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Journal of the Pan African Thoracic Society

Original Article

In-hospital mortality of acute HIV-associated pulmonary morbidity among COVID-19 negative medical admissions to Dr. George Mukhari Academic Hospital

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Received: 22 December 2022
Accepted: 21 May 2023
EPub Ahead of Print: 26 June 2023
Published: 30 September 2023

DOI
10.25259/JPATS_45_2022

Quick Response Code:

ABSTRACT

Objectives: Human immunodeficiency virus (HIV)-related complications remain a frequent cause of hospital admissions. Pulmonary complications are among the most frequent causes of morbidity and mortality in HIV-infected individuals. We aimed to describe the in-hospital mortality of medical admissions with an acute HIV-associated pulmonary pathology.

Materials and Methods: This was an observational study undertaken at a tertiary care center over 12 months. Variables of interest were as follow: Diagnoses, diagnostic work-up, treatment, mortality rate, and impact of comorbidities and HIV-associated factors on mortality.

Results: Two-hundred and seventy-two patients were studied. The mean age was 42.0 ± 10.8 years. Males constituted 62.4% of the cases. One hundred and thirty patients (47.8%) were anti-retroviral therapy (ART) naive. The median CD4 count was 76 cells/mm^3. The most frequent pulmonary diagnosis was community-acquired pneumonia (CAP) (212; 78%). Gram-negative pathogens were isolated in the majority of patients admitted with infectious complications. Pulmonary tuberculosis (PTB) was confirmed in only 27 (0.9%) of the cases. Significantly more female patients were on ART compared to males (P = 0.0436). Survival rates were not significantly different between the two genders (P = 0.1670). Overall, in-hospital mortality was 25.7%. CD4 counts and comorbidities were not predictive of mortality.

Conclusion: HIV-associated acute pulmonary disease is associated with significant mortality. A large number of patients are diagnosed at an advanced stage of HIV. Programs that encourage voluntary testing and treatment are likely to reduce the high number of late presentations and reduce the poor outcomes. Adherence to the South African thoracic society guideline recommended evaluation for PTB in HIV-infected patients diagnosed with CAP cannot be over-emphasized.

Keywords: HIV, Acute pulmonary morbidity, Mortality

INTRODUCTION

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) remains a cause of significant ill health and death world-wide, with 1.5 million people becoming newly infected with HIV and 650,000 AIDS-related deaths in 2021.[1] South Africa is estimated to have an overall HIV prevalence rate of 13.7%, with approximately 8.2 million individuals living with the disease.[2] HIV-related admissions remain very common in the country.[3,4] Almost 86,000 (85,769) South Africans succumbed to AIDS-related deaths in 2022.[5]

Anti-retroviral therapy (ART) has decreased the incidence of opportunistic infections and allowed for an increase in the life expectancy of HIV-infected persons.[6-8] ART has been freely available to South Africans for more than a decade and a half. Adherence to ART is an important determinant of virologic suppression and has been shown to reduce morbidity and mortality.[9-11]

Pulmonary complications are among the most frequent causes of morbidity and mortality in HIV-infected individuals.[12-14] The spectrum includes infectious and non-infectious complications.[15-17]

Pulmonary infections remain the most frequent cause of hospital admissions for HIV-infected people.[18-20] South African studies suggest pulmonary tuberculosis (PTB), bacterial community-acquired pneumonia (CAP), and *Pneumocystis jirovecii* pneumonia (PJP) be the more common infectious complications.[21,22]

Comorbid conditions have been suggested to significantly increase the odds of poorer health outcomes in HIV-infected persons.[23]

Our primary aim was to determine the in-hospital mortality of COVID-19 negative HIV-positive patients admitted with an acute pulmonary illness. Secondary objectives were to describe the diagnoses, diagnostic work-up, and treatment of the cohort and to assess the contribution of comorbidities and HIV-associated factors to mortality. The focus of our study was on COVID-19 negative patients as we felt concomitant COVID infection would be a significant confounder to our results and, in general, less attention was being paid to this group during the pandemic.

