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# The bacterial profile and antibiotic susceptibility pattern in respiratory tract samples from art-experienced HIV-positive adults in Uganda

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## Abstract

### Introduction

Microbial infections are a major cause of morbidity and mortality among people living with HIV (PLWH). Respiratory tract infections (RTIs) are responsible for approximately 70% of illnesses among PLWH. Drug resistant bacteria are highly prevalent among PLWH and this is a public health concern.

### Methods

This is a retrospective analysis of data collected during the COSTOP trial between 2011 and 2013. Sputum collected on spot from participants presenting with a productive cough was examined using Gram, Ziehl-Neelsen stains and cultured on suitable bacteriological media. Antimicrobial sensitivity testing was done on isolated pathogens, by disc diffusion technique.

### Results

We included 687 participants with mean age 41.3 (SD 8.2) years of whom 76.4% were female. Two hundred one sputum samples grew bacteria; *Moraxella species* (27.4%), *Streptococcus pneumoniae*(25.4%), *Haemophilus influenza*(22.4%), *Mycobacterium species*(4.5%), *Pseudomonas species*(4.0%), *Staphylococcus aureus*(4.0%), *Escherichia coli* (1.0%), *Klebsiella species* (1.0%), other bacteria (10.4%). A higher monthly income greater than or equal to 30$ (aOR = 0.63, 95%CI: 0.40–0.99) and longer duration since HIV diagnosis (aOR = 1.06, 95%CI: 1.0–1.11) were found to be independently associated with a positive bacterial culture. Moraxella *sp*, H. *influenza* and Pseudomonas had zero sensitivity towards cotrimoxazole. Sensitivity to erythromycin was low among Moraxella *sp* (28.6%), H.

*influenza* (31.6%) and S. *aureus*(42.9%) and other bacteria (42.9%). Most isolates were sensitive to Amoxicillin + Clavulanic acid and ceftriaxone.

## Conclusion

There is a very low sensitivity of isolated bacteria to commonly prescribed antibiotics that are more available through the national supply chain, which is of public health concern. Urgent steps to tackle the high antimicrobial resistance among PLWH is required.

## Introduction

For over three decades, Human Immunodeficiency Virus (HIV) infection remains a disease of public health importance with approximately 37.6 million people living with HIV (PLWH) globally in 2020 [1]. Sub-Saharan Africa (SSA) suffers the highest burden of HIV with nearly 70% of global HIV infections [2]. Since the introduction of antiretroviral therapy (ART), PLWH have an improved quality of life however, microbial infections are still a major cause of morbidity and mortality among this population [3], with approximately 70% of illnesses being respiratory tract infections (RTIs) [4, 5]. Ojha et al. reported a high prevalence (47%) of respiratory tract infections caused by bacterial pathogens among PLWH [5] and, factors associated with these infections include low CD4 counts (<200 cells/μl) and detectable viral loads [5, 6].

HIV infection causes a progressive depletion of CD4 T cells as well as an impairment of cellular and humoral immunity through a dysfunction of the T and B cells respectively [7]. A dysfunction of T cells leads to abnormal cellular responses while a dysfunction of B cells leads to a lack of antibody responses to infections. The resultant immune dysfunction, deregulation and depletion of CD4 lymphocytes causes an increased susceptibility to infections and the subsequent risk of other complications like resistant pathogens [8, 9]. HIV infection causes an alteration in lung host defences for example, it affects mucociliary function which may contribute to an increase RTIs among PLWH [9]. PLWH are at increased risk of hospital acquired infections due to their frequent contact with health care system through frequent clinic visits and admissions [10]. The frequent infections and admissions among PLWH, pill burden leading to unfinished doses and inappropriate use of drugs through self-medication due to easy access to over the counter drugs are some of the factors that have led to the development of antimicrobial resistance among this population [11].

