Detection of pulmonary tuberculosis and COVID-19 co-infection in the city of Ouagadougou, Burkina Faso

Arouna ZOUNGRANA[1,3], Tani SAGNA[1,2*], Koudbi Jacob ZONGO[5], W. Yasmine Astrid SANA[1], Dinanibè KAMBIRE[2], Tinoaga Léon SAWADOGO[4], Albert SOUDRE[5], Serges SOUGUE[3], Arzouma Paul YOODA[4], Naâ-Imwine Stanislas Dimitri MEDA[6], Kouka Zoéwentallé Thibaut OUEDRAOGO[1], Tegwinde Rebeca COMPAORE[1,2], Lassina TRAORE[1], Wendkuuni Florencia DJIGMA[1], Ollo YOUL[3], Adjima COMBARY[4], Adama ZIGANI[4], Abdou Azaque ZOURE[1,2], Absatou KY/BA[1], Amadou TRAORE[5, 6], Henri Gautier OUEDRAOGO[2], Elie KABRE[3], Jacques SIMPORE[1]

Abstract

Introduction: Pulmonary tuberculosis and COVID-19 have shared some similarities in term of clinical manifestations and modes of transmission. COVID-19 could increase the mortality rate of tuberculosis. Consequently, pulmonary tuberculosis and COVID-19 co-infection could be a major public health concern. The aim of this study was to establish the prevalence of pulmonary tuberculosis and COVID-19 co-infection in the city of Ouagadougou, Burkina Faso. *Method*: *Mycobacterium tuberculosis* DNA, was detected using GeneXpert (Cepheid, USA), on the sputum of suspected pulmonary tuberculosis. Anti-SARS-CoV-2 antibodies (IgM and IgG) was detected using the Accu-Tell rapid kit (AccuBio Techn Co, Ltd kit) on the blood plasma of suspected pulmonary tuberculosis cases. SARS-CoV-2 RNA amplification

[1] Laboratoire de Biologie moléculaire et de génétique (LABIOGENE), Université Joseph KI-ZERBO, tel +22625307064, BP 7021, Ouagadougou, Burkina Faso
[2] Institut de Recherche en Sciences de la Santé (IRSS/CNRST), tel +22625363215, 03 BP 7047, Ouagadougou, Burkina Faso
[3] Agence Nationale pour la Sécurité Sanitaire de l'Environnement, de l'Alimentation, du Travail et des Produits de Santé (ANSSEAT), tel +22625373232, 09 BP 24, Ouagadougou, Burkina Faso
[4] Centre National de Lutte Anti-Tuberculeuse (CNLAT), Ouagadougou, tel +22625252525, 01 BP 6632, Ouagadougou, Burkina Faso
[5] Université Norbert ZONGO de Koudougou, tel +25440122, BP 376, Koudougou, Burkina Faso
[6] Institut de l'Environnement et des Recherches Agricoles (INERA/CNRST), tel +22650347112, 04 BP 8645, Ouagadougou, Burkina Faso
***Corresponding author:** Dr Tani SAGNA. Tel : 0022670397440, stanilinda@gmail.com, ORCID: https://orcid.org/0000-0002-8775-0693

was then performed using the TaqPath kit (Applied Biosystems), with the QuantStudio 5 thermocycler on nasopharyngeal swabs from patients found positive for pulmonary tuberculosis. *Results*: The prevalence of pulmonary tuberculosis was 27.54% (65/236). Among tuberculosis-positive patients who accepted the COVID-19 serological test, co-infection was 12.5% (3/24). The prevalence of *Mycobacterium tuberculosis* resistance to rifampicin was 9.23%. Males and patients aged 40 and below were the most likely to be infected with pulmonary tuberculosis at 76.90% and 66.20% respectively. Seroprevalence of COVID-19 was 12.63%. *Conclusion*: Pulmonary tuberculosis and COVID-19 co-infection was a reality in this study.

Keywords: Co-infection; Tuberculosis; COVID-19; *Mycobacterium tuberculosis*; SARS-CoV-2; Burkina Faso.

Introduction

Tuberculosis (TB) is an infectious disease with human-to-human transmission, mainly via the airborne route. TB is a highly contagious, fatal but curable disease that affects developing countries. *Mycobacterium tuberculosis* (*M. tuberculosis*) is the main causative agent of human tuberculosis. Several species of Mycobacteria, including *M. tuberculosis* or Koch's Bacillus (KB), are grouped together under the name of *M. tuberculosis* Complex (1).

According to the World Health Organisation's (WHO) 2021 report, 9.9 million people contracted tuberculosis in 2020, with a significant number (1.5 million) dying from this disease (2). The highest number of new TB cases was recorded in Asia (43% of all new cases), followed by Africa (25%) and the Pacific region (18%) (2).

