

Full Length Research Paper

Contribution of COVID-19 diagnosis in patients seen at the tuberculosis laboratory in the response to the COVID-19 pandemic in the Kayes Heath district

MAIGA A.^{1,2*}, CISSE A. B.⁴, SOUMANO I.⁶, Ag. BARAIKA M.^{3,4}, SANGARE A. K.⁵, DIARRA B², TRAORE B.⁵, TRAORE A.⁷, HAMIDOU A⁶, SAMAKE H⁴, MAIGA I. I.^{1,2} and GUINDO I.^{3,4}

¹Laboratory of Medical Biology and Hospital Hygiene, Point-G University Hospital, Bamako, Mali.

²Faculty of Medicine and Odontostomatology, University of Sciences, Technics and Technologies of Bamako (USTTB), Bamako, Mali.

³Laboratory of Chemistry, Faculty of Pharmacy (FAPH), University of Sciences, Technics and Technologies of Bamako (USTTB), Bamako, Mali.

⁴National Institute of Public Health, Bamako, Mali.

⁵Charles Merieux Infectiology Center, Bamako, Mali.

⁶Kayes Reference Health Center, Mali.

⁷National Institute for Training in Health Sciences, Bamako, Mali.

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The COVID-19 pandemic has posed challenges to tuberculosis (TB) services, leading to an increase in TB deaths for the first time in a decade. The aim of our study was to investigate the presence of SARS-CoV-2 in patients attending the Kayes Reference Health Center for tuberculosis diagnosis and anti-tuberculosis treatment monitoring. This was a cross-sectional and prospective study conducted at the Reference Health Center (CSREF) laboratory in Kayes from December 1, 2021, to February 28, 2022. Sputum and nasopharyngeal samples were collected from all patients suspected of tuberculosis and those undergoing anti-tuberculosis follow-up. The search for acid-fast bacilli (AFB) and the detection of SARS-CoV-2 were performed using fluorescence microscopy and the GeneXpert Xpert Xpress SARS-CoV-2 test, respectively. A total of 463 patients were included in the study, with males representing the majority at 67% (N=308), and the age group of 35 to 44 being the most represented at 19% (N=86). SARS-CoV-2 was detected in 70 patients, with 69% (N=48) being male and 31% (N=22) female. The age group of 65 and over was the most affected by SARS-CoV-2, followed by the age group of 55 to 64, with 21% and 17% of cases detected, respectively. In this study, 16% of patients undergoing tuberculosis diagnosis and 12% of patients undergoing microscopic monitoring of anti-tuberculosis treatment tested positive for SARS-CoV-2. A total of 1.9% (N=9) of patients were co-infected, with 7 cases detected during tuberculosis diagnosis and 2 during treatment monitoring. Based on these results, bidirectional screening for COVID-19 and tuberculosis should be integrated into our health system.

Key words: Tuberculosis, Covid-19, CSREF, Kayes, Mali.

INTRODUCTION

Coronavirus Disease-19 (COVID-19) is caused by the novel severe acute respiratory syndrome coronavirus 2

(SARS-CoV-2), which primarily targets the respiratory system (Lu et al., 2020). The disease was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Globally, there have been over 126 million confirmed cases of COVID-19, resulting in 2.7 million deaths, with the majority occurring in the Americas and Europe regions (Sy et al., 2020). According to the WHO report from February 2023, Mali recorded 32,998 cases of COVID-19 and 743 deaths (WHO, 2023). COVID-19 is primarily transmitted through respiratory droplets, such as those produced by coughing and sneezing, or by touching contaminated surfaces (WHO, 2021). The symptoms of COVID-19 can vary widely, including headache, fatigue, body aches, cough, sore throat, fever, gastrointestinal issues, diarrhea, nausea, muscle pain, difficulty breathing, and pneumonia (Ren et al., 2020; Huang et al., 2020; Yang et al., 2020; Mao et al., 2020). Individuals aged 65 and older, as well as those with underlying health conditions such as hypertension, heart or lung problems, diabetes, obesity, or cancer, are at higher risk of developing severe forms of the disease (Mahieu, 2020).

