

The Impact of Infection Control Policies on Hospital Acquired Infections by MDROs from 2016 to 2023

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Purpose: Hospital-acquired infections (HAIs) caused by multidrug-resistant organisms (MDROs) pose a significant challenge to healthcare systems. The present study aimed to evaluate the impact of the infection policy to COVID-19 on the incidence of HAIs caused by MDROs.

Methods: We conducted an eight-years retrospective analysis at a hospital in Shanghai, China. Bloodstream, sputum, and urinary tract cultures of MDROs obtained 48h after admission were collected monthly from January 2016 to Dec 2023. Occupied bed days (OBDs) were used to generate monthly HAI incidences per 10,000 OBDs. The study period was divided into pre-control, in-control, and post-control cohorts, in January 2020 and January 2022. The incidence was compared using interrupted time-series regression.

Results: In total, 6763 MDRO cultures were identified, comprising 1058 bloodstream, 4581 sputum, and 1124 urine cultures derived from 4549 patients. The incidence rates of all HAIs were 8.68 per 10,000 OBDs in the pre-control cohort, 9.76 per 10,000 OBDs in the in-control cohort and 12.58 per 10,000 OBDs in the post-control cohorts, respectively. A downward trend in the incidence of HAI was observed in the post-control cohort ($p < 0.05$).

Conclusion: This study demonstrates that while the COVID-19 pandemic poses a significant challenge to infection control within hospitals, it provides a unique opportunity to enhance infection control measures and evaluate their effectiveness. In addition, these findings highlight the need for more targeted prevention and control strategies against different pathogens in future epidemics.

Keywords: hospital required infection, multidrug-resistant organism, infection control, policy, Covid-19, surveillance

Introduction

Hospital-acquired infections (HAIs), also known as nosocomial infections, are infections occurring in patients 48 h after admission or upon discharge. HAIs lead to adverse outcomes such as prolonged hospitalization, increased healthcare expenses, and elevated mortality rates.¹ Multidrug-resistant bacteria (MDRO) pose a significant threat in this context.

ESKAPE, a group of bacteria capable of evading antibiotic action, has emerged within hospital settings, with *Enterobacter spp*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* identified as the most critical by the World Health Organization (WHO).²

The COVID-19 pandemic has posed significant challenges to healthcare systems worldwide. However, its impact on global antimicrobial resistance and associated HAIs remains unclear, and is likely to vary across different populations and disease hotspots.^{3–5} Countries with relatively lax infection control policies, such as the US and Italy, may experience more severe repercussions of antimicrobial resistance and HAIs.^{6,7} However, certain changes in human behavior and healthcare practices prompted by the pandemic, such as enhanced infection control measures and improved hygiene, may have mitigated the impact of COVID on HAIs.⁸

The Chinese government has implemented a “dynamic zero-clearance” policy based on national circumstances, continuously reinforcing prevention and control measures to avert large-scale pandemic resurgences,⁹ which reduces the incidence of HAIs, though further research on drug-resistant bacteria is warranted.¹⁰ In December 2022, following the issuance of the “New 10 Guidelines”, which means reopening measures, China experienced an initial wave of infection peaks.

This study evaluates the impact of the infection control policy of COVID-19 on HAIs caused by MDROs.

Methods

Study Design

This retrospective single-center study involved an eight-year analysis of inpatient laboratory data.

Setting and Population

Data were sourced from a teaching hospital affiliated with Shanghai Jiao Tong University School of Medicine, with a total of 2300 beds, between January 2016 and December 2023. We constructed three cohorts: the pre-control cohort was defined as inpatients who had their specimens collected between January 2016 and December 2019. Second, the in-control cohort comprised inpatients with specimens collected between January 2020 and December 2022. Third, the post-control cohort was defined as inpatients with specimens collected between January 2022 and December 2023. This time point was chosen following the first identification of a COVID-19 case with the “dynamic zero-clearance” policy in China in December 2019, and the COVID-19 reopening measures announced in December 2022.

