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Microbiological blood profile among COVID-19 patients hospitalized in a tertiary care hospital: An observational study

Mamta Meena[1], Priyanka Singh[2], Arvind Kumar Mittal[3], Deepti Chaurasia[4]

[1,2]Assistant Professor, [4]Professor, Department of Microbiology, [3]Assistant Professor, Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal, Madhya Pradesh, India

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ABSTRACT

Background: Bacterial coinfection contributes to increase morbidity and morbidity of viral respiratory infections and may lead to fatal outcome during its course of illness. **Aims and Objectives:** The main objective of this study was to determine the bacteriological profile of COVID-19 patients admitted in hospital, their antibiotic susceptibility, and their association with severity. **Materials and Methods:** The present study was retrospective observational cross-sectional study of all patients admitted for COVID-19 at Gandhi Medical College and Hamidia Hospital, Bhopal (MP) between (March 2020 and December 2020). Demographic, comorbid conditions, and microbiological data were compared HBD and intensive care unit (ICU) admissions and role secondary coinfection in severity and mortality. **Results:** Thirty percentages of percent of patients showed bacterial growth, *Staphylococcus aureus* was most common, followed by *Pseudomonas aeruginosa*. Mean ± SD of age was 43.6 ± 21.6. Antibiotic resistance of cefoxitin, cotrimoxazole, and azithromycin was seen in maximum Gram-positive growth, whereas sensitivity for linezolid and gentamicin was present in 10–16% cases. Highest antibiotic resistance in Gram-negative growth was seen for ceftozidime, amikacin, imipenem, and meropenem, whereas sensitivity of colistin antibiotic was highest in Gram-negative growth. **Conclusion:** Coinfection rates increase in patients admitted to the ICU, despite frequent prescription of broad-spectrum antibiotics. Infectious diseases practitioners carry the burden of life-saving and provide for societal trust that is effective antibiotic therapy in the face of these changes. With a growing body of evidence supporting short-course, antimicrobial therapy "Shorter Is Better" should be the new mantra.

Key words: Super infection; Coinfection; COVID-19; Antibiotic resistance

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the Novel corona virus originating from Wuhan, China, responsible for the illness named coronavirus disease 2019 (COVID-19) that has rapidly spread worldwide.[1] COVID-19 has a significant morbidity and mortality rate, and due to bacterial super infections, its complications and lethality have grown.[2]

In critically sick patients with COVID-19, Chinese and American reports reveal a dismal prognosis with a high mortality rate, particularly in those requiring invasive mechanical ventilation. Due to the severity of these critically ill patients at the outset, as well as the difficulty of excluding a bacterial coinfection based on clinical, biological, or radiological findings, more than 90% of critically ill patients with severe SARS-CoV-2 pneumonia received empiric antibiotic therapy on intensive care unit (ICU) admission.[1]

A similar coinfection has been reported in COVID-19 patients, as it has been seen in other respiratory disorders such as influenza, where roughly 25% of older patients get secondary coinfections.[3] However, information on the impact of fungal coinfection and accompanying

Address for Correspondence:
Dr. Priyanka Singh, Assistant Professor, Department of Microbiology, Gandhi Medical College and Associated Hamidia Hospital, Bhopal - 462 001, Madhya Pradesh, India. **Mobile:** +91-9424723491. **E-mail:** priyankasingh27031982@gmail.com

clinical outcomes is scarce. The empirical usage of antibiotics for the majority of COVID-19 patients has been documented in a number of studies.[3] However, there is evidence that inflammatory serological markers such as increased procalcitonin and C-reactive protein, which are generally linked with bacterial infection, may develop in COVID-19 patients who do not have a bacterial coinfection. As a result, there is a clinical need for a thorough examination into the function of coinfection in COVID-19 patients.[4]

However, evidence on the prevalence of bacterial coinfections in critically sick patients with severe SARS-CoV-2 pneumonia is sparse, and the microorganisms responsible for these bacterial coinfections are unclear. In patients with severe SARS-CoV-2 pneumonia requiring ICU hospitalization, there are few data on viral coinfections, particularly influenza coinfections.

