

# COVID-19/Tuberculosis Co-Infection at the Epidemic Treatment Center (ETC) of Saint-Louis (Senegal): About 9 Cases

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## Abstract

**Introduction:** COVID-19 is a global public health emergency that can cause acute respiratory distress syndrome. In countries where tuberculosis (TB) is endemic, co-infection of COVID-19 and TB is often encountered, which increases the risk of developing severe forms of COVID-19. **Objectives:** The aim of this study was to determine the prevalence of COVID-19/TB co-infection at the Epidemic treatment center (ETC) in Saint-Louis (Senegal) and to describe the epidemiological, clinical, paraclinical, and outcome profile of co-infected patients. **Patients and Methods:** This is a retrospective, cross-sectional, descriptive cohort study based on the records of COVID-19/TB co-infected patients who were hospitalized at the ETC in Saint-Louis (Senegal) over an 18-month period from March 2020 to September 2021. **Results:** Out of a total of 454 hospitalizations, we collected records of 9 patients co-infected with COVID-19/TB, resulting in a prevalence of 2%. The study included patients with a median age of 34 years (range: 10-86 years), with a male predominance (7 cases) and a sex ratio of 3.5. The majority of patients (88.9%) had severe forms of COVID-19. Dyspnea and cough were reported in all patients (100%). Pulmonary TB was the most frequent localization, with 9 cases. The diagnosis of COVID-19 was confirmed by nasopharyngeal PCR in all patients (100%). Bacilloscopy was positive in 3 out of 5 cases. One patient tested positive for GeneXpert<sup>®</sup> MTB/RIF without rifampicin resistance. All patients were prescribed the hydroxychloroquine-azithromycin combination and anti-tuberculosis treatment. Out of the nine patients, four recovered (44.4%) and five died (55.5%). **Conclusion:** COVID-19/TB coinfection had a low

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prevalence in our cohort, but was associated with a high mortality due to the frequent occurrence of severe forms of the disease.

## Keywords

COVID-19, Tuberculosis, Saint-Louis, Senegal

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## 1. Introduction

COVID-19 (Coronavirus Disease-19), caused by the SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), is a respiratory illness that was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. It can lead to severe forms of acute respiratory distress requiring hospitalization in intensive care units and resulting in high mortality rate [2] [3]. As of December 29<sup>th</sup>, 2021, there were 281 million recorded cases of COVID-19 worldwide, resulting in 5.4 million deaths [4]. On the same date, Senegal had reported 74,672 confirmed cases, 72,422 recoveries, and 1890 COVID-19-related deaths [5]. Tuberculosis, on the other hand, is an infectious disease caused by *Mycobacterium tuberculosis* that primarily affects the lungs. It is also a significant global public health issue. In 2020, the World Health Organization (WHO) recorded 9.9 million cases of tuberculosis (TB) resulting in 1.5 million deaths worldwide. TB is the 13<sup>th</sup> leading cause of death globally and the second leading cause of death due to an infectious disease, after COVID-19 (and before AIDS) [6]. In Senegal, 13663 cases of TB of all forms were reported in 2019 [7].

These two conditions share similarities. They are both airborne diseases, although SARS-CoV-2 is more contagious [8] [9]. They also have common symptoms such as fever, cough, and dyspnea, as well as the same risk factors such as advanced age, diabetes, and immunosuppression [10]. The co-infection of COVID-19 and TB worsens the prognosis of patients, with an increased risk of developing acute respiratory distress syndrome (ARDS) [11]. This association has been referred to as a “deadly duo” [12]. The immunosuppression caused by the SARS-CoV-2 infection [13] can reactivate latent TB or worsen active TB [14]. Similarly, the pulmonary sequelae of COVID-19 increase the risk of developing TB [14]. Conversely TB increases the risk of developing severe forms of COVID-19 [15] and is a significant factor in the spread of SARS-CoV-2 by promoting longer viral excretion in sputum and feces [16]. In this regard, we conducted a study to determine the prevalence of COVID-19/TB coinfection at the ETC of Saint-Louis (Senegal) and to describe the epidemiological, clinical, paraclinical and evolution profile of coinfecting patients.

## 2. Patients and Methods

This is a retrospective, cross-sectional, and descriptive cohort study conducted from March 2020 to September 2021. The study included all patient records of

those hospitalized with COVID-19/TB co-infection at the ETC of Saint-Louis (Senegal). Patients whose files were incomplete or could not be found were excluded.

