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ORIGINAL RESEARCH

Impact of the COVID-19 Pandemic on Multidrug-Resistant Organism Infections in Infected Pancreatic Necrosis: A Post-Hoc Cohort Analysis

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Background: This study aimed to elucidate the impact of COVID-19 pandemic on multidrug-resistant organism (MDRO) infection in patients with infected pancreatic necrosis (IPN).

Methods: This post-hoc analysis of a prospective cohort included patients with IPN stratified into three phases: pre-pandemic (2016–2019), pandemic period (2020–2022), and post-pandemic period (2023–2024). Logistic regression and interrupted time-series analysis (ITSA) were employed to identify risk factors and longitudinal trends.

Results: MDRO infection decreased significantly during the pandemic period compared to pre-pandemic levels (44.8% vs 81.1%, $P<0.001$). There was no significant difference in the incidence of MDRO infection between the pandemic and post-pandemic period (44.1% vs 44.8%, $P=0.924$). During the pandemic, both prophylactic antimicrobial usage (64.8% vs 85.1%, $P<0.001$) and ICU stays (median: 6.0 vs 15.0 days, $P<0.001$) were significantly reduced compared to the pre-pandemic period. Logistic regression identified prophylactic antimicrobial usage (OR 17.28, $P<0.001$), ICU stays (OR 1.07, $P<0.001$), and the COVID-19 pandemic (OR 0.21, $P<0.001$) as independent factors associated with MDRO infection. ITSA revealed a significant decrease in the trend of MDRO infection during the pandemic compared to the pre-pandemic period ($P=0.006$). An immediate level of MDRO infection increased during the post-pandemic period compared to the pandemic ($P=0.040$). The similar trend variations were observed in the proportion of prophylactic antimicrobial usage.

Conclusion: The COVID-19 pandemic has led to a notable reduction in MDRO infection among IPN patients, likely attributable to stringent infection prevention and control measures which led to reduced prophylactic antimicrobial usage and ICU stays during this period.

Keywords: antimicrobial resistance, acute pancreatitis, COVID-19, antimicrobial usage, interrupted time-series analysis

Introduction

Acute pancreatitis (AP) is the most common gastrointestinal indication requiring acute admission to the hospital. Infected pancreatic necrosis (IPN) is a severe complication of AP.[1] Recent years have witnessed an increasing proportion of infection caused by multidrug-resistant organisms (MDROs) in patients with IPN. Antimicrobial resistance (AMR) is not only prevalent, but also associated with adverse clinical outcomes and increased mortality in IPN.[2]

The COVID-19 pandemic has profoundly impacted healthcare systems worldwide. Data from the United States Centers for Disease Control and Prevention (CDC) suggests the pandemic has resulted in rising rates of AMR, mostly due to inappropriate antibiotic usage. However, the truth is far from that simple. Enhanced infection prevention and

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control (IPC) measures, such as heightened hygiene protocols and the widespread use of personal protective equipment (PPE), may mitigate the transmission of MDROs in both healthcare and community setting. Given potentially opposing effects, it is unclear how AMR will change among different districts, hospitals, and diseases during the pandemic. Emerging evidence suggests considerable heterogeneity in AMR trends across hospitals and regions during the pandemic, reflecting variability in healthcare capacities, infection prevention adherence and levels of intervention adoption.[3]

The COVID-19 pandemic provides a window to uncover key infection control practices and a valuable insight into sustainable and long-term strategies for AMR mitigation.[4] China, well known for the strict enforcement of a dynamic zero-COVID approach, quickly implemented lockdowns in impacted urban locations during the pandemic from January 2020 until December 2022. The sudden lifting of these COVID-19 restrictions signaled a major shift in policy. For IPN patients who are vulnerable to nosocomial MDRO transmission due to prolonged ICU stays, invasive interventions and frequent antibiotic exposure, these policy shifts may have created distinct infection patterns. It remains unclear how the pandemic has affected MDRO incidence in IPN. This study post-hoc analyzes a large prospective cohort of IPN, investigating key factors associated with changes in AMR during the COVID-19 pandemic and the period of the subsequent policy shifts, with the goal of guiding future infection control and treatment strategies for IPN patients.

Methods

Study Design and Setting

This study was a post-hoc analysis of a prospective database of patients with IPN at Xiangya Hospital, Central South University. The prospective database was initiated in 2010 following institutional ethical approval (No. 201012067), with ongoing patient enrollment and data collection conducted under the approved protocol. The present analysis focuses on patients admitted between 2016 and 2024. All data were derived from this longitudinal cohort.

The primary aim was to compare the incidence of MDRO infection in different phases of in relation to COVID-19. The pandemic phase included patients who presented from January 1, 2020 to December 31, 2022, during which stringent IPC policy had been implemented in China. Patients who presented during the relaxed IPC policy period in China were included in the post-pandemic cohort from January 1, 2023 to December 31, 2024. The pre-pandemic cohort covered the period from January 1, 2016 to December 31, 2019.[5,6] The secondary aim was to identify the risk factors for MDRO infection.