Data Sources

Microbiological data were sourced from the laboratories of the teaching hospital from January 2016 to December 2023 (inclusive), including positive bloodstream, sputum, and urine cultures. Patient-level information was gathered for each positive culture, including age, sex, date of admission, date of specimen collection, and organism name. To compute the incidence rate, monthly occupied bed-day (OBD) data were collated for the same duration. For consistency, the organisms identified as carbapenem-resistant *Enterobacterales*(CRE) are listed in [Supplementary Tables S1–S3](#).

Definitions

For the purposes of this study, the following definitions for HAIs were applied, with all infections requiring diagnosis by clinicians:

- Bloodstream infection (BSI): Positive cultures collected > 48h post admission.
- Lower respiratory tract infection (LRTI): Positive cultures collected > 48h post admission.
- Urinary tract infection (UTI): Positive cultures collected > 48h post admission.

Target Detection of Bacterial Species

MDROs include methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), carbapenem-resistant *Klebsiella pneumoniae* (CRKP) and carbapenem-resistant *Enterobacterales* (CRE). Carbapenem-resistant organisms are resistant to meropenem or imipenem. Antimicrobial susceptibility testing was performed according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI).¹¹

Statistical Analysis

Interrupted time series (ITS) regression analyses with Newey-West autocorrelated errors¹² were conducted to evaluate disparities in the log-transformed level and trend of HAIs among the pre-control, in-control, and post-control periods. The ITS models assessed the baseline rate of HAI (intercept), the trend during the pre-control interval (slope), and the change in slope among the three time periods. To validate the transformation, a small pseudo-count was added to the values, with a response variable of zero. Before the analyses, the model assumptions were assessed by inspecting the autocorrelations and model residuals. The infection rates were also scrutinized for potential seasonal trends, and no discernible patterns were

detected. To ensure proper accounting for the autocorrelation structure, the Baum and Schaffer autocorrelation test was used to test for up to 12 lags. Lags with significant autocorrelations are integrated into the model.¹³ A nominal alpha level of 0.05, was applied in all statistical analyses to interpret the significance test results.

For the construction of the time series, the number of infections and OBD was aggregated by month. HAI rates were computed as the ratio of infections (numerator) in a given month to the corresponding OBD (denominator) and expressed as the rate per 10,000 OBDs. Changes in HAI, bloodstream infection (BSI), lower respiratory tract infection (LRTI), and urinary tract infection (UTI) rates were assessed collectively across all MDROs, and individually for each MDRO.

All the analysis was done using Stata 17.0 (MP—Parallel Edition). The interrupted time series (ITS) regression analyses were performed using the ITSA command in Stata. ITSA is specifically designed to handle and analyze data where an intervention may have caused a disruption in the time series, allowing for precise estimation of both immediate and gradual effects of interventions.

Results

Positive cultures were collected from the specimens obtained between January 2016 and December 2023. A total of 6763 positive multidrug-resistant organism (MDRO) cultures were identified, comprising 1058 bloodstream, 4581 sputum, and 1124 urine cultures derived from 4549 patients were included in the final analysis.

The median age of the patients in the pre-control cohort was 62.79 years old (SD=17.81), with 68% (1308/1920) of them being male. In the in-control cohort, the median age of the patients was 65.31 years old (SD=17.06) and 68.88% (1222/1774) were male. In the post-control cohort, the median age of the patients was 66.08 years old (SD=17.42), and 66.32% (567/855) were male (Table 1).

The mean monthly number of OBD combined in the pre-control cohort was 68,141 compared to 75015 for the in-control cohort and 85,326 for the post-control cohort. Notably, there is a decline in February 2020 and April 2022. However, by March 2020 and June 2022, the numbers returned to levels similar to those in other periods.

The incidence rates of all HAIs in the pre-control cohort were 8.68 per 10,000 OBDs, 9.76 per 10,000 OBDs in the in-control cohort and 12.58 per 10,000 OBDs in the post-control cohort (Table 2).

CRKP and CRAB contributed to more than half of the positive culture episodes and in every subgroup (Table 3). The detailed classification and frequency of CRE are shown in Tables S1–S3.

