



Impact of comorbidities on the severity of illness of COVID-19 patients managed in a Southern Nigerian State

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is characterized by varying clinical manifestations ranging from asymptomatic disease, mild upper respiratory illness, severe pneumonia and acute respiratory distress syndrome. Patients with COVID-19 who have comorbidities are at risk of having a more severe disease course, longer duration of hospitalization, complications and need for intensive care. The pattern of comorbidities in patients with COVID-19 in Nigeria has not been adequately described yet.

Objective: This study aimed to access the actual burden of comorbidities and their impact on the severity of COVID-19.

Materials and Methods: This was a retrospective cohort study of patients with confirmed COVID-19 using reverse transcription polymerase chain reaction. All confirmed COVID-19 patients diagnosed in Akwa Ibom State from April 1, 2020 to September 30, 2020 and admitted in the isolation facilities were enrolled into this study. A proforma was used to obtain the sociodemographic characteristics of the patient, the type(s) of comorbidity and the severity class. Data was analyzed using SPSS 23.

Results: One hundred and forty-nine patients were included in this study. The most common comorbidities were hypertension (32.2%) and diabetes mellitus (19.5%). Severe or critical disease was significantly found in 17 (35.4%) of the patients with hypertension and 15 (51.7%) of the patients with diabetes with p-value <0.01 on univariate analysis. After multivariate logistic regression, having diabetes mellitus (OR: 4.48, 95% CI: 1.37 – 14.70) and age (OR: 1.07, 95% CI: 1.02 – 1.13) were independent predictors of severity in COVID-19 patients with p-value <0.01. Conclusion: The presence of comorbidities is associated with worsening clinical outcomes in patients with SARS-CoV-2 infection. There is therefore need for closer monitoring of COVID-19 patients having comorbid conditions.

Keywords: COVID-19, Comorbidity, Clinical outcome

Introduction

Coronavirus disease 2019 (COVID-19) is a clinical syndrome caused by severe acute respiratory syndrome- coronavirus 2 (SARS-CoV-2). The

disease is characterized by varying clinical manifestations ranging from asymptomatic disease, mild upper respiratory illness, severe pneumonia and acute respiratory distress syndrome.¹ Coronaviruses are a group of RNA viruses. They are enveloped, non-segmented and have positive sense.¹ Previously, most human infections caused by coronaviruses result in mild, self-limiting flu-like illness. However, over the last 2 decades, Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) had

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emerged prior to this current pandemic as severe coronavirus infections.

Patients with COVID-19 who have comorbidities such as diabetes mellitus, hypertension, chronic respiratory diseases are at risk of having a more severe disease course, longer duration of hospitalization, complications and need for intensive care.² Some of these chronic medical conditions and COVID-19 share a basic feature of being pro-inflammatory. The more severe pattern of illness observed in COVID-19 patients have also been noted in patients with other respiratory viral infections such as Influenza and MERS.²

The pattern and prevalence of comorbidities in patients with COVID-19 may differ between countries. The pattern of comorbidities in patients with COVID-19 in Nigeria has not been adequately described yet. This study will help to provide more insight on the actual burden of comorbidities and their impact on severity of COVID-19. A study in the United States found comorbidities in 93.9% of hospitalized patients. The most common comorbidities were hypertension (56.6%), obesity (41.7%) and diabetes mellitus (33.8%).³ In China, Yang et al in a meta-analysis of 7 studies reported Hypertension (21.1%), Diabetes mellitus (9.7%), cardiovascular diseases (8.4%) and chronic respiratory diseases (1.5%) as the common comorbidities in patients with COVID-19.² A study involving 104 travelers who had COVID-19 on a cruise ship, Diamond Princess found comorbidities in 50% of them.⁴

Knowledge of the pattern and impact of comorbidities in COVID-19 patients in Nigeria will help guide the health authorities in making policies aimed at protecting this vulnerable population. This group of patients have been suggested as a possible priority group for vaccination.² Since the management of COVID-19 is largely supportive, awareness of the pattern of comorbidities will help clinicians to offer more targeted attention to the management of this comorbid conditions in order to improve outcomes. This study aimed to assess the actual burden of comorbidities and their impact on the severity of COVID-19.