The diagnosis of COVID-19 was confirmed by positive PCR tests from nasopharyngeal samples, rapid antigen tests, or suggestive peripheral and subpleural ground-glass opacities on CT scans. The diagnosis of TB was based on a combination of epidemiological, clinical, and paraclinical evidence, including positive bacilloscopy and GeneXpert<sup>®</sup> MTB/RIF results, as well as radiological findings. We analysed epidemiological factors such as age, gender, marital status, anti-COVID-19 vaccination, comorbidities, and lifestyle, as well as clinical factors such as symptoms at admission, TB localisations, and severity. Paraclinical factors such as COVID-19 PCR, antigenic COVID RDT, and haemogram were also considered. The study collected data on CRP, creatinine levels, transaminases, fasting blood glucose, retroviral serology (SRV), bacilloscopy, GeneXpert<sup>®</sup> MTB/RIF, chest X-ray, and chest CT scans. The therapeutic aspects, such as the administered molecules, and the evolution of the disease, such as the duration of hospitalization and the outcome, were also recorded. All these data were collected from patients' files.

Data entry and analysis were performed using Excel and Epi info 7 software. Categorical variables were expressed in frequencies and percentages. No comparison was made as this is a purely descriptive study. Throughout our study, medical confidentiality and privacy were respected.

### 3. Results

#### 3.1. Epidemiological Data

A total of 9 patients with co-infection of COVID-19 and TB were identified out of 454 hospitalizations, resulting in a prevalence of 2%. The median age was 34 years [range: 10 - 86 years]. The most common age group was 21 to 40 years old with 3 cases (33.3 %). There was a male predominance with 7 cases, resulting in a sex ratio of 3.5. Seven patients were single (77.8%) and 2 patients were married (22.2%). The main comorbidities were HIV infection (1 case) and sickle cell disease SS (1 case). One case of active smoking was noted (**Table 1**).

#### 3.2. Clinical Data

According to severity, there were 8 severe cases (88.9%) and 1 moderate case (11.1%). Upon admission, the predominant functional symptoms were dyspnea and cough, each with 9 cases. The most common general symptoms were night fever, weight loss, anorexia, and physical asthenia, each with 9 cases. All patients presented with a pulmonary consolidation syndrome and acute respiratory distress syndrome. In 9 cases, TB was located in the lungs, followed by 2 cases each of pleural and lymph node locations (**Table 2**).

#### 3.3. Paraclinical Data

A nasopharyngeal COVID-19 PCR test was performed on admission for all

**Table 1.** Distribution of COVID-19/TB co-infected patients according to epidemiological data.

Epidemiological data	Number (n)	Percentage (%)
<b>Age (n = 9)</b>		
0 - 20 ans	2	22.2
21 - 40 ans	3	33.3
41 - 60 ans	1	11.1
61 - 80 ans	2	22.2
>80 ans	1	11.1
<b>Sex (n = 9)</b>		
Male	7	77.8
Female	2	22.2
<b>Marital status (n = 9)</b>		
Married	2	22.2
Single	7	77.8
Divorced	0	0
Widowed	0	0
<b>Comorbidities (n = 9)</b>		
HIV infection	1	11.1
Sickle cell disease SS	1	11.1
<b>Lifestyle (n = 9)</b>		
Active smoking	1	11.1

**Table 2.** Distribution of COVID-19/TB co-infected patients according to clinical data.

Clinical data	Number (n)	Percentage (%)
<b>Forms by severity (n = 9)</b>		
Severe forms	8	88.9
Moderate forms	1	11.1
Mild forms	0	0
<b>Functional signs (n = 9)</b>		
Dyspnea	9	100
Cough	9	100
Agueusia	4	44.4
Flu syndrom	3	33.3
Hemoptysis	2	22.2
Anosmia	2	22.2
<b>General signs (n = 9)</b>		
Night fever	9	100
Weigh loss	9	100
Anorexia	9	100
Physical asthenia	9	100

**Continued****Physical signs (n = 9)**

Pulmonary condensation syndrome	9	100
Acute respiratory distress syndrome	9	100
Slow cord compression syndrome	1	11.1
Psoitis	1	11.1
Oral candidiasis	1	11.1
Cachexia	1	11.1

**TB location (n = 9)**

Pulmonary	9	100
Pleural	2	22.2
Lymph node	2	22.2
Peritoneal	1	11.1
Vertebral	1	11.1

