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Article

Risk Factors Related to HIV Infection among TB Patients in Luanda, Angola

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Abstract: TB and HIV continue to increase and constitute major public health concerns worldwide, mainly in resource-limited countries, showing that we are not going to end HIV if we do not also end TB. Herein, we investigated the risk factors related to HIV infection among TB patients in Luanda, the capital city of Angola. This was a retrospective cohort study conducted on the medical records of 117 TB patients from January to September 2016. Overall, the HIV/TB co-infection rate was 12%. The mean age of coinfected patients was 37.7±10.1 years. No statistically significant relationship was observed between sociodemographic or clinical features with HIV/TB co-infection ($p>0.05$). TB patients aged 30 years or older (OR: 4.13, p=0.072), female (OR: 1.08, p=0.898), residing in urbanized areas (OR: 1.90, p=0.578), with a history of treatment abandonment (OR: 3.74, p=0.083), with polyresistance (OR: 1.62, p=0.603), and MDR-TB (OR: 2.00, p=0.454), were more likely to have HIV/TB co-infection, while latent TB infection (OR: 0.63, p=0.559) and treatment-susceptible TB patients (OR: 0.56, p=0.616), presented a lower chance of HIV/TB coinfection. Our finding showed a slightly high HIV/TB coinfected rate, which suggests that the dual HIV/TB epidemic keeps evolving and poses a huge concern to the public health in Angola. Further studies on features related to HIV/TB coinfection and its impact on disease progression and clinical outcome in adults from high-risk Angolan communities, should be carried out to intensify and strengthen collaborative activities between national TB and HIV programs in Angola.

Keywords: Tuberculosis; HIV; coinfection; Risk factors; Luanda; Angola

1. Introduction

Tuberculosis (TB) remains the most common cause of death in people living with human immunodeficiency virus (HIV).[1, 2] In some African countries, 80% of persons with TB have HIV infection.[3] People who live with HIV are up to 34 times more likely to develop active TB than HIV-negative people.[4] Of the total new TB patients, there were about 787,000 HIV/TB-coinfected patients, accounting for about 8% and 204,000 TB deaths among people living with HIV (PLWH) in 2020 globally.[1, 2] The HIV/TB coinfection prevalence in sub-Saharan Africa was estimated at 31.8%.[5] A previous study reports an apparent decrease in the estimate of HIV in TB African patients from 33.7% in the period before 2000 to 25.7 in the period after 2010.[5] The Eastern and Southern sub-Saharan Africa region had a higher prevalence (34.4%) than the Western and Central regions (27.3%).[5] The interaction between TB and HIV is complex since HIV infection weakens the immune system by reducing TCD4 lymphocytes which play an important role in the body's defense and increases susceptibility to MTB infection.[3, 4]

A recent review of autopsy studies among HIV-infected individuals found a mean TB prevalence of 43% (95% CI: 38–48) in sub-Saharan Africa, with almost half of undiag-

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nosed fatal TB cases in their lifetime.[6, 7] The World Health Organization (WHO) recommended that PLHIV be routinely screened for TB. [1, 2, 8] Until now, Angola is one of the 14 countries with a triple burden of TB, HIV/TB, and MDR-TB (multidrug-resistant TB) and it is between three countries, alongside Congo and Liberia that never completed a drug-resistance survey.[9] Despite that, the epidemiological impact of TB screening in HIV patients, or vice versa, has been little explored in Angola. In this study, we investigated the sociodemographic and clinical determinants as well as risk factors related to HIV infection among TB patients in Luanda, the capital city of Angola. The results of this study could help to intensify and strengthen collaborative activities between national TB and HIV programs in Angola.