Antimicrobial resistance is an emerging global problem of public health importance [4]. Previous studies have reported a much higher prevalence of drug resistant bacteria among PLWH (79%) compared to their HIV negative counterparts (30%) [10, 12]. Prophylactic cotrimoxazole given to PLWH over prolonged periods of time to prevent opportunistic infections has been reported to give rise to antibiotic resistance [13]. Resistant microbes are more difficult to manage since they require alternative medications and or higher doses of drugs, both of which are more expensive, not readily available in SSA and or toxic to the patient [13]. Additionally, laboratory capacity for identifying AMR is still limited in many parts of SSA; data are therefore still limited on antimicrobial susceptibility patterns among PLWH in SSA [10]. It is important to understand the common disease-causing pathogens among PLWH and current antibiotic susceptibility patterns for better management. We studied the susceptibility pattern of microorganisms isolated from respiratory samples taken from PLWH in central Uganda.

# Methods

## Study design and setting

We conducted a retrospective analysis of data collected during the COSTOP trial *(Safety of discontinuing cotrimoxazole prophylaxis among HIV infected adults in Uganda*: *a randomised controlled trial*, *ISRCTN44723643)* conducted between January 2011 and March 2013 in two HIV care clinics in Masaka and Entebbe in central Uganda [14, 15].

The COSTOP trial enrolled HIV positive adults (≥18 years) who had been on ART and cotrimoxazole prophylaxis for at least six months, clinically asymptomatic and had CD4 cell counts of >250 cells/$mm^3$ prior to enrolment. Individuals who had an acute illness, grade three or four anaemia, neutropenia or thrombocytopenia, known hypersensitivity to cotrimoxazole, and pregnant women were excluded.

## Participants and eligibility

The current analysis included COSTOP trial participants who presented to the clinic with a productive cough and provided sputum at any time during the trial. Participants were asked to collect sputum in a dry, leak proof, sterile container after rinsing their mouth with water. Samples were immediately transported to the laboratory for microscopy, culture, and sensitivity.

## Laboratory

Samples were examined microscopically using Gram, Ziehl-Neelsen stains and cultured on suitable bacteriological media (Blood, Chocolate, MacConkey agar and Subouroid agar). Samples were incubated at 37˚c for 24hrs, the pathogens that grew from incubated samples were identified microscopically and biochemically using analytical profile index (API) and by sensitivity testing. Antimicrobial sensitivity testing was done on isolated pathogens, by disc diffusion technique [16]. The diameter of the zone of inhibition was measured and compared to that of European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards [17] to determine resistance or sensitivity of a pathogen to the antimicrobial.

## Study variables

The dependent variable was bacterial culture positivity of sputum collected during the study. The independent variables were gender, age (years) categorized under age groups <35years, 35–55 years and >55 years, recent and initial CD4 counts categorized into <200, 200–300 and >300 cells/ul, study arm in the COSTOP trial (cotrimoxazole arm, placebo arm), highest education level attained categorized into none, primary and secondary school, marital status categorized into married, divorced and single, monthly income ($) categorized into those earning <30 and >/ = 30, ART regimen categorized into First line and second line, duration on ART (years) and period since HIV diagnosis (years).

## Statistical analysis

The data collected were managed in MS Access, 2003 (Microsoft Corporation, Redmond, WA) and data analyses were performed using Stata 14 (Stata Corp, College Station, Texas 77845 USA) [11]. Continuous variables were presented as means with standard deviation (SD) and categorical variables as frequencies and percentages. The proportion of bacterial culture positivity overall, and by different participant characteristics were determined as number culture positive divided by the total sample, expressed as a percentage. A bar graph was used to display the frequency of bacterial isolates, and frequency and percentages used to summarise antibacterial susceptibility of bacteria isolated in sputum. We did not consider multiple

samples per participant in our analysis because we considered the primary out as binary (positive or negative). For the fewer participants 249/687 (36%) with more than one samples, we considered the results of the last sample for those that remained negative and the first positive result for those that had a positive result at any point during follow up. Only 11 had at least two culture positive samples. The reason for not considering this as a repeat measure analysis was informed by the fact that majority of the participants 438/687 (64%) had only one sample tested.

To determine factors associated with bacterial culture positivity, we fitted both univariable and multivariable logistic regression models. At univariable analysis, all factors in logit models with likelihood ratio test p-value $<0.2$, were selected for multivariable logit model. Factors were retained in the multivariable logit model if their inclusion did not make the model fit significantly worse at $p<0.05$ on likelihood ratio test. We present the results as adjusted odds ratios (AOR) with corresponding 95% confidence intervals (CI)

### Ethical approval statement

All participants enrolled into the main COSTOP trial gave written informed consent prior to any study procedures. The COSTOP study received approval from Uganda Virus Research Institute Ethics committee, National Drug Authority and Uganda National Council for Science and Technology.