The COVID-19 pandemic has also posed challenges to tuberculosis (TB) services, leading to an increase in TB deaths for the first time in a decade (WHO, 2022). According to MacLean et al. (2022), in 2020, at least 1.5 million people died from tuberculosis, a figure not seen since 2017. In many countries, COVID-19 testing rates are below WHO targets, and TB case notification rates have fallen (Guirelli et al., 2022). Cases of co-infection of tuberculosis and COVID-19 have been reported since the beginning of the COVID-19 pandemic (WHO, 2022). High mortality, associated with an increased need for intensive care, has been noted in active and treated TB patients co-infected with COVID-19 (MacLean et al., 2022). However, the differential diagnosis between these two conditions remains difficult due to the similarity of the clinical pictures. Countries were recommended to adopt diagnostic algorithms following WHO guidelines for screening for TB or COVID-19 based on clinical characteristics and patient history as well as the local TB burden (Guirelli et al., 2022). Several countries (Indonesia, South Africa, Nigeria, and India) have tested simultaneous screening strategies for COVID-19 and tuberculosis during the pandemic. Particularly, the Indian ministry released a rapid response plan to mitigate the impact of the COVID-19 pandemic on tuberculosis in September 2020, which included COVID-19 screening for all patients diagnosed with tuberculosis and tuberculosis screening for all patients with confirmed COVID-19 (Ruhwald et al., 2022). Faced with this problem, the aim

of our study was to search for SARS-COV-2 in patients received at the Kayes Reference Health Center for the diagnosis of tuberculosis or for the monitoring of anti-tuberculosis treatment.

METHODOLOGY

This was a cross-sectional study conducted at the Kayes Reference Health Center (CSREF) laboratory over a period of three months, from December 1, 2021, to February 28, 2022. All healthcare facilities referring patients for tuberculosis diagnosis were notified about the study. Participation in the study was systematically offered to all new suspected patients and those undergoing anti-tuberculosis treatment, and they were sampled for the Xpert Xpress SARS-CoV-2 test after obtaining their free and informed consent. The COVID-19 care units were also informed of the study to ensure compliance with the code of ethics.

Study population

The study population consisted of patients seen in the laboratory diagnoses of tuberculosis and the monitoring of anti-tuberculosis treatment during the study period of the Kayes Reference Health Center.

Inclusion criteria

All patients in the study population seen at the Kayes Reference Health Center who agreed to give their free and informed consent were included in our study.

Non-inclusion criteria

Not included : patients who did not give their free and informed consent; patients who have not benefited from the SARS-CoV-2 detection test.

The authors sampling approach was exhaustive, including all patients meeting the predefined inclusion criteria. The variables studied encompassed socio-demographic factors (such as age, sex, and patient type) as well as biological parameters (including microscopy and Xpert Xpress SARS-CoV-2 test results). Sputum samples were collected using dedicated spittoons recommended by the national tuberculosis control program. Patients were instructed on proper sputum collection techniques, with two samples obtained from those suspected of TB and one from those undergoing microscopic monitoring of anti-TB treatment, following national guidelines. Sputum collection took place early in the morning on an empty stomach, either at the patient's home or at a designated center outdoors, away from others. Upon receipt, each sputum sample was assessed for appearance and volume, with patients asked to provide a new sample if the quality was deemed poor (e.g., saliva-like appearance). All samples were accompanied by an information sheet detailing patient identity, sex, age, type of patient, and contact information, with this data recorded in the microscopy register. Additionally, oropharyngeal swabs were obtained from

*Corresponding author. E-mail: mimimaiga@yahoo.fr. Tel: +223 75 89 80 54.

Table 1. Socio-demographic characteristics of patients (N=463).