2. Materials and Methods

2.1. Study design and setting

This was a retrospective cohort study conducted on the medical histories of 117 TB patients followed up at the referral medical care unit for respiratory illnesses from January to September 2016, which is located in Luanda, the capital city of Angola. The survey was conducted at the National Institute of Health Research of Angola (INIS), also located in Luanda, the capital of Angola. INIS is a public institution of the Ministry of Health of Angola, whose main purpose is to develop scientific research in health care and its determinants for the strengthening of public health policies. The explanatory variables collected included sociodemographic data of TB patients (age, sex, and area of residence) and clinical data such as smear level, treatment dropout, treatment status, and resistance profile. The dependent variable of the survey was HIV infection, dichotomized into negative and/or positive. The study was revised and approved by the Angolan National Ethics Commission (approval n.º 11/2021). Anonymous information was used for analysis, and the need for the individual informed agreement was waived by the National Ethics Commission of Angola.

2.2. Sample collection and laboratory testing

Laboratory procedures have been performed at the TB research laboratory of the INIS. The patients were subjected to MTB identification tests and antibiotic sensitivity tests (AST). The specimens were stained with Ziehl-Neelsen [10] and susceptibility to first-line drugs containing streptomycin, isoniazid, rifampicin, and ethambutol was carried out using the automatic BACTEC MGIT 960 system (Becton Dickinson, Franklin Lakes, NJ). The susceptibility test was carried out in liquid culture. The TB patients were classified as non-resistant when they were susceptible to all drugs, while resistant patients were classified as monoresistant (resistant to at least one of the drugs), polyresistant (resistant to more than one drug), and MDR-TB (at least resistant to isoniazid and rifampicin). Moreover, the TB patients were screened for HIV infection using the rapid antibodies detection test Determine HIV1/2™ (Alere, Japan) and the Unigold™ HIV (Trinity Biotech, Ireland), following national guides for HIV testing in Angola.

2.3. Statistical analysis

Data generated in this study were processed SPSS v28. Absolute or relative frequencies were determined in the descriptive analysis. The chi-square (X^2) and logistic regression tests were used to evaluate the relation between the categorical variables. The odds ratio (OR) and its 95% confidence intervals (CI) were calculated to evaluate the strength and direction of the existing relationship. All reported p-value are two-tailed and considered to be significant when $p<0.05$.

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3. Results

A total of 117 TB patients were part of this study. The age of the studied patients ranged from 14 to 68 years. The mean age was 33.7±11.2 years. TB patients aged 30 years or older (37.6%, 44/117), male (65.8%, 77/117), from non-urbanized regions (95.7%, 112/117), classified with the level of exposure to MTB (74.4%, 87/117), without a history of treatment abandonment (91.5%, 107/117), untreated (99.1%, 116/117), and with monoresistance (75%, 33/44), were the most predominant. Overall, the HIV/TB co-infection rate was 12% (14/117). The mean age of HIV-infected patients (37.7 ± 10.1 years) was higher compared to HIV-negative patients (33.1 ± 11.3 years), although there were no significant differences (p=0.151). HIV/TB co-infection was higher among patients aged 30 years or over (85.7%), male (64.3%), living in non-urbanized areas (92.9%), exposed to MTB (85.7%), without a history of treatment abandonment (78.6%), untreated (100%), non-susceptible to the treatment (83.3%), and monoresistant (100%). No statistically significant relationship was observed between sociodemographic or clinical characteristics with HIV/TB co-infection (p>0.05). TB patients aged 30 years or older [OR: 4.13 (95 CI: 0.88 – 19.4), p=0.072], female [OR: 1.08 (95 CI: 0.23 – 3.47), p=0.898], residing in urbanized areas [OR: 1.90 (95 CI: 0.20 – 18.4), p=0.578], with a history of treatment abandonment [OR: 3.74 (95 CI: 0.84 – 16.6), p=0.083], with polyresistance [OR: 1.62 (95 CI: 0.26 – 9.93), p=0.603], and MDR-TB [OR: 2.00 (95 CI: 0.33 – 12.3), p=0.454], were more likely to have HIV/TB co-infection compared to the other groups. On the other hand, latent TB infection [OR: 0.63 (95 CI: 0.13 – 3.02), p=0.559] and treatment-susceptible TB patients [OR: 0.56 (95 CI: 0.56 – 5.39), p=0.616], presented a lower chance of HIV/TB coinfection compared to the other groups.