## Results

### Participants' characteristics

The characteristics of participants included in the analysis are summarised in Table 1. We included 687 participants in the analysis with mean age was 41.3 years (SD ±8.23) and 76.4% were female. Overall, 51.1% of participants received cotrimoxazole, 70.2% earned less than $30 monthly and 60.3% had primary level education. We observed that the mean period since HIV diagnosis was 5.49 years (SD ±4.50) and the mean period on ART was 3.79 years (SD ±1.86) with 97.9% of participants on a first line ART regimen. Regarding CD4 counts, 89.7% had a recent CD4 of >300cell/μl however, 68.4% had a nadir CD4 count of <200cell/μl.

### Bacterial culture positivity and prevalence of isolated microorganisms

A total of 201 (29.3%) samples had bacterial growth, with 9 samples growing more than one bacterial organism. Isolated bacteria included *Moraxella species* (55, 27.4%), *Streptococcus pneumoniae* (51, 25.4%), *Haemophilus influenza* (45, 22.4%), *Mycobacterium species* (11, 4.5%), *Pseudomonas species* (8, 4.0%), *Staphylococcus aureus* (8, 4.0%), *Escherichia coli* (2, 1.0%), *Klebsiella species* (2, 1.0%) and other bacteria (19, 10.4%) (Fig 1).

### Factors associated with bacterial culture positivity

The factors found to be independently associated with having a bacterial culture positive sample shown in Table 1 where; monthly income ≥ $30 (aOR = 0.63, 95%CI 0.40–0.99) compared to those earning below $30 and longer duration of years since HIV diagnosis [aOR = 1.06, 95% CI 1.01–1.11]. Participants who received placebo were more likely to have a positive sputum culture than those who received cotrimoxazole however this was not found to have statistical significance (aOR = 1.37, 95% CI 0.94–1.98).

**Table 1. Factors associated with bacterial growth in sputum cultures among ART-experienced HIV-positive individuals in Uganda (N = 687).**

| Characteristic | N = 687 n(%) | Culture positive (%) | OR (95% CI) | P-value | AOR (95% CI) | P-value |
|---|---|---|---|---|---|---|
| Sex | | | | | | |
| Female | 525 (76.4) | 113 (21.5) | 1 | | 1 | |
| Male | 162 (23.6) | 43 (26.5) | 1.32 (0.88–1.98) | 0.183 | 1.37 (0.89–2.11) | 0.156 |
| Age (years) | | | | | | |
| <35 | 161 (23.4) | 40 (24.8) | 1 | | | |
| 35–55 | 482 (70.2) | 110 (22.8) | 0.89 (0.59–1.36) | 0.599 | 0.91 (0.59–1.41) | 0.666 |
| >55 | 44 (6.4) | 6 (13.6) | 0.48 (0.19–1.21) | 0.120 | 0.43 (0.17–1.13) | 0.086 |
| Receiving cotrimoxazole | | | | | | |
| cotrimoxazole | 351 (51.1) | 71 (20.2) | 1 | | | |
| placebo | 336 (48.9) | 85 (25.3) | 1.34 (0.93–1.91) | 0.113 | 1.37 (0.94–1.98) | 0.098 |
| Education level | | | | | | |
| None | 101 (14.7) | 26 (25.7) | 1 | | | |
| Primary | 414 (60.3) | 91 (22.0) | 0.81 (0.49–1.34) | 0.419 | | |
| Secondary | 172 (25.0) | 39 (22.7) | 0.85 (0.48–1.50) | 0.566 | | |
| Marital status | | | | | | |
| Married | 284 (41.3) | 62 (21.8) | 1 | | | |
| Divorced | 377 (54.9) | 88 (23.3) | 1.09 (0.75–1.58) | 0.646 | | |
| Single | 26 (3.8) | 06 (23.1) | 1.07 (0.41–2.79) | 0.883 | | |
| Monthly income ($) | | | | | | |
| <30 | 448 (70.2) | 109 (24.3) | 1 | | | |
| >/ = 30 | 190 (29.8) | 38 (20.0) | 0.78 (0.51–1.18) | 0.236 | 0.63 (0.40–0.99) | 0.049 |
| Recent CD4* | | | | | | |
| <200 | 11 (1.6) | 1 (9.1) | 1 | | | |
| 200–300 | 58 (8.4) | 18 (31.0) | 4.50 (0.53–37.85) | 0.166 | 5.09 (0.58–44.60) | 0.141 |
| >300 | 616 (89.7) | 137 (22.2) | 2.86 (0.36–22.54) | 0.318 | 2.86 (0.35–23.44) | 0.326 |
| Nadir CD4* | | | | | | |
| <200 | 470 (68.4) | 105 (22.3) | 1 | | | |
| 200–300 | 123 (17.9) | 30 (24.4) | 1.12 (0.70–1.79) | 0.629 | | |
| >300 | 18 (2.6) | 4 (22.2) | 0.99 (0.32–3.08) | 0.991 | | |
| ART regimen* | | | | | | |
| First line | 662 (97.9) | 151 (22.8) | 1 | | | |
| Second line | 14 (2.1) | 1 (7.1) | 0.26 (0.03–201) | 0.196 | 0.24 (0.03–1.94) | 0.180 |
| Duration on ART, (mean (SD)) yrs | 3.79 (1.86) | 3.75 (1.84) | 0.98 (0.89–1.08) | 0.726 | | |
| Years since HIV diagnosis, (mean (SD)) yrs | 5.49 (4.50) | 6.20 (6.83) | 1.04 (1.00–1.09) | 0.053 | 1.06 (1.01–1.11) | 0.025 |

