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Brief Report

Impact of Underlying Chronic Medical Conditions on COVID-19 Outcomes Among People Living with HIV: A Retrospective Analysis from the Minnesota Fairview Network

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Abstract: (1) Background: The Coronavirus Disease 2019 (COVID-19) pandemic has raised concerns about the impact of underlying medical conditions on the health outcomes of people living with HIV (PLWH). This study aimed to assess how pre-existing chronic medical conditions affect the health outcomes of PLWH infected with COVID-19. (2) Methods: A retrospective study using data from the Minnesota Fairview network (1 January 2020–31 December 2022) was conducted. Fisher's exact test, the Kruskal–Wallis rank-sum test, and ordinal logistic regressions with a Benjamini–Hochberg (BH) adjustment on p-values were used to assess the influence of chronic conditions on COVID-19 severity, adjusting for age and gender. (3) Results: Among 216 records, significant associations were found for a stroke, chronic kidney disease, lung disease, and neurologic conditions ($p < 0.05$). Type 1 diabetes was marginally significant ($0.05 < p < 0.1$). After adjusting for age and sex, a stroke ($p = 0.0008$, BH-adjusted $p = 0.0044$) and chronic kidney disease ($p = 0.0003$, BH-adjusted $p = 0.0033$) significantly increased the risk of severe COVID-19 outcomes. (4) Conclusions: Pre-existing medical conditions should be considered in the clinical management and public health interventions for PLWH infected with COVID-19. Tailored strategies are essential to mitigate the higher risk of severe outcomes in PLWH with specific chronic comorbidities.

Keywords: COVID-19 severity; comorbidities; people living with HIV; stroke; chronic kidney disease

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1. Introduction

The Human Immunodeficiency Virus (HIV) infection has a dramatic and historically significant origin, akin to many major viral discoveries in medical history. First identified in 1983 through the cloning and sequencing of its genome, HIV was recognized as the causative agent of acquired immunodeficiency syndrome (AIDS) [1–4]. Since that pivotal discovery, the virus has spread globally, impacting millions of individuals across various demographics and regions. In the United States alone, approximately 1.2 million people are currently living with HIV (PLWH), with an estimated 31,800 new infections reported in 2022 [5,6]. Although trends in HIV incidence have shown a decline over the past 40 years, the virus remains a formidable public health challenge that continues to necessitate attention and action [7].

HIV is not only associated with direct health effects but also complicates the management of a range of associated health issues, particularly for individuals who have pre-existing medical conditions [8]. The presence of such comorbidities can significantly lead to poorer health outcomes for those living with HIV, emphasizing the urgent need for comprehensive management strategies that take these underlying issues into account. Researchers have been working diligently to enhance HIV management, aiming to empower individuals living with the virus to lead fulfilling and productive lives despite their diagnosis [9].

The emergence of the Coronavirus Disease 2019 (COVID-19) pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has further complicated this landscape. For individuals living with HIV, particularly those who also have chronic medical conditions, the COVID-19 infection poses heightened risks and challenges [10]. The intersection of these two public health crises raises crucial questions about how comorbidities influence health outcomes for PLWH. As healthcare professionals adapt treatment approaches during the COVID-19 and HIV infection dual pandemic, it becomes increasingly important to understand the implications of these underlying medical conditions on overall health and well-being [11,12].

This study aims to assess the impact of chronic medical conditions on the health outcomes of PLWH who are also infected with SARS-CoV-2. By examining this population, this research seeks to provide valuable insights into how comorbidities affect disease progression and recovery in the context of both HIV and COVID-19. Understanding these dynamics is essential for informing best practices and improving the standard of care for individuals facing the dual challenges of HIV and COVID-19 infections. Ultimately, the findings could lead to better-targeted interventions and support systems that enhance the quality of life for those navigating the complexities of these intertwined health issues.

2. Materials and Methods

2.1. Study Design and Data Collection

This retrospective study utilized data obtained from the Minnesota Fairview network via electronic health records (EHRs). Using a templated chart, the dataset comprised demographic information and clinical diagnoses of various chronic diseases, focusing on patients living with HIV who tested positive for SARS-CoV-2 via a nasal swab. Only those who received care within the Minnesota Fairview network between 1 January 2020 and 31 December 2022 were included in this analysis. This same dataset was previously described in Aremu et al. (2023) [10].