In Burkina Faso, according to data provided in 2022 by the technical guide to tuberculosis control, the mortality rate of tuberculosis was estimated at 46 cases per 100,000 inhabitants, the incidence of mortality was 9.7 cases per 100,000 inhabitants among tuberculosis patients; and the prevalence of rifampicin-resistant TB (RR-TB) was 2.1% among new patients and 14% among patients previously treated (3). Investigations show a frequency of over 70% of laboratory-confirmed cases among presumptive TB on admission to hospital (4). After a more or less long period of stabilisation in the incidence of the disease, high morbidity and mortality remain linked to co-infection with HIV and resistance to anti-tuberculosis drugs. The epidemiological profile of respiratory infections has worsened with the advent of COVID-19, which has a high morbidity and mortality rate (5).

COVID-19 is caused by SARS-CoV-2 which is a single-stranded polarity-positive RNA virus. The first cases of the disease were

observed in December 2019, in Wuhan, China, and the disease was declared a pandemic in March 2020 (6). Since the start of this pandemic, a rapid increase in the number of cases of infection has been reported worldwide. Indeed, as of November 30, 2020, there were an estimated 62,746,222 cases of COVID-19 worldwide, with 1,459,497 deaths. The number of cases reported in Africa was 1,613,249, including 39,402 deaths. In Burkina Faso, the first case of COVID-19 was recorded on March 9, 2020, and by the end of August 2021, there were 13,777 cases with 171 deaths. The rapid increase in the number of people affected worldwide led the WHO to declare, on March 11, 2020, that COVID-19 had reached pandemic status (7,8).

Pulmonary tuberculosis and COVID-19 share some similarities in terms of clinical manifestations and mode of transmission. In addition, COVID-19 could increase the morbidity and mortality rate of tuberculosis (2). Pulmonary tuberculosis and COVID-19 co-infection is therefore a public health problem and require further documentation. Investigating this co-infection is a worthy objective, which motivated our study. We targeted patients received for pulmonary tuberculosis screening in the city of Ouagadougou.

I. Material and methods

I.1. Study design

This was a descriptive cross-sectional study conducted from May 18 to October 18, 2021.

I.2. Sampling

Participant enrolment, sputum, blood and nasopharyngeal sampling, and PCR detection of *M. tuberculosis* were carried out at the National Reference Laboratory for Mycobacteria (LNR-M) located at the National Tuberculosis Control Centre (CNLAT) in Ouagadougou. Participants in the study were patients over 18 years of age who came to the CNLAT with suspected tuberculosis. Sample size was estimated from resistance prevalence data of 18.75%, reported by Ilboudo et al in Burkina (9). A total of 236 sputum samples were collected for the detection of *M. tuberculosis*. All 236 participants had the choice of blood sampling for SARS-CoV-2 serological testing or nasopharyngeal sampling for molecular diagnosis. Ninety-five blood samples were taken in EDTA tubes from tuberculosis patients and non-tuberculosis patients for the detection of SARS-CoV-2 antibodies. For the molecular

diagnosis of SARS-CoV-2, twenty-nine nasopharyngeal swabs were taken from patients confirmed positive for *M. tuberculosis* by GeneXpert and preserved in the viral transport medium (DNA/RNA preservation kit dewei). A total of 95 whole blood samples were collected from tuberculosis-positive or -negative patients who had given informed consent to participate in the study.

I.3. Serological and molecular analyses

The various serological and molecular tests were carried out at the Institut de Recherche en Sciences de la Santé (IRSS) and the national agency for environmental, food, occupational and health product safety (ANSSEAT). Molecular analysis of *M. tuberculosis* was carried out using the commercial Xpert MTB/RIF kit (Cepheid) on the GeneXpert instrument (Cepheid, USA) at the LNR-M. SARS-CoV-2 serology was performed with the AccuBio Techn Co, using plasma. Molecular testing (RT-PCR) of SARS-CoV-2 in *M. tuberculosis*-positive patients was then carried out using ANDiS350 reagents and instrument for nucleic acid extraction from twenty-nine (29) nasopharyngeal swabs. Amplification was performed using the QuantStudio5 instrument and Taqpath COVID-19 CE-IVD reagents (Applied Biosystems) targeting the ORF1ab, N and S genes of SARS-Cov-2 RNA.

I.4. Statistical analysis

After the collection on paper, the data were entered into Excel 2010 and analysed using R software version 2016. Qualitative variables were analysed using frequency distribution with chi-square adjustment. The difference was statistically significant for $p < 0.05$.