ART = antiretroviral therapy; HIV = Human Immunodeficiency Virus

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## Antibiotic sensitivity of isolated microorganisms

The sensitivity of bacterial isolates is shown in Table 2. Most isolates were highly sensitive to Amoxicillin + Clavulanic acid and ceftriaxone with *Moraxella sp*. *and*, *Streptococcus pneumoniae* having 100% sensitivity to both. *Pseudomonas* had 100% sensitivity to gentamycin while H. *influenza* showed 100% sensitivity to ceftriaxone and 88.6% sensitivity to Amoxicillin + Clavulanic acid. Other bacteria showed the highest sensitivity to ceftriaxone and gentamycin (85.7%).

All isolates had very low sensitivity to cotrimoxazole (<17%). *Moraxella sp*, H. *influenza* and *Pseudomonas* showed zero sensitivity to cotrimoxazole. *Moraxella* sp (28.8%), H. *influenza* (31.6%), S. *aureus* (42.9%) and other bacteria (42.9%) also had low sensitivity towards

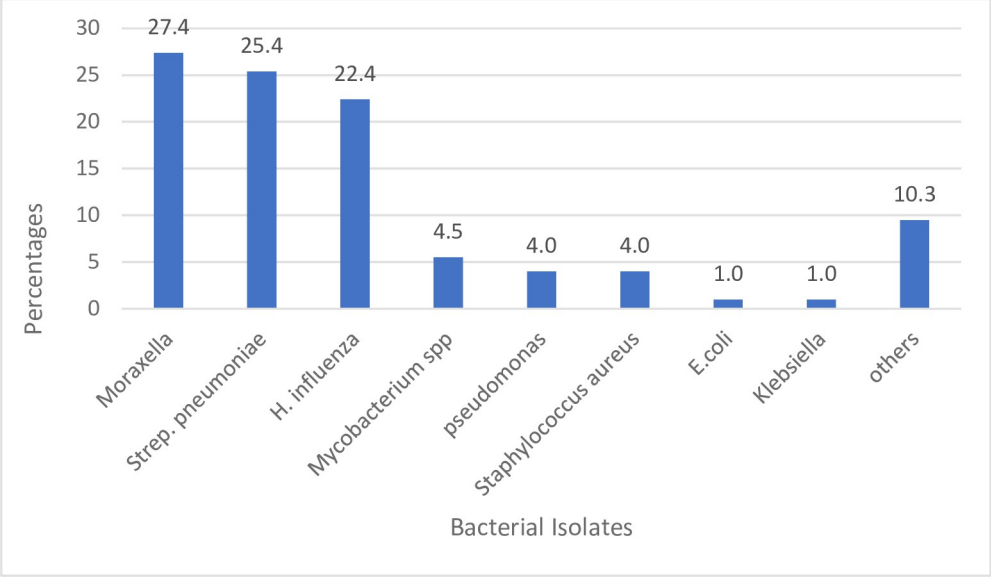


**Fig 1. Frequency of bacterial isolates.**

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erythromycin. H. *influenza* (50.0%) and other bacteria (69.2%) had relatively low sensitivity towards ciprofloxacin.