Data	Effective	Percent
Sex		
Female	155	33
Male	308	67
Age group (year)		
0 à 14	19	4
15 - 24	47	10
25-34	82	18
35-44	86	19
45-54	85	18
55-64	74	16
65 and more	69	15
Type of patients		
New patient	378	82
Patient Follow-up	85	18

patients on their first laboratory visit after providing consent. The COVID-19 collection kit comprised a nylon flocked swab with viral transport medium, totaling 3 ml, following standard precaution procedures. These samples were transported, analyzed, or refrigerated at +4°C before testing. Smear slides were prepared and identified with the patient's serial number, corresponding to the entry in the microscopy register and the spittoon. Under a microbiological safety station (PSM), the cuspidor was carefully opened, and purulent or mucous patches were identified. A portion of these patches was taken and spread using a single-use loop onto an area approximately 2 by 1 centimeter in the center of the slide. The smears were then made, dried, and fixed under the PSM. Following national guidelines, the smears were stained with auramine and observed under a Primo Star iLED fluorescence microscope for acid-fast bacilli (AFB). This microscope, recommended by the WHO for tuberculosis diagnosis, combines optical microscopy with fluorescence visualization. Smears were read the same day they were stained due to the light sensitivity of fluorescent staining. Smears were initially read using the 20X objective, with confirmation at 40X in case of doubt. Results were interpreted according to the national algorithm, classifying as negative, weakly positive, or graded from 1+, 2+ and 3+.

The Xpert Xpress SARS-CoV-2 test was conducted using the four-module GeneXpert system with GeneXpert Xpert® Xpress SARS-CoV-2 test cartridges. These single-use disposable cartridges contain the necessary reagents for polymerase chain reaction (PCR) amplification of genetic material. Cartridges were prepared and loaded according to the manufacturer's instructions, with device information input and barcode reading to initiate testing. Results were automatically interpreted by the GeneXpert system and displayed clearly in the "Show results" window. Interpretations included "SARS-CoV-2 POSITIVE" for detected target RNA, "SARS-CoV-2 NEGATIVE" for undetected target RNA, "INVALID" for criteria not met and absence of SARS-CoV-2 RNA, "ERROR" for indeterminate RNA presence, and "NO RESULT" for undetermined RNA presence or absence. Results were recorded in microscopy and COVID-19 registers and on results forms. Patients' positive for

either or both diseases that did not collect their results within one day of the appointment were contacted by telephone or traced following ethical and professional conduct rules. Data were analyzed and processed using Excel and Word software.

RESULTS

Socio-demographic data

The male gender was the most represented at 67% (N=308), with the age group of 35 to 44 being the most prevalent at 19% (N= 86). New patients or suspected patients comprised 82% (N=378) of the total (Table 1). SARS-CoV-2 was detected in 70 patients, with 69% (N=48) being male and 31% (N=22) female, resulting in a sex ratio of 2.18 favoring men (Figure 1). The age group of 65 and over was the most affected by SARS-CoV-2, followed by the age group of 55 to 64, accounting for 21 and 17% of cases detected, respectively. In this study, 16% of patients undergoing tuberculosis diagnosis and 12% of patients undergoing microscopic monitoring of anti-tuberculosis treatment tested positive for SARS-CoV-2 (Figure 2). Among microscopy-positive patients, 13% (N=9) tested positive for SARS-CoV-2, while among microscopy-negative patients, 15% (N=61) tested positive. The overall rate of tuberculosis and COVID-19 co-infection in the study was 1.9% (N= 9). Among microscopy-positive patients, 13% (N=7) were detected positive for SARS-CoV-2, and among microscopy-negative patients, 16% (N=53) were detected positive. Two cases of tuberculosis diagnosis and seven cases of treatment monitoring were co-infected, all of which were male (Table 2).

DISCUSSION

Our study aimed to diagnose COVID-19 in tuberculosis patients seen at the CSREF laboratory in Kayes. Sociodemographically, over three months, 463 patients participated in our study, with 81.64% (N=378) undergoing tuberculosis diagnosis and 18.36% (N=85) undergoing treatment monitoring. The male sex was the most represented, accounting for 67% of the participants. This proportion is comparable to the study conducted by Chahboune et al. (2022) in Morocco, which reported 60.08% male sex, but lower than that of Patel et al.(2023) in India, where 71.9% were male. The over-representation of the male sex in our context could be attributed to factors such as tobacco consumption among men and occupational exposure to harmful particles or smoke. The average age of our patients was 44 years old, similar to the findings of Patel et al. (2023) in India, who reported an average age of 40 years. This could be attributed to patients' reluctance to seek healthcare due