The study was approved by the Institutional Research and Ethics Committee (Sefako-Makgatho University and Dr. George Mukhari academic hospital]) (SMUREC/M32/2020:PG). Due to the observational nature of the study, informed consent was waived.

MATERIALS AND METHODS

This was a cohort study of unselected COVID-19 negative HIV-infected patients admitted to the medical wards of Dr. George Mukhari Academic Hospital with an acute respiratory illness (defined as presentation to hospital within 10 days of symptom onset). The hospital is located in the Tshwane district of the Gauteng Province, South Africa and is surrounded by low- and middle-income communities. The study was conducted between April 1, 2020, and March 31, 2021.

All consecutive admissions of medical patients with a known diagnosis of HIV or who were highly suspected of having and subsequently confirmed with HIV and an acute respiratory illness were included in the study. The researchers were made aware of these cases by the admitting medical teams. The teams had been made aware of the project after approval had been granted by the Institutional Review Board. The investigations and treatment of the patients were at the discretion of the medical teams. We observed the clinical progress of the patients and prospectively documented the results of the diagnostic investigations, the management of the patients and outcomes. The variables of interest were as follows: The degree of immunosuppression as evidenced by the CD4 count and viral load (VL), comorbidities, pathogens isolated and sources of isolation (in cases of suspected infections), % on ARTs, treatment administered, and outcome (death or discharge).

Data analysis

All the data from the study was captured into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS, version 21.0 IBM, USA). Categorical variables are presented as *n* (%). The distribution of non-parametric data was expressed as median and interquartile range (IQR). Continuous variables with a normal distribution are presented as mean ± standard deviation. Comparison of proportions was done using the Fishers exact test. All statistical tests were two-sided at $P = 0.05$.

RESULTS

The study took place over a period of 12-month (April 1, 2020–March 31, 2021). Our study cohort consisted of 272 patients. The mean age of the group was 42.0 ± 10.8. The majority (62.4%) were male.

One hundred and forty-four patients (52.6%) were on ART. There were significantly more female patients on ART than males (64.1% vs. 45.6%; $P = 0.0436$).

The median CD4 count of the cohort was 76 cells/mm^3 (IQR 39–310). The median CD4 count of the male patients was 63 (IQR 20–172) cells/mm^3). Female patients had a median CD4 count of 98 cells/mm^3. This difference was not statistically significant ($P = 0.1630$).

Two hundred and seven patients (76.1%) had a CD4 count below 200 cells/mm^3; 93 (45%) of these patients were on ART.

Seventy-one patients (26%) had a concomitant comorbid illness with 17 (24%) of these having two or more comorbidities [Table 1]. The most frequent clinical diagnosis was community-acquired pneumonia. Other respiratory reasons for admission are summed up in [Table 2].

A number of diagnostic investigations were carried out on the patients as deemed appropriate by the treating clinicians. All patients underwent chest radiography. Four patients (3.3%) underwent CT pulmonary angiography; three were positive for pulmonary emboli. Six patients underwent non-contrast chest CT scans. The remainder of the investigations and

Table 1: Comorbidities and their frequency of occurrence.

Comorbidity	*n* (%)
T2DM	11 (4.0)
HTN	21 (7.7)
COPD	10 (3.6)
Bronchiectasis	19 (6.9)
CKD	17 (6.2)
CHF	12 (4.4)

*T2DM: Type 2 diabetes mellitus; HTN: Hypertension; COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, CHF: Congestive heart failure *n*: number of patients with the comorbid illness

Table 2: Diagnoses.

	n (%)
Pulmonary condition/morbidity	
Community-acquired pneumonia	212 (78)
Opportunistic pneumonias	
PTB	27 (0.9)
Other infective causes	
COPD exacerbation	10 (3.6)
Bronchiectasis exacerbation	17 (6.3)
Non-infectious	
Pulmonary embolism	3 (0.01)

COPD: Chronic obstructive pulmonary disease, PTB: Pulmonary tuberculosis, *n*: number of patients with the diagnosis

the frequency with which they were done is summed up in [Table 3]. Sixty patients (28.3%) with CAP had microbiological documentation of infection. [Table 4] is a summary of the isolates, frequency of detection, and sample source.