We aimed to determine the prevalence of bacterial super infection and bacteriological profile in adults with COVID-19, hospitalized in Hamidia hospital, and its distribution according to sociodemographic and other clinical conditions.

These findings are critical for identifying priority clinical groups, improving the treatment of concurrent COVID-19 infections in people who have been exposed to the risk factors in the population investigated, and identifying microorganisms of public health concern.

Aims and objectives

The aims of this study were as follows:

1. To identify the bacteriological profile of COVID patients admitted in HDU and ICU and to assess the antibiotic susceptibility
2. To find association of bacteriological invasion with comorbidities and severity of COVID-19.

MATERIALS AND METHODS

This retrospective observational cross-sectional study was conducted on inpatient department patients of General Medicine Department of Gandhi Medical College and Hamidia Hospital, Bhopal, MP from March 2020 to December 2020. The study was approved by the Institutional Ethical Committee 20498/MC/IEC/2021 date-July 19, 2021.

Sample size was calculated based on prevalence of one of the reference study which was 49.6% which came out to be n=99.4 rounding it to 100. All COVID-19 confirmed cases (by any of the laboratory methods) admitted in Hamidia Hospital. We exclude all COVID-19 confirmed cases dying before blood sample collection and in adequate/leakage samples received against COVID guidelines/protocol. Blood samples were collected as per COVID – protocol from medicine department (COVID and ICU ward) and sent to microbiology department for their culture and drug susceptibility.

The blood culture incubation was reduced from 7 day to 5 day. Moreover, culture after or at 6 day considers possible contamination. In subsets of patients for whom data were collected, the interval was taken from time of blood culture collection to time of Gram stain was performed which is used to calculate time to blood culture positivity during our study period.

For the purposes of classifying blood cultures by SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) status, we used the following parameter. (i) Blood cultures were labeled positive if they were performed within 2 days of a positive SARS-CoV-2 RT-PCR result and considered positive for all subsequent blood cultures after a positive SARS-CoV-2 – RT-PCR result. (ii) Blood cultures were labeled negative if they were performed within 2 days of a positive SARS-CoV-2 RT-PCR result and considered negative for all subsequent blood cultures unless the patient had a subsequent positive SARS-CoV-2 – RT-PCR result, at which point, the status was changed to positive for any blood cultures performed within 2 days of the positive SARS-CoV-2 RT-PCR result.

All other blood cultures were labeled SARS-CoV status not tested. The 2-day interval was used to account for turnaround time from test ordering to SARS-CoV-2 test. Results as blood culture and SARS-CoV-2 RT-PCR tests ordered on the same day may have taken up to 2 days for the SARS-CoV-2 RT-PCR result to become available.

The main outcome of interest was the overall proportion of confirmed acute bacterial infections in patients with COVID-19 stratified by coinfection on initial presentation and secondary infection during the course of the illness.

Statistic analysis

Data were entered in Microsoft Excel and analysis was done with Epi-info 7 software. Frequency and percentage were calculated to describe the proportion of different types of Gram-positive and Gram-negative bacteria. Chi-square test was applied to see the association between comorbidity in patients and bacterial growth in their samples; $P<0.05$ was taken as statistical significant.

RESULTS

Majority patients did not show any growth, that is, 70%, whereas 30% of the patients showed bacterial growth. Among these 30% patients, *Staphylococcus aureus* was seen in 9% of patients, followed by *Pseudomonas aeruginosa* in 7% of patients and least proportion showed Cons (1%) and *Klebsiella oxytoca* (1%) (Table 1).