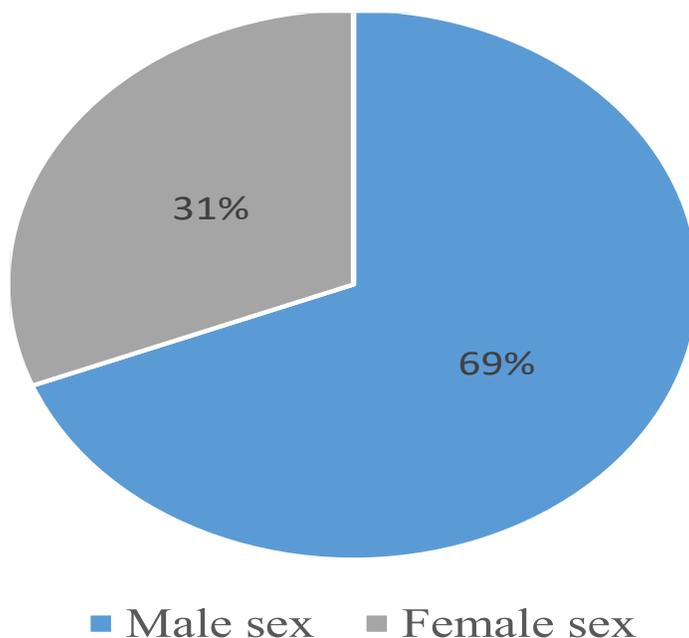


Figure 1. Distribution of SARS-CoV-2 detection in study patients based on gender.

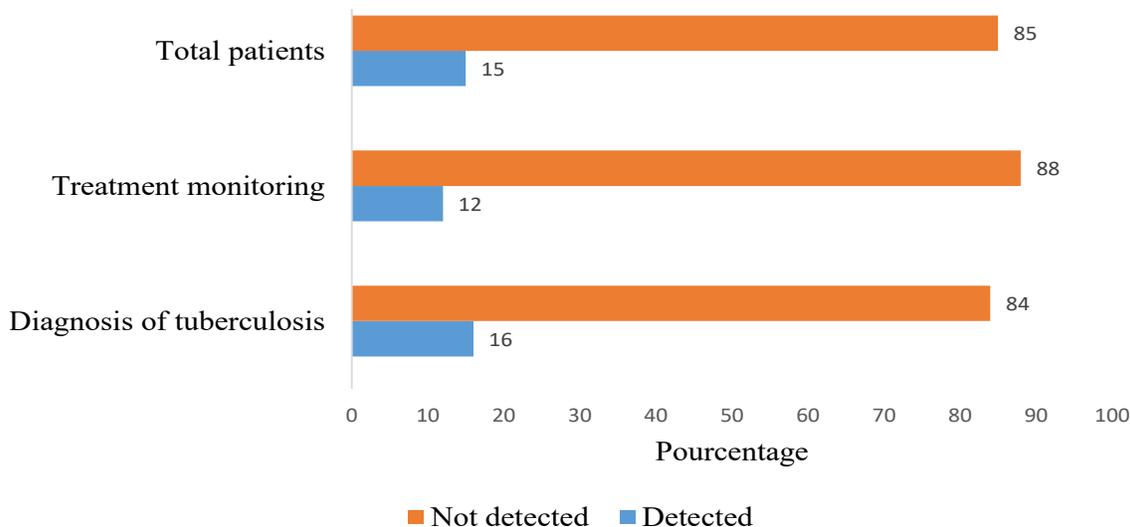


Figure 2. Detection of SARS-CoV-2 depending on the reason for attending the laboratory.

to financial constraints, low levels of education, or crowded living conditions. However, the age groups 65 years old and over and 55 to 64 years old were the most affected by COVID-19, accounting for 21 and 17% of cases, respectively. Our results align with existing literature indicating that elderly individuals are more susceptible to COVID-19 compared to the general population (Gidado et al., 2020).

The detection rate of SARS-CoV-2 was 15% among all patients in our study, which was higher than that reported by Adusi-Poku and colleagues in Ghana in 2023, who found a rate of 11.7% (95% CI: 5.2 to 18.2%). Among patients suspected of tuberculosis, the detection rate was 16%, higher than the 13.7% (95% CI: 6.8-20.6%) reported by Adusi-Poku et al. (2023). This disparity could be attributed to the timing of our study, conducted during

Table 2. Characteristics of co-infected patients.