The proportion of patients with Gram-negative isolates was higher in those with comorbidities compared to patients without (18.3% vs. 6.0%; $P = 0.004$).

Two hundred and seventy patients (99.3%) received empiric antibiotic therapy (combination of a beta-lactam/beta-lactamase penicillin and a macrolide) as initial treatment. Half of these patients (49.63%) also received concomitant anti-tuberculosis (TB) therapy and just over a quarter (26.47%) received doses of cotrimoxazole appropriate for PJP.

The median length of hospital stay of the patients was 11 (IQR 7.0–17.5 days). The hospital length of stay was not significantly different between survivors and non-survivors (13.8 [±9.86] vs. 14.8 [±14.44]; $P = 0.568$).

Overall, in-hospital mortality was 25.7% ($n = 70$). Survival rates were not statistically significantly different between male and female patients (70.8% vs. 80.4%; $P = 0.1679$). The presence of a comorbid illness did not adversely affect patient survival [Table 5]. HIV-related variables had no impact on mortality rates [Table 6].

Table 3: Additional diagnostic investigations.

Investigation	*n* (%)
Expectorated sputum	89 (32.7)
Induced sputum	6 (2.2)
Blood culture	93 (34.2)
Serum CrAg	82 (30.15)
Urine antigen (for *Legionella*)	1 (0.45)

*CrAg: Cryptococcal antigen, *n*: number of samples submitted

Table 4: Microbial isolates, source of isolation versus number of cases on ART.

	n (%)	Sample	on ART
Pathogen			
Pseudomonas aeruginosa	11 (18.3)	2 BC/9 SPT	9
Enterobacteriaceae	13 (21.6)	2 BC/11SPT	9
Staphylococcus aureus	6 (10)	4 BC/2 SPT	1
Acinetobacter baumannii	1 (1.6)	BC	1
Polymicrobial	10 (16.6)	SPT	6
Streptococcus pneumoniae	1 (1.6)	SPT	0
Haemophilus influenzae	1 (1.6)	SPT	0
Pathogens of unclear significance			
CNS	20 (33)	18 BC/2 SPT	6
Candida albicans	2 (3.3)	SPT	1
MAC	3 (0.01)	SPT	2

*MAC: Mycobacterial avium complex, BC: Blood culture, SPT: Sputum, CNS: *Coagulase negative staphylococcus*, ART: Anti-retroviral therapy, n: number of pathogens isolated

Table 5: Comorbidities versus survival.

Comorbidity	Survivors (%)	Non-survivors (%)	*P*-value
T2DM	9 (26.1)	2 (18.1)	0.73
HPT	17 (26.3)	4 (19.0)	0.60
CHF	11 (26.5)	1 (8.3)	0.31
COPD	7 (25.5)	3 (30)	0.72
Bronchiectasis	15 (26.1)	4 (21.1)	0.80
CKD	12 (25.5)	5 (29.4)	0.78

COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, CHF: Congestive heart failure, HPT: Hypertension

The proportion of patients with comorbid illness and on ART who demised was not statistically significantly different from those with comorbidities, not on ART (2.96% vs. 2.59%; $P = 1.00$).

DISCUSSION

The study confirms previous findings that CAP is a common respiratory infectious complication of and a frequent reason for hospitalization (including intensive care unit

Table 6: HIV-related variables versus survival.

