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Assessing the Prevalence of COVID-19 and Associated Outcomes among People Living with HIV/AIDS at Kitwe Teaching Hospital between 1st July-30th September, 2021

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Abstract

Aim: COVID-19 has created a global public health emergency with significant mortality and morbidity for People Living with HIV (PLWH). Preliminary data reveals persons with immune-compromised status are at risk of developing adverse clinical outcomes from SARS-CoV-2. This study intended to characterise clinical outcomes of HIV patients co-infected with SARS-CoV-2 infection at Kitwe Teaching Hospital (KTH).

Materials and methods: A retrospective cross-sectional study was conducted among patients admitted with COVID-19 at KTH between 1st July and 30th September, 2021. All necessary data was collected from files and records of patients admitted between 1st July and 30th September, 2021, using a data extraction sheet. Data was entered, coded and analysed using SPSS version 26*64.

Results: 17.4% of admitted patients were HIV positive, with 40.5% were HIV negative and 42.0% had their HIV status unknown. There was no correlation between HIV status and clinical outcomes (p-value=0.146), instead, there was significance between gender and clinical outcome (p-value=0.026). There was an observed overall mortality rate of 80% for all patients admitted due to COVID-19, regardless of their HIV status.

Conclusion and recommendations: There was no observed influence of HIV on clinical outcomes of COVID-19 patients. The increased mortality rate of HIV infected patients could be attributed to many other things. That is why recommendations to seek medical attention early, improving management of patients with special needs and encouraging seeking medical care for related symptoms were made.

Keywords: Acquired immunodeficiency syndrome • Aspartate transaminase • Coronavirus disease

Abbreviations: AIDS: Acquired Immunodeficiency Syndrome; ANOVA: Analysis of Variance; ALB: Albumin; ALP: Alanine Phosphatase; ALT: Alanine Transaminase; AST: Aspartate Transaminase; CD_4: Cluster of Differentiation 4; COVID-19: Coronavirus Disease of 2019; GGT: Gamma-Glutamyl Transferase; HIV: Human Immunodeficiency Viruses; IDU: Injection Drug Users; KTH: Kitwe Teaching Hospital; LFT: Liver Function Tests; PLWH: People Living with Human Immunodeficiency Viruses; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SPSS: Statistical Package for Social Sciences; TDRC: Tropical Disease Research Centre; UNAIDS: United Nations Joint Program on HIV and AIDS WHO: World Health Organization

Introduction

Background

In December 2019, a novel Coronavirus, now known as SARS-CoV-2, caused a series of acute atypical respiratory diseases in Wuhan, Hubei Province, China. The disease caused by this virus was termed COVID-19. The virus is transmittable between humans and has caused pandemic worldwide [1]. According to WHO Corona virus dashboard Globally as of 24th January 2022, there have been 349,641,119 confirmed cases of COVID-19, including 5,592,266 deaths, reported to WHO. Before COVID-19 there exists an epidemic disease known as HIV/AIDS which has lived with us for many years

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since it's discovery traced from as early as 1980's which has led to over 32.7 million deaths worldwide [2]. The global HIV and AIDS statistics (2021) also reveals that 28.2 million people were accessing antiretroviral therapy as of 30 June 2021. 37.7 million (30.2 million–45.1 million) people globally were living with HIV in 2020. 1.5 million (1.0 million–2.0 million) people became newly infected with HIV in 2020. 680 000 (480 000–1.0 million) people died from AIDS related illnesses in 2020. 79.3 million (55.9 million–110 million) people have become infected with HIV since the start of the epidemic. 36.3 million (27.2 million–47.8 million) people have died from AIDS related illnesses since the start of the epidemic. These alarming figures demands special attention and strategic interventions in this special population. Furthermore, it also worth noting that Southern Africa is the region worst affected by HIV and accounts for one third of the global burden of HIV. Thus, achieving the UNAIDS 90-90-90 target by 2020 and ending the AIDS epidemic by 2030 depend on success in Southern Africa region [3].

The coming of the COVID-19 has brought about massive anxiety among people from all walks of life and has burdened the health care practitioners in trying to fight the COVID-19 and has caused diversion of attention and resources to this rapidly growing pandemic. However, with the available information it is still unclear whether people living with human immunodeficiency virus are at increased risk of COVID-19 and severe disease manifestation as information about incidence, clinical characteristics and outcomes of HIV-infected individuals with severe acute respiratory syndrome corona virus-2 infection is still scarce. Therefore, it is crucial that HIV infected individuals are included in investigational anti-COVID-19 strategies to gain insight into the best approach for this population and if the fight should be won against both HIV/AIDS epidemic and COVID-19 pandemic. This study is aimed at assessing the outcomes of COVID-19 among PLWH in comparison to non-HIV infected populations.