Time Series Analysis of Pre COVID-19 Cohort and COVID-19 Cohort Combined Hospital Acquired Infections

When analyzing the aggregate data for all infections across MDROs, the incidence rate of infections was observed to have a downward trend in the post-control cohort ($p<0.05$), as shown in Figure 1. The trends for MRSA($p<0.01$) and CRAB($p<0.001$) followed a similar pattern, with immediate increases in MRSA($p<0.01$) and CRAB($p<0.001$) following the unlocking policy. CRKP showed an upward trend in the pre-control cohort ($p<0.05$), whereas CRPA showed an upward trend during the in-control cohort ($p<0.05$). CRE showed an upward trend in the pre-control cohort($p<0.001$) and post-control cohort($p<0.01$), with an immediate decrease following the control policy($p<0.001$).

Table 1 The Demographic Characteristics of Patients of All Cohorts

	Pre-control	In-control	Post-control
Age (SD)	62.77(±17.82)	65.31(±17.06)	66.08(±17.42)
Gender [N (%)]			
Male	1291(68.20)	1222(68.88)	567(66.32)
Female	602(31.80)	552(31.12)	288(33.68)

Notes: Continuous variables are represented by $\bar{x} \pm s$ and categorical variables are represented as n (%).

Table 2 Incidence Rates per 10,000 OBDs of All Cohorts by Infection Site

	Pre-control		In-control		Post-control	
	Number	Incidence per 10,000 OBDs	Number	Incidence per 10,000 OBDs	Number	Incidence per 10,000 OBDs
BSI	419	1.28	419	1.55	202	1.97
LRTI	1969	6.02	1744	6.46	840	8.2
UTI	399	1.22	473	1.75	246	2.4
Total	2787	8.52	2636	9.76	1288	12.58
OBDs/year	817699		900,191		1,023,920	

Abbreviation: OBDs, Occupied bed days.

Table 3 Proportion of MDROs of All Cohorts from 2016 to 2023 [N (%)]

	BSI	LRTI	UTI	Total
MRSA	157(15.08%)	796(17.51%)	47(4.2%)	1000(14.91%)
CRAB	227(21.81%)	1670(36.73%)	229(20.48%)	2126(31.7%)
CRKP	448(43.04%)	975(21.44%)	431(38.55%)	1854(27.65%)
CRPA	116(11.14%)	849(18.67%)	144(12.88%)	1109(16.54%)
CRE	93(8.93%)	257(5.65%)	267(23.88%)	617(9.2%)
Total	1041(100%)	4547(100%)	1118(100%)	6706(100%)

Abbreviations: MRSA, Methicillin-resistant *Staphylococcus aureus*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CRKP, carbapenem-resistant *K. pneumoniae*; CRE, carbapenem-resistant *Enterobacterales*.

Bloodstream Infections

When combining all the BSI data, the incidence rate of infections was observed to be a downward trend in the post-control cohort ($p < 0.05$), as shown in Figure 2. The trends for MRSA ($p < 0.01$) and CRAB ($p < 0.01$) followed similar patterns, with significant immediate increases in MRSA ($p < 0.01$) and CRAB ($p < 0.01$) following the unlocking policy. CRKP showed no significant changes. CRPA showed an upward trend in the in-control cohort ($p < 0.05$). CRE showed an increase following the unlock policy ($p < 0.01$).

Lower Respiratory Tract Infections

When combining all LRTI data, the incidence rate of infections was observed to be a notable decreasing trend in the post-control cohort ($p < 0.05$), as shown in Figure 3. The trends for MRSA ($p < 0.01$) and CRAB ($p < 0.001$) followed similar patterns, with significant immediate increases in MRSA ($p < 0.001$) and CRAB ($p < 0.01$) following the unlocking policy. No significant changes were observed in the CRKP and CRPA. CRE showed an upward trend in the pre-control cohort ($p < 0.05$) with an immediate decrease following the control policy ($p < 0.001$).