Among the Gram-positive bacteria, cefoxitin and cotrimoxazole resistance was seen in 14%, penicillin resistance was seen in 13%, azithromycin resistance was seen in 12%, and ciprofloxacin in 8%. Other drug resistance seen was clindamycin in 4%, doxycycline in 6%, gentamicin in 6%, teicoplanin in 3%, and vancomycin in 1%. Sixteen percentages were sensitive to linezolid and 10% were sensitive to gentamicin (Table 2).

Among the Gram-negative bacteria, highest resistance was seen of ceftozidime, that is, in 10%, amikacin in 9%, imipenem and meropenem in 9%, gentamicin in 6%, amoxyclav in 4%, ciprofloxacin in 3%, cefoperazone sulbactum, and levofloxacin in 2%. Maximum Gram-negative growth was sensitive to colistin, that is, 12% followed by levofloxacin, that is, in 8% (Table 3). Out of 60 patients that had pre-existing comorbidity 15 (25%) showed positive cultures and out of 40 patients who did not have any comorbidity 15 (37.5%) showed positive bacterial growth (Table 4).

Out of 64 patients that were discharged 24 (37.4%) had positive bacterial growth and out of 31 patients who died 6 (19.3%) showed bacterial coinfection (Table 5).

Table 1: Proportional distribution according to bacterial growth seen on culture

Organism	Percentage
No growth	70.0
Klebsiella pneumoniae	2.0
Acinetobacter	2.0
Citrobacter	2.0
Enterococcus species	2.0
Klebsiella oxytoca	1.0
MRSA *Staphylococcus aureus*	2.0
Pseudomonas aeruginosa	7.0
Staphylococcus aureus	9.0
Staphylococcus spp	2.0
Cons	1.0
Total	100.0

Table 2: Drug sensitivity among the gram positive bacteria

Drug	Sensitive (%)	Resistance (%)
Azithromycin	4	12
Cefoxitin	2	14
Ciprofloxocin	3	8
Clindamycin	2	4
Doxycycline	9	6
Gentamicin	10	6
Linezolid	16	0
Penicilin	2	13
Teicoplanin	2	3
Cotrimoxazole	2	14
Vancomycin	2	1

DISCUSSION

In this observational of 100 patients admitted to Hamidia hospital with COVID-19, coinfection identified was secondary. *S. aureus* was the most frequently recovered pathogens from respiratory and blood cultures.

Maximum proportion of patients belonged to age group of 61–70 years, mean±SD of age was 43.6±21.6.

About 30% of the patients showed bacterial growth of which *S. aureus* was most common, followed by *P. aeruginosa*, and least obtained were Cons and *K. oxytoca*. Among the Gram-positive bacteria, cefoxitin resistance was most common followed by penicilin, cotrimoxazole, azithromycin, and

Table 3: Drug sensitivity among Gram negative bacteria

Drug	Sensitive (%)	Resistance (%)
Amikacin	5	9
Amoxyclav	6	4
Ceftozidime	0	10
Cefoperazone-sulbactum	3	2
Imipenem	5	7
Ciprofloxacin	3	3
Levofloxacin	8	2
Colistin	12	0
Gentamicin	5	6
Meropenem	2	9

Table 4: Association between bacterial growth and comorbidity

Comorbidity	Growth		Total
	Absent	Present	
Absent	25	15	40
Present	45	15	60
Total	70	30	100

Table 5: Association between bacterial growth and outcome

Outcome	Growth		Total
	Absent	Present	
Discharge	40	24	64
Death	25	6	31
LAMA	5	0	5
Total	70	30	100

ciprofloxocin. Among the Gram-negative bacteria, highest resistance was seen for ceftozidime, followed by amikacin, imipenem, meropenem, and gentamicin. About 27% had comorbidities such as hypertension, DM-II, and COPD. Mean±SD duration of hospitalization was 1.5±0.57.

Our results show that there is currently insufficient evidence to support widespread empirical use of antibiotics in most hospitalized patients, as the overall proportion of bacterial infections in patients with COVID-19 was low.

