burden of chronic non-communicable diseases like diabetes, hypertension, and obesity [2,3]. These conditions had been identified as significant risk factors for severe COVID-19 illness and mortality in numerous studies worldwide [4,5].

By December 2022, Belize had reported over 70,000 confirmed COVID-19 cases and 697 deaths, with a significant proportion of these deaths linked to pre-existing health conditions. This concerning trend highlights the urgent need to understand the specific risk factors within the Belizean population that contribute to severe COVID-19 outcomes.

This study aims to address this critical need by identifying the socio-demographic and health-related risk factors associated with severe and critical COVID-19 illness among hospitalized patients in Belize. The findings sought to guide clinical identification and management of high-risk individuals, prioritizing patient care, and informing targeted public health interventions to mitigate the impact of COVID-19 and future health threats

on the vulnerable Belizean population.

Population and Methods

A hospital-based case-control study was conducted on patients with laboratory-confirmed COVID-19 who were hospitalized across the six districts of Belize, including patients at the Karl Heusner Memorial Hospital. This institution, being the only tertiary hospital in Belize and the national referral center for severe and critical COVID-19 cases, played a crucial role. The study spanned from March 2020 to December 2022. Out of the 3,258 patients admitted with a COVID-19 diagnosis during this period, one was excluded due to insufficient data, leaving 3,257 for analysis. Of these, 1,763 were hospitalized specifically for COVID-19 or a respiratory illness that was later confirmed to be COVID-19, as opposed to other diagnoses. The defined criteria for a COVID-19 case in this study included individuals who meet clinical or epidemiological criteria and have tested positive for SARS-CoV-2 via PCR or antigen rapid diagnostic tests [6].

These 1,763 patients were subsequently categorized based on the World Health Organization's severity classifications for COVID-19 [6], including these two categories 1) severe COVID-19: patients with oxygen saturation <90% on room air, respiratory distress, or signs of pneumonia; and 2) critical COVID-19: patients experiencing acute respiratory distress syndrome (ARDS), sepsis, septic shock, or those requiring life-sustaining therapies such as mechanical ventilation [7]. In this study, patients with severe or critical disease were considered cases, while controls were patients admitted during the same period with confirmed SARS-CoV-2 infection who did not meet the WHO criteria for severe or critical illness (i.e., non-severe COVID-19). Patients were excluded if they were admitted for non-COVID-19-related reasons or had incomplete data.

Regarding inclusion, any person with a confirmed SARS-CoV-2 infection admitted for COVID-19 treatment within the specified timeframe was considered. The exclusion

criteria eliminated anyone admitted for treatment of illnesses other than COVID-19.

Data was collected through the Belize Health Information System, which aggregates comprehensive information on each patient at every encounter with the health system. This includes socio-demographic data, geographical information, lab results, prescriptions, diagnoses, and clinical notes. Secondary data analysis was performed using Microsoft Access and R software with various packages for data organization and analysis.

The required sample size was calculated using the method described elsewhere [8]. Assuming a prevalence of hypertension of 40% among controls and 52% among cases, corresponding to an odds ratio of 1.63, a 95% confidence level, and 80% power, the minimum sample size required was 180 cases and 540 controls, maintaining a 1:3 case-to-control ratio, for a total of 720 participants.

To ensure temporal and geographic representation, stratified random sampling was conducted by District and lab order date. Within each stratum, one case and up to three controls were randomly selected. Final selection was adjusted to meet the total required sample size, ensuring balanced representation across key demographic and temporal variables while maintaining the independence of cases and controls.

Data analysis

In the data analysis phase of the study, information was meticulously organized in a line list format, incorporating socio-demographic details and risk factors such as age, sex, geographical location, and clinical history of chronic illnesses. Descriptive analysis was employed to understand the demographics and characteristics of the population. For categorical and continuous variables, frequencies were expressed as percentages and medians, respectively. Statistical comparisons between cases (severe or critical COVID-

19 patients) and controls (non-severe COVID-19 patients) were made using the Chi-squared or Fisher's exact test, depending on the appropriateness for the data. The odds ratio with a 95% confidence interval was calculated to measure the strength of association between risk factors and severe COVID-19 outcomes, with a *P*-value of less than 0.05 indicating statistical significance. Subsequently, multivariable logistic regression was used to further explore the relationships between risk factors and disease severity.

