Original Article

Dissemination of Carbapenem-Resistant Bacteria During the COVID-19 Pandemic in A Tertiary Hospital in Northern India

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Abstract

Background: Carbapenemase-producing Enterobacteriaceae (CRE), carbapenem-resistant Pseudomonas aeruginosa (CRPA) and Acinetobacter baumannii (CRAB) have spread rapidly in the recent years. ***Objective:*** To look for the impact of COVID-19 pandemic on carbapenem-resistance. ***Methods:*** This retrospective, cross-sectional study was done, from March 2018 to April 2022, on an adult population of ICU patients who were found resistant to carbapenem group drugs in tracheal culture. ***Results:*** During the COVID-19 pandemic CRE, CRPA and CRAB infections were found significantly increased. ***Conclusion:*** Our results suggested the need to focus on CRE, CRPA and CRAB infections post-COVID-19. We explore how COVID-19 pandemic affects health-care systems by amplifying AMR. Further studies are needed to understand the epidemiology and molecular profile of CRE, CRPA and CRAB associated infections post COVID-19. Screening is necessary when a patient has been in a hospital where carbapenem-resistant microorganisms are common, and every institution should have a specific policy in place for the management of organisms that are resistant to carbapenem that is periodically reviewed.

Keywords: Antibiotics, carbapenem, drug resistance, COVID-19 pandemic, intensive care units

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Introduction

Antimicrobial resistance (AMR) is a comprehensive health menace which has caused approximately five million mortalities in the year 2019 alone, with the highest burden in low and middle-income countries.[1] The increasing number of multidrug-resistant (MDR) bacteria is a severe problem and a challenge for the entire medical community, particularly in intensive care units (ICUs).[2,3] In 2017, the World Health Organization (WHO) published a list of "priority pathogens" which exhibit high antibiotic resistance. The list included carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Pseudomonas aeruginosa (CRPA), and carbapenem-resistant Enterobacteriaceae (CRE) at the highest priority.[4]

Carbapenem is an important antibiotic class offering the largest spectrum activity, effective against both Gram-negative and Gram-positive bacteria. They were used as "drugs of last resort" in the treatment of Gram-negative bacterial infections. CRAB is responsible for various nosocomial infections e.g., hospital acquired pneumonia, urinary tract infections and blood stream infections and is associated with high mortality rates and treatment failures.[5-7] CRAB is responsible for AMR outbreaks in critical care settings which are difficult to contain. The CRE are another group of gram-negative bacteria that are resistant to a variety of antibiotics, including carbapenem. The infections are difficult to treat and are associated with high mortality, morbidity, and healthcare expenses.

The arrival of a novel coronavirus (SARS-CoV-2) and the resulting pandemic has been the greatest threat to overall wellbeing in this century. The pandemic has posed significant challenges and

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necessitated major adjustments in the healthcare system along with overburdening healthcare worldwide.

A simultaneous rise in multidrug resistant infection because of inappropriate empirical antibiotic therapy in these patients is a cause of concern. However, there is still a significant knowledge gap regarding the impact of COVID-19 on antimicrobial resistance, especially in Indian context. We therefore conducted retrospective cross-sectional research with adult population of intensive care units (ICUs) to evaluate the influence of COVID-19 pandemic on the incidence of CRAB, CRPA and CRE in a tertiary care hospital of northern India.

Methods

This retrospective, cross-sectional study was conducted from March 2018 to April 2022. This period was subdivided into two periods i.e., pre-COVID and post-COVID. In our study, March 2018 to March 2020 has been assigned as pre-COVID period while April 2020 to April 2022 as post-COVID. ICU patients who were resistant to carbapenem group antibiotics were identified from ICU surveillance unit records after university ethics committee approval Following that, all identified patients’ medical records were evaluated for data gathering.

Data were collected and recorded in the structured case record form. Statistical analyses were done using the SPSS version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Values were calculated and expressed by frequencies and percentages. Data were presented through graphs, pie charts and tables.

Results

Out of 389 total numbers of isolates, 119 Carbapenem resistant organisms were identified in the ICU settings during pre-COVID-19, while post-COVID-19, it was 169 out of 421 (Table1 & Figure 1). Post COVID-19, CRAB was predominant, followed by CRPA. E. coli, and Klebsiella pneumonia. Carbapenem-resistant Klebsiella oxytoca, Citrobacter species, Proteus vulgaris, Enterobacter cloacae, Providencia rettagiri, or Steno malto showed no significant change (Figure 2 & 3).

