

**Determinants of antibiotic use in SARS-CoV-2 positive patients during the COVID-19 pandemic. A retrospective cohort study conducted in an Epidemic Treatment Center in Dakar (ETC)**

**Abstract**

**Introduction**

COVID-19, like most viral respiratory diseases, can be associated with bacterial infections requiring antibiotic prescription. However, the prescription of antibiotics must be based on clinical and biological arguments, with clear recommendations. The aim of this study was to identify the factors associated with antibiotic prescription in patients hospitalized for COVID-19.

**Methodology**

This was a retrospective cohort study including patients hospitalized for COVID-19 at the Epidemic Treatment Center of Fann Hospital from July 31, 2021 to March 31, 2022. Data were collected using a form and entered using Excel software. Analysis was performed using R software version 4.2.2. Factors associated with antibiotic prescribing were investigated using logistic regression.

**Results**

A total of 248 patients were included. The median age was 65 years [53, 73], with a male predominance (sex ratio M/F 2.25). Comorbidities were mainly hypertension (35.88%), cardiovascular disease (23.38%) and diabetes (21.77%). The main clinical signs were cough (60.17%), fever (40.41%) and dyspnea (22.56%). On imaging, a ground-glass appearance was found in the majority of cases (84.52%), with severe lung involvement in 31.25%. Almost all patients were treated with anticoagulation (96%) and corticosteroids (95%). **Azithromycin** was the most prescribed antibiotic (56.38%), and 77% of patients were on oxygen. Case fatality was 21%.

In bivariate analysis, antibiotic prescription was associated with heart disease (81.25% vs. 47.83%,  $p=0.01$ ), smoking (81.82% vs. 48.51%,  $p=0.03$ ), signs of lung consolidation (55, 43% vs 34.43%,  $p=0.004$ ), oxygen therapy (55.97% vs 36.84%,  $p=0.03$ ) and the existence of a complication (62.24% vs 41.73%,  $p=0.002$ ). In multivariate analysis, only smoking (OR: 5.78 [1.30-42]), fever (OR: 1.82 [1.04-3.24]) and signs of lung consolidation (OR: 2.52 [1.30-5.05]) were associated with antibiotic prescription.

## **Conclusion**

In patients infected with COVID-19, antibiotic prescription is indicated in those with clinically or biologically documented bacterial infection.

**Key words:** Antibiotics, Covid-19, ETC, Fann

## **Introduction**

The year 2020 was profoundly shaped by the COVID-19 pandemic, initially detected in China in December 2019 (1). Globally, the number of confirmed cases reached around 776 million, with over 7 million deaths recorded (2). In West Africa, Senegal had recorded 88,998 confirmed cases of COVID-19, including 1,971 deaths, underlining the significant impact of the pandemic in the region (3).

Although COVID-19 is primarily a viral infection, the fear of superimposed bacterial infections, particularly in severe cases, has often led to widespread prescription of antibiotics. Indeed, around 50-70% of patients hospitalized for COVID-19 received antibiotic therapy despite a low proportion of confirmed cases of secondary bacterial infections, raising concerns about the overuse of antibiotics in this context (4,5).

Superimposed bacterial infections in respiratory viral infections, are well documented for influenza, however they are relatively rare in COVID-19 patients. Studies show that only 3% to 8% of patients with covid-19 develop such co-infections (4,6). In this context, antibiotic prescription should be guided by precise clinical and biological criteria, in line with international recommendations aimed at avoiding antibiotic overuse and the selection of bacterial resistance (7). Despite this, significant disparities persist in the implementation of recommendations for antibiotic use in COVID-19 patients, influenced by clinical, logistical and socio-cultural factors. Understanding the prevalence and determinants of antibiotic use during the COVID-19 pandemic is essential for adapting practices and preserving antibiotic efficacy in the face of growing resistance risk. Our study aims to describe the sociodemographic, clinical and paraclinical aspects of Covid-19 and identify factors associated with antibiotic prescribing in hospitalized patients.

## **Methodology**

### ***Type of study***

This retrospective cohort study was conducted in patients hospitalized for COVID-19 at the Epidemic Treatment Center of Fann Hospital, Dakar, Senegal, from July 31, 2021 to March 31, 2022.

### ***Study population***

Patients included in this study were all adults admitted for confirmed SARS-CoV2 infection (PCR or positive antigenic test). Inclusion criteria included age over 18 years, hospitalization of at least 24 hours, and availability of complete medical records. Patients with incomplete data or hospital stays of less than 24 hours were excluded from the analysis.