Inclusion and Exclusion Criteria

Patients included in the analysis were HIV-positive individuals who tested positive for SARS-CoV-2. Patients with incomplete or duplicate data and those who tested negative for SARS-CoV-2 were excluded from this study. A visual representation of the selection process is provided in Figure 1.

2.2. Exposure Variables

The primary exposure variables were chronic diseases identified by the CDC, including heart disease, a stroke, cancer, diabetes, cognitive impairment, lung complications, and chronic kidney disease (CKD) [13]. We classified and grouped chronic diseases, creating additional aggregations for further analysis. For instance, diabetes status included both Type 1 and Type 2 diabetes, while lung disease encompassed chronic obstructive pulmonary disease (COPD), asthma, cystic fibrosis, and other lung disorders.

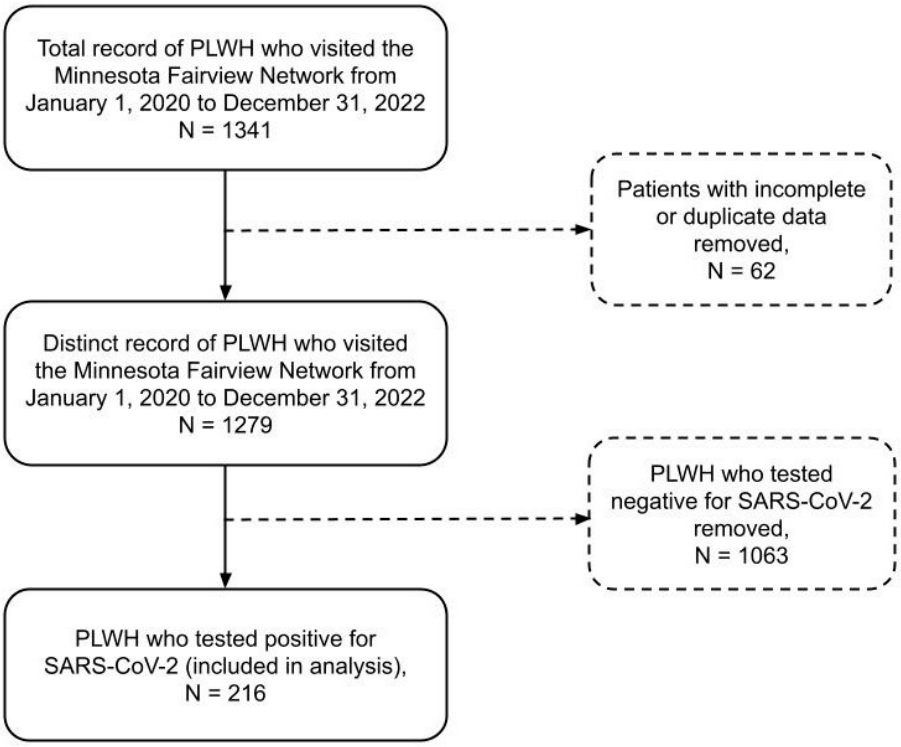

Figure 1. Study population flow chart.

2.3. Outcome Variables

The primary outcome was the severity of COVID-19 infection, classified into four levels: (1) tested positive for SARS-CoV-2 without additional records, (2) admitted to the hospital or hospitalized due to COVID-19, (3) admitted to the ICU due to COVID-19, and (4) death possibly related to COVID-19.

2.4. Statistical Analysis

Descriptive statistics were computed to summarize baseline patient characteristics and chronic comorbidities across the four severity groups. Continuous variables were summarized using means and standard deviations, while categorical variables were expressed as counts and percentages.

To assess differences in characteristics and chronic disease statuses among the four severity groups, we used the Kruskal–Wallis rank-sum test for continuous variables and Fisher's exact test for categorical variables. An ordinal regression model was fitted for each chronic disease and aggregation, adjusting for age and sex, to evaluate the impact of chronic comorbidities on COVID-19 disease severity. A Benjamini–Hochberg (BH) adjustment was applied to account for multiple comparisons. The significance level (alpha) was set at 0.05. Given the limited sample sizes of patients with relatively more severe outcomes, we considered testing the robustness of our results by dichotomizing the patients into two groups: (a) those who tested positive for COVID-19 without additional records, and (b) those who tested positive for COVID-19 with at least one additional record. A sensitivity analysis was conducted using logistic regression on comorbidities that were found significant. All statistical analyses were conducted using R software, version 4.2.1.