patients, with 100% positivity. An antigenic COVID-19 RDT test was performed on 3 patients, all of whom tested positive. Bacilloscopy was positive in 3 out of 5 cases. GeneXpert<sup>®</sup> MTB/RIF was performed on only one patient and was positive without resistance to rifampicin (**Table 3**). The median leukocyte count was 9810/uL [4410 - 18,850/uL]. Hyperleukocytosis (>10,000/uL) was noted in 4 patients (44.4%). The median lymphocyte count was 1110/uL [510 - 2270/uL]. Lymphopenia (<1500/mm<sup>3</sup>) was observed in 8 patients (88.9%). The median haemoglobin (Hb) level was 10 g/dL [8.4 - 12.7 g/dL]. Anaemia (Hb < 11 g/dL) was found in 6 patients (66.7%). The median CRP level was 36 mg/L [12 - 96 mg/L]. CRP > 12 mg/L was found in 4 patients (44.4%). The median ALAT level was 14 UI [08 - 41 UI]. The median creatinine level was 9.4 mg/L [5.3 - 12.1 mg/L]. The fasting blood glucose level was 0.9 g/L [0.7 - 1.1 g/L]. All patients underwent HIV-1 testing, with one case testing positive. Chest X-ray was performed on four patients, revealing the following abnormalities: hematogenous miliary (two cases), left apical cavity (one case), and left apical infiltrate (one case). Chest CT scan was performed on 7 patients, with the majority showing ground-glass opacities (7 cases), followed by cavitations (4 cases) and hematogenous miliary (2 cases). A spine CT scan was performed on 1 patient, revealing tuberculous spondylodiscitis from D6 to D10 associated with a paravertebral abscess collection (**Table 3**).

**3.4. Treatment and Outcome Data**

Treatment regimens included: hydroxychloroquine-azithromycin (09), RHZE (09), ceftriaxone (09), dexamethasone (09), enoxaparin (09), oxygen therapy (09), vitamin B therapy (09), vitamin C therapy (09) and cART (TDF-3TC-DTG) (01), co-trimoxazole 960 mg/day (01). The median hospital stay was 20 days [10 - 27 days]. Four patients (44.4%) recovered, while five (55.6%) died. The causes of death were respiratory distress in four cases and septic shock in one case. The

majority of deaths occurred in patients aged 60 and over, as shown in **Table 4**.

**Table 3.** Distribution of COVID-19/TB co-infected patients according to paraclinical data.

Paraclinical data	Number (n)	Percentage (%)
<b>COVID PCR (n = 9)</b>		
Positive	9	100
Negative	0	0
<b>COVID RDT (n = 3)</b>		
Positive	3	100
Negative	0	0
<b>Bacilloscopy (n = 5)</b>		
Positive	3	60
Negative	2	40
<b>GeneXpert® MTB/RIF (n = 1)</b>		
Positive	1	100
Negative	0	0
<b>Chest CT (n = 7)</b>		
Frosted glass appearance	7	100
Caverns	6	85.7
Miliary	2	28.6
Small right pleurisy	2	28.6
Interstitial syndrome	1	14.3
Pulmonary emphysema	1	14.3
Right hilo-apical calcifications	1	14.3
Left apical fibrosis	1	14.3
<b>Spine CT (n = 1)</b>		
Spondylodiscitis	1	100
Abscessed paravertebral collection	1	100
<b>Chest X-ray (n = 4)</b>		
Hematogenous miliary	2	50
Left apical cavern	1	25
Left apical infiltrate	1	25

**Table 4.** Distribution of death by age group.

Age group	Number of deaths	Percentage (%)
<30	1	20
30 to 60	1	20
>60	3	60
<b>Total</b>	<b>5</b>	<b>100</b>

## 4. Discussion

Our study was limited by its retrospective nature, the insufficient number of bacilloscopy and GeneXpert<sup>®</sup> MTB/RIF to confirm tuberculosis, especially when imaging revealed suggestive signs. In most cases, the diagnosis of TB was based on a range of arguments. The low prevalence found meant that it was not possible to carry out in-depth statistical analyses to understand the determinants of this co-infection.

Tuberculosis (TB) and COVID-19 are respiratory illnesses that primarily affect the lungs. While TB progresses slowly, COVID-19 develops rapidly within a few days after exposure [17] [18]. Physiopathologically, SARS-CoV-2 infection may cause transient immunosuppression [13] due to a significant decrease in TCD4+ and CD8+ lymphocytes combined with low IgG antibody production, which may favor reactivation of latent TB or exacerbate active TB in COVID-19/TB co-infected patients. Additionally, corticosteroid therapy used in COVID-19 treatment exacerbates this immunosuppression [16]. In addition, viral excretion lasts twice as long in sputum and five times as long in stool for COVID-19/TB co-infected patients compared to COVID+ patients without TB. This results in a higher potential for the spread of SARS-CoV-2 [17].

COVID-19 may contribute to the detection of pulmonary TB, especially in high endemic areas, due to the clinical similarity and overlapping symptoms [19] [20]. Our patient series showed a 2% prevalence of COVID-19/TB co-infection. In India, Gupta N *et al.* reported an increase in the incidence of active TB and treated TB from 1.21 and 0.83 per 100 hospitalizations for COVID-19, respectively [21]. In the Philippines, the prevalence was 1% [22]. In South Africa, a prevalence of 9.5% was reported [23]. In 2020, Tadolini *et al.* found a higher prevalence of COVID-19/TB co-infection at 18.3% in Belgium [24].