Statement of the problem

COVID-19 is threatening gains against the HIV epidemic, and alleviating the burden among nations in the fight to ending the HIV epidemic goals. The ongoing collision of these two global pandemics will continue to need both study and interventions to mitigate the effects of COVID-19 on HIV efforts worldwide. Hence, the need to assess whether the co-infection of these two pandemics result in severe disease manifestations and/or worse outcome. This is of tantamount necessity in being alert and the preparedness to fight these two major diseases which are posing huge threats worldwide and especially on developing countries that are still trying to find ground in creating a health system that is stable and well equipped.

Significance of the study

Conducting this study will provide region specific data which can then be used to plan for Kitwe teaching hospital and its catchment area with reference to responding to COVID-19 in this population of people and help authorities in the allocation of financial and human resources to mitigate the impact of the pandemic.

General objective

To determine the prevalence of COVID-19 and its associated outcomes among people living with HIV who were admitted to KTH between 1st July-30th September, 2021.

Specific objectives

- To determine the prevalence of COVID-19 among people living with HIV at KTH during the period 1st July-30th September, 2021.
- To determine the outcomes of COVID-19 among people living with HIV who were admitted to KTH between 1st July-30th September, 2021.

Literature Review

General overview

COVID-19 is threatening gains against the HIV epidemic, including the United States ending the HIV epidemic goals. The ongoing collision of these two global pandemics will continue to need both study and interventions to mitigate the effects of COVID-19 on HIV efforts worldwide [4]. These threats pose a great challenge especially on developing countries like Zambia and quick attention is needed in the preparedness to combat the impact of COVID-19 pandemic on HIV epidemic. Regarding researches which have been done so far especially in the western side of the world, it still remains unclear whether PLWH are at an increased risk of COVID-19 and severe disease manifestations, though there also controversial suggestions from some studies that HIV infected individuals could be protected from severe COVID-19 by means of antiretroviral therapy or HIV-related immune-suppression and such suggestions need further investigations. However, evidence from the preliminary analysis of available data as summarised by Kanwugu and Adadi shows that PLWH are not protected from COVID-19 or severity of the disease. They further added that, HIV related immunosuppression may increase risk of severity of COVID-19 instead confer protection. Even though the study by Kanwungu and Adadi did not show excess morbidity and mortality among PLWH, especially those with viral load suppression on ART, they then advised that PLWH ought to be vigilant and adhere strictly to guidelines and recommendations of how to keep themselves safe from SARS

COV-2 infection

A number of researches have been conducted around the world in trying to assess the impact of COVID-19 on PLWHIV in terms clinical presentations and outcomes, though it is unfortunate that not much has been done on the African side despite it being the continent with a majority of PLWH. According to Varsheny, et al. in a scoping review found the following factors to predispose an individual to COVID-19, having a black racial background, living with comorbidities, being an IDU, being older, having a low CD_4 count and being male. Despite the conclusion of their review not showing any high risk for death by COVID-19 among PLWH, they proposed the need for targeted interventions and pandemic control efforts towards individuals with these risk factors to effectively save lives during the COVID-19 pandemic. Similarly, another study by Karmen, et al. it was found that patient with co-infection of HIV and SARS-CoV-2, when compared

with matched non-HIV patients showed notable trends towards increased rates of intensive care unit admission, mechanical ventilation, and mortality in HIV positive patients though not statistically significant this can be owed to the fact that the target population was small, hence they proposed that a larger study is required to determine whether the trends they observed apply to all HIV positive patients. In a systematic review on COVID-19 outcomes in HIV/AIDS patients by Cooper, et al. found that PLWH with well controlled disease are not at risk of poorer COVID-19 disease outcomes than the general population. They further suggest that it is not clear whether those with poorly controlled HIV disease and AIDS have poorer outcomes, thus leaving room for comparison studies to determine whether a difference exists between those with poorly controlled disease and those with well controlled with COVID -19. Cooper et al. defined well controlled HIV disease as undetectable viral load and adequate CD_4 count. They also proposed the need for further research to elucidate whether superimposed bacterial pneumonia is a risk factor for more severe COVID-19 for people living with HIV as compared to the general population, which showed some indication.