### ***Data collection***

Data were collected retrospectively from hospitalized patients' medical records. A structured questionnaire was designed to collect sociodemographic (age, sex), clinical (severity of COVID-19 infection, comorbidities, clinical signs), laboratory (results of relevant biological tests) and therapeutic information (antibiotic prescription, duration and type of treatment).

### ***Data analysis***

Data were entered using Epi Data 3.1 and analyzed using R version 4.4.0. Categorical variables were described in terms of relative and absolute frequencies. Quantitative variables were presented as means  $\pm$  standard deviation or median with interquartile range (IQR), depending on the type of distribution. Factors associated with antibiotics prescription were initially determined in bivariate analysis, using the Chi-square test or Fisher's exact test for comparison of proportions and the Wilcoxon test for comparison of means. Variables with  $p$ -value  $< 0.20$  were then entered into the logistic regression model for multivariate analysis. In the event of collinearity between two variables, one was excluded from the model. Variables included in the final model were selected using a bottom-up stepwise method based on the AKAIKE information criterion (AIC). The association between explanatory variables and outcome (death) was expressed using adjusted Odds ratios (OR), framed by their 95% confidence intervals. A  $p < 0.05$  was considered significant.

### ***Analysis of factors associated with antibiotic prescribing***

To identify factors associated with antibiotic prescribing, a binary logistic regression was performed. The dependent variable was antibiotic prescription (yes/no). The

independent variables included relevant sociodemographic, clinical and biological characteristics, as well as variables specific to the hospital stay (length of hospitalization, presence of complications). Logistic regression results were expressed as odds ratios (OR) with their 95% confidence intervals (95% CI), and a statistical significance threshold of  $p < 0.05$  was retained.

### ***Ethical considerations***

The study was conducted in compliance ethical principles and was approved by the hospital ethics committee. Patient anonymity and data confidentiality were strictly observed throughout data collection and analysis.

### **Results**

#### ***Epidemiological and clinical aspects***

A total of 248 patients were included. The median age was 65 years [IQR:53, 73], with the majority in the 60-80 age group (48%). The patients were predominantly male (55.65%), with sex ratio M/F 2.25.

The majority of our participants were married (78.02%) and mostly from central Dakar (57.53%) and its suburbs (23.29%). Nationalities other than Senegalese accounted for 5.02% of the participants. In the case histories, 23.3% of participants reported previous vaccination against covid-19 and 2.42% reported a history of tuberculosis. Comorbidities were predominantly arterial hypertension (35.88%), cardiovascular disease (23.38%) and diabetes (21.77%) (Table 1).

**Table 1:** Distribution of patients hospitalized for covid 19 at the ETC of Fann Hospital from July 31, 2021 to March 31, 2022 according to comorbidities found

<b>Variables</b>	<b>Number</b>	<b>Percentage</b>
Arterial Hypertension	89	35.88
Cardiopathy	57	22.98
Diabetes	54	21.77
Obesity	18	7.82
Asthma	7	2.82
Smoking	11	4.43
Immunosuppressive treatment	8	3.22
Chronic obstructive pulmonarydisease	2	0.81

The main clinical signs presented by the participants were cough (60.17%), fever (40.41%), chest pain (22.52%) and dyspnea (22.56%).

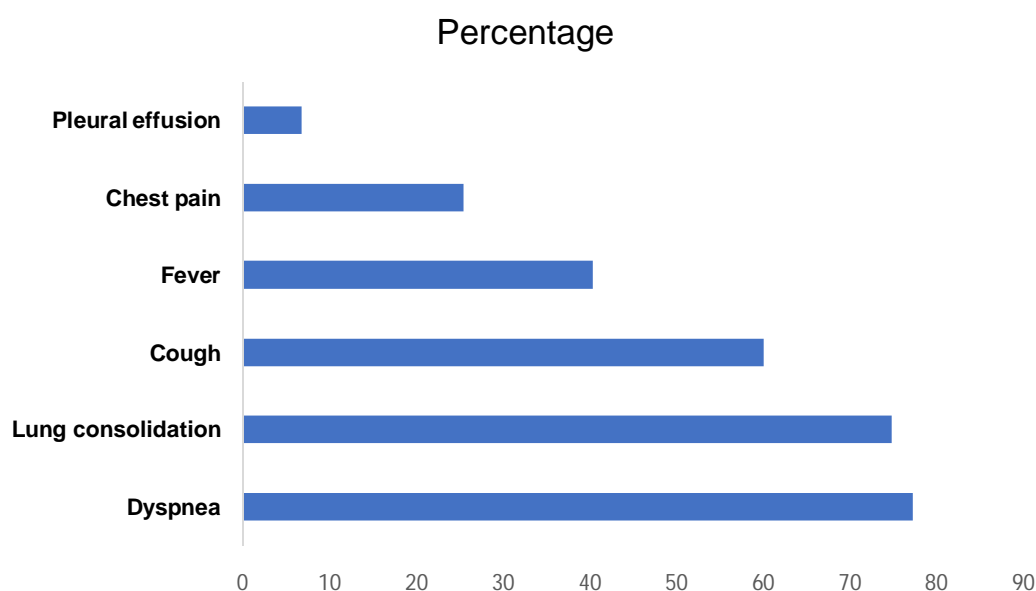


Figure 1: Distribution of patients hospitalized for COVID-19 at the ETC of Fann Hospital from July 31, 2021 to March 31, 2022 according to clinical presentation