2.5. Ethical Considerations

This study adhered to the principles of the Declaration of Helsinki and received approval from the Institutional Review Board at the University of Minnesota as an exempt human research study (IRB ID: STUDY00013254) on 23 July 2021.

3. Results

3.1. Patient Cohort and Severity Groups

A total of 216 patients living with HIV who tested positive for SARS-CoV-2 were included in the analysis. The cohort was categorized into four groups based on the severity of their COVID-19 condition: those without additional records (N = 161), those admitted to the hospital (N = 42), those admitted to the ICU (N = 9), and those who died from COVID-19 (N = 4). Table 1 presents a comprehensive data summary of the four patients who died from COVID-19.

Table 1. Data matrix for patients who died from COVID-19 infection.

Patient ID	Type 1 Diabetes	Type 2 Diabetes	HTN	Stroke	Cancer	CKD	Lung Disease	Neurologic Conditions	Heart Conditions
A	No	No	No	No	No	No	Yes	No	No
B	No	No	No	No	No	No	No	Yes	No
C	No	No	No	No	No	No	No	Yes	No
D	No	No	Yes	Yes	Yes	Yes	No	No	Yes

3.2. Baseline Characteristics

Table 2 summarizes the baseline characteristics of the patients. The median age across all groups did not vary significantly, with those admitted to the hospital, admitted to the ICU, and deceased having a median age of 54, 60, and 49, respectively ($p = 0.7$). The interquartile range of age across groups spanned from 41 to 65 years. Gender distribution revealed that males were the majority in each severity category, accounting for 67.6% of the patient cohort overall and 100% of the deceased group ($p = 0.3$).

Table 2. Baseline patient characteristics for COVID-19 specific mortality.

	Without Additional Records, N = 161	Admitted to Hospital, N = 42	Admitted to ICU, N = 9	COVID-19 Death, N = 4	*p*-Value
Age	54 (44, 61)	54 (41, 65)	60 (48, 63)	49 (49, 49)	0.7
Sex					0.3
Female	54 (34%)	15 (36%)	1 (11%)	0 (0%)	
Male	107 (66%)	27 (64%)	8 (89%)	4 (100%)	
Type 1 Diabetes					0.065
No	157 (98%)	37 (88%)	9 (100%)	4 (100%)	
Yes	4 (2.5%)	5 (12%)	0 (0%)	0 (0%)	
Type 2 Diabetes					0.3
No	128 (80%)	33 (79%)	5 (56%)	4 (100%)	
Yes	33 (20%)	9 (21%)	4 (44%)	0 (0%)	
Any Diabetes					0.3
No	128 (80%)	32 (76%)	5 (56%)	4 (100%)	
Yes	33 (20%)	10 (24%)	4 (44%)	0 (0%)	
Hypertension					0.3
No	74 (46%)	17 (40%)	2 (22%)	3 (75%)	
Yes	87 (54%)	25 (60%)	7 (78%)	1 (25%)	
Stroke					<0.001
No	156 (97%)	40 (95%)	5 (56%)	3 (75%)	
Yes	5 (3.1%)	2 (4.8%)	4 (44%)	1 (25%)	

Table 2. *Cont.*

	Without Additional Records, N = 161	Admitted to Hospital, N = 42	Admitted to ICU, N = 9	COVID-19 Death, N = 4	*p*-Value
Cancer					0.4
No	148 (92%)	37 (88%)	9 (100%)	3 (75%)	
Yes	13 (8.1%)	5 (12%)	0 (0%)	1 (25%)	
Chronic Kidney Disease					0.001
No	135 (84%)	26 (62%)	4 (44%)	3 (75%)	
Yes	26 (16%)	16 (38%)	5 (56%)	1 (25%)	
Any Lung Disease					0.3
No	126 (78%)	29 (69%)	5 (56%)	3 (75%)	
Yes	35 (22%)	13 (31%)	4 (44%)	1 (25%)	
Neurologic Condition					0.035
No	152 (94%)	38 (90%)	9 (100%)	2 (50%)	
Yes	9 (5.6%)	4 (9.5%)	0 (0%)	2 (50%)	
Heart Condition					0.2
No	130 (81%)	29 (69%)	6 (67%)	3 (75%)	
Yes	31 (19%)	13 (31%)	3 (33%)	1 (25%)	

Fisher's exact test was conducted for categorical variables and the Kruskal–Wallis rank-sum test was conducted for continuous variables.