Variable	Survivors	Non-survivors	*P*-value
CD4 (mean)	152.5 (±201.34)	142.1 (±215.97)	0.718
CD4: ≥200 versus <200	N/A	22% versus 25.2%	0.75
% on ART	0.36	0.32	0.678

HIV: Human immunodeficiency virus, ART: Anti-retroviral therapy
N/A: Not applicable

[ICU] admissions) among HIV-infected individuals despite widespread availability of ART.[12,21,24-26]

Studies in South Africa that have reported on the causes of respiratory infections among admitted HIV-infected patients have suggested TB and Gram-positive bacteria to be the more common isolates.[4,21,22] The proportion of patients diagnosed with PTB in this study was much lower than would be expected from the low to middle income communities that the hospital serves. The explanation for this is several-fold. It should be noted that in the three South African studies cited, there was a concerted/deliberate effort to systematically screen every patient for PTB by obtaining multiple samples for TB diagnosis. Our study was, in effect, a review of everyday "standard of care" of such patients by our physician colleagues. In addition, only 35% of the patients had a sputum sample submitted and not all were for TB diagnosis.

Gram-negative pathogens were the more frequent isolates in our study. While this may be a true reflection of the status of isolates in the community we serve, we would recommend a cautious interpretation of this finding as the bulk of the bacterial isolates which were on sputum. The quality of the sputum samples was not assessed. The usefulness of sputum culture in making a microbiological diagnosis of pulmonary bacterial infections has been controversial.[27,28]

About 16% of the infections were poly-microbial. Respiratory infections with more than one pathogen are not unusual in HIV-infected individuals, especially with advanced immunosuppression.[20,21,29] While it is usually encouraged to work with a single diagnosis and treat accordingly, it is worth bearing in mind that respiratory infections in HIV-infected patients may be the result of multiple pathogens that may require their own unique treatments.[11] In a study undertaken by Barbier *et al.* of the causes and outcomes of acute respiratory failure in HIV-associated admissions to an ICU, two or more respiratory processes were identified in 22% of the cases.[20]

Community-acquired *Pseudomonas aeruginosa* and *Staphylococcus aureus* infections were isolated in 18% and 10% of the CAP cases in this study, respectively. Both pathogens have been reported to occur as community-acquired pathogens with increased frequency in HIV-infected persons.[14,25] The number of cases with PTB in our cohort was unusually low compared to studies previously undertaken in the country.[4,22] This is most likely an underestimate as not only does South Africa have a high TB burden, but HIV-positive individuals are much more likely to develop TB. It is worth noting that only 35% (n = 95) of the patients had a sputum sample submitted. We did not pay attention to the quality of the sputum samples collected.

Two hundred and seven patients (76%) had CD4 counts below 200 during the current admission. Almost half of them (47.4%) were ART naïve. Admission of patients with advanced HIV disease and ART naivety in South African hospitals is not uncommon.[4,21,26] ART is freely available in South Africa and, globally, South Africa is reported to support the largest ART program.[9] This finding likely reflects delays in diagnosis and/or patient reluctance to be initiated on ART.

Of particular concern was the large number of patients (45%) on ART that still had evidence of inadequate immune reconstitution (CD4 counts <200 cells/mm^3). Challenges with adherence to treatment and/or drug resistance may be the reasons behind this. Reports of short-term ART adherence among South African patients from multiple urban HIV clinics indicated adherence rates of between 63% and 88%.[30,31] Challenges of retaining people in HIV care through treatment programs in South Africa have been highlighted.[1]

A study of long-term adherence and successful treatment outcomes by Moosa *et al.* concluded that long-term adherence was possible within a structured ART program with close adherence monitoring.[9]

There are significantly more women than men on ART. The explanation for this finding remains obscure. The previous studies have suggested that fewer men go for voluntary counseling and testing and were less likely to initiate ART if they tested positive.[32,33] Other studies have disputed this, suggesting that men are as willing to be tested and treated as non-pregnant women.[34-37]