Urine Tract Infections

When combining all UTI data, the incidence rate of infections was observed to be an upward trend in the pre-control cohort ($p < 0.001$), as shown in Figure 4. MRSA showed a downward trend in the post-control cohort ($p < 0.05$). CRAB showed an immediate increase following the unlock policy ($p < 0.05$), with a downward trend in the post-control cohort ($p < 0.001$). The CRKP levels showed an upward trend in the pre-control cohort ($p < 0.01$). CRPA showed an upward trend in the in-control

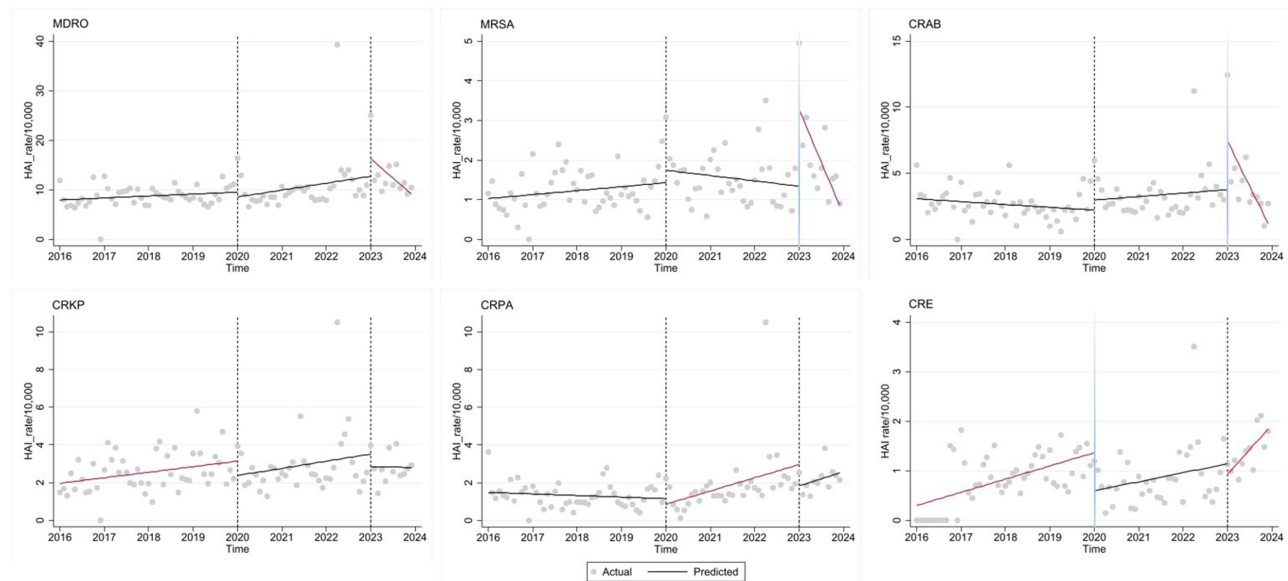


Figure 1 Hospital-acquired infections rates using interrupted time-series analysis. Gray dots (Actual): These represent the observed incidence rates of hospital-acquired infections over time. Horizontal solid line (Model fitted): Red line represents the model-fitted incidence rates where the change in infection rates is statistically significant. Black line represents the model-fitted incidence rates where the change is not statistically significant. Vertical lines indicate the time (in months) when the control policy started and withdrawn respectively. Blue line indicates the time points where there is a statistically significant difference in infection rates before and after the intervention. Black line indicates the time points where there is no statistically significant difference in infection rates before and after the intervention.