Methods

This was a retrospective cohort study of patients with confirmed COVID-19, with SARS-Cov-2

detected using reverse transcription polymerase chain reaction. All COVID-19 patients diagnosed in Akwa Ibom State from April 1, 2020 to September 30, 2020 and admitted in the isolation facilities were enrolled into this study. Ethical approval was obtained from the Health Research Ethics Committee of Ibom Multi-Specialty Hospital, Uyo, with patients' confidentiality ensured. The patients were classified based on severity of illness into asymptomatic, mild, moderate, severe, and critical.⁵ A proforma was used to obtain sociodemographic characteristics of the patients such as age and sex. The type(s) of comorbidity and the severity class of the patients' illnesses were also recorded on the proforma. The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23 (Armonk, N. Y., USA).⁶ Qualitative data was reported as percentages while quantitative variables was reported as mean \pm standard deviation (SD). Chi-square was used to compare proportion of patients with severe COVID-19 with or without comorbidities. Multivariate logistic regression was done to identify factors that were independently associated with severe COVID-19. The variables included in the model were the major comorbidities that had significant association with severe disease following univariate analysis, which were hypertension and diabetes as well as age and male gender, which have also been associated with higher risk of COVID-19.^{7,8}

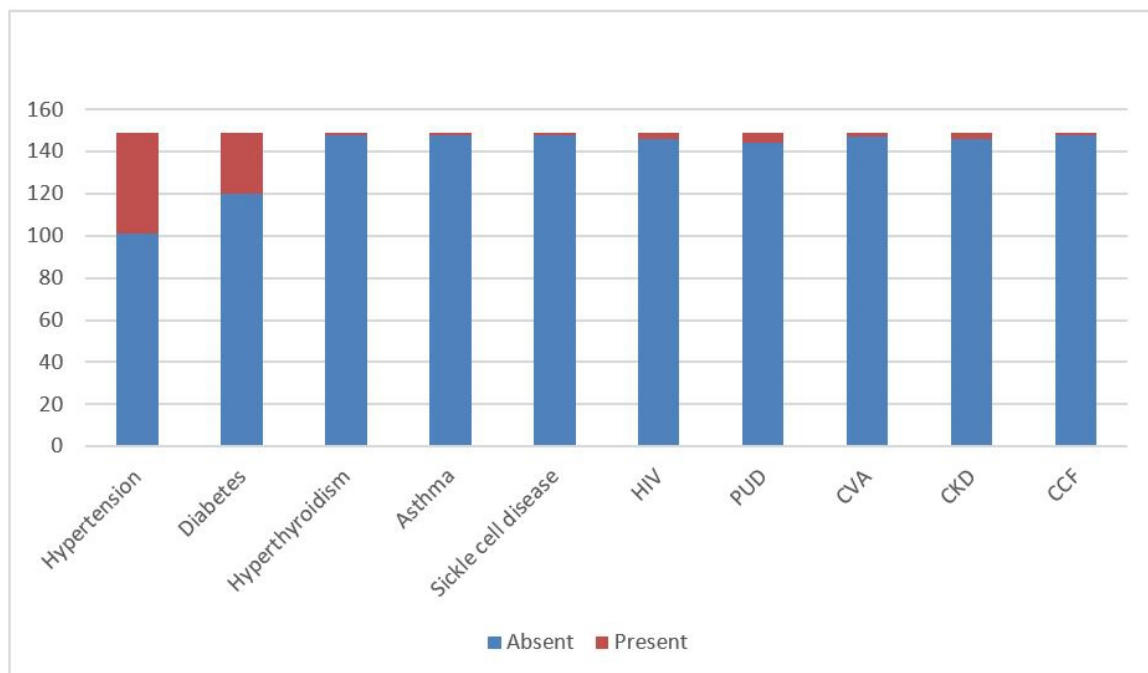
Results

One hundred and forty-nine patients were included in this study. Majority (70.5%) of the participants were males. About half (51.7%) of the patients were between 21-40 years and only 2 (1.3%) were less than 20 years (See Table 1). The most common comorbidities were hypertension (32.2%) and diabetes mellitus (19.5%). Other comorbidities included peptic ulcer disease (3.2%), chronic kidney disease (2%) and human immunodeficiency virus (2%) (See Figure 1).