The investigations carried out for an infectious etiology in this study appear standard. There is no consensus among clinicians on an algorithm for diagnosis of pulmonary infections in HIV patients. The recommendation has been for the diagnostic approach to be guided by the local epidemiologic findings.[14] Flexible bronchoscopy was conspicuously absent as an investigational tool. Communication with the local respiratory team indicated that the study took place just as the COVID-19 pandemic was starting, with concerns about the risk of transmission of the infection to the staff posed by the technique. In addition, some patients were deemed too unwell for the procedure to be undertaken safely. Ordinarily bronchoscopy is a procedure

with a high yield for pulmonary disease in HIV-infected patients.[14]

The majority of the patients with a suspected infective etiology were initiated on empiric standard antibiotic therapy. About a quarter of the patients received also empiric cotrimoxazole for PJP. Both the World Health Organization (WHO) and South African thoracic society (SATS) advise addition of empiric therapy for PJP when patients fulfill the WHO case definition.

Empiric anti-TB therapy was started in almost half of the patients. Guidelines recommend that empiric anti-TB treatment should not be routinely initiated unless there is a miliary pattern on a chest X-ray or the patient is severely ill and the suspicion for TB is high.[38,39]

A mortality rate of 26% is unacceptably high. We could not find comparative data (mortality data related to pulmonary morbidity in HIV-infected admitted patients) from our review of the literature. Most published studies referring to mortality as an outcome has focused on HIV-associated complications in general and not specifically as they relate to pulmonary morbidity. Barbier *et al*. found in-hospital mortality of 19.7% among their cohort of HIV-infected patients admitted to an ICU in acute respiratory failure.[20] Spanish researchers found an overall 30-day mortality of 7% among HIV-infected admissions for community-acquired pulmonary sepsis.[28] Results of admissions for CAP in a teaching hospital in Kwazulu-Natal Nyamande found a 15.9% in-hospital mortality among patients infected with HIV.[22] These comparisons are to be interpreted cautiously given the differences in patient populations.

Being male was not associated with an increased risk of death in this study. For reasons not clearly understood, increased mortality has been reported among HIV-infected men on ART over women.[40-42] Some of the reasons offered by the researchers were late initiation of treatment and challenges with follow-up.

We could not establish a relationship between CD4 count and in-hospital mortality. Similar results were described by Barbier *et al*. in France as well as by Meintjes's and Mkoko's groups in South Africa.[4,20,26] Shortcomings of using the CD4 as a sole determinant of the degree of immune-depression have been well described.[43] Data on VL were not available. VL is a better predictor of mortality and HIV/AIDS progression than CD4 cell count.[44] Suppression of VL to undetectable levels has been associated with reduced HIV-related mortality.[45] Compliance with ART in our cohort was not examined. Adherence to ART has been associated with better chances of survival for HIV-infected patients.[10]

Survival rates were not significantly different between patients with comorbidities and those without. This finding should be interpreted as being equivocal, because the numbers of patients computed for comorbid illnesses were too small (analysis was under-powered). HIV-infected patients are living longer and develop comorbidities related to aging and the HIV infection itself.[12,13,17] We believe that it would be reasonable to evaluate the impact of comorbidities on survival in HIV-infected patients presenting with an acute respiratory illness.

CONCLUSION

Patients admitted with HIV-associated acute pulmonary morbidity have significant mortality. Approximately half of the patients were ART naïve, with advanced disease despite ready availability of ART. Programs that encourage voluntary testing and treatment are likely to reduce the high number of late presentations and reduce the poor outcomes. More studies looking at the pathogens in CAP in our community are necessary to clarify the dominant pathogens. Future studies looking at other HIV-associated variables such as the VL and treatment adherence in relation to mortality are indicated. The SATS guidelines for the management of CAP in adults recommends among others, that in HIV-infected patients presenting with CAP, clinicians should have a low-threshold for carrying out testing for PTB.[38] TB-LAM antigen testing is advised in those with CD4 counts below 100 cells/mm^3 or stage 3 or 4 disease if sputum is unavailable.[38]

Study strengths

The data collection tool was piloted on the first ten patients to ensure collection of appropriate data. Our cohort of patients was unselected thereby minimizing selection bias. The sample size was statistically derived to be representative.