I.5. Ethical considerations

The approval of the Institutional Ethics Committee for Health Research (CEIRES) was obtained for the study under the reference N/Ref. A04-2021/CEIRES. All participants in the study gave their agreement and informed consent. For patients who could not read, consent was obtained after oral interpretation in the presence of an impartial witness.

II. Results

II.1. Prevalence of pulmonary tuberculosis

The proportion of tuberculosis was 27.54% (65/236) in all sputum samples. The frequency of rifampicin resistance among positive cases

was 9.23% (65). The infection rate in men was statistically higher than in women ($p<0.05$). Table I shows the proportion of patients with pulmonary tuberculosis according to sex and age.

Table I: Summary of GeneXpert results by age and sex

Characteristics	*p*-value	Positive *Mtb* (n=65)	*p*-value	Rifampicin Resistant (n=6)
Age group (year)				
≤ 40 (56.78%)	0.386	43 (66.20%)	0.086	4 (66.67%)
> 40 (43.22%)		22 (33.80%)		2 (33.33%)
Sex				
Female (36%)	< 0.05	15 (23.10%)	0.011	1 (16.67%)
Male (64%)		50 (76.90%)		5 (83.33%)

Mtb: Mycobacterium tuberculosis

II.2. Prevalence of COVID-19

For serology, 95 SARS-CoV-2 tests were carried out. Of those tested, 12 (12.63%) were seropositive, with six (06) being positive for both IgG and IgM; but no single case of IgM was detected. A total of 29 patients accepted the nasopharyngeal swab for molecular diagnosis of SARS-CoV-2, i.e. an acceptance rate of 44.62%. PCR results for SARS-CoV-2 were all negative for those patients who tested positive for *M. tuberculosis*. Table II shows the results of SARS-CoV-2 serology according to sex and age. The predominance of people under 40 years of age is observed in the study population, with a statistically significant difference ($p<0.05$).

Table II: Summary of SARS-CoV-2 serology results according to age and sex

Characteristics	*p*-value	IgG	IgM/IgG
Age group (year)			
≤ 40 (65.30%)	0.034	3 (50.00%)	3 (50.00%)
> 40 (34.70%)		3 (50.00%)	3 (50.00%)
Sex			
Female (29.50%)	0.085	1 (16.67%)	2 (33.33%)
Male (70.50%)		5 (83.33%)	4 (66.67%)

IgG: type G immunoglobulin; IgM: type M immunoglobulin

II.3. Tuberculosis and COVID-19 co-infection

Of the 65 cases of tuberculosis patients, 24 accepted the SARS-CoV-2 serological test, of which three (03) were positive for COVID-19. The prevalence of *M. tuberculosis* cases detected and associated with the presence of SARS-CoV-2 antibodies was 12.50% (3 cases). Table III shows the cross-tabulation of results between *M. tuberculosis* RT-PCR and SARS-CoV-2 serology.

Table III: Cross-referencing of GeneXpert results for *M. tuberculosis* and SARS-CoV-2 serology

Results		SARS-CoV-2 serology	
		IgG	IgG/IgM
GeneXpert *M.tb*	Negative	3 (50%)	6 (100%)
	Positive	3 (50%)	0 (00%)

IgG: type G immunoglobulin; IgM: type M immunoglobulin

III. Discussion

The aim of this study was to estimate the prevalence of co-infection with tuberculosis and COVID-19. The prevalence of pulmonary tuberculosis was 27.54% and that of COVID-19 co-infection 12.5%. In this study, the frequency of tuberculosis (27.54%), was lower than that reported by Ilboudo and collaborators in Burkina Faso (9). The difference between the prevalence frequency could be explained by the fact that our study population was composed exclusively of people with suspected tuberculosis. Other studies carried out in the USA (10), Ethiopia (11) and South Africa (12) reported lower rates of 8.4%, 14.4% and 17.8% respectively. Of a total of 236 patients referred for tuberculosis screening, 64.00% were men. The proportion of *M. Tuberculosis* cases detected among those with suspected of having tuberculosis was 76.90% in men, as against versus 23.10% in women ($p<0.05$). This study reveals not only the high attendance of men at tuberculosis screening centers, but also that men were the most infected. This situation is the most common worldwide, where men are more at risk of contracting tuberculosis (13). Other studies had also found a high rate of male participation and/or infection (11,14–17), in contrast to those by Wani and collaborators or Daulay and collaborators who reported the opposite trend in gender participation (18,19).

Among the patients enrolled in this study, 56.78% were below or equal to 40 years of age, while 43.22% were strictly above 40 years of age. These results are corroborated by those of Diandé and collaborators (20) who reported in their study, a 58.40% participation rate of patients whose age was less than or equal to 40 years.