There were 104 (69.8%) patients with asymptomatic/mild illness, 19 (12.8%) patients with moderate illness and 26 (17.4%) patients with severe/critical disease. There was no gender difference in severity of the illness in this cohort of patients ($p = 0.45$). The age of the participants were categorized in years into groups of 1-20, 21-40, 41-

Table 1: Sociodemographic characteristics of the study participants

Characteristic	Frequency (n)	%
Gender		
Female	44	29.5
Male	105	70.5
Total	149	100.0
Age group (years)		
1 - 20	2	1.3
21 – 40	77	51.7
41 – 60	61	40.9
61 – 80	9	6.0
Total	149	100.0

**Figure 1: Pattern of comorbidities of the study participants**

(HIV- Human immunodeficiency virus, PUD- Peptic ulcer disease, CVA- Cerebrovascular accident, CKD- Chronic kidney disease, CCF- Congestive cardiac failure)

Table 2: COVID – 19 severity by gender and by age

Characteristic	Severity				p-value
	Asymptomatic/ mild	Moderate	Severe/ Critical	Total	
Gender					
Female (n)	33	6	5	44	0.45
Male (n)	71	13	21	105	
Frequency (%)	69.8	12.8	17.4	100.0	
Age group					
1 – 20 n (%)	2 (100.0)	0 (0)	0 (0)	2 (100.0)	<0.01
21 – 40 n (%)	64 (83.1)	9 (11.7)	4 (5.2)	77 (100.0)	
41 – 60 n (%)	35 (57.4)	9 (14.8)	17 (27.9)	61 (100.0)	
61 – 80 n (%)	3 (33.3)	1 (11.1)	5 (55.6)	9 (100.0)	

Table 3: COVID – 19 severity by comorbidity

Comorbidity	Asymptomatic /Mild	Moderate	Severe/ Critical	Total	p-value
Hypertension	24	7	17	48	<0.01
Diabetes	10	4	15	29	<0.01
Hyperthyroidism	1	0	0	1	0.70
Asthma	1	0	0	1	0.70
SCD	0	1	0	1	0.13
HIV	3	0	0	3	0.52
CVA	0	0	2	2	0.03
CKD	0	0	3	3	0.01
CCF	0	0	1	1	0.17

Table 4: Multivariate regression on predictors of severity

Variables	Odds ratio	95% confidence interval		p-value
		Lower	Upper	
Age	1.08	1.02	1.14	<0.01
Male gender	0.50	0.14	1.76	0.28
Hypertension	1.50	0.48	4.70	0.49
Diabetes	3.98	1.34	11.80	0.01

60 and 61-80, and was found to significantly vary with the severity of illness ($p = 0.01$). Severe/critical illness were found in 55.6% of the participants in the 61-80 age category when compared with 27.9% and 5.2% of those in the 41-60 and 21-40 age categories respectively (See Table 2). The most common comorbidities were hypertension (32.2%) and diabetes mellitus (19.5%). Severe or critical disease was significantly found in 17 (35.4%) of the patients with hypertension and 15 (51.7%) of the patients with diabetes with p -value < 0.01 on univariate analysis. There were 2 patients with cerebrovascular accidents and 3 patients with chronic kidney disease and they also presented with severe or critical illness (See Table 3). After multivariate logistic regression, having diabetes mellitus (OR: 4.48, 95% CI: 1.37 – 14.70) and age (OR: 1.07, 95% CI: 1.02 – 1.13) were independent predictors of severity in COVID-19 patients with p -value < 0.01 (Table 4).

Discussion

The most common comorbidities that were associated with COVID-19 infection in the patients studied was hypertension and diabetes mellitus. Hypertension, diabetes mellitus, cerebrovascular accidents and chronic kidney disease were the comorbidities that were significantly associated with worsening severity on univariate analysis, though only diabetes mellitus remained an independent predictor of severity on multivariate analysis. Similarly, Yang et al² from their systematic review and meta-analysis of 7 studies had found hypertension, diabetes, cardiovascular disease and respiratory system disease as the commonly associated comorbidities with COVID-19 infection. A meta-analysis of the comorbidities showed that hypertension, respiratory system disease and cardiovascular diseases were significantly associated with severe disease and not diabetes mellitus, which was unlike the finding in our study. However, a meta-analysis involving 76 studies has significantly associated diabetes mellitus with severe infection and increased mortality in patients with COVID-19 infection.⁹ Diabetics have a predisposition to infections and are increasingly susceptible to hyper-inflammation and cytokine storm which are associated with poorer outcomes in COVID-19 patients.¹⁰ Other studies have also associated cerebrovascular accidents and

chronic kidney diseases with worsening COVID-19 illness.^{11,12}

Patients that were advanced in age had a higher proportion of severe and critical illness when compared to younger patients, who were more likely to have asymptomatic or mild disease. Older age group has been associated with a higher risk of SARS-CoV-2 positivity.⁷ Given that comorbid conditions worsen with advances in age, this could explain the worsening clinical manifestations of COVID-19 in this cohort of patients.¹³ Starke et al¹⁴ in assessing the risk of age-related severe outcomes from COVID-19 infection found that age accounted crudely for a 5.2% increase risk of severity but after adjusting for the effect of comorbidities, the effect of age as an independent risk factor for disease severity reduced to 2.7% for two studies thereby underscoring the impact of comorbidities in worsening clinical outcomes. There is therefore need to consider COVID-19 patients with comorbidities as a vulnerable population that should be prioritized for SARS-CoV-2 vaccination.²