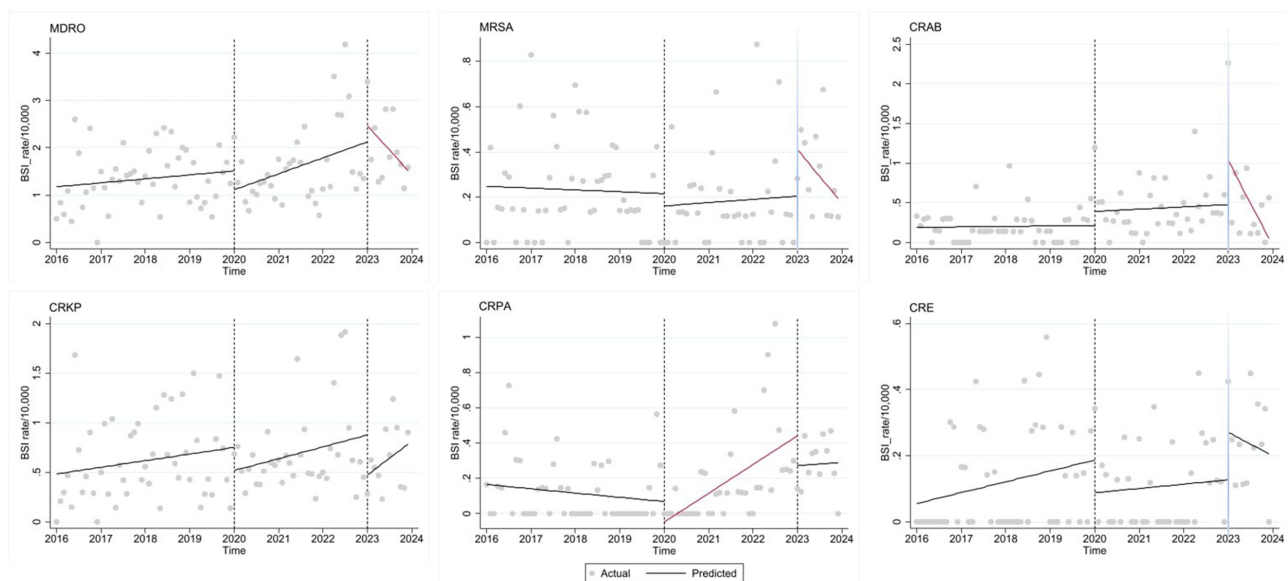


Figure 2 Hospital-acquired bloodstream infections rates using interrupted time-series analysis. Gray dots (Actual): These represent the observed incidence rates of hospital-acquired infections over time. Horizontal solid line (Model fitted): Red line represents the model-fitted incidence rates where the change in infection rates is statistically significant. Black line represents the model-fitted incidence rates where the change is not statistically significant. Vertical lines indicate the time (in months) when the control policy started and withdrawn respectively. Blue line indicates the time points where there is a statistically significant difference in infection rates before and after the intervention. Black line indicates the time points where there is no statistically significant difference in infection rates before and after the intervention.

cohort ($p < 0.05$) with a decrease following the unlock policy. CRE showed an upward trend in the pre-control cohort ($p < 0.001$) and post-control cohort ($p < 0.05$), with an immediate decrease following the control policy ($p < 0.05$).

Discussion

This study investigated the impact of infection control policies of COVID-19 on Hospital-Acquired infections (HAIs) caused by Multidrug-Resistant organisms (MDROs). This single-center study was conducted at a tertiary teaching hospital in