In our series, the median age of patients was 34 years [10 - 86 years] with a male predominance. Co-infection of COVID-19 and TB was generally found in young male patients in the literature. For example, Tadolini M *et al.*, describing the first Italian cohort of 49 patients with COVID-19 and TB coinfection, found the mean age to be 48 years with 81.6% male [24]. Motta I *et al.* (in Italy) found a mean age of 37 years [22]. Stochino C *et al.* (in Italy) found a mean age of 39 years and a male predominance (60%) [25]. A meta-analysis conducted on 34 countries with a total of 767 COVID-19/TB co-infected patients highlighted the same trend, with a median age of 44 years and a male predominance (70.4%) [26]. Men are more likely to contract TB and COVID-19 because of their activities and behaviour. Throughout their lives, they take more risks and engage in more harmful behaviours such as tobacco and alcohol use. In contrast, women tend to be more health-conscious and seek medical attention more frequently [27]. Regarding clinical symptoms, a meta-analysis showed that fever (71.7%), dry cough (57.8%), dyspnoea (35.7%), headache (24.7%), fatigue (21.2%) and sore throat (17.8%) predominated in COVID-19/TB coinfection [26]. In our series, the main symptoms were dyspnoea (9 cases), cough (9 cases), evening/night

fever (9 cases), weight loss (9 cases), anorexia (9 cases), physical asthenia (9 cases) and ageusia (4 cases).

In our series, pulmonary tuberculosis was found in all 9 cases (100%), followed by pleural and lymph node involvement with 2 cases each (22.2%). Stochino *et al.* also found a predominance of pulmonary tuberculosis with 19 cases (95%), followed by renal and neurological tuberculosis, each with 2 cases [25]. In their series, Tadolini *et al.* had 36 cases out of 49 of isolated pulmonary TB, 12 cases out of 49 of pulmonary TB associated with extra-pulmonary TB, and 1 case of isolated extra-pulmonary TB (1/49) [24]. In fact, the lungs are the primary site for tuberculosis, followed by the pleura and lymph nodes. Tuberculosis is an infectious disease transmitted mainly by air. The passage of BK via the haematogenous and lymphatic routes explains the extra-pulmonary localizations [28] [29].

Diagnosing co-infection can be challenging due to the clinical similarities and the presence of ground-glass opacities in both cases on imaging. It is worth noting that 20% of tuberculosis patients also present with ground-glass opacities [30] [31], although this feature is more commonly found in SARS-CoV-2 infection [24]. This could explain the low prevalence of COVID-19/TB co-infection in our series.

Regarding severity, 8 patients (88.9%) had severe COVID. This is consistent with the literature as TB is associated with a 2.17 times higher risk of developing severe COVID-19 [22], making this association a ‘deadly duo’ [12]. We found a mortality rate of 55.6%, which is higher than that reported by Tadolini M *et al.* (Italy) with a mortality rate of 10.2% [24]. Motta *et al.* (Italy) reported a mortality rate of 11.6% [22], while Gupta *et al.* found a mortality rate of 27.3% in India [2]. The high mortality observed in TB/COVID-19 co-infection may be due to parenchymal destruction leading to fibrosis and cavitation, exacerbated by COVID-19, further compromising already impaired lung function [2]. In our series, the majority of deaths (60%) occurred in patients aged 60 and over. Tadolini *et al.* found 5 patients aged over 60 among the 6 deaths in their study (83.3%) [24]. This could be explained by the fact that advanced age is a negative factor for both TB and COVID-19 [32] [33].

## 5. Conclusion

Co-infection of COVID-19 and TB was infrequent in our cohort. However, it was associated with high mortality, making this combination a “cursed couple”, particularly in areas where TB is endemic. The use of COVID PCR, bacilloscopy and medical imaging played a crucial role in diagnosing this co-infection. Popularizing the use of masks, physical distancing, vaccination, early diagnosis and treatment could help control both diseases.

## Authors Contribution

List of authors who contributed to the study:



- Moustapha Diedhiou: contributed to the analysis, interpretation, and correction;
- Papa Latyr Junior Diouf: contributed to the english traduction;
- Mba Bambo Diakhaby: contributed to the proofreading;
- Demba Makalou: contributed to the proofreading;
- Samba Niang: contributed to the proofreading;
- Diatou Dia-Gueye: contributed to the proofreading;
- Amadou Diop Dia: contributed to the proofreading;
- Ibrahima Louis Martin Dieng: contributed to the proofreading;
- Seynabou Lô: contributed to the proofreading;
- Ndéye Méry Dia-Badiane: contributed to the proofreading.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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