#### ***Distribution according to biological and radiologic signs***

Leucocytosis was found in 44% of cases, with neutrophils predominating in only 35.61%. C-Reactive protein was elevated in 62.21% of cases, and Procalcitonin in 30 patients (14.08%). In our series, plasma D-Dimer levels were elevated in 40.20% of cases. On imaging, a ground-glass appearance was found in the majority of cases (**84.52%**), and lesions were bilateral in 73.17%. The extent of lesions was considered severe in 31.25% of cases and critical in 23.75%.

#### ***Distribution according to therapeutic and evolutionary aspects***

Almost all patients were on anticoagulation (96%) and corticosteroids (95%). Azithromycin (56.38%) and **ceftriaxone** (35.10%) were the most commonly prescribed antibiotics, and 77% of patients were on oxygen therapy, administered

with a high-concentration mask in 49.37%. Over time, 41.18% of patients developed complications. Pleuropulmonary complications accounted for the majority (31.91%), followed by electrolyte imbalances (12.50%) and metabolic disorders (4.98%). A total of 52 patients died, representing a case-fatality rate of 22.51%.

### **Factors associated with antibiotic therapy**

In bivariate analysis, antibiotic prescription was associated with heart disease (81.25% vs. 47.83%,  $p=0.01$ ), smoking (81.82% vs. 48.51%,  $p=0.03$ ), lung consolidation (55.43% vs 34.43%,  $p=0.004$ ), oxygen therapy (55.97% vs 36.84%,  $p=0.03$ ) and the existence of at least one complication (62.24% vs 41.73%,  $p=0.002$ , (Table 2)

**Table 2:** Factors associated with antibiotic prescribing in patients hospitalized for COVID-19 at ETC of Fann Hospital from July 31, 2021 to March 31, 2022 (Bivariate analysis).

<b>Variables</b>	<b>No antibiotics</b>	<b>With antibiotics</b>	<b>p-value</b>
<b>Obesity</b>			
- Yes	5 (27.78%)	13 (72.22%)	0.059
- No	107 (50.95%)	103 (49.05%)	
<b>Heart Disease</b>			
- Yes	3 (18.75%)	13 (81.25%)	<b>0.010</b>
- No	120 (52.17%)	110 (47.83%)	
<b>Smoking</b>			
- Yes	121 (51.49%)	114 (48.51%)	<b>0.031</b>
- No	2 (18.18%)	9 (81.82%)	
<b>Lung Consolidation</b>			
- Yes	40 (65.57%)	21 (34.43%)	<b>0.004</b>
- No	82 (44.57%)	102 (55.43%)	
<b>Complications</b>			
- Yes	81 (58.27%)	58 (41.73%)	<b>0.002</b>
- No	37 (37.76%)	61 (62.24%)	
<b>Oxygen therapy</b>			
- Yes	36 (63.16%)	21 (36.84%)	<b>0.034</b>
- No	87 (46.03%)	102 (53.97%)	

After multivariate analysis, only smoking (OR: 5.78; 95% CI [1.30-42]), fever (OR: 1.82; 95% CI [1.04-3.24]) and pulmonary condensation (OR: 2.52; 95% CI [1.30-5.05]) were associated with antibiotic prescription.

**Table 3:** Factors associated with antibiotic prescription in patients hospitalized for COVID-19 at ETC of Fann Hospital (Multivariate analysis).

Variables	OR-adjusted	95% CI	P-value
<b>Smoking</b>	<b>5.78</b>	1.30 – 42,0	<b>0.039</b>
<b>Comorbidity</b>	1.58	0.92 – 2.76	0.10
<b>Fever</b>	<b>1.82</b>	1.04 – 3.24	<b>0.039</b>
<b>Pleural effusion</b>	0.43	0.13 – 1.30	0.14
<b>Lung consolidation</b>	<b>2,52</b>	1,30 – 5,05	<b>0.007</b>
<b>Oxygen therapy</b>	1.76	0.88 – 3.58	0.11

### Discussion

We conducted a retrospective cohort study of patients with COVID-19 hospitalized at the Epidemic Traitement Center (ETC) of the Fann infectious and tropical diseases department, to determine the factors associated with antibiotic prescription in this population. The cohort was predominantly elderly, with a predominance of males. Smoking, fever and lung consolidation were the main determinants of antibiotic prescription.