Globally

According to review of various documented literature by Brown, Spinelli and Gandhi as of to date in the United States and Europe they stated that the conclusion of all of these studies signified that PLWH did not seem to be at increased risk of severe outcomes with COVID-19. Another systemic review of epidemiology and outcome of COVID-19 in HIV infected individuals by Ssentongo, et al. reveals that HIV was associated with a significantly higher risk of SARS-CoV-2 infection (RR 1.24, 95% CI 1.05–1.46). Between study variation was high (I2=85, p=0.0003). The pooled prevalence of HIV in COVID-19 patients was 1.22% (95% CI 0.61–2.43%; I2=98%; p<0·01). The prevalence of HIV in COVID-19 patients ranged from a low of 0.26% (95% CI 0.23–0.29%) in Catalonia, Spain to a high of 4.17% (95% CI 0.58–24.35%) in Seattle, USA. The point estimates for the prevalence of HIV of the general population in the analysed cities was half the HIV prevalence in among COVID-19 patients: 0.65% (95% CI 0.48–0.89%). When they stratified the analysis by the country, they found a noticeable difference in the pooled HIV prevalence among COVID-19 patients in the United Sates (1.43%, 95% CI 0.98–2.07%) compared to Spain (0.26%, 95% CI 0.23–0.29%) but the difference was not significant compared to the prevalence in China (0.99%, 95% CI 0.25–3.85%).

The interpretation of results from a study in the UK was that people with HIV in the UK seem to be at increased risk of COVID-19 mortality. The study included 17 282 905 adults, of whom 27 480 (0·16%) had HIV recorded. 14 882 COVID-19 deaths occurred during the study period, with 25 among people with HIV. People living with HIV had higher risk of COVID-19 death than those without HIV after adjusting for age and sex: Hazard Ratio (HR) 2·90 (95% CI 1·96–4·30; p <0·0001), [5].

African region

A large cohort done in South Africa showed that HIV was associated with a higher mortality rate due to COVID-19. They further added that the larger population-based study in South Africa may better estimate the impact of HIV on severe COVID-19 disease, or differing comorbidity burdens and viral suppression between these settings could explain these differences. Comorbidities such as diabetes and cardiovascular disease that are prevalent among PLWH may compound potential risks of HIV itself, and controlling modifiable risk factors previously associated with COVID-19 disease severity among PLWH is therefore important for multiple reasons [6-8].

Zambia

A study by Chanda, et al. of which 612 hospitalized patients who were eligible for the study, 443 (72%) had HIV status recorded. Among those patients, 122 (28%) were HIV positive, and among the 102 HIV positive persons who provided information on ART status, 91 (89%) were receiving ART. Although sex and mean age did not differ by HIV status, among HIV negative patients, the proportion of those aged ≥ 60 years was higher than the proportion of those aged <60 years (p=0.002). The study did not show different outcomes from the studies done in South Africa, the United Kingdom and most of the other regions. Finally, longitudinal data from diverse settings across the world and across the spectrum of COVID-19 disease severity will eventually provide a more complete picture of the impact of HIV on COVID-19 disease over time. Thus, the need for studies such as this one (Table 1 and Figure 1).

Definition of variables and measurement

Variable	Definition	Indicator	Scale of measurement
Clinical outcome	The clinical fate of the patient. Either death or discharge	0. Death	Categorical
		1. Discharge	
		2. Referral	
COVID-19 positive	Patients that were confirmed COVID-19 positive by either RDT or PCR	1. RDT	Categorical
		2. PCR	
Age	The amount of time the respondent has lived	1. 0-25 year's	Categorical
		2. 26-35 year's	
		3. 36-45 year's	
		4. 46-55 year's	

		5. 56-65 year's	
		6. 66-75 year's	
		7. 75 plus year's	
Gender	Sex of the respondent	1. Female	Categorical
		2. male	
Residence	The place a the respondent stay	1. low density	Categorical
		2. High density	
HIV status	Whether the patient is reactive or non -reactive.	1. Negative	Categorical
		2. Positive	
		3. Unknown	
Other comorbidities	Medical condition that is simultaneously occurring with COVID-19 in the respondent	1. Diabetes	Categorical
		2. Hypertension	
		3. Others	

Table 1. Definition of variables and measurements.