Study limitations

This was a single-center study and the surrounding communities may have a different epidemiology of acute respiratory illnesses; compromising the generalizability of the results. The study was limited to acute respiratory conditions only. There are other non-acute HIV-associated respiratory conditions that can be a significant risk to people's health. Adherence to ART was not systematically studied. This could have offered an understanding of continued immunologic failure in those patients on ART.

Acknowledgments

The authors wish to express their sincere gratitude to Prof. Olankule Towobola for assistance with the statistical calculations and to Andrew Scoltz for his professional editing services.

Declaration of patient consent

The Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS. UNAIDS Global AIDS Update-confronting Inequalities-lessons for Pandemic Responses from 40 Years of AIDS. Switzerland: Joint United Nations Programme on HIV/AIDS; 2021. Available from: https://www.unaids.org/en/resources/documents/2021/2021-global-aids-update [Last accessed on 2023 May 21].
2. Statistics South Africa. Mid-year Population Estimates-2021. Statistical Release P0302. Pretoria: Statistics South Africa; 2021. Available from: https://www.statssa.gov.za/publications/P0302/P03022021.pdf [Last accessed on 2023 May 21].
3. Laher AE, Venter WD, Richards GA, Paruk F. Profile of presentation of HIV-positive patients to an emergency department in Johannesburg, South Africa. South Afr J HIV Med 2021;22:1177.
4. Meintjes G, Kerkhoff AD, Burton R, Schutz C, Boulle A, Van Wyk G, *et al*. HIV-related medical admissions to a South African district hospital remain frequent despite effective antiretroviral therapy scale-up. Medicine (Baltimore) 2015;94:e2269.
5. Statistics South Africa. Number of Deaths from AIDS in South Africa 2002-2022. Pretoria: Statistics South Africa; 2022. Available from: https//:www.statista.com [Last accessed on 2023 May 21].
6. Wandeler G, Johnson LF, Egger M. Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: Comparisons with general population. Curr Opin HIV AIDS 2016;11:492-500.
7. Bor J, Herbst AL, Newell ML, Bärnighausen T. Increases in life expectancy in rural South Africa: Valuing the scale-up of HIV treatment. Science 2013;339:961-5.
8. Lloyd-Smith E, Brodkyn E, Wood E, Kerr T, Tyndall MW, Montaner JS, *et al*. Impact of HAART and injection drug use on life expectancy of two HIV-positive cohorts in British Columbia. AIDS 2006;20:445-50.
9. Moosa A, Gengiah TN, Lewis L, Naidoo K. Long-term adherence to antiretroviral therapy in a South African adult patient cohort: A retrospective study. BMC Infect Dis 2019;19:775.
10. Rai S, Mahapatra B, Sircar S, Raj PY, Venkatesh S, Shaukat M, *et al*. Adherence to antiretroviral therapy and its effect on survival of HIV-infected individuals in Jharkhand, India. PLoS One 2013;8:e66860.
11. Grimwood A, Fatti G, Mothibi E, Malahlela M, Shea J, Eley B. Community adherence support improves programme retention in children on antiretroviral treatment: A multicentre cohort study in South Africa. J Int AIDS Soc 2012;15:17381.