COVID-19 is a common disease that can be severe in elderly subjects (8). The median age of patients in our study was 65 years, comparable to the ages of 63 and 61 years reported respectively in a large American study (9) and a large Italian study (10). The predominance of the male sex in our cohort (55.65%) was similar in a series of COVID-19 patients described by Diarra et al (54%) during the first wave of the pandemic in Senegal. However, percentage was lower than in some European studies (>60%), possibly due to gender differences in access to care (9-11). Furthermore, for socio-cultural reasons, in Africa, men with financial and decision-making power within the household are more likely to visit healthcare facilities and when they are ill, unlike women, who often wait for their husbands' decisions (12,13). Comorbidities identified were mainly hypertension (35.88%) and diabetes (21.7%). Similar results were reported in Kenya, with 33.1% and 27.3 respectively (14). However, these data were lower than those found by Richardson et al in the USA,

Hypertension (56.6%) and diabetes (33.8%), potentially due to epidemiological and socio-economic differences (9). The vaccine coverage rate of 23.3% was slightly higher than that recorded in Nigeria (15%) and far lower than the 70% rate found in Europe and America, possibly due to limited access and reluctance. Our results are similar to African trends, showing differences with developed countries and highlight the need for approaches adapted to the regional context to improve management and prevention of COVID-19 (15,16).

In the cohort as a whole, the most frequent symptoms were cough 60%, fever 44%, and shortness of breath 22%. These symptoms were described as the cardinal signs of COVID-19 and formed the basis of case definition during the pandemic. Among the radiological signs, a ground-glass appearance was found in the majority of cases (84.52%), with severe pulmonary involvement in 31.25%, similar to aspects described in the Algerian series (70%) (17). At the initial stage, ground-glass images predominated, progressing to a combination of ground-glass, reticular opacities and consolidation foci at an advanced stage (18).

Azithromycin (56.38%) and ceftriaxone (35.10%) were the most commonly prescribed antibiotics in our study, with antibiotic consumption well above the Brazilian cohort at 15.33% for azithromycin and 16.61% for cefalexin. However, the authors mentioned an overconsumption of antibiotics during the covid pandemic, potentially in response to early studies of the pandemic that suggested azithromycin as a treatment for COVID-19 (22,23). A systematic review showed that 71.8% of patients received an antibiotic at some point during admission, while only 3.5% of patients were diagnosed with a community-acquired bacterial infection and 14.3% had a hospital-acquired bacterial infection (6).

Our study reveals that antibiotic prescription in patients hospitalized for COVID-19 is influenced by factors such as smoking, fever and lung consolidation. In Africa, several studies have highlighted the complexity of managing bacterial superinfections during the pandemic. A review of African guidelines by Adebisi et al. and a Nigerian study by Oladunni et al. revealed that antibiotic prescription in patients with COVID-19 was often empirical, based mainly on symptoms such as fever and dyspnea. Our results, showing a significant association between fever and antibiotic therapy, corroborate with this observation.

With regards smoking, our study concurs with the findings of a large meta-analysis which found that smoking patients had an increased risk of developing respiratory

complications requiring antibiotic therapy (19). These findings reinforce the hypothesis that smoking aggravates pulmonary involvement, making patients more likely to be placed on antibiotics for fear of bacterial superinfections (19,20).

The presence of lung consolidation has also been documented as a determinant of antibiotic prescribing by Stoichitoiu et al. (21) where chest imaging was used as a key criterion for the decision to prescribe antibiotics. Although our study revealed a similar trend, it is important to note that variability in the interpretation of imaging findings can influence prescribing, highlighting the need for standardized protocols. These results are in contrast with WHO recommendations, which state that antibiotic therapy should be reserved for cases of confirmed bacterial infection (7). However, observations made in several studies from resource-limited countries show that in settings where laboratory infrastructure is lacking, clinicians often have to rely on clinical and radiological signs to make diagnostic and therapeutic decisions (21).

## **Conclusion**

Antibiotic prescription is not uncommon in Covid-19 patients, but must be based on clear indications in patients with clinically or biologically documented bacterial infection. Our study has shown that the factors associated with antibiotic prescription were: smoking, the existence of fever and the presence of lung consolidation. It is crucial to strengthen diagnostic capabilities and improve adherence to international protocols to limit the excessive use of antibiotics and the risk of antibiotic resistance.

## **Disclaimer (Artificial intelligence)**

### **Option 1:**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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