Regarding comorbidities, certain chronic conditions were more prevalent among patients with severe outcomes. A stroke showed a statistically significant association with worse outcomes, particularly among ICU patients (44%) and those who died (25%), with a *p*-value of <0.001. Chronic kidney disease (CKD) also showed a significant association with COVID-19 severity, affecting 56% of ICU patients and 25% of those who died ($p = 0.001$). Other conditions, such as hypertension and cancer, were not statistically significant ($p = 0.3$ and $p = 0.4$, respectively). The presence of diabetes, whether Type 1 or Type 2, did not show significant variation across groups.

3.3. Ordinal Logistic Regression Analysis

Table 3 outlines the odds ratios (ORs) from ordinal logistic regression models for various chronic conditions in relation to more severe COVID-19 outcomes, including hospital admissions, ICU admissions, and COVID-19-related death.

Age was not a significant predictor of more severe COVID-19 outcomes across all models. Similarly, sex was not a significant predictor of more severe COVID-19 outcomes in any model, with ORs ranging from 1.2514 to 1.3902 across the models.

A stroke emerged as a strong predictor of more severe COVID-19 outcomes, including COVID-19-related death, with an OR of 8.5864 (95% CI: 2.4098, 30.7546; $p = 0.0008$; BH-adjusted $p = 0.0044$). In essence, the odds of having a more severe outcome for a patient with a stroke is 8.5-times as much as those for a patient without a stroke. CKD was also significantly associated with a higher possibility of having more severe COVID-19 outcomes (OR = 3.6544; 95% CI: 1.8063, 7.4236; $p = 0.0003$; BH-adjusted $p = 0.0033$). In essence, the odds of having a more severe outcome for a patient with CKD is 3.7-times as much as those for a patient without CKD. After accounting for age and sex, CKD and a stroke remain significantly associated with COVID-19 severity. Other comorbidities, including neurologic conditions, heart conditions, and diabetes, did not show a statistically significant association with more severe COVID-19 outcomes after adjustment. While Type 1 diabetes showed a potential trend toward more severe COVID-19 outcomes (OR = 2.8073; $p = 0.0931$; BH-adjusted $p = 0.2048$), this association did not reach statistical significance.

Table 3. Summary of ordinal logistic regression models, with BH adjustment for multiple testing on *p*-values, death being COVID-19-specific.

Model	Odds Ratio	95% CI	*p*-Value	Adjusted *p*-Value
Any Lung Disease				
Age	0.9986	0.9783, 1.0198	0.8971	
Sex: Male vs. Female	1.3902	0.7172, 2.7942	0.3398	
Pulmonary Conditions: Yes vs. no	1.8205	0.9140, 3.5607	0.0828	0.2048
All Chronic Disease				
Age	0.9954	0.974, 1.0176	0.6790	
Sex: Male vs. Female	1.2882	0.6677, 2.5696	0.4591	
All Chronic Disease: Yes vs. no	1.6996	0.8061, 3.7858	0.1760	0.2766
Any Type Diabetes				
Age	0.9995	0.9791, 1.0207	0.9586	
Sex: Male vs. Female	1.3150	0.6836, 2.6177	0.4216	
Any Type Diabetes: Yes vs. no	1.3250	0.6287, 2.6936	0.4456	0.5888
Type 1 Diabetes				
Age	1.0003	0.9801, 1.0213	0.9798	
Sex: Male vs. Female	1.3183	0.683, 2.6338	0.4198	
Type 1 Diabetes: Yes vs. no	2.8073	0.7887, 9.2146	0.0931	0.2048
Type 2 Diabetes				
Age	0.9999	0.9796, 1.0212	0.9957	
Sex: Male vs. Female	1.3188	0.6858, 2.6244	0.4166	
Type 2 Diabetes: Yes vs. no	1.2139	0.5665, 2.4925	0.6057	0.6057
Hypertension				
Age	0.9979	0.9761, 1.0206	0.8539	
Sex: Male vs. Female	1.2924	0.6695, 2.5798	0.4537	
Hypertension: Yes vs. no	1.2556	0.6397, 2.5013	0.5112	0.5888
Stroke				
Age	0.9909	0.9702, 1.0123	0.3973	
Sex: Male vs. Female	1.2514	0.6447, 2.5097	0.5157	
Stroke: Yes vs. no	8.5864	2.4098, 30.7546	0.0008	0.0044
Cancer				
Age	0.9999	0.9795, 1.0211	0.9914	
Sex: Male vs. Female	1.3361	0.6941, 2.6616	0.3956	
Cancer: Yes vs. no	1.3808	0.4633, 3.6831	0.5353	0.5888
CKD				
Age	0.9906	0.9698, 1.012	0.3838	
Sex: Male vs. Female	1.2213	0.6235, 2.4668	0.5667	
CKD: Yes vs. no	3.6544	1.8063, 7.4236	0.0003	0.0033
Neurologic Conditions				
Age	0.9967	0.9759, 1.0184	0.7631	
Sex: Male vs. Female	1.3075	0.6777, 2.6095	0.4332	
Neurologic Conditions: Yes vs. no	2.3019	0.709, 6.9595	0.1465	0.2686
Heart Conditions				
Age	0.9977	0.9772, 1.0189	0.8258	
Sex: Male vs. Female	1.2787	0.6615, 2.5546	0.4734	
Heart Conditions: Yes vs. no	1.8300	0.8985, 3.65	0.0895	0.2048