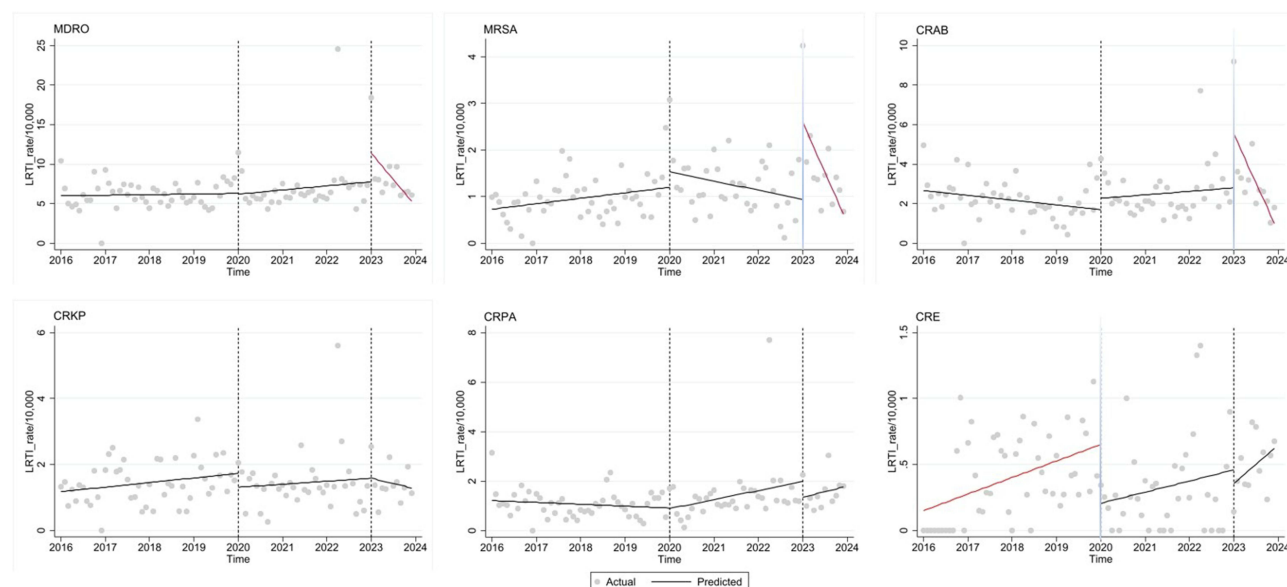


Figure 3 Hospital-acquired lower respiratory tract infections rates using interrupted time-series analysis. Gray dots (Actual): These represent the observed incidence rates of hospital-acquired infections over time. Horizontal solid line (Model fitted): Red line represents the model-fitted incidence rates where the change in infection rates is statistically significant. Black line represents the model-fitted incidence rates where the change is not statistically significant. Vertical lines indicate the time (in months) when the control policy started and withdrawn respectively. Blue line indicates the time points where there is a statistically significant difference in infection rates before and after the intervention. Black line indicates the time points where there is no statistically significant difference in infection rates before and after the intervention.

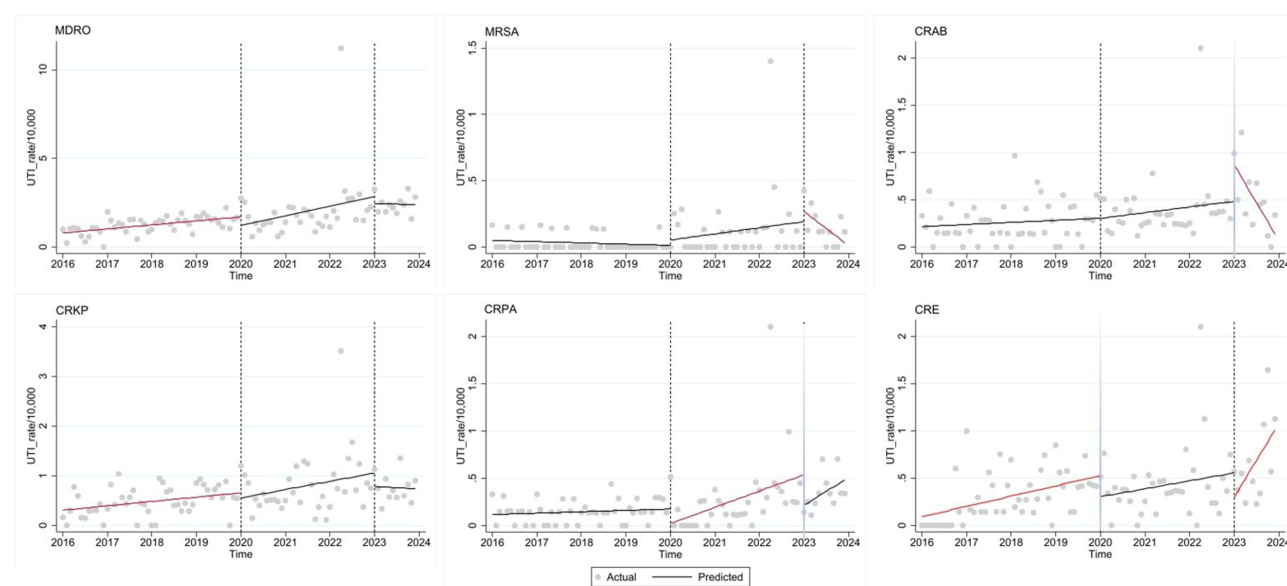


Figure 4 Hospital-acquired urine tract infections rates using interrupted time-series analysis. Gray dots (Actual): These represent the observed incidence rates of hospital-acquired infections over time. Horizontal solid line (Model fitted): Red line represents the model-fitted incidence rates where the change in infection rates is statistically significant. Black line represents the model-fitted incidence rates where the change is not statistically significant. Vertical lines indicate the time (in months) when the control policy started and withdrawn respectively. Blue line indicates the time points where there is a statistically significant difference in infection rates before and after the intervention. Black line indicates the time points where there is no statistically significant difference in infection rates before and after the intervention.