## Discussion

We cultured sputum from ART experienced PLWH with a productive cough and approximately 30% of the sputum samples had bacterial growth. This is similar to what was reported by Akingbade OA et al who found a prevalence of 24.2% positive cultures from sputum collected from participants with lower RTIs [18], but lower than approximately 44% prevalence reported by Adhanom et al [19]. Adhanom et al included both ART experienced and ART naïve participants that were suspected of pneumonia, which more a severe disease than the presentation of cough that was considered in our study. Our participants were all ART experienced, indicating they might have had a better immunity than those included in Adhanom et al study. Additionally, Adhanoum et al's study was conducted in three years after the COSTOP study, during which period there might have been an increase in antimicrobial

**Table 2. Antibacterial susceptibility rates of bacterial isolated from sputum of PLWH.**

| | *Moraxella species* | | | *Streptococcus pneumoniae* | | | *Haemophilus influenza* | | | *Pseudomonas species* | | | *Staphylococcus aureus* | | | *Others* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N = 55 | | | N = 51 | | | N = 45 | | | N = 8 | | | N = 8 | | | N = 34 | | |
| | T | S | S% | T | S | S% | T | S | S% | T | S | S% | T | S | S% | T | S | S% |
| **Cotrimoxazole** | **43** | **0** | **0.0** | **39** | **1** | **2.6** | **37** | **0** | **0.0** | **3** | **0** | **0.0** | **6** | **1** | **16.7** | **21** | **2** | **9.5** |
| Erythromycin | 42 | 12 | **28.6** | 38 | 30 | **78.9** | 38 | 12 | **31.6** | 0 | 0 | **n/a** | 7 | 3 | **42.9** | 7 | 3 | **42.9** |
| Amoxyl+clavulanic acid | 42 | 42 | **100.0** | 4 | 4 | **100.0** | 35 | 31 | **88.6** | 0 | 0 | **n/a** | 6 | 6 | **100.0** | 7 | 6 | **85.7** |
| ciprofloxacin | 0 | n/a | **n/a** | 0 | n/a | **n/a** | 2 | 1 | **50.0** | 5 | 4 | **80.0** | 0 | n/a | **n/a** | 13 | 9 | **69.2** |
| Ceftriaxone | 2 | 2 | **100.0** | 35 | 35 | **100.0** | 1 | 1 | **100.0** | 2 | 1 | **50.0** | 0 | n/a | **n/a** | 13 | 10 | **76.9** |
| Gentamycin | 0 | n/a | **n/a** | 0 | n/a | **n/a** | 0 | 0 | **n/a** | 5 | 5 | **100.0** | 0 | n/a | **n/a** | 14 | 12 | **85.7** |

NOTE: Amoxyl + clavulanic acid = Amoxicillin + Clavulanic acid, T = number tested, S = sensitivity

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resistance, leading to reduced response by the bacteria to antibiotics hence increased bacterial growth on culture.

We found a high prevalence of *Moraxella species* (28%) in our sputum samples. *Moraxella species* is usually normal flora of the respiratory tract, however, previous studies have reported *Moraxella* as a pathogen of the lower respiratory tract in immunosuppressed patients [20]. Abdullah et al reported a relatively high prevalence of *Moraxella* in patients with lower RTIs among the elderly and immunosuppressed [20]. Our finding of high proportion of participants with *Moraxella species* may indicate a less than complete immune recovery in these patients.

A study done by Genetu et al in Ethiopia in 2019 reported Klebsiella *pneumoniae* (29.7%) and Staphylococcus *aureus* (25%) [21] as the most prevalent isolates while a study done by Mihret et al also from Ethiopia in 2021 isolated Streptococcus *pneumoniae* (28%), Klebsiella *pneumonia* (26.3%) and Pseudomonas *euroginosa* (19.4%) [22]. Our study isolated *Moraxella species* (27.4%), *Streptococcus pneumoniae* (25.4%), *Haemophilus influenza* (22.4%). The differences between isolates could be due to the time difference between our study and the other two studies, and the different locations where the studies were conducted.