3.4. Sensitivity Analysis

The results of the sensitivity analysis using logistic regressions on the effect of a stroke and CKD are summarized in Table 4. The patients were dichotomized into two groups: (a) those who tested positive for COVID-19 without additional records, and (b) those who tested positive for COVID-19 with at least one additional record, including hospital admission, ICU admission, or death. Logistic regression indicated that a stroke is a strong predictor of more severe outcomes, with an odds ratio of 5.0135 and a *p*-value of 0.0118. CKD was also identified as a significant predictor, with an odds ratio of 3.8313 and a *p*-value of 0.0003.

Table 4. Summary of logistic regression models with dichotomized outcomes.

Model	Odds Ratio	95% CI	*p*-Value
Stroke			
Age	0.9930	0.9719, 1.0149	0.5213
Sex: Male vs. Female	1.1757	0.6013, 2.3706	0.6420
Stroke: Yes vs. no	5.0135	1.4449, 18.7388	0.0118
CKD			
Age	0.9891	0.9673, 1.0113	0.3324
Sex: Male vs. Female	1.1184	0.5635, 2.2816	0.7526
CKD: Yes vs. no	3.8313	1.8532, 8.0308	0.0003

4. Discussion

In this study, we identified key comorbidities associated with poor outcomes in patients infected with COVID-19, particularly among those living with HIV. Although age and sex did not emerge as significant predictors of more severe COVID-19 outcomes, the presence of a stroke and CKD were strongly associated with increased risks of poor COVID-19 outcomes, including in-hospital admission, ICU admission, and death. These findings are consistent with prior research that underscores the elevated risk posed by pre-existing conditions such as cerebrovascular disease and CKD in the context of COVID-19 [14,15].

A stroke emerged as the most impactful predictor of severe COVID-19 outcomes, with an odds ratio (OR) of 8.5864. This significant association highlights the heightened vulnerability of patients with cerebrovascular disease, which may exacerbate the inflammatory response triggered by SARS-CoV-2. Similar to prior studies, our results emphasize the need for rigorous monitoring and management of stroke patients, particularly in the context of a viral infection like COVID-19 [16,17].

CKD also demonstrated a strong association with severe outcomes, with an OR of 3.6544. This link is attributed to impaired renal function and the additional strain CKD places on the immune system, both of which exacerbate the severity of viral infections [18]. A study conducted in Spain found a significant independent association between CKD and poor COVID-19 outcomes [19]. In line with these findings, several studies have provided moderate-certainty evidence suggesting that CKD increases both the risk of mortality and the severity of COVID-19 infection [20,21]. Our results also support the need for close renal monitoring and early intervention for COVID-19 patients with CKD, consistent with previous research [22,23].