12. Fitzpatrick ME, Kunisaki KM, Morris A. Pulmonary disease in HIV-infected adults in the era of antiretroviral therapy. AIDS 2018;32:277-92.
13. Triplette M, Crothers K, Attia EF. Non-infectious pulmonary diseases and HIV. Curr HIV/AIDS Rep 2016;13:140-8.
14. Benito N, Moreno A, Miro JM, Torres A. Pulmonary infections in HIV-infected patients: An update in the 21st century. Eur Respir J 2012;39:730-45.
15. Staitieh B, Guidot DM. Noninfectious pulmonary complications of human immunodeficiency virus infection. Am J Med Sci 2014;348:502-11.
16. Gingo MR, Morris A. Pathogenesis of HIV and the lung. Curr HIV/AIDS Rep 2013;10:42-50.
17. Crothers K, Huang L, Goulet JL, Goetz MB, Brown ST, Rodriguez-Barradas MC, *et al*. HIV infection and risk for incident pulmonary diseases in the combination antiretroviral therapy era. Am J Respir Crit Care Med 2011;183:388-95.
18. Brown J, Lipman M. Community-acquired pneumonia in HIV-infected individuals. Curr Infect Dis Rep 2014;16:397.
19. Feldman C, Anderson R. HIV-associated bacterial pneumonia. Clin Chest Med 2013;34:205-16.
20. Barbier F, Coquet I, Legriel S, Pavie J, Darmon M, Mayaux J, *et al*. Etiologies and outcome of acute respiratory failure in HIV-infected patients. Intensive Care Med 2009;35:1678-86.
21. Maartens G, Griesel R, Dube F, Nicol M, Mendelson M. Etiology of pulmonary infections in human immunodeficiency virus-infected inpatients using sputum multiplex real-time polymerase chain reaction. Clin Infect Dis 2020;70:1147-52.
22. Nyamande K, Lalloo UG, John M. TB presenting as community-acquired pneumonia in a setting of high TB incidence and high HIV prevalence. Int J Tuberc Lung Dis 2007;12:1308-13.
23. Rodriguez-Penney AT, Iudicello JE, Riggs PK, Doyle K, Ellis RJ, Letendre SL, *et al*. Co-morbidities in persons infected with HIV: Increased burden with older age and negative effects on health-related quality of life. AIDS Patient Care STDS 2013;27:5-16.
24. Gordin FM, Roediger MP, Girard PM, Lundgren JD, Miro JM, Palfreeman A, *et al*. Pneumonia in HIV-infected persons: Increased risk with cigarette smoking and treatment interruption. Am J Respir Crit Care Med 2008;178:630-6.
25. Afessa B, Green B. Bacterial pneumonia in hospitalized patients with HIV infection: The pulmonary complications, ICU support, and prognostic factors of hospitalized patients with HIV (PIP) study. Chest 2000;117:1017-22.
26. Mkoko P, Raine RI. HIV-positive patients in the intensive care unit: A retrospective audit. S Afr Med J 2017;107:877-81.
27. Ogawa H, Kitsios GD, Iwata M, Terasawa T. Sputum gram stain for bacterial pathogen diagnosis in community-acquired pneumonia: A systematic review and Bayesian meta-analysis of diagnostic accuracy and yield. Clin Infect Dis 2020;71:499-513.
28. Fukuyama H, Yamashiro S, Kinjo K, Tamaki H, Kishaba T. Validation of sputum gram stain for treatment of community-acquired pneumonia and healthcare-associated pneumonia:

A prospective observational study. BMC Infect Dis 2014;14:534.
29. Cilloniz C, Torres A, Polverino E, Gabarrus A, Amaro R, Moreno E, *et al*. Community-acquired lung respiratory infections in HIV-infected patients: Microbial aetiology and outcome. Eur Respir J 2014;43:1698-708.
30. El-Khatib Z, Ekstrom AM, Coovadia A, Abrams EJ, Petzold M, Katzenstein D, *et al*. Adherence and virologic suppression during the first 24 weeks on antiretroviral therapy among women in Johannesburg, South Africa-a prospective cohort study. BMC Public Health 2011;11:88.
31. Maqutu D, Zewotir T, North D, Naidoo K, Grobler A. Factors affecting first-month adherence to antiretroviral therapy among HIV-positive adults in South Africa. Afr J AIDS Res 2010;9:117-24.
32. Venkatesh KK, Madiba P, De Bruyn G, Lurie MN, Coates TJ, Gray GE. Who gets tested for HIV in a South African urban township? Implications for test and treat and gender-based prevention interventions. J Acquir Immune Defic Syndr 2011;56:151-65.
33. Muula AS, Ngulube TJ, Siziya S, Makupe CM, Umar E, Prozesky HW, *et al*. Gender distribution of adult patients on highly active antiretroviral therapy (HAART) in Southern Africa: A systematic review. BMC Public Health 2007;7:63.
34. Dovel K, Yeatman S, Watkins S, Poulin M. Men's heightened risk of AIDS-related death: The legacy of gendered HIV testing and treatment strategies. AIDS 2015;29:1123-5.
35. Njeru MK, Blystad A, Shayo EH, Nyamongo IK, Fylkesnes K. Practising provider-initiated HIV testing in high prevalence settings: Consent concerns and missed preventive opportunities. BMC Health Serv Res 2011;11:87.
36. Ministry of Health. Integrated HIV Program Report (January-March 2014). Lilongwe, Malawi: Ministry of Health; 2014.
37. Sloan DJ, van Oosterhout JJ, Malisita K, Phiri EM, Lalloo DG, O'Hare B, *et al*. Evidence of improving antiretroviral therapy treatment delays: An analysis of eight years of programmatic outcomes in Blantyre, Malawi. BMC Public Health 2013;13:490.
38. Boyles TH, Brink A, Calligaro GL, Cohen C, Dheda K, Maartens G, *et al*. South African guideline for the management of community-acquired pneumonia in adults. J Thorac Dis 2017;9:1469-502.
39. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach. Available from: https://www.who.int/entity/hiv/pub/guidelines/keypopulations-2016/en/index.htm [Last accessed on 2023 May 21].
40. Bärnighausen T, Herbst AJ, Tanser F, Newell ML, Bor J. Unequal benefits from ART: A growing male disadvantage in life expectancy in rural South Africa. In: Rizza SA, Temesgen Z, editors. In: 21st Conference on Retroviruses and Opportunistic Infections (CROI 2014) Boston, Massachusetts, USA-March 3-6; 2014.
41. Kanters S, Nansubuga M, Mwehire D, Odiit M, Kasirye M, Musoke W, *et al*. Increased mortality among HIV-positive men on antiretroviral therapy: Survival differences between sexes explained by late initiation in Uganda. HIV AIDS (Auckl) 2013;5:111-9.
42. Cornell M, Schomaker M, Garone DB, Giddy J, Hoffmann CJ, International Epidemiologic Databases to Evaluate AIDS Southern Africa Collaboration, *et al*. Gender differences in survival among adult patients starting antiretroviral therapy in South Africa: A multicentre cohort study. PLoS Med 2012;9:e1001304.
43. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents. Bethesda (MD): Department of Health and Human Services; 2015. Available from: https://aidsinfo.nih.gov/contentfiles/adultandadolescentgl.pdf [Last accessed on 2023 May 21].
44. Shoko C, Chikobvu D. A superiority of viral load over CD4 cell count when predicting mortality in HIV patients on therapy. BMC Infect Dis 2019;19:169.
45. Chakraborty H, Iyer M, Duffus WA, Samantapudi AV, Albrecht H, Weissman S. Disparities in viral load and CD4 count trends among HIV-infected adults in South Carolina. AIDS Patient Care STDS 2015;29:26-32.

How to cite this article: Seema L, Mpe MJ. In-hospital mortality of acute HIV-associated pulmonary morbidity among COVID-19 negative medical admissions to Dr. George Mukhari academic hospital. J Pan Afr Thorac Soc 2023;4:124-30.