Conceptual framework

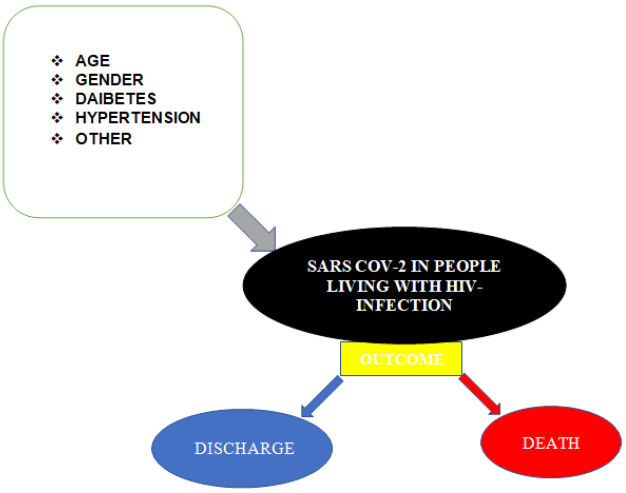

Figure 1. Conceptual framework.

Methodology

Study design

The proposed study is to be a hospital based cross-sectional study. Data will be retrieved from the hospital files of COVID-19 patients that were admitted from July 1st to September 30th 2021 so as to document what their HIV status were, how long they were admitted for and their outcome so as to find out if at all there is a relation between HIV and severity of disease and therefore outcome.

Time period being assessed

Data collection commenced on 1st April 2022, using patients' records who were admitted to the COVID-19 ward from July 1st to September 30th 2021.

Study site

The study was conducted at the Kitwe teaching hospital in Kitwe, Zambia. Kitwe teaching hospital is currently a major tertiary referral hospital and receives patients from the Northern and North Western regions of Zambia.

Study population

The study population comprised adult male and female patients who presented at KTH with Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) during the specified study period.

Selection of patients

Inclusion criteria: Male and female patients 16 years and above who presented to KTH with Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) during the study period.

Exclusion criteria: Patients with a diagnosis of COVID-19 that presented outside the stipulated study time. Those not diagnosed with COVID-19.

Sampling method: Total enumerative sampling method was used.

Sample size

The sample size required for this study included all the reported cases of COVID-19 disease among in the isolation ward at Kitwe Teaching Hospital from 1st July 2020 to 30th September 2021.

The required sample size after knowing the prevalence with a study population of 100 was calculated as follows

$n=z^2PQ/d^2$

Where Z was the level of confidence measure, P was the prevalence rate, Q was 100-P, D was the margin error and n was the sample size.

Taking the sample population as 100, the final sample size was

$n1+(n-1)/n$

Where N was the study population.

Using the information in Table 2, the sample size needed was 309

Level of confidence measure	1.96 (at 95% confidence level)
Margin of error	5%
Baseline levels of the indicators	72%

Table 2. Sample size parameters.

Data collection and tools

The data abstraction sheet that was used is included in the appendix section. This was used to collect all relevant medical records from the hospital files.

Follow up was made using patient file numbers on laboratory results that may be missing from the patient files with records kept at the laboratory.

Data analysis

The data collected from the hospital records was cross-checked by the research supervisor. The demographic, clinical and laboratory statistics collected were coded and cleaned using summary statistics. The data that was entered in to SPSS was checked entry by entry to ensure accuracy and completeness. SPSS v 26 was then employed for statistical analysis. *Chi square* test will be used to determine associations between categorical variables. Data which was collected include:

- File number
- Sex of the patient
- Age
- Residence
- Days of admission
- Clinical outcomes (discharge or death)
- HIV status
- Viral load
- CD4 count
- AST
- ALT
- Total bilirubin
- Plasma albumin
- GGT
- What cause of death was indicated if patient died?

Ethical considerations

Issues of confidentiality: Ethical approval to conduct the study was collected at Tropical Disease Research Centre (TDRC) at Ndola Teaching Hospital through the Michael Chilufya Sata Copperbelt University School of Medicine authorities. Institutional consent to access patient records was sought. Confidentiality and respect were accorded to every participant record and all the information collected during the research was handled according to stipulated guidelines.

Cases were assigned study numbers in series starting from one. Each study number was then paired to the patient's Kitwe teaching hospital lab number and Kitwe teaching hospital file number. This process was known and accessible only to the main researcher involved in this study. Under no circumstances were the names to be included in the study. The data forms were then placed in an encrypted file whose password was known by the histopathology unit head and the senior medical superintendent.

Time frame: After ethical approval is granted a period of 1 month is expected to be enough to collect and analyse all the data.