Sensitivity analysis confirmed the robustness of our findings, particularly regarding a stroke and CKD. Due to the relatively small number of stroke cases in our dataset, we investigated whether the association between a stroke and severe COVID-19 outcomes might be influenced by its overlap with CKD, as approximately half of the stroke patients in our cohort (7 out of 12) also had CKD. Despite this overlap, the analysis showed that the association of a stroke with severe outcomes was not entirely explained by CKD. Patients with a stroke alone were more likely to experience worse outcomes than those without a stroke or CKD, while patients with both a stroke and CKD had even worse outcomes than those with CKD alone. This highlights the distinct impact of a stroke as a comorbidity in

COVID-19 patients, separate from its overlap with CKD. These results are presented in Supplementary Table S1.

While diabetes and hypertension are frequently highlighted as risk factors for severe COVID-19 outcomes in the general population [14], these conditions did not reach statistical significance in our cohort after multivariable adjustment. This lack of significance suggests that in the presence of more critical comorbidities such as a stroke and CKD, these conditions alone may not independently drive the severity of outcomes. This finding aligns with some recent studies that indicate that the interplay of multiple comorbidities, rather than any single condition, may play a crucial role in determining COVID-19 outcomes [23]. However, a study using national administrative healthcare open data of Mexico identified hypertension and diabetes mellitus as independent predictors of severe COVID-19 outcomes [21].

Additionally, despite the trends suggesting higher risks for patients with diabetes and heart conditions, our findings indicate that these factors may not uniformly increase more severe COVID-19 outcomes, including mortality risk in PLWH infected with COVID-19. This highlights the complexity of interactions between HIV status, chronic conditions, and other viral infections, warranting further exploration [17].

These findings highlight the importance of early identification and focused clinical care for high-risk groups, particularly patients with a stroke and CKD. Tailored interventions that address these comorbidities may mitigate the risk of severe outcomes, including COVID-19-related mortality, in vulnerable populations such as those living with HIV. Given their strong links to severe outcomes, a stroke and CKD should receive prioritized attention in clinical practice.

5. Limitations

A limitation of our study is the small number of COVID-19-specific deaths reported, with only four occurrences, increasing the possibility of a type II error due to insufficient statistical power. To address this, we used the nonparametric test, Fisher's exact test, and the Kruskal–Wallis rank-sum test for descriptive statistics, which are more suitable for small sample sizes and help provide more reliable results in cases of sparse data. Additionally, the data obtained from the Minnesota Fairview Network did not include dates for the SARS-CoV-2 test results, which restricts our ability to perform time-dependent analyses. This limitation prevents us from examining the influence of infection timing on outcomes, understanding epidemiological trends over time, or assessing latency and duration effects between infection and health outcomes. Consequently, our findings may be impacted by the inability to adjust for these important time-related factors.

Moreover, our study assumes that the presence of comorbidity is associated with more severe COVID-19 outcomes. This assumption, while supported by existing literature, may oversimplify the complex interactions between comorbidities and COVID-19 severity, potentially overlooking individual differences or other mitigating factors that could influence outcomes. Future studies with larger sample sizes and more comprehensive time-stamped data would enhance our understanding of these nuanced relationships.

6. Conclusions

Our study emphasizes the critical role of pre-existing medical conditions in influencing COVID-19 outcomes among people living with HIV (PLWH). Specifically, chronic diseases such as a stroke and chronic kidney disease (CKD) were found to significantly affect the severity of outcomes, including mortality associated with COVID-19 infection, in this vulnerable population. These findings highlight the need for tailored clinical management strategies that address the unique risks faced by PLWH with specific chronic comorbidities.

By implementing targeted interventions, healthcare providers can mitigate the heightened risk of severe COVID-19 outcomes and improve overall health for individuals with HIV. Also, these insights are essential for guiding public health initiatives aimed at preventing worse outcomes, such as in-hospital and ICU admissions, and reducing mortality rates

in high-risk groups. Future research should focus on exploring the cumulative effects of multiple chronic conditions and refining intervention strategies to enhance health outcomes for PLWH facing the challenges posed by COVID-19 infection.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/covid4110127/s1, Table S1: COVID-19 Severity by conditions of CKD and Stroke.

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Informed Consent Statement: Patient consent was waived because medical record data were only obtained from the EPIC for patients that had opted in to allow their deidentified record to be used for research.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons.

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Abbreviations

HTN (hypertension), CKD (chronic kidney disease), CDC (center for disease prevention and control), PLWH (people living with HIV).

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