

# “Secondary Microbial Infections in Covid-19 Patients”

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## Abstract

Secondary infections are known complication of viral respiratory infections, often leads to deterioration of the patient. Secondary infections are commonly seen in severe respiratory viral infections. Critically ill novel coronavirus disease 19 (COVID-19) patients need hospitalization which increases their risk of acquiring secondary infections. The practice of empiric antibiotics due to limited diagnostic capabilities of many hospitals has the potential to escalate an already worrisome antimicrobial resistance (AMR) situation. This study is undertaken to find out most effective antibiotic for empirical treatment. We aimed to define the impact of secondary microbial infections on the clinical course in COVID-19 patients.

A retrospective study was carried out for a period of one year at RMCH& RC, Kanpur, and U.P. India. The patients admitted in intensive care units (ICUs) and wards of the hospitals were undertaken.

In our study a total of 262 SARS CoV-2 positive patient's pulmonary culture were assessed. Out of 262 cases, 53 (20.2%) were culture positive. Prevalence of bacterial culture positive was 46 (86.8%) and fungal positive culture was 7 (13.2%). The most common bacterial isolate was *Klebsiella pneumoniae* 18 (39.1%) followed by *Acinetobacter baumannii* 12 (26.1%), *Pseudomonas aeruginosa* (17.4%), *Escherichia coli* 6 (13.0%), and *Staphylococcus aureus* 2 (4.4%). The overall mortality was high among culture positive patients. The antimicrobial susceptibility pattern in *K. pneumoniae* showed highest resistance against commonly used cephalosporins.

Predominance of Gram-negative bacteria (GNB) in COVID-19 patients coupled with high rates of resistance to higher generation antimicrobials is an alarming finding. A high rate of mortality in patients with secondary infections warns to improve the infection control practices and antimicrobial stewardship interventions, not only to save patient lives but also prevent drug-resistant, to which the current situation is very conducive.

**Keywords:** COVID-19, secondary infections, antimicrobial resistance.

## INTRODUCTION

Secondary microbial infections are a known complication of viral respiratory infections, often responsible for clinical deterioration of the patient, previously well-studied influenza pandemics and seasonal influenza, also shows secondary microbial infection is responsible [1,2] for increase morbidity and mortality [1,2]. Disruption of airway epithelium, its barrier function caused by SARS coronavirus 2 (SARS CoV-2) leads to immune-mediated damage, and impaired regulation of both the innate and adaptive immune responses results increases the colonization of various fungal and bacterial organisms [3,4].

COVID-19 has caused 119.2 million illnesses and 2.64 million deaths worldwide as of 14 March 2021 [5]. India had 11.35 million illnesses and 0.15 million fatalities as of March 14, 2021 [6]. Secondary microbial infections in COVID-19 hospitalized patient's shows similar consequences like in other viral pneumonias. Severely infected individuals are more likely to require prolonged hospitalization which increases risk of hospital-acquired infections.

Secondary microbial infection is due to impaired ability of the host to clear infection owing to release of specific cytokines like IL-6, IL-10, IL-17 and IL-23, reduced the function of dendritic cells, macrophages, NK cells, CD4+ and CD8+ T-cells, and also certain phagocyte-independent mechanisms by which virus infection may facilitate secondary bacterial infection [7,8].

Although many study shows highly variable, bacterial co-infection in patients with influenza has been reported to be as high as 20–30% and is associated with a greater severity of illness; greater use of health resources increases the risk of

mortality. The prevalence, incidence or the features of the bacterial infection in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is not well understood and has been raised as an important knowledge gap [9].

The secondary infections in COVID-19 patients are known for negative outcomes. As per recent studies, bacterial co-infection upon admission has been reported in 3.1 to 3.5% of COVID-19 patients, while secondary bacterial infections, following hospitalization, seen up to 15% [9-10]. Higher risk of mortality in COVID-19 patients with bacterial co-infection has been previously reported, and a number of other recommendations encourage empirical use of antibiotics in severely ill patients [11-12].

The prevalence and profile of secondary infections in COVID-19 is not studied well. Thus, this study was carried out with an objective to know the etiology and antimicrobial resistance profile of secondary microbial infections and subsequent clinical outcomes in hospitalized COVID-19 patients. The overarching aim is to use this evidence to guide the optimal antimicrobial use in COVID-19 patients.