Ethical considerations were carefully observed throughout the research process. Access to the data from the Belize Health Information System was restricted to authorized personnel and the principal investigator. Privacy of individuals was preserved as no personal information was disseminated and the dataset remained solely with the principal investigator and the senior biostatistician from the Ministry of Health and Wellness. The study, a secondary data analysis, received the necessary approval from the national Ethics Committee of the Belize Ministry of Health and Wellness, ensuring that all research activities adhered to ethical standards.

Results.

Table 1 presents the characteristics and clinical history of hospitalized patients with COVID-19 in Belize from March 2020 to December 2022, comparing 176 severe or critical cases to 528 non-severe controls. Among the cases, the majority were over 45 years of age, with 137 individuals (76%) falling into this older age group, compared to only 265 (49%) of controls. Conversely, younger individuals under 45 comprised 51% of the control group but only 24% of the cases, suggesting a strong association between older age and severe illness.

With regard to sex, a higher proportion of cases were male (97 individuals, 54%), whereas females comprised the majority of the control group (302 individuals, 56%). This suggests

that men were more likely to experience severe or critical COVID-19 in this cohort.

District-level distribution showed that Cayo had the highest proportion of cases at 55 (31%), followed by Belize with 41 (23%). Controls were more evenly distributed, with Belize accounting for the largest share (146, or 27%), and smaller but consistent proportions across Cayo (23%), Corozal (12%), Orange Walk (13%), Stann Creek (14%), and Toledo (12%).

In terms of clinical history, diabetes was highly prevalent among the cases, affecting 110 individuals (61%) compared to only 181 (34%) of controls. Similarly, hypertension was present in 97 cases (54%) and 213 controls (40%), indicating a higher burden of these comorbidities among those with severe disease. Obesity was also more frequent in cases (54 individuals, 73%) compared to controls (153 individuals, 61%).

Asthma and chronic renal failure (CRF) were prevalent in both groups at similar proportions. Asthma was present in 16 cases (33%) and 22 controls (31%), while CRF affected 62 cases and 109 controls, both at a rate of 75%. The presence of HIV and cancer was relatively low overall but slightly more frequent in the control group: HIV was reported in 15 controls (23%) versus 4 cases (10%), and cancer in 19 controls (27%) versus 4 cases (9.8%).

Table 1. Characteristics and clinical history of persons hospitalized with diagnoses of COVID-19 illness in Belize, during the period March 2020 - December 2022.

Characteristic	Cases and Controls	
	Cases N = 176	Control N = 528
Age Group		
≤45	43(24%)	276 (51%)
>45	137 (76%)	265 (49%)
Sex		
Female	83 (46%)	302 (56%)
Male	97 (54%)	238 (44%)
District		
Belize	41 (23%)	146 (27%)
Cayo	55 (31%)	123 (23%)
Corozal	25 (14%)	63 (12%)
Orange Walk	21 (12%)	68 (13%)
Stann Creek	24 (13%)	76 (14%)
Toledo	14 (7.8%)	64 (12%)
Diabetes	110 (61%)	181 (34%)
Hypertension	97 (54%)	213 (40%)
HIV	4 (10%)	15 (23%)
Cancer	4 (9.8%)	19 (27%)
CRF	62 (75%)	109 (75%)
Asthma	16 (33%)	22 (31%)
Obesity	54 (73%)	153 (61%)

Table 2 presents an analysis of risk factors associated with severe and critical COVID-19 illness among hospitalized patients in Belize. Patients aged over 45 years had significantly higher odds of severe illness compared to younger individuals, with an odds ratio (OR) of 3.3 (95% CI: 2.3–4.9, $P < 0.001$), indicating that older adults were more

than three times as likely to develop severe disease. Male patients were also at increased risk, with nearly twice the odds of severe illness compared to females (OR: 1.48, 95% CI: 1.1–2.1, $P = 0.02$).