4. Discussion

TB is an opportunistic infection among PLHIV worldwide, however, HIV/TB co-infection modifies the clinical course of the infection as well as the outcome of tuberculosis, especially in resource-limited settings.[3, 4] Up to the present date, approximately 34 million people are living with HIV worldwide, and of these, about a third are also infected with TB, mostly in resource-limited African countries.[3] Angola is a country with a triple burden of TB, HIV/TB, and MDR-TB.[9] The dual epidemics of HIV and TB are particularly widespread with different epidemicities in the different regions urbanized or non-urbanized from Angola, where HIV has been one of the most important factors for the increase in the incidence of tuberculosis.[11–15] Despite this, HIV/TB co-infection has been little studied in Angola. To the best of our knowledge, this study is one of the first to present in detail a picture of HIV/TB co-infection in the last five years in Luanda, the capital city of Angola, a sub-Saharan African country. The overall estimate of HIV/TB coinfection in sub-Saharan Africa was reported at 31.8%,[5] indicating that it is 2.7 times higher than that observed in the present study. Also, we identified an HIV/TB co-infection rate of around 12%, which is similar to those reported by Chen et al (13.7%) in China,[4] and Bjerrum et al (13%) in Ghana,[6] high compared to a study performed by Cui et al (0.8%) in Guangxi province, China,[16] but low when compared to the results reported by Nyamogoba et al (42%) in Kenya [17] and the global HIV/TB co-infection rate (14.8%).[1] The quality of health services and cultural, socioeconomic, political, and biological factors could make individuals disproportionately vulnerable to TB, HIV, or HIV/TB coinfection and might help to explain differences in infection rates in different countries.

A previous study indicated that gender, age, educational level, marital status, per capita monthly income, patient residence, family size, distance from a health institution, knowledge of HIV/TB co-infection, and knowledge of HIV might be risk factors for HIV/TB co-infection.[4] In the present study, although statistically insignificant, there was a high prevalence of HIV/TB co-infection for patients aged 30 years or older, men, living in non-urbanized regions, exposed to *Mycobacterium tuberculosis* (MTB), with a history of treatment abandonment or no treatment, non-susceptible to the TB drugs, with mono-

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resistance, poly-resistant, and MDR-TB, indicating on the one hand that sociodemographic, behavioral and clinical characteristics play an important role in the course of dissemination of these infectious agents (MTB and HIV) in the community, and on the other hand, these findings indicate that HIV infection prevention strategies in the TB population should target these vulnerable groups.[4] Patients over 30 years of age (OR: 4.13, p=0.072), female (OR: 1.08, p=0.898), and living in urbanized areas (OR: 1.90, p=0.578) had a higher risk of HIV/TB coinfection, which was similar to that observed by Datiko et al in Ethiopia, where TB patients over 35 years of age (OR: 7.10, p=0.001) and living in urbanized areas (OR: 1.77, p=0.001) also had a higher risk of coinfection.[18] Other studies reported that HIV/TB coinfection is more common among urban people, which was different from the results observed in the present study.[4, 19] A previous study carried out by our research team showed that urbanized areas have a higher rate of HIV, as they concentrate most of the population at risk, such as injecting drug users and sex workers.[12] However, in this study, we found contrary results, since residents in non-urbanized regions represented 93% of the HIV-positive population. However, it is worth mentioning that 97% of TB patients were from non-urbanized areas, which would not be surprising, since this population faces great socioeconomic difficulties, limited access to health services, extreme poverty, and a low nutritional index, compared to the resident population, in urbanized areas, where in addition to being close to health services, they benefit from a more functional healthcare system. Our results reinforce the hypothesis that TB is a disease of the poor, especially for rural people in the context of limited resources. On the other hand, our findings contradict the study by Datiko et al., which indicates that the rate of HIV/TB co-infection depends on the prevalence of HIV infection in a community,[18] adding that sociodemographic and behavioral characteristics also play an important and independent role in increasing the co-circulation of MTB and HIV. Further studies, including sociodemographic, behavioral, clinical, and nutritional status, should be carried out in different urbanized and non-urbanized regions to help guide decision-making regarding strategies to control infectious agents such as HIV and MTB, in the communities.