In our study, post COVID-19, Carbapenem resistance was increased by 9.64% in ICU setting. The highest increase was in CRAB (20.5%) followed by CRPA (18.44%). Carbapenem-resistant Escherichia coli and carbapenem-resistant Klebsiella pneumoniae was observed to rise by 10.7% and 6% respectively. Carbapenem-resistant Klebsiella oxytoca and carbapenem-resistant Citrobacter species does not show any significant change. Similarly, no significant effect of COVID-19 is observed in Proteus vulgaris, Enterobacter cloacae, Provdencia rettagiri and Steno malto. (Figure 4).

Table 1: Carbapenem-resistant pathogens in tracheal culture pre- and post-COVID-19

Pathogen	No. of carbapenem resistance (pre COVID-19)/Total no. of isolate	No. of carbapenem resistance (post COVID-19)/ Total no. of isolate
Escherichia coli	21/60	32/70
Klebsiella pneumoniae	33/75	42/84
Proteus vulgaris	3/30	4/40
Enterobacter cloacae	3/24	8/32
Klebsiella oxytoca	12/44	8/30
Citrobacter species	6/36	5/30
Pseudomonas aeruginosa	7/31	16/39
Acinetobacter baumaani	30/52	50/64
Provdencia rettagiri	2/18	2/15
Steno malto	2/19	2/17
Total	119/389	169/421

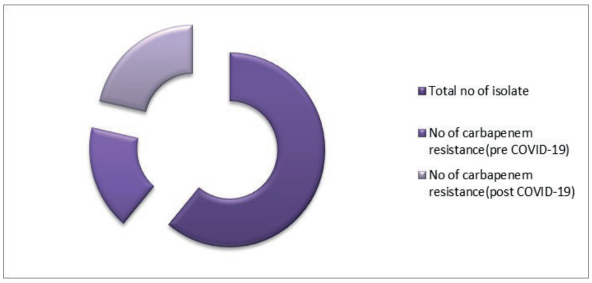

Figure 1: Carbapenem resistance in tracheal culture pre- and post-COVID-19

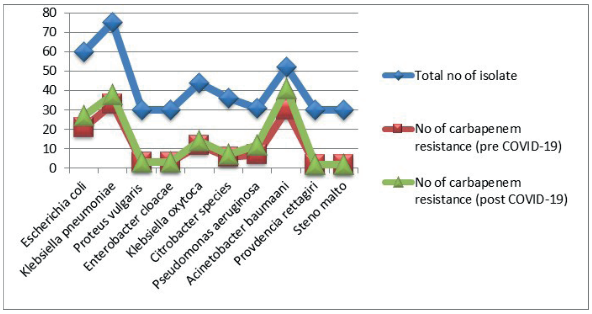

Figure 2: Carbapenem resistance bacteria in tracheal culture pre- and post-COVID-19

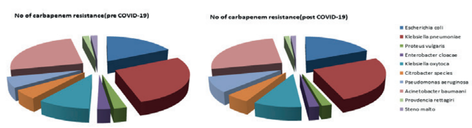

Figure 3: Carbapenem resistance isolates in tracheal culture pre and post COVID-19

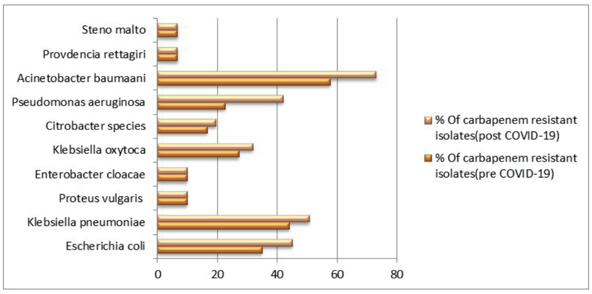

Figure 4: Percentage of carbapenem resistant isolates (pre- and post-COVID-19)

Discussion

Infections with gram negative bacteria are amongst the most common and problematic issues affecting the critically ill patients. Among the pathogens on the list of ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.), Enterobacteriaceae and Acinetobacter are the bacteria of major concern due to unique antibiotic resistance characteristics.

Antibiotics from the carbapenem group are usually used as drugs of last resort in the treatment of gram-negative bacterial infections, however the widespread use of carbapenems in hospital settings, particularly when infection control procedures are weak, has contributed to an increase in the prevalence of carbapenem-resistant Acinetobacter and carbapenem resistant Enterobacteriaceae.