Similar results were observed by Kariyawasam et al.,[5] 2022 in meta-analysis of 1331 articles identified, a total of 1959 unique isolates were identified with 29% (569) resistant organisms identified. Coinfection with resistant bacterial or fungal organisms ranged from 0.2% to 100% among included studies. Pooled prevalence of coinfection with resistant bacterial and fungal organisms was 24% (95% CI 8–40%; n=25 studies: I2=99%) and 0.3% (95% CI 0.1–0.6%; n=8 studies: I2=78%), respectively. Among multi-drug resistant organisms, methicillin-resistant *S. aureus*, Carbapenem-resistant *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *P. aeruginosa,* and multi-drug resistant *Candida auris* were most commonly reported.

Lensbury et al[6] in their systemic review and meta –analysis approx thirty studies included 3834 patients. Overall, 7% of hospitalized COVID-19 patients had a bacterial coinfection (95% CI 3–12%, n=2183, I2=92·2%). A higher proportion of ICU patients had bacterial coinfections than patients in mixed ward/ICU settings (14%, 95% CI 5–26, I2=74·7% vs. 4%, 95% CI 1–9, I2=91·7%). The most common bacteria were *Mycoplasma pneumonia*, *P. aeruginosa,* and *Haemophilus influenzae*.

Rawson et al.,[7] 2020 in his review study of nine studies, observed reporting bacterial coinfection in COVID-19 cases, 62/806 (8%) cases of bacterial/fungal coinfection were reported. The use of broad-spectrum antimicrobial therapy was widely reported with 72% of COVID-19 cases receiving antibacterial therapy.

Our study has few limitations. First, the retrospective mono-center design with inherently associated bias may limit its generalizability to other centers with a different bacterial ecology. Second, the study done was too early in the 1st wave of pandemic; hence, a complete picture could not be obtained and potentially underestimated the real rate of bacterial coinfection and anti-microbial resistance. Third, we did not consider bacterial count which could have helped to distinguish between an infection and respiratory tract colonization.

Further larger studies are needed to assess the real prevalence and the predictors of coinfection together with its prognostic impact on critically ill patients with severe SARS-CoV-2 pneumonia.

Limitations of the study

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CONCLUSION

The practice of medicine is constantly evolving as the results of new research become available, and as secular trends change over time (e.g., fluctuations in antibiotic resistance and new antibiotic development). Coinfection rates increase in patients admitted to the ICU, despite frequent prescription of broad-spectrum antibiotics. Infectious diseases practitioners carry the burden of life-saving and provide for societal trust that is effective antibiotic therapy in the face of these changes. Antimicrobial stewardship principles should be re-considered to avoid development and transmission of drug resistant organisms in health-care facilities.

Judicious use of antimicrobials will be vital to ensure access to therapy by those with confirmed bacterial infection. With a growing body of evidence supporting short-course, antimicrobial therapy "Shorter Is Better" should be the new mantra.

When antimicrobials are required, the choice of antimicrobial should be tailored to likely pathogens and local resistance patterns, with treatment duration limited to 5 days if lower respiratory tract infection is suspected.

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Authors' Contributions:
MM- Concept and design of study, prepared first draft of manuscript; **PS-** Interpreted the result, reviewed the literature and manuscript preparation; and **AKM-** Concept coordination, statistical analysis and interpretation, preparation of manuscript, and revision of manuscript; **DC-** Permission for study.

Work attributed to:
Gandhi Medical College and Associated Hamidia Hospital Bhopal - 462 001, Madhya Pradesh, India.

ORCID ID:
Dr. Mamta Meena - https://orcid.org/0000-0001-8189-7945
Dr. Priyanka Singh - https://orcid.org/0000-0003-2376-5148
Dr. Arvind Kumar Mittal - https://orcid.org/0000-0001-6879-3850
Dr. Deepti Chaurasia - https://orcid.org/0000-0001-5780-5254

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