We found no difference in the rate of HIV infection between the different types of TB, which was similar to the results reported by Chen et al.[4] No patient with active TB was coinfected with HIV, which differs from the findings of Cui et al., where they showed that active TB increases the chances of HIV/TB co-infection, especially in those without antiretroviral treatment (ART).[20] However, we do not know whether the HIV patients in our study were on ART which could affect the coinfection rate with TB. Nonetheless, future studies that assess the impact of ART use on the HIV/TB co-infection, disease progression, and clinical outcome, should be carried out in Angola.

It is worth mentioning that the fact that more than 90% of TB or HIV/TB coinfected patients were from non-urbanized regions, reinforces the need to set up screening posts for these two infections in the poor regions, as well as better diagnostic training for healthcare professionals. Also, 83% of the HIV/TB coinfected showed resistance to treatment, and of these, 67% were classified as polyresistant or MDR-TB, respectively. This finding suggests the need to increase awareness on the one hand of the general population about the correct use of antimicrobial drugs, and on the other hand, health professionals must ensure the follow-up of a treatment and patient adherence to treatment using antibiotics. Indeed, we observed that all (100%) HIV/TB coinfected patients were untreated or who had a history of treatment dropout (79%). Previous studies have shown that MDR-TB outbreaks were generated in HIV treatment clinics and then spread to communities.[2, 21] Indeed, our results agree with this study, as more than 50% of TB patients in our study had polyresistance or MDR-TB, and at the same time, 67% of HIV/TB coinfected had polyresistances and MDR-TB, respectively.

Our results have some limitations that must be considered. Firstly, the small sample size might have affected the significance and robustness of our results. Secondly, the stage of HIV infection, viral load, and/or CD4/CD8 cell count were not described. Finally, the clinical outcome of TB and HIV/TB coinfected patients was not presented, which limited

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information, on the one hand, the impact of HIV/TB coinfection on clinical outcome and well-being, and on the other hand the epidemiological impact on the population level, which is crucial to guide public health choices and investments. Despite these limitations, our study presents important data or determinants of the HIV/TB co-infection rate in Luanda, the capital city of Angola, which could help to intensify and strengthen collaborative activities between national TB and HIV programs as well as improve the management of HIV/TB co-infected patients in Angola.

In conclusion, we observed a slightly high HIV/TB coinfection rate, indicating that the dual HIV/TB epidemic continues to evolve and constitutes a huge concern for the public health team in Angola. PLHIV needs early diagnosis and treatment of active TB, and equally, people living with TB need early diagnosis and treatment of HIV. The following concerns should be addressed in future studies: (i) the impact of sociodemographic, behavioral, clinical, and nutritional status in the TB or HIV/TB coinfection in Angola, should be carried out in different urbanized and non-urbanized regions, (ii) the impact of ART use on the HIV/TB co-infection, disease progression, and clinical outcome in Angola, should be carried out to help guide decision-making regarding strategies to control infections both infectious agents (HIV and MTB) in the Angolan population, and (iii) activities to intensify and strengthen collaborative activities between national TB and HIV programs should be carried out to ensure medical assistance and adequate treatment of HIV/TB coinfected Angolan patients.