The Moraxella species isolated in our study was sensitive to amoxicillin+ clavulanic acid and ceftriaxone and had very low sensitivity to erythromycin and cotrimoxazole, which is similar to what Abdullah et al reported [20]. The very low sensitivity of all the bacterial isolates to cotrimoxazole is not surprising since our study participants were either on active cotrimoxazole prophylaxis or had previously used cotrimoxazole prophylaxis.

HIV infection leads to a low CD4 count and a defective immune system which renders people infected with the HIV virus susceptible to microbial infections leading to a greater use of antibiotics among people living with HIV. The increased use of antibiotics may explain the observed low sensitivity of isolated bacteria to cotrimoxazole [23], and erythromycin [20] among PLWH in this study and other studies. There is an urgent need to invest in the control and prevention of increased use of antibiotics which, may be done through regulation of over-the-counter antibiotics dispensed through pharmacies. It is also critical to invest in affordable point-of-care tests that can help in quick diagnosis, thus preventing unnecessary prescription of antibiotics, and in regular surveillance to detect drug resistant strains early.

Participants that received placebo were more likely to have a positive sputum culture compared to those receiving cotrimoxazole, however this was not statistically significant. This implies that use of Cotrimoxazole did not provide protection against respiratory infections in this study population. This could be due to the fact that the study participants were ART experienced, had improved and stabilised immunity, and thus were no longer susceptible to infections associated with compromised immunity. Although the study was not powered to answer the question on the effect of cotrimoxazole on respiratory bacterial infections, this finding supports the 2020 Uganda HIV prevention and treatment guidelines that recommends use of prophylactic cotrimoxazole only in adults with advanced HIV disease, those newly diagnosed with HIV, children below 18years, pregnant and breastfeeding women [24]. An association of long term use of cotrimoxazole among PLWH with an increase in resistance to cotrimoxazole has been reported in previous studies [25, 26] therefore, reduced use of cotrimoxazole in this population may reduce resistance of microbes to it.

The participants in the study were generally low earners as majority of them were earning less than $30 a month. Participants who earned more than $30 were less likely to have positive bacterial cultures compared to those who earned less than $30. This is similar to evidence that suggests that those with lower socio-economic status are more vulnerable, have higher burden of disease and thus more prone to frequent respiratory infections [27]. Participants who had a longer duration since HIV diagnosis were more likely to have a positive bacterial culture. This

finding requires further investigation since there is no clear biological explanation between duration of HIV infection and risk of bacterial infections.

### Strengths and limitations

This study among ART experienced participants has applicable results as majority of PLWH are on ART following the test and treat policy. Previous studies have mainly reported antimicrobial sensitivity among ART naïve patients. The study was however, a secondary data analysis and this limited the number of antimicrobial drugs that could have been tested for bacterial sensitivity. We could also not explore other factors for example viral load, that could be associated with a positive sputum culture.

## Conclusion

There was no significant difference in bacterial growth in sputum cultures from participants on the placebo arm and those on cotrimoxazole arm. High prevalence of bacterial isolates with most being susceptible to Amoxicillin + Clavulanic acid and ceftriaxone. However, majority of organisms showed very low sensitivity to cotrimoxazole and erythromycin that are cheaper and readily available. As antibiotic choices are becoming limited due to low sensitivity of microbes to these drugs, there is an urgent need to invest in the prevention and control of increasing antibiotic resistance.

## Supporting information

**S1 Appendix.**
(XLSX)

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We would like to acknowledge the contributions of the COSTOP trial team and the contribution of the study participants.

## Author Contributions

**Conceptualization:** Gloria Lubega.

**Data curation:** Andrew Abaasa.

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**Supervision:** Joseph Lutaakome, Eugene Rugazira.

**Validation:** Eugene Rugazira.

**Writing – original draft:** Gloria Lubega.

**Writing – review & editing:** Gloria Lubega, Andrew Abaasa, Willyfred Ochola, Bernard Kikaire, Joseph Lutaakome, Eugene Rugazira, Yunia Mayanja.