Study limitations: The study had limitations in terms of laboratory results records which were not available for every patient. This hindered analysis of any other factors and the influence they had on the patients' outcome. The HIV status for 42% of the patients were unknown, this would have an effect on the prevalence and measure of outcomes as it could either underestimate or overestimate the prevalence and mortality rate for HIV infected patients with COVID-19 (Table 3).

Results

Patient information

	Frequency	Percent	Cumulative percent
Age			
15-25	2	1.2	1.2
26-35	6	3.7	4.9
36-45	16	9.8	14.6
46-55	13	7.9	22.6
56-65	47	28.7	51.2
66-75	45	27.4	78.7
76-85	24	14.6	93.3

86-95	10	6.1	99.4
More than 95	1	0.6	100
Total	164	100	
Sex			
Male	101	59.8	59.8
Female	68	40.8	100
Total	169	100	
RVD status			
Negative	56	40.5	40.6
Positive	24	17.4	58
Unknown	58	42	100
Total	138	100	
Type of residence			
Low density	59	51.3	51.3
High density	56	48.7	100
Total	115	100	
Days admitted			
Less than 24 hours	3	1.9	1.9
1–2	24	15.3	17.2
3–6	40	25.5	42.7
7–10	45	28.7	71.3
11–14	22	14	85.4
15–21	11	7	92.4
More than 21	12	7.6	100
Total	157	100	
Diabetes			
No	110	68.8	68.8
Yes	50	31.3	100
Total	160	100	
Hypertension			
No	87	53.4	53.4
Yes	76	46.6	100
Total	163	100	

Table 3. Participant information.

Despite the sample size being 169, the total number of patients could not be considered for various entries, for instance, 5 patients were missing on age, 31 patients on RVD status, 54 entries on residential area details of the patient, and 12 entries on days admitted. This could be attributed to failure to record uniform details of all patients in the hospital's patient file system. For co-morbidities, on obesity, there were more than 100 (against a sample size of 169) missing entries so it could not be recorded among the co-morbidities as it did not represent the picture of the study patients (Figure 2).

Patient outcome

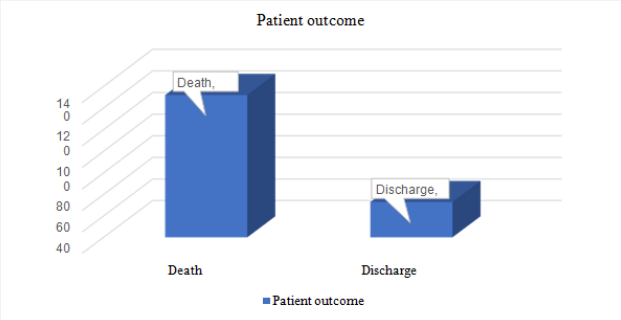

Figure 2. Patient outcomes.

From the Figure 2 above, it could be noted that majority of the patients regardless of their HIV status ended up with death as an outcome of their COVID-19 infection. Only 33 patients were discharged of the patients whose information was recorded for the study (Table 4).

Prevalence of COVID-19 and correlation with patient information

Age group	Sum of squares	df	Mean square	F	Sig.
Between groups	7.026	2	3.513	1.474	0.232
Within groups	383.852	161	2.384		
Total	390.878	163			

Table 4. Analysis of Variance (ANOVA) between patient age and their outcome.

The above Table 4 depicts results for Analysis of variance for age groups of COVID-19 infected patients in relation to their clinical outcome. The results show lack of significance between age group and clinical outcome with significant value of 0.232 (Table 5).

CODVID-19 patient outcome			
Total	Death	Discharge	P-value
Sex			
Male	46	20	0.026
Female	86	13	
Total	127	33	
RVD status			
Negative	37	17	0.086
Positive	21	3	
Total	58	20	
Type of residence			
Low density	50	9	0.052
High density	40	13	
Total	90	22	

Table 5. Correlation between sex, HIV status type of residence and Clinical outcome for COVID-19 infected patients.

Chi-square was used to determine whether there was a relationship between the clinical outcome and patient's gender, HIV status, and their type of residence. The only variable that seemed to influence the clinical outcome was gender (p-value=0.026) (Table 6).

Diabetes			
No	87	21	0.987
Yes	39	10	
Total	126	31	

Hypertension			
No	69	15	0.130
Yes	60	16	
Total	126	31	

Table 6. Correlation between the co-morbidities and clinical outcome.

Chi-square was used to determine presence of a relationship between patient's co-morbidities and their clinical outcome. The co-morbidities considered in this study were diabetes and hypertension. There was no correlation found between these diseases and the patients outcomes (Table 7).