## MATERIAL AND METHODS

A retrospective study was carried out in the Department of Microbiology and Medicine for a period of one year (December 2020 to December 2021) after obtaining ethical approval from ethical committee of Rama Medical College, Hospital & Research Centre, Kanpur, UP, India

Patients with COVID-19 infections admitted in intensive care units (ICUs) and wards were included in our study. The respiratory samples were taken into consideration. The samples were cultured on blood agar, chocolate agar and MacConkey agar and then incubated at 37°C for 24 to 48 hours under standard conditions. The biochemical tests for the identification of microbial species were performed accordingly. The antibiotic susceptibility test was performed according to Clinical Laboratory Standard Institute (CLSI) guideline [16]. Patients with confirmed or clinically defined cases of SARS-CoV-2 infection with pneumonia were eligible for inclusion in the study. Patients with asthma and previous history of lung infection were excluded in the study.

## RESULTS

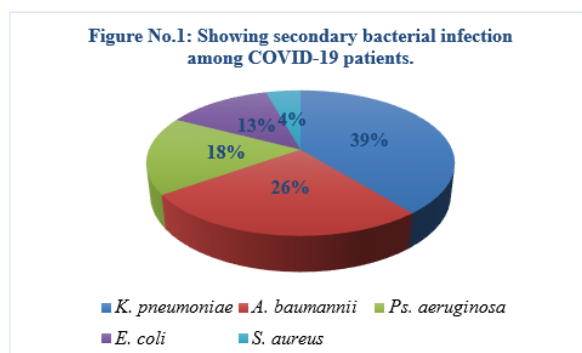
In our study a total of 262 SARS CoV-2 positive patient's culture were assessed. Out of 262 cases, 53 (20.2%) were culture positive. Males were more commonly infected compared to female i.e. 71.3% (187/262) was male and 28.7% (75/262) was female.

The respiratory samples were cultured to check the secondary microbial infection. Out of 262 patients, 53 (20.2%) cultures were positive, in which 46 (86.8%) were bacteria and 7 (13.2%) were fungus.

According to culture results, the commonest co-pathogens identified were mainly Gram-negative bacteria (GNB). The most common bacterial isolate in our study was *Klebsiella pneumoniae* 18(39.1%) followed by *Acinetobacter baumannii* 12(26.1%), *Pseudomonas aeruginosa* 8(17.4%), *Escherichia coli* 6(13.0%) and *Staphylococcus aureus* 2(4.4%). (Table No.1) It was also noted that the Gram-negative bacteria were more in number as compared to the Gram-positive bacteria (GPC).

Bacterial isolates (n=46)	No. of Isolates	Percentage
<i>K. pneumoniae</i>	18	39.1%
<i>A. baumannii</i>	12	26.1%
<i>Ps. aeruginosa</i>	8	17.4%
<i>E. coli</i>	6	13.0%
<i>S. aureus</i>	2	4.4%
<b>Total</b>	<b>46</b>	<b>100%</b>

**Table-1:** Showing secondary bacterial infection among COVID-19 patients.



Approximately the median length of hospital stay and the median duration of ICU stay were 22 and 17 days, respectively. The overall mortality of the total population in both ICU and ward was 16 (6.1%). The mortality was observed more in ICU patients i.e., 11 (4.2%). Mortality among COVID-19 patients who acquired secondary microbial infections was 34.5% (13/53), whereas it was 1.4% (3/209) among patients without secondary infection.

In our study we observed that there was a significantly higher rate of mortality among patients with secondary microbial infection compared to those without any secondary infection.

The antimicrobial susceptibility pattern was also observed in which the highest drug resistance was seen in *K. pneumoniae* isolates followed by *A. baumannii*, *Ps. aeruginosa*, and *Escherichia coli* isolates. *K. pneumoniae* showed highest resistance 88.9% (16/18) against piperacillin/tazobactam (PTZ) followed by ceftazidime (CAZ) 83.33% (15/18), cefepime (CPM) 83.33% (15/18), gentamicin (GEN) 66.67% (12/18), ciprofloxacin (CIP) 55.55% (10/18), and Imipenem (IMP) 5.55% (1/18).

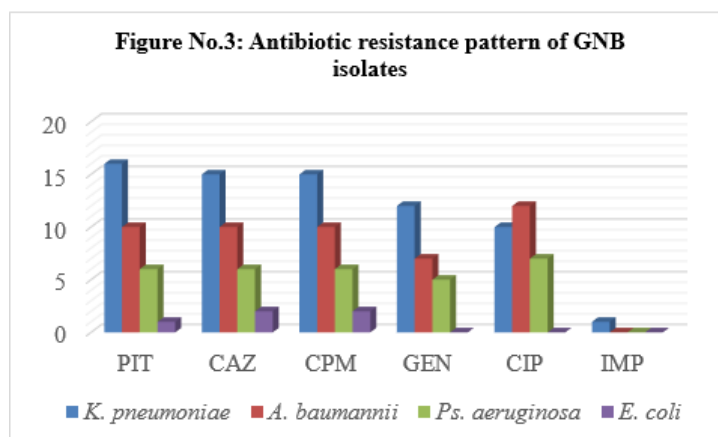
*A. baumannii* was the second most common isolate showed 100% resistance against CIP followed by PTZ, CAZ, CPM i.e. 83.33% (10/12) and GEN 58.33% (7/12). *A. baumannii* was 100% sensitive to IMP.