Declarations

Authors' contributions: Conceptualization: CSS. Methodology: CSS. Formal analysis: CSS. Investigation: CSS and JS. Data curation: CSS. Writing—original draft preparation: CSS. Writing—review and editing: CSS, JNV, and JM. Supervision: CSS, JS, and JP. Project administration: CSS, JP, AM, ZD, JNV, and JM. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: The individual informed agreement was waived by the National Ethics Commission of Angola.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. WHO. Global tuberculosis report. 2020.
2. WHO. Global TB Report. 2021. https://www.who.int/publications/i/item/9789240037021.
3. Granich R, Akolo C, Gunneberg C, Getahun H, Williams P, Williams B. Prevention of tuberculosis in people living with HIV. Clin Infect Dis. 2010;50 SUPPL. 3:215–22.
4. Chen J, Cao W, Chen R, Ren Y, Li T. Prevalence and determinants of HIV in tuberculosis patients in Wuxi City, Jiangsu province, China: a cross-sectional study. Int J STD AIDS. 2016;27:1204–12.
5. Gelaw YA, Williams G, Soares Magalhães RJ, Gilks CF, Assefa Y. HIV Prevalence Among Tuberculosis Patients in Sub-Saharan Africa: A Systematic Review and Meta-analysis. AIDS Behav. 2019;23:1561–75. doi:10.1007/s10461-018-02386-4.

 doi:10.20944/preprints202211.0022.v1

6. Bjerrum S, Oliver-Commey J, Kenu E, Lartey M, Newman MJ, Addo KK, et al. Tuberculosis and non-tuberculous mycobacteria among HIV-infected individuals in Ghana. Trop Med Int Heal. 2016;21:1181–90.
7. Gupta RK, Lucas SB, Fielding KL, Lawn SD. Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource-limited settings: A systematic review and meta-analysis. Aids. 2015;29:1987–2002.
8. Perch M, Andersen P, Kok-Jensen A. HIV testing of patients diagnosed with tuberculosis increased in Denmark during the period from 2007 to 2009. HIV Med. 2013;14 SUPPL.3:42–3.
9. Robbiati C, Tosti ME, Mezzabotta G, Dal Maso F, Lulua Sachicola OM, Siene Tienabe P, et al. Improving TB Surveillance and Patients' Quality of Care Through Improved Data Collection in Angola: Development of an Electronic Medical Record System in Two Health Facilities of Luanda. Front Public Heal. 2022;10 March:1–8.
10. MacGregor-Fairlie M, Wilkinson S, Besra GS, Oppenheimer PG. Tuberculosis diagnostics: Overcoming ancient challenges with modern solutions. Emerg Top Life Sci. 2020;4:435–48.
11. National Institute of Statistics. Inquérito de Indicadores Múltiplos e de Saúde (IIMS) em Angola. 2016. https://dhsprogram.com/pubs/pdf/FR327/FR327.pdf.
12. Sebastião CS, Neto Z, Jandondo D, Mirandela M, Morais J, Brito M. HIV, hepatitis B virus, hepatitis C virus, and syphilis among pregnant women attending antenatal care in Luanda, Angola: Seroprevalence and risk factors. J Med Virol. 2020;92:3265–70.
13. Sebastião CS, Neto Z, Jandondo D, Mirandela M, Morais J, Brito M. Dengue virus among HIV-infected pregnant women attending antenatal care in Luanda, Angola: an emerging public health concern. Sci African. 2022;17:e01356.
14. Sebastião CS, Morais J, Brito M. Clinical and public health implications of hiv-1 genetic diversity and drug resistance mutations in angola: A systematic review. AIDS Rev. 2020;22:1–9.
15. Sebastião CS, Morais J, Brito M. Factors Influencing HIV Drug Resistance among Pregnant Women in Luanda, Angola: Findings from a Cross-Sectional Study. Trop Med Infect Dis. 2021;6:29.
16. Cui Z, Huang F, Liang D, Huang Y, Qin H, Ye J, et al. Tuberculosis among Ambulatory People Living with HIV in Guangxi Province, China: A Longitudinal Study. Int J Environ Res Public Health. 2022;19:12280.
17. Nyamogoba HDN, Mbuthia G, Mining S, Kikuvi G, Biegon R, Mpoke S, et al. HIV co-infection with tuberculous and non-tuberculous mycobacteria in western Kenya: Challenges in the diagnosis and management. Afr Health Sci. 2012;12:305–11.
18. Datiko DG, Yassin MA, Chekol LT, Kabeto LE, Lindtjørn B. The rate of TB-HIV co-infection depends on the prevalence of HIV infection in a community. BMC Public Health. 2008;8:1–8.
19. Post FA, Grint D, Werlinrud AM, Panteleev A, Riekstina V, Malashenkov EA, et al. Multi-drug-resistant tuberculosis in HIV positive patients in Eastern Europe. J Infect. 2014;68:259–63.
20. Cui Z, Lin M, Nie S, Lan R. Risk factors associated with Tuberculosis (TB) among people living with HIV/AIDS: A pairmatched case-control study in Guangxi, China. PLoS One. 2017;12:1–12.
21. Corbett EL, MacPherson P. Tuberculosis screening in high human immunodeficiency virus prevalence settings: Turning promise into reality. Int J Tuberc Lung Dis. 2013;17:1125–38.