In terms of clinical comorbidities, diabetes showed a strong association with severity, with diabetic patients having over three times the odds of severe illness compared to non-diabetics (OR: 3.1, 95% CI: 2.2–4.4, $P < 0.001$). Similarly, hypertension was significantly associated with increased severity (OR: 1.8, 95% CI: 1.3–2.5, $P = 0.001$). While obesity appeared to increase risk (OR: 1.7, 95% CI: 1.0–3.1), the association was not statistically significant ($P = 0.06$). No significant associations were observed for chronic renal failure (CRF) (OR: 1.0, $P = 0.93$), asthma (OR: 1.1, $P = 0.7$), or HIV (OR: 0.1, $P = 0.1$), though the direction of the odds for HIV suggests a potential protective trend that warrants further investigation.

Interestingly, patients with a history of cancer were found to have significantly lower odds of severe illness (OR: 0.3, 95% CI: 0.1–0.9, $P = 0.03$), though this finding should be interpreted with caution given the small number of cancer cases. Regarding geographic variation, none of the districts showed statistically significant differences when compared to Belize District. However, patients from Cayo District had borderline higher odds of severe illness (OR: 1.6, 95% CI: 1.0–2.6, $P = 0.05$), while other districts including Corozal, Orange Walk, Stann Creek, and Toledo did not differ significantly from the risk of the residents of Belize District.

Table 2. Association of risk factors with Severe and Critical COVID 19 illness in hospitalized patients, Belize, March 2020 – December 2022.

Risk Factors	Cases	Controls	OR	IC	P-value
	n	n			
Sex					
Male	97	238	1.5	1.1-2.1	0.02
Age					
≤45	137	264	3.3	2.3-4.9	<0.00
>45					
District					
Belize	41	146	1	-	-
Cayo	55	123	1.6	1.0-2.6	0.05
Toledo	14	64	0.8	0.4-1.5	0.5
Orange Walk	21	68	1.1	0.6-2.0	0.7
Stann Creek	24	76	1.1	0.6-2.0	0.7
Corozal	25	63	1.4	0.8-2.5	0.2
Clinical Risk Factor					
Diabetes	110	181	3.1	2.2-4.4	<0.00
Hypertension	97	213	1.8	1.3-2.5	0.00
Obesity	54	153	1.7	1.0-3.1	0.06
CRF	62	109	1.0	0.5-1.8	0.93
Cancer	4	19	0.3	0.1-0.9	0.03
Asthma	16	22	1.14	0.5-2.5	0.75
HIV	4	15	0.11	0.1-1.2	0.11

Table 3, derived from a logistic regression analysis, reveals key risk factors associated with severe COVID-19. Notably Diabetes was significantly associated with increased odds of severe illness (OR = 5.1, 95% CI: 1.2–22.4, $P = 0.031$). Obesity also showed a strong and statistically significant association (OR = 4.9, 95% CI: 1.5–16.4, $P = 0.009$). Asthma was significantly associated with increased severity (OR = 8.8, 95% CI: 1.1–72.2, $P = 0.042$), though the wide confidence interval suggests uncertainty and a need for cautious interpretation. While not statistically significant, CRF had an inverse association (OR = 0.6, 95% CI: 0.2–1.9, $P = 0.4$). Other factors, such as sex (male) (OR = 1.9, $P = 0.27$) and age ≥ 45 (OR = 0.9, $P = 0.92$), were not statistically significant in

this model. Compared to Belize District, none of the other districts showed statistically significant differences. However, Toledo District showed the highest estimated odds (OR = 12.1, 95% CI: 0.5–290.6, $P = 0.125$), again with a wide CI suggesting imprecision due to small sample size. These findings suggest that diabetes, obesity, and asthma are key predictors of severe COVID-19 among hospitalized patients in Belize, independent of age, sex, and location.