Shanghai, China. During the active control period, hospitals not only conduct rigorous screening for COVID-19, but also increase the frequency of surface disinfection of objects. The staff, patients, and visitors were required to adhere to hand hygiene and personal protective measures. These findings indicate no differences in HAIs across different infection sites; however, significant differences exist among various MDROs, which may have multiple interpretations.

During the active control period, the incidence of HAIs caused by MRSA and CRAB remained relatively constant. However, as control measures were lifted, the infection rates increased, which is consistent with the findings of some studies.^{3,14} Research indicates that the high prevalence of CRAB during the COVID-19 period was due to the clonal spread of OXA-23 positive CRAB,¹⁵ which also resulted in higher mortality rates.¹⁶ The spike in infection rates caused by MRSA and CRAB was only temporary, likely because of the surge in COVID-19 patients overwhelming healthcare facilities, and the limited effectiveness of hand hygiene and other basic infection control measures against these pathogens. Over time, as hospitals strengthened and optimized these measures, and as the number of COVID-19 cases decreased, the infection rates subsequently declined.

CRKP continues to pose significant challenges despite increased infection control measures, as the incidence and resistance levels remain concerning. Research has highlighted the complexities of controlling CRKP in hospital settings, noting that while increased hand hygiene and isolation practices might reduce some infections, these alone are not sufficient to significantly affect the prevalence of CRKP.^{17–19}

Over the past decade, the global spread of CRE infections has become a significant healthcare concern, owing to its association with high morbidity and mortality rates.^{4,20} This study suggests that the enhanced disinfection and isolation practices were effective in controlling the spread of CRE, excluding CRKP. This suggests that, while CRKP remains a challenging pathogen to control, other types of CRE were more effectively contained with the strengthened measures implemented during the control period. These findings emphasize the varying effects of infection control protocols on different bacterial strains within the CRE group, and highlight the need for tailored strategies to combat specific types of resistant bacteria.

CRPA exhibited a unique trend, with an increase during the control period, in contrast with other studies.^{21,22} The effectiveness of infection control measures in reducing CRPA incidence remains controversial owing to moderate evidence and diverse transmission sources and mechanisms among different strains.²³ However, the implementation of these measures is highly recommended. This increase in infection rates may also be due to the CRPA's capability to survive in the environment for prolonged periods,²⁴ widespread antibiotic use, and resource constraints.^{14,25}

This study has several limitations. First, this was a single-center study, limited to a tertiary-level teaching hospital in Shanghai. Second, Shanghai, where the study was located, was closed from March to May 2022, which may have had a certain impact on the conclusion. Third, only one year has passed since the epidemic was released, and no long-term changes in drug-resistant bacterial infections have been observed due to the release.

Conclusion

This study demonstrates that while the COVID-19 epidemic poses a significant challenge to infection control within hospitals, it also provides a unique opportunity to enhance infection control measures and evaluate their effectiveness. In addition, these findings highlight the need for more targeted prevention and control strategies against different pathogens in future epidemics.

Consent to Participate

Obtained.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval

This study is approved by the Ethics Committee of Ruijin Hospital, Jiaotong University School of Medicine with a waiver of informed consent for the following reasons: (1) the retrospective nature of the study, (2) all identifiable personal information was removed for privacy protection, (3) only medical records were reviewed. This study complies with the Declaration of Helsinki.

Consent for Publication

Obtained.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China (81670569), Shanghai Shen Kang Hospital Development Center (SHDC2020CR6025), Shanghai Jiao Tong University School of Medicine Hospital Infection Committee 2022 (Jyyg2209) and Shanghai Medical and Health Development Foundation, Apply Continuous Quality Improvement to Prevent Central Venous Catheter-Associated Bloodstream Infections (CLABSI) Study.

Disclosure

The authors report no conflicts of interest in this work.

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