In this study, we evaluated the incidence of CRAB, CRE and CRPA during the COVID-19 pandemic. A comparison was done with pre-COVID-19 era and we found that the incidence of carbapenem resistance increased by 9.64% in ICU setting during Covid 19 era. The highest incidence was in carbapenem resistant Acinetobacter baumanii (20.5%) followed by Pseudomonas aeruginosa (18.44%). A rise in the incidence of carbapenem resistant Enterobacteriaceae (E. coli by 10.7% & Klebsiella by 6%) was also noted.

The preparation to manage Covid 19 pandemic crisis began at our hospital, a tertiary care hospital by the 15th of March 2020. The hospital was declared as Level 2 COVID care hospital to deal with complicated and critical cases. We observed that conversion of our hospital to dedicated Level 2 COVID care centre resulted in an increase in the incidence of carbapenem resistant gram-negative bacteria. To the best of our knowledge this is the first study in India comparing the incidence of carbapenem resistant gram-negative bacteria during covid 19 pandemic with pre covid era.

As a result of the COVID-19 pandemic, Polly et al. found an increase in the incidence of CRAB and MRSA in both ICU and non-ICU settings in a hospital in Brazil.[8] As compared to the study by Polly et al. we extracted data only in ICU settings and an increased incidence was observed only in gram-negative organisms. Similarly, Perez et al. and Gottesman et al. reported outbreak of carbapenem-resistant Acinetobacter baumanii during the COVID-19 in their studies.[9,10] Gasperini et al. studied the impact of COVID-19 pandemic on multidrug resistant bacterial infections in geriatric patients. The authors reported that MDR bacteria in bloodstream increased significantly in post-COVID-19 period.[11] Those findings are similar to our study. Interestingly, in the abovementioned study, E. coli was the main organism isolated, while we observed an increased incidence of CRAB, CRE and CRP in tracheal cultures. Moreover, we analysed only a subset of hospital patients and this lacked generalisability in overall adult population.

Carbapenemase enzyme production is the main mechanism of resistance in Enterobacteriaceae, whereas in pseudomonas aeruginosa the main mechanism leading to resistance is mutational inactivation of oprD porin gene. Acinetobacter baumanii shows carbapenem resistance by three mechanism that includes carbapenemase enzyme production, porins membrane protein alteration and activation of drug efflux pump.[12-14]

The significance of an efficient infection control strategy was recognised in our institution and put into practise in accordance with the hospital infection control committee (HICC) guidelines of the institution. Consistent with this strategy we expected a decrease in the incidence of MDR bacterial infections, however in sharp contrast to our expectations we found an increase in the incidence of MDR pathogens. In fact, the COVID-19 pandemic acted as a catalyst to amplify AMR. There could have been several possible reasons for this increase in MDR bacteria.

Since SARS-COV-2 pneumonia was difficult to identify from other viral and bacterial pneumonia, broad spectrum antimicrobials like carbapenems were empirically and frequently administered.[15] Routine surveillance measures were suspended and emphasis on preventing transmission of covid 19 resulted in lapses in routine infection control measures. The COVID-19 emergency deprioritized planned activities and diverted human and financial resources that had been contributing to AMR surveillance and response activities, instead channelling them to the COVID-19 response.[16] Untrained staff from general wards were deployed in critical care areas which resulted in disruptions of infection prevention and control practices in an already overburdened health system. The COVID-19 pandemic emerged as a rare type of medical emergency. We lacked the necessary experience in our set up to handle such a circumstance. Initial practise policies and protocols were not established, and authorities continually modified them in response to the circumstance, which was dynamic and quickly changing.

There are several limitations of our study. The study being retrospective cross-sectional research, the temporal link between COVID-19 and antibiotic resistance could not be determined. The sample size was less, and the data included was from a single centre. Most of the patients were on empirical antibiotic therapy and in some cases a culture could have been negative despite the presence of an infection. We also did not define the in-hospital mortality rate in our study. Despite those limitations our study emphasizes that the COVID-19 related changes in antibiotic usage, infection control and health systems affect the development, spread and burden of AMR in hospitals.

Conclusion

To summarize, our data suggested that during the COVID-19 pandemic CRE, CRPA and CRAB infections were found significantly increased. We also recommend that further research from different institutions in India is needed to identify the epidemiology and molecular profile of carbapenem resistance infection during the COVID-19 era.

Conflict of interest: None declared by the authors.

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Ethical approval: The study was approved by the Institutional Ethical Committee of Jawaharlal Nehru Medical College Hospital, Aligarh, UP, India (IECJNMC/681).

Author's contribution: All authors were equally involved in conception, study design, data collection, statistical analysis, writing, editing, and final approval of the manuscript.

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