Code	Reason for attendance	Sex	Age (an)	Microscopy result	Test SARS-CoV-2	Sampling date
TB/C-15	Suspect of TB	M	43	Positif 3+	Detected	1/12/2021
TB/C-53	Follow-up 2nd month of treatment	M	68	Positif F+	Detected	5/12/2021
TB/C-77	Suspect of TB	M	56	Positif 3+	Detected	7/12/2021
TB/C-10	Suspect of TB	M	64	Positif 3+	Detected	24/12/2021
TB/C-19	Suspect of TB	M	42	Positif 2+	Detected	24/12/2021
TB/C-96	Suspect of TB	M	70	Positif F+	Detected	26/12/2021
TB/C-23	Follow-up 2nd month of treatment	M	19	Positif F+	Detected	25/01/2022
TB/C-59	Suspect of TB	M	50	Positif 2+	Detected	1/02/2022
TB/C-68	Suspect of TB	M	29	Positif 3+	Detected	2/02/2022

Positive F+: weakly positive (1-19) b/a length; Positive 2+: 5-50 b/field; Positive 3+: more than 50 b/field.

the peak of the COVID-19 pandemic, and the size of our sample. The detection rate of SARS-CoV-2 among patients undergoing anti-tuberculosis treatment was 12%, lower than the 23.92% reported by Kayali (2022) in Turkey. This difference could be explained by our smaller sample size and the presence of higher comorbidity factors in the Turkish study.

SARS-CoV-2 and *Mycobacterium tuberculosis* infections can both lead to an unbalanced inflammatory immune response and a common dysregulation of the immune response, suggesting an increased risk of severity and progression of both diseases (Luke et al., 2022). TB/COVID-19 co-infection was reported in 9 patients, accounting for 1.9% of patients in the study. This result is comparable to the findings of Adun-Poku et al. (2022), who reported a rate of 1%, but lower than that reported by Sarınoğlu et al. (2020), who found a rate of 6.66%. The disparity with the latter study could be explained by the timing of Sarınoğlu's study in 2020, when COVID-19 cases were higher during the peak of the epidemic.

Additionally, the impact of SARS-CoV-2 on TB patients and the pathological pathways linking SARS-CoV-2 and *M. tuberculosis* have been highlighted (Shah et al., 2022). The detection of SARS-CoV-2 in 15% of patients in our study likely contributed to a reduction in the transmission of COVID-19 within the CSREF of Kayes and the community, as well as a decreased risk of severe disease development through prompt treatment in those co-infected with tuberculosis and COVID-19. The detection of SARS-CoV-2 in 15% of microscopy-negative patients underscores the importance of using both tests for tuberculosis and COVID-19 diagnosis during the pandemic to prevent missed cases of either disease, aligning with WHO recommendations.

One limitation of our study is that we did not utilize the GeneXpert system for tuberculosis diagnosis. The use of this equipment could have potentially increased the detection rate of co-infection cases due to its higher

sensitivity compared to microscopy.

Conclusion

This study enabled the detection of SARS-CoV-2 in a percentage of patients, particularly in those aged over 50 years. Based on these findings, we recommend that both public and private healthcare facilities adhere to WHO guidelines by adopting an integrated approach to bidirectional screening for COVID-19 and tuberculosis.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

- Adusi-Poku Y, Wagaw ZA, Frimpong-Mansoh RP, Asamoah IO, Sorvor F, Afutu FK, Sarpong C, Amoussou-Gohoungo LO, Abdulai FN, Ahmedov S (2023). Bidirectional screening and testing for TB and COVID-19 among outpatient department attendees: outcome of an initial intervention in Ghana. *BMC Infectious Diseases* 23(1):1-7.
- Chahboune M, Barkaoui M, Iderdar Y, Alwachami N, Mourajid Y, Ifleh M, Boumendil K, Bachar K, El Madani S (2022). Profil épidémiologique, aspects diagnostiques et évolutifs des patients tuberculeux au centre de diagnostic de la tuberculose et des maladies respiratoires de Settat, Maroc. *The Pan African Medical Journal* 42 p.
- Gidado M, Odume B, Ogbudebe C, Useni S, Tukur M, Chukwuogo O, Ajiboye P, Sadiq I, Yahaya K, Adebola L (2020). Early experience in implementation of an integrated COVID-19 and TB community-based active case finding in Nigeria. *African Journal of Respiratory Medicine* 15(2).
- Guirelli AO, Bispo TR, Colpas DR, de Campos IB, Chimara E, Cergole-Novella MC, Rodart IF, dos Santos Candido V, Segura-Ramírez PJ, Dos Santos Menezes Gaiotto Daros V, dos Santos Carmo AM (2022). Tuberculosis/COVID-19 co-infection detected in a single sputum sample using a rapid molecular test. *Brazilian Journal of Microbiology* 53(2):633-639.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 395(10223):497-506.