Table 3. Association of risk factors with Severe COVID -19 Disease presentation, adjusted through application of logistic regression analysis.

Risk factors	OR	Lower CI	Upper CI	<i>P</i> -value
Male Sex	1.9	0.6	6.1	0.27
Age > 45	0.9	0.2	4.0	0.92
Diabetes	5.1	1.2	22.3	0.03
Hypertension	2.4	0.7	7.9	0.16
CRF	0.6	0.2	1.9	0.40
Obesity	4.9	1.5	16.3	0.00
Asthma	8.8	1.1	72.2	0.04
Male	1.9	0.6	6.1	0.25

Discussion

This study identified diabetes, obesity, and asthma as independent risk factors for severe and critical COVID-19 illness among hospitalized patients in Belize. These findings align with global research and underscore the importance of chronic disease management in the context of pandemic preparedness.

Diabetes was consistently shown to be a significant predictor of severe COVID-19 in both univariate and multivariate analyses. Similar findings have been reported across diverse populations. A meta-analysis by Kumar et al. found that diabetes doubled the risk of

severe illness and mortality in COVID-19 patients [9]. Likewise, Geng et al. in China and Pandita et al. in the United States reported adjusted odds ratios (aORs) of 2.0 and 2.2 respectively for severe disease among diabetic individuals [10,11]. These results reinforce the global evidence base and emphasize the urgency of targeted interventions for diabetic patients in Belize.

Obesity also emerged as a statistically significant risk factor, with an adjusted OR of 4.9. This aligns with studies by Sattar & Valabhji, who observed a linear increase in COVID-19 hospitalization risk with rising BMI [12]. Given the high burden of obesity in Belize, this association has major implications for clinical risk stratification and resource prioritization during public health emergencies.

Asthma, though less frequently reported as a major driver of severity in some studies, showed a strong association in our analysis. The wide confidence interval, however, suggests potential instability in the estimate, possibly due to small sample size. Nonetheless, this finding is consistent with the physiological plausibility that pre-existing respiratory disease may exacerbate COVID-19-related pulmonary complications.

Interestingly, variables commonly associated with severe COVID-19, such as older age and male sex, were not statistically significant in the multivariable model. This contrasts with studies from Ethiopia [13], and India [14], where advanced age and male sex remained consistent predictors. The discrepancy in our findings may reflect contextual factors in Belize, such as early presentation, healthcare-seeking behavior, or treatment accessibility, which warrant further exploration.

Other conditions like chronic renal failure, cancer, and HIV were not associated with increased severity in this study. This may be due to their lower prevalence in the study population or residual confounding. Notably, cancer was associated with decreased odds in univariate analysis, but the small number of cancer cases limits definitive conclusions.

Overall, this study contributes novel insights to the limited literature on COVID-19 in Central America. It reinforces the importance of identifying locally relevant risk profiles to guide evidence-based public health responses.

Limitations

This study is limited by its use of retrospective administrative data, which may contain incomplete or misclassified information in the context of the overwhelming circumstances faced by staff during the surge of patients. Also, the comparison of severe or critical cases with non-severe cases may not be influenced by the factors compared such as some of the chronic diseases or age, and rather these risk factors, age and comorbidities may be predictors of mortality from COVID-19 as shown in some other studies. Selection was limited to hospitalized patients, which may limit generalizability to milder cases or the broader community. Some risk factors (e.g., asthma, cancer, HIV) had low counts, reducing statistical power to detect associations.

Conclusion

This study highlights the role of diabetes, obesity, and asthma as key predictors of severe COVID-19 among hospitalized patients in Belize. These findings reinforce the need for targeted prevention and clinical monitoring of patients with chronic diseases. Further research is needed to explore the complex interplay of demographic and clinical risk factors, especially in light of unexpected findings related to age and sex.

Public health strategies should prioritize high-risk individuals, especially those with obesity and diabetes, for vaccination, early testing, and access to advanced care.

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