## References

1. UNAIDS. Global HIV & AIDS statistics—Fact sheet 2021 [Available from: https://www.unaids.org/en/resources/fact-sheet#:~:text=GLOBAL%20HIV%20STATISTICS,AIDS%2Drelated%20illnesses%20in%202020.

2. Barankanira E, Molinari N, Niyongabo T, Laurent C. Spatial analysis of HIV infection and associated individual characteristics in Burundi: indications for effective prevention. BMC Public Health. 2016; 16 (1):118. https://doi.org/10.1186/s12889-016-2760-3 PMID: 26847711
3. Ford N, Shubber Z, Meintjes G, Grinsztejn B, Eholie S, Mills EJ, et al. Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis. The lancet HIV. 2015; 2(10):e438–44. https://doi.org/10.1016/S2352-3018(15)00137-X PMID: 26423651
4. Gauchan P, Lekhak B, Sherchand JB. The prevalence of lower respiratory tract infection in adults visiting Tribhuvan University Teaching Hospital. Journal of Institute of Medicine Nepal. 2007; 28(2):10–4.
5. Ojha CR, Rijal N, Khagendra KC, Palpasa K, Kansakar P, Gupta BP, et al. Lower respiratory tract infections among HIV positive and control group in Nepal. VirusDisease. 2015; 26(1):77–81. https://doi.org/10.1007/s13337-015-0254-z PMID: 26436125
6. Lamas CC, Coelho LE, Grinsztejn BJ, Veloso VG. Community-acquired lower respiratory tract infections in HIV-infected patients on antiretroviral therapy: predictors in a contemporary cohort study. Infection. 2017; 45(6):801–9. https://doi.org/10.1007/s15010-017-1041-0 PMID: 28660356
7. Cairns G. HIV damages B-cells as well as T-cells: new treatment targets identified NAM-aidsmap2011 [Available from: https://www.aidsmap.com/news/jun-2011/hiv-damages-b-cells-well-t-cells-new-treatment-targets-identified.
8. Okoye AA, Picker LJ. CD4(+) T-cell depletion in HIV infection: mechanisms of immunological failure. Immunol Rev. 2013; 254(1):54–64. https://doi.org/10.1111/imr.12066 PMID: 23772614
9. 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. American journal of respiratory and critical care medicine. 2011; 183(3):388–95. https://doi.org/10.1164/rccm.201006-0836OC PMID: 20851926
10. Olaru ID, Tacconelli E, Yeung S, Ferrand RA, Stabler RA, Hopkins H, et al. The association between antimicrobial resistance and HIV infection: a systematic review and meta-analysis. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2021; 27(6):846–53. https://doi.org/10.1016/j.cmi.2021.03.026 PMID: 33813126
11. Rameshkumar MR, Narasingam Arunagirinathan, editors. Drug-Resistant Bacterial Infections in HIV Patients2018.
12. Marbou WJT, Kuete V. Bacterial resistance and immunological profiles in HIV-infected and non-infected patients at Mbouda AD LUCEM Hospital in Cameroon. Journal of Infection and Public Health. 2017; 10 (3):269–76. https://doi.org/10.1016/j.jiph.2016.04.009 PMID: 27133911
13. Arunagirinathan MRRaN. Drug-Resistant Bacterial Infections in HIV Patients, Advances in HIV and AIDS Control. IntechOpen. 2018.
14. Anywaine Z, Abaasa A, Levin J, Kasirye R, Kamali A, Grosskurth H, et al. Safety of discontinuing cotrimoxazole prophylaxis among HIV infected adults on anti-retroviral therapy in Uganda (COSTOP trial): Design. Contemporary clinical trials. 2015; 43:100–4. https://doi.org/10.1016/j.cct.2015.05.015 PMID: 26009024
15. Anywaine Z, Levin J, Kasirye R, Lutaakome JK, Abaasa A, Nunn A, et al. Discontinuing cotrimoxazole preventive therapy in HIV-infected adults who are stable on antiretroviral treatment in Uganda (COSTOP): A randomised placebo controlled trial. PloS one. 2018; 13(12):e0206907. https://doi.org/10.1371/journal.pone.0206907 PMID: 30596666
16. Novick WJ Jr. Development of in vitro susceptibility testing criteria and quality control parameters. Elsevier; 1989. p. 60–2.
17. Leclercq R, Cantón R, Brown DFJ, Giske CG, Heisig P, MacGowan AP, et al. EUCAST expert rules in antimicrobial susceptibility testing. Clinical Microbiology and Infection. 2013; 19(2):141–60. https://doi.org/10.1111/j.1469-0691.2011.03703.x PMID: 22117544
18. A A, Ogiogwa J, Okerentugba P, Innocent-Adiele C, Onoh C, Nwanze J, et al. Prevalence of Antibiotic Susceptibility Pattern of bacterial Agents Involve In lower Respiratory Tract Infection in Abeokuta, Ogun State, Nigeria. Report and Opinion. 2012.
19. Adhanom G, Gebreegziabiher D, Weldu Y, Gebreyesus Wasihun A, Araya T, Legese H, et al. Species, Risk Factors, and Antimicrobial Susceptibility Profiles of Bacterial Isolates from HIV-Infected Patients Suspected to Have Pneumonia in Mekelle Zone, Tigray, Northern Ethiopia. BioMed Research International. 2019; 2019:8768439. https://doi.org/10.1155/2019/8768439 PMID: 31192259
20. Abdullah FE, Ahuja KR, Kumar H. Prevalence and emerging resistance of Moraxella catarrhalis in lower respiratory tract infections in Karachi. JPMA The Journal of the Pakistan Medical Association. 2013; 63 (11):1342–4. PMID: 24392515