- Kayali S, Karacorlu FN, Yilmaz M, Toraman ZA, Pirincci E (2022). Clinical Characteristics of COVID-19 in Active or Previously Treated Tuberculosis Patients in Turkey. *Medical Bulletin of Haseki/Haseki Tip Bulteni* 60(5):453-460.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet* 395(10224):565-574.
- Luke E, Swafford K, Shirazi G, Venketaraman V (2022). TB and COVID-19: An Exploration of the Characteristics and Resulting Complications of Co-infection. *Frontiers in bioscience (Scholar edition)* 14(1):6.
- MacLean EL, Villa-Castillo L, Ruhwald M, Ugarte-Gil C, Pai M (2022). Integrated testing for TB and COVID-19. *Med* 3(3):162-166.
- Mao R, Qiu Y, HE J-S, Tan J'Y, Li XH, Liang J, Shen J, Zhu LR, Chen Y, Iacucci M, Ng SC, Ghosh S, Chen MH (2020). Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterology and Hepatology* 5:667-668.
- Mahieu R (2020). Vincent Dubée. Caractéristiques cliniques et épidémiologiques de la Covid-19. *Actualités Pharmaceutiques* 59(599):24-26.
- Patel N, Kaur M, Aggarwal R, Ganesh V, Ayub A, Kumar R, Kodan P, Singh Y, Soni KD, Trikha A. (2023). Clinical characteristics, course and outcome of critically ill COVID-19 patients with previous or current TB admitted in ICU of a tertiary care COVID centre of Indian subcontinent. *Lung India* 40(1):91-93.
- Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu T, Jiang YZ, Xiong Y, Li YJ, Li XW, Li H (2020). Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chinese Medical Journal* 133(09):1015-1024.
- Ruhwald M, Hannay E, Sarin S, Kao K, Sen R, Chadha S (2022). Considerations for simultaneous testing of COVID-19 and tuberculosis in high-burden countries. *The Lancet Global Health* 10(4):e465-e466.
- Sarinoğlu RC, Sili U, Eryuksel E, Yildizeli SO, Cimsit C, Yagci AK (2020). Tuberculosis and COVID-19: An overlapping situation during pandemic. *The Journal of Infection in Developing Countries* 14(7):721-725.
- Shah T, Shah Z, Yasmeen N, Baloch Z, Xia X (2022). Pathogenesis of SARS-CoV-2 and Mycobacterium tuberculosis coinfection. *Frontiers in Immunology* 13:909011.
- Sy KTL, Haw NJL, Uy J (2020). Previous and active tuberculosis increases risk of death and prolongs recovery in patients with COVID-19. *Infectious Diseases* 52(12):902-907.
- World Health Organization (WHO) (2021). *Maladie à coronavirus 2019 (COVID-19): How does COVID-19 spread between people?*. Disponible sur <https://www.who.int/fr/>
- World Health Organization (WHO) (2022). *Tuberculosis deaths and disease increase during the COVID-19 pandemic. Global tuberculosis report 2022*. Geneva: Licence: CC BY-NC-SA 3.0 IGO.
- World Health Organization (WHO) (2023). *Bulletin on outbreaks and other emergencies - week 10: 27 February to 5 March 2023 [Consulté le 7 mai, 2023]* », *Health Emergency Information and Risk Assessment* P 23.
- Yang J, Zhenga Y, Goua X, Pua K, Chena Z, Guoa Q, Jia R, Wang H, Wang Y, Zhou Y (2020). Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *International Journal of Infectious Diseases* 94:91-95.