Differences in gender was not significantly associated with worsening outcomes in our study though there were more males on admission than females. This contrasts with the findings in other studies that have associated male gender with increasing disease severity when compared to females.^{8,15} Larger studies may corroborate the conventional finding. The female hormonal milieu has been considered more immuno-protective when exposed to infectious pathogens.¹⁶

Conclusion

The presence of comorbidities is associated with worsening clinical outcomes in patients with SARS-CoV-2 infection. There is therefore need for closer monitoring of patients having comorbid conditions while prioritizing them for COVID-19 vaccination.

References

1. Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E. COVID-19, SARS and MERS: are they closely related? *Clin Microbiol Infect.* 2020;26:729–34.
2. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a

- systematic review and meta-analysis. *Int J Infect Dis.* 2020;94:91–5.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* [Internet]. 2020;323(20):2052–9. Available from: <https://doi.org/10.1001/jama.2020.6775>
 4. Tabata S, Imai K, Kawano S, Ikeda M, Kodama T, Miyoshi K, et al. Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2 infection on the Diamond Princess cruise ship: a retrospective analysis. *Lancet Infect Dis* [Internet]. 2020;20(9):1043–50.
 5. Pongpirul WA, Wiboonchutikul S, Charoenpong L, Panitantum N, Vachiraphan A, Uttayamakul S, et al. Clinical course and potential predictive factors for pneumonia of adult patients with coronavirus disease 2019 (COVID-19): A retrospective observational analysis of 193 confirmed cases in Thailand. *PLoS Negl Trop Dis* [Internet]. 2020;14(10):1–17. Available from: <http://dx.doi.org/10.1371/journal.pntd.0008806>
 6. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY, USA: IBM Corp.; 2015.
 7. De Lusignan S, Dorward J, Correa A, Jones N, Akinyemi O, Amirthalingam G, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *Lancet Infect Dis* [Internet]. 2020;20(9):1034–42. Available from: [http://dx.doi.org/10.1016/S1473-3099\(20\)30371-6](http://dx.doi.org/10.1016/S1473-3099(20)30371-6)
 8. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. *Front Public Heal.* 2020;8:152.
 9. Shang L, Shao M, Guo Q, Shi J, Zhao Y, Xiaokereti J, et al. Diabetes Mellitus is Associated with Severe Infection and Mortality in Patients with COVID-19: A Systematic Review and Meta-analysis. *Arch Med Res.* 2020;51:700–9.
 10. Ugwueze C V., Ezeokpo BC, Nnolim BI, Agim EA, Anikpo NC, Onyekachi KE. COVID-19 and Diabetes Mellitus: The Link and Clinical Implications. *Dubai Diabetes Endocrinol J.* 2020;1–9.
 11. Nannoni S, de Groot R, Bell S, Markus HS. Stroke in COVID-19: A systematic review and meta-analysis. *Int J Stroke.* 2020;1–13.
 12. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. *PLoS One* [Internet]. 2020;15:e0238215. Available from: <http://dx.doi.org/10.1371/journal.pone.0238215>
 13. Yanez ND, Weiss NS, Romand J, Treggiari MM. COVID-19 mortality risk for older men and women. *BMC Public Health* [Internet]. *BMC Public Health*; 2020;20:1742. Available from: <https://doi.org/10.1186/s12889-020-09826-8>
 14. Starke KR, Petereit-Haack G, Schubert M, Kämpf D, Schliebner A, Hegewald J, et al. The age-related risk of severe outcomes due to covid-19 infection: A rapid review, meta-analysis, and meta-regression. *Int J Environ Res Public Health.* 2020;17(16):1–24.
 15. Ueyama H, Kuno T, Takagi H, Krishnamoorthy P, Vengrenyuk Y, Sharma SK, et al. Gender Difference Is Associated With Severity of Coronavirus Disease 2019 Infection: An Insight From a Meta-Analysis. *Crit Care Explor.* 2020;2:e0148.
 16. Pradhan A, Olsson PE. Sex differences in severity and mortality from COVID-19: are males more vulnerable? *Biol Sex Differ. Biology of Sex Differences*; 2020;11:53.