Table 1. Putative sociodemographic and clinical determinants related to HIV infection among TB patients in Luanda, Angola

Independent variables	N (%)	HIV infection			Univariate analysis	
		Negative (%)	Positive (%)	p-value	OR (95% CI)	p-value
Overall	117 (100)	103 (88.0)	14 (12.0)			
Age, mean ± SD	33.7 ± 11.2	33.1 ± 11.3	37.7 ± 10.1	0.151		
Age distribution						
<30y	44 (37.6)	42 (40.8)	2 (14.3)	0.055	1.00	
≥30y	73 (62.4)	61 (59.2)	12 (85.7)		4.13 (0.88 – 19.4)	0.072
Gender						
Female	40 (34.2)	35 (34.0)	5 (35.7)	0.898	1.08 (0.23 – 3.47)	0.898
Male	77 (65.8)	68 (66.0)	9 (64.3)		1.00	
Residence area						
Non-urbanized	112 (95.7)	99 (96.1)	13 (92.9)	0.572	1.00	
Urban	5 (4.30)	4 (3.90)	1 (7.10)		1.90 (0.20 – 18.4)	0.578
TB category						
Exposure	87 (74.4)	75 (72.8)	12 (85.7)	0.464	1.00	
Latent	22 (14.3)	20 (19.4)	2 (14.3)		0.63 (0.13 – 3.02)	0.559

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TB disease	8 (6.80)	8 (7.80)	0 (0.00)		0 (0.00 – 0.00)	0.999
Treatment dropout						
No	107 (91.5)	96 (93.2)	11 (78.6)	0.066	1.00	
Yes	10 (8.50)	7 (6.80)	3 (21.4)		3.74 (0.84 – 16.6)	0.083
Patient status						
Untreated	116 (99.1)	102 (99.0)	14 (100)	0.711	1.00	
Treated	1 (0.90)	1 81.00)	0 (0.00)		0 (0.00 – 0.00)	1.000
Treatment profile§						
Susceptibility						
No	33 (75.0)	28 (73.7)	5 (83.3)	0.612	1.00	
Yes	11 (25.0)	10 (26.3)	1 (16.7)		0.56 (0.06 – 5.39)	0.616
Monoresistance						
No	11 (25.0)	11 (28.9)	0 (0.00)	0.128	0 (0.00 – 0.00)	0.999
Yes	33 (75.0)	27 (71.1)	6 (100)		1.00	
Polyresistance						
No	19 (43.2)	17 (44.7)	2 (33.3)	0.600	1.00	
Yes	25 (56.8)	21 (55.3)	4 (66.7)		1.62 (0.26 – 9.93)	0.603
MDR-TB						
No	21 (47.7)	19 (50.0)	2 (33.3)	0.448	1.00	
Yes	23 (52.3)	19 (50.0)	4 (66.7)		2.00 (0.33 – 12.3)	0.454

Abbreviations: CI – confidence interval; OR – odds ratio; MDR – Multi-Drug Resistance

§ missing value = 73