Furthermore, the proportion of *M. tuberculosis* cases detected was 66.20% in participants aged 40 or under, compared with 33.80% in those aged 40 or above. Our results could also be explained not only by the consumption of tobacco and alcohol, which are factors favoring the onset of tuberculosis in young men, but also by the diversity of economic activities they engage in, where tuberculosis transmission can occur (21,22).

In this study, the rate of *M. tuberculosis* resistance to rifampicin was 9.23%. This result is considerably lower than that of Sangaré and collaborators in 2010, which was 51.6%, and slightly lower than that of Selfegna and Alelign (2022), which was 15.80% (16). But the proportion of *M. tuberculosis* resistance to rifampicin in our study is almost similar to those obtained in Ethiopia by Abay, Mulu, Derbie, Arega and their collaborators who reported 9.10%; 10.20%; 9.9%; and 9.3% respectively in their studies (23–26). Our results could be explained by the fact that, according to the WHO, when the Directly Observed Treatment Short-course (DOTS) strategy is properly applied to new cases, the rate of resistance to at least one anti-tuberculosis drug is less than 10% (27,28).

Regarding SARS-CoV-2 serology, the results of the study showed a seroprevalence of 12.63%. This seroprevalence was almost similar to that of Cissé and collaborators who also reported 14.3% in their study in Burkina Faso (29). These results were slightly higher than those of Anand and collaborators or Pollán and collaborators, who reported seroprevalence of 8% and 5% respectively (30,31).

Among SARS-CoV-2 seropositive subjects (n=12), half were positive for both IgM and IgG at the time of testing and half for IgG alone. The presence of IgM antibodies associated with IgG shows that these patients had the disease, and the presence of IgG alone proves that these patients had contact with the SARS-CoV-2 virus but not through vaccination. Indeed, none of the people enrolled in our study had received doses of vaccine against COVID-19 because the vaccine was not yet available in Burkina Faso at the time of the study.

For PCR detection of SARS-CoV-2, all samples tested were negative. These samples came from patients who tested positive for *M. tuberculosis*. These results could be explained by the short recovery time (less than 2 weeks) of people affected by the COVID-19 pandemic (32). Indeed, in Burkina Faso, tuberculosis is detected after at least two weeks of coughing, because this is when patients come to health centers. Most TB patients refused the nasopharyngeal swab. Because this was at a time when cases of COVID-19 were systematically interned in dedicated health facilities.

The prevalence of TB and COVID-19 co-infection was 12.5% (3/24). TB and COVID-19 share common features in terms of mode of transmission and symptomatology. This similarity could lead to a delayed differential diagnosis between TB and COVID-19. This serological evidence of COVID-19 among TB cases does not allow us to distinguish asymptomatic carriers from SARS-CoV-2, even though studies have revealed a high proportion of asymptomatic carriers both within the population in general (33,34) and in vulnerable groups (35). The results of the present study are relatively similar to those of Bruyn and collaborators, who reported a prevalence of TB cases associated with COVID-19 of 14.4% in 2023 (12). Similarly, in 2021, Faye and collaborators and Doutchi and collaborators respectively reported 3 and 2 cases of TB and COVID-19 co-infection in Senegal and Niger (36,37). These low rates may reflect the fact that barrier measures were already being applied to tuberculosis cases before the advent of COVID-19, thereby reducing the rate of co-infection. Moreover, lower rates of co-infection (0.21%) were reported in Thailand by the Siranart's team in 2023, who instead surveyed TB among COVID-19 cases, (17). Thus, just as TB should be screened among cases of COVD-19 cases (17), attention should also be paid to screening for COVID-19 among pulmonary TB cases, given the high case-fatality in co-infected patients.

Conclusion

This study revealed a prevalence of pulmonary tuberculosis of 27.54% in our study population. Among TB-positive patients who accepted the COVID-19 serological test, 12.5% were carriers of anti-SARS-CoV-2 antibodies. Co-infection with pulmonary tuberculosis and COVID-19 is a reality. Thus, COVID-19 screening should be carried out systematically in suspected cases of pulmonary tuberculosis during the pandemic period.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors' Contributions

Conceptualization: ZA, ST and ZKJ.; methodology: ST, STL, SS, YAP and YO; validation: MNSD, SA, TL, ST, BKA and OHG.; sample collection: Z A, SWYA, OKZT, and YAP; formal analysis: ZA, YAP and SS; investigation; ST and SJ; resources: ST, KE, CA, ZA and SJ; writing-original draft preparation: ZA, ST; writing-review and editing: ST, ZKJ, KD, CTR, DWF, ZAA and TA; supervision: ST. All authors have read and agreed to the published version of the manuscript.

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