Similarly, *Ps. Aeruginosa* showed highest resistance against PTZ, CAZ and CPM 75% (6/8) followed by GEN, CIP *Ps. aeruginosa* was 100% sensitive to IMP.

*E. coli* was 100% sensitive to GEN, CIP and IMP. *E. coli* showed 33.33% (2/6) against CAZ and CPM whereas 16.67% (1/6) resistance against PIT.

Bacteria	Number of isolates	PIT	CAZ	CPM	GEN	CIP	IMP
<i>K. pneumoniae</i>	18	16	15	15	12	10	1
<i>A. baumannii</i>	12	10	10	10	7	12	0
<i>Ps. aeruginosa</i>	8	6	6	6	5	7	0
<i>E. coli</i>	6	1	2	2	0	0	0

**Table-3:** Showing antibiotic resistance pattern of GNB isolates.



## DISCUSSION

Thus, this study was carried out with an objective to know the etiology and antimicrobial resistance pattern of secondary microbial infections and subsequent clinical outcomes in hospitalized COVID-19 patients in a tertiary care centre, Kanpur.

In our study a total of 262 SARS CoV-2 positive patient's culture were assessed. Out of 262 cases, 53 (20.2%) were culture positive. Males were more commonly infected compared to female i.e., 71.3% (187/262) was male and 28.7% (75/262) was female, our findings were in agreement with study conducted by Sushma Yadav Boorgula et al (13) may be due to more outdoor activity by males.

Our results indicate a higher incidence of mortality in ICU compared to wards. The other article published by Ehsan Sharifipouret al(14) also shows similar findings may be due to increased equipment use and procedures like arterial line, central line, high work load/nurse ratio.

In a study conducted by Gurung K et al(15) shows 44 percent positivity of pathogen in which gram negative organism was predominant, in our study also shows similar findings like gram negative were predominant, fungal organism followed by gram positive bacteria.

The most common bacteria isolated in our study were *K. pneumonia* followed by *A. baumannii*, *Ps. aeruginosa*, *E.coli*. It was also noted that two Gram-positive bacterial isolates were *S.aureus*. The study conducted by Sharifipour et al., (14) in 2020 were also shows similar findings.

In addition, we observed 7 cases of fungal co-infections caused by *Candida* species. In a systematic review in 2020, Lansbury and colleagues have reported that the rate of fungal infections was low among COVID-19 patients, (Lansbury et al., 2020) [16].

In our study all the seven fungal isolates was caused by the *Candida* species. The study conducted by other researcher Vijay S. et al, shows that the *Candida auris* was responsible for the fungal culture positive cases [17].

Approximately the median length of hospital stay and the median duration of ICU stay was 22 and 17 days, Sharifipour et al. (2020) [14], also reported a length of stay of 15 days (2–39) of all patients with COVID-19 admitted to their ICU.

The percentages of resistance to other antimicrobial agents among *K. pneumoniae* were *K. pneumoniae* showed highest 88.9% (16/18) resistance against piperacillin/tazobactam (PTZ) followed by ceftazidime (CAZ) 83.33% (15/18), cefepime (CPM) 83.33% (15/18), gentamicin (GEN) 66.67% (12/18), ciprofloxacin (CIP) 55.55% (10/18), and Imipenem (IMP) 5.55% (1/18).

*A. baumannii* was the second most common isolate showed 100% resistance against CIP followed by PTZ, CAZ, CPM i.e. 83.33% (10/12) and GEN 58.33% (7/12). *A. baumannii* was, 100% sensitive to IMP. *S. aureus* was resistant to most of the antibiotics except vancomycin and tecoplanin.

The frequent prescription of broad-spectrum empirical antimicrobials in COVID-19 patients could increase antibiotic resistance in the near future. Therefore, strict programs of antimicrobial stewardship required to improve prudent antibacterial use.

## CONCLUSION:

In conclusion, the predominance of Gram-negative pathogens in COVID-19 patients coupled with high rates of resistance to higher generation antimicrobials is an alarming finding. The secondary infection among patients admitted to the ICU and wards was a serious problem in the COVID-19 pandemic, which can lead to increase in morbidity and mortality. Hence, there is a need to reinforce the principles of antimicrobial susceptibility pattern and infection control interventions not only to save patient's life but also to prevent drug-resistant infections to which the current situation is very conducive.

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**Consent to participate:** Consent from participants was taken to participate in the study.

**Availability of data and material:** The entire data and materials were self-generated.

**Author's Contribution:** All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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