21. Genetu DE, Zenebe Y. Bacterial Profile and Their Antibiotic Resistance Pattern Among HIV Patients Diagnosed with Pneumonia in Felege-Hiwot Referral Hospital, Bahir Dar, Northwest Ethiopia. Research Square; 2020.

22. Tilahun M, Gebretsadik D, Seid A, Gedefie A, Belete MA, Tesfaye M, et al. Bacteriology of community-acquired pneumonia, antimicrobial susceptibility pattern and associated risk factors among HIV patients, Northeast Ethiopia: cross-sectional study. SAGE Open Medicine. 2023; 11:20503121221145569. https://doi.org/10.1177/20503121221145569 PMID: 36632083

23. Oguche JI-o, Bolaji RO, Onaolapo JA, Abah SE, Kwaghe VG, Akor SE, et al. BACTERIAL INFECTION AND ANTIBIOTIC RESISTANCE IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS PRESENTING LOWER RESPIRATORY TRACT INFECTION IN NIGERIA. medRxiv. 2021: 2021.09.05. https://doi.org/10.1212/WNL.0b013e318208f492

24. Health Mo. CONSOLIDATED GUIDELINES FOR THE PREVENTION AND TREATMENT OF HIV AND AIDS IN UGANDA 2020 [Available from: https://differentiatedservicedelivery.org/Portals/0/adam/Content/HvpzRP5yUUSdpCe2m0KMdQ/File/Uganda_Consolidated%20HIV%20and%20AIDS%20Guidelines%202020%20June%2030th.pdf.

25. Martin JN, Rose DA, Hadley WK, Perdreau-Remington F, Lam PK, Gerberding JL. Emergence of trimethoprim-sulfamethoxazole resistance in the AIDS era. The Journal of infectious diseases. 1999; 180 (6):1809–18. https://doi.org/10.1086/315132 PMID: 10558935

26. Zachariah R, Harries AD, Spielmann MP, Arendt V, Nchingula D, Mwenda R, et al. Changes in Escherichia coli resistance to co-trimoxazole in tuberculosis patients and in relation to co-trimoxazole prophylaxis in Thyolo, Malawi. Malawi medical journal: the journal of Medical Association of Malawi. 2002; 14 (2):10–2. https://doi.org/10.4314/mmj.v14i2.10759 PMID: 27528931

27. Kiwanuka SN, Ekirapa EK, Peterson S, Okui O, Rahman MH, Peters D, et al. Access to and utilisation of health services for the poor in Uganda: a systematic review of available evidence. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2008; 102(11):1067–74. https://doi.org/10.1016/j.trstmh.2008.04.023 PMID: 18565559