Age group	Sum of squares	df	Mean square	F	Sig.
Between groups	1.568	1	1.568	0.891	0.348
Within groups	126.432	73	1.759		
Total	130	74			

Table 7. ANOVA for days admitted and RVD status.

ANOVA done to determine significance of the relationship between days admitted and HIV status revealed no significance with a significant value of 0.348 which was above the value of significance (0.05).

Majority of the patients were reported to have spent 7–10 days in the hospital. This duration was the mean duration patients would spend during their admission before an outcome. This is based on information from 130 patients whose duration of admission was recorded, from the 169 patients this study targeted.

Discussion

The study used COVID-19 patients information to look at the prevalence of COVID-19 and associated outcomes in COVID-19 patients living with HIV. The study also wanted to establish the outcomes of COVID-19 patients living with HIV. The patients information pertaining to investigations had a huge number above 50% of patients missing so they could not be included in the analysis. The analysis therefore concentrated on age, sex, RVD status, type of residence, history of diabetes and hypertension, and the number of days spent in the hospital [9-12].

Prevalence of COVID-19 among patients living with HIV and the outcomes of the 169 patients who were admitted due to COVID-19 infection, 17.4% (n=24) were HIV positive, compared with 69% and 53% who reported a history of diabetes and hypertension respectively. The study observed no significant relationship between duration of hospital stay and RVD status. The mean duration of hospital stay was 7–10 days [13]. The majority of HIV positive patients (42%) were reported to stay up to 7–10 days before a clinical outcome could be recorded. However, for the HIV negative patients, majority of the patients were reported to have spent 3–6 days prior to a clinical outcome [14]. This was statistically insignificant, showing no relationship between HIV status, and duration of hospital stay (Sig.=0.348).

Gender was a factor observed to influence clinical outcomes for COVID-19 patients, with females reporting more mortalities (87%) than males (70%). This relationship was represented by a p-value of 0.026. Nevertheless, there was no relationship noted between age, RVD status, diabetes and hypertension, and the clinical outcome of COVID-19 infection. The noted lack of relationship between COVID-19 and HIV status has been postulated to be as a result of the protection incurred from retroviral therapy, making PLWH to be protected and not prone to developing more severe cases of COVID-19 disease. However, the lack of an association between diabetes and hypertension, and COVID-19 are in contradiction to what Varsheny, et al. found indicating an increased risk of mortality and morbidity in people with co-morbidities (diabetes and hypertension).

It was observed in the study that HIV infected patients had a higher mortality rate compared with the HIV negative patients and those whose status was undefined, with an 88% of HIV infected patients dying compared with 69% mortality for the HIV negative patients. However, there was no correlation observed between HIV status and a mortality rate (p-value=0.086). The higher rate of mortality in HIV infected individuals resulting from COVID-19 is also supported by Karmen, et al. who mentions that HIV infected individual are at a higher risk to develop more serious illness needing Intensive care management and ventilation and eventually death as opposed to their HIN negative counterparts. However, Karmen, et al. also found this to be of no statistical significance, a reason attributable to the study sample size being too small. Cooper, et al. on the other hand, found that people living with HIV where no different from the general population, where clinical outcomes are concerned and hence postulated that there has to be a disparity between people with well controlled and poorly controlled HIV and AIDS, a hypothesis needing further studies.

Conclusion

The studys aims which were to establish prevalence of COVID-19 among people living with HIV and assessing their outcomes, were achieved. Indicating that people living with HIV did

not stand a higher chance of developing COVID-19 as compared with the rest of the population. The study also indicated a relationship between HIV status and duration of stay of the patient in the hospital, however, the clinical outcomes of the disease were not influenced by the patients HIV status, their co-morbidities such as diabetes and hypertension or their age, but by the gender.

Recommendations

- Improve patient information system so that in case of a pandemic, information is readily available for research that may prompt immense research and hence improvement of management and prognosis.
- Increase awareness among the general population to make them understand that everyone is at risk of developing COVID-19 regardless of their HIV status. Making them understand that COVID-19 outcomes may be fatal regardless of HIV status.
- Increase access to better treatment for patients with special needs, especially those with co-morbidities who may need special care. This will enable the access treatment before worsening of their condition.
- Promote awareness through community outreaches to encourage people with co-morbidities to seek medical attention, for evaluation, when they notice any early symptoms.
- For further studies on the matter, information must be readily available so that the information obtained from the research can be generalized to the entire population seeking COVID-19 treatment. Moreover, a fairly large sample size is needed for further studies.

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