This study was reported according to the "Strengthening the Reporting of Observational studies in Epidemiology" (STROBE) guidelines and conducted in accordance with the principles of the Declaration of Helsinki.[7] The study was registered on www.researchregistry.com (Unique identifying number: researchregistry9293). Written informed consent was obtained from all participants or their legal representatives for the participation in the study.

Data Collection and Definitions

Prospectively collected data included baseline characteristics and potential risk factors for MDRO infection: demographics (age, gender, comorbidities, etiology and severity), microbial culture, prophylactic antimicrobial usage, surgical intervention (step-up approach, number of surgical interventions and time from onset to first surgical intervention), ICU stays, hospital stays, complications and outcomes (intestinal fistula, hemorrhage, pancreatic fistula and death).

The diagnosis of AP was based on the Revised Atlanta Classification criteria.[1] The presence of transient (within 48 hours) organ failure and/or local complications was classified as moderately severe AP (MSAP). Severe AP (SAP) was defined as AP with persistent (lasting >48 hours) organ failure.[1] Pancreatic necrosis was defined as the presence of diffuse or focal areas of pancreatic non-enhancement on enhanced CT. IPN was defined as positive culture of peripancreatic fluid or pancreatic necrosis obtained during the first percutaneous drainage or during the first surgical intervention.[1] Patients with fungal infection alone were excluded in the study.

MDROs were defined as microorganisms resistant to at least one agent in three or more antimicrobial categories.[8] MDROs in this study mainly included Carbapenem-resistant Acinetobacter baumannii (CRAB), Escherichia coli producing extended-spectrum beta-lactamase (ESBLp), Carbapenem-resistant Klebsiella pneumoniae (CRKP), Carbapenem-resistant Citrobacter freundii, Carbapenem-resistant Enterobacter cloacae, Carbapenem-resistant Pseudomonas aeruginosa (CRPA) and Methicillin-resistant Staphylococcus aureus (MRSA).

Prophylactic antimicrobial usage was defined as antibiotics administered in the absence of any evident peripancreatic or extrapancreatic infections, including cholangitis, catheter-related infections, blood stream infections, urinary tract infections and pneumonia.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviations or median (interquartile range, IQR) for statistical description, and categorical variables were expressed as absolute numbers with percentages. The two-tailed Fisher's exact test was used to compare categorical variables, and a Student's *t*-test was used to compare continuous variables. The post-hoc multiple comparisons were conducted with the Nemenyi multiple comparison or chi-square segmentation method. All variables that were significant in univariate analysis were included in multivariable analysis using logistic regression. Odds ratio (OR) with 95% confidence interval (CI) was calculated. P-value < 0.05 was considered to be statistically significant. Interrupted time-series analysis (ITSA) is a widely used robust quasi-experimental method for evaluation of longitudinal effects of interventions or incidents. The impact of the COVID-19 pandemic was evaluated by the change in the level (immediate effect) and trend of the proportion of MDRO infection quarterly. The ITSA model included: (1) Segmented regression to estimate baseline trends and immediate level changes at policy transition points; (2) Autocorrelation adjustment using *Prais-Winsten* regression; (3) Effect size quantification via β coefficients for trend differences (slope changes) and immediate level shifts. All statistical analysis was performed in R, version 4.2.0 statistical language (R Foundation for Statistical Computing).

Results

Patient Characteristics

This study post-hoc analyzed data from a prospectively maintained database of 336 patients with IPN at Xiangya Hospital, Central South University. The cohort were stratified into three periods, with 148 (42.8%) during pre-pandemic, 105 (31.3%) during the pandemic, and 93 (27.7%) during the post-pandemic period. The median age was 47.0 years, and 259 patients (74.9%) were male. 203 (58.7%) were SAP, and the remaining 143 patients (41.3%) had MSAP. 208 (60.1%) had MDRO infection. Prophylactic antimicrobials were administered to 74.3% of patients, and 87.9% underwent a step-up surgical approach. The median (IQR) number of surgical interventions was 4.0 (2.0, 6.0), with a median (IQR) time of 22.0 (14.0, 33.0) days from symptom onset to the first procedure. Median (IQR) length of hospital stay was 56.0 (37.0, 75.0) days and median (IQR) length of ICU stay was 10.0 (0.0, 23.0) days. Overall mortality was 22.0% (n = 76) (Table 1).

Table 1 Baseline Demographic and Clinical Characteristics in IPN Patients

Variable		
Demographic data		
Total no. of patients		336 (100%)
Time period classification, n (%)	Pre-pandemic 2016–2019	148 (42.8%)
	Pandemic 2020–2022	105 (31.3%)
	Post-pandemic 2023–2024	93 (27.7%)
Gender, n (%)	Male	259 (74.9%)
	Female	87 (25.1%)
Age, years [Median (IQR)]		47.0 (37.0 to 56.0)
DM, n (%)	No	267 (77.2%)
	Yes	79 (22.83%)

(*Continued*)

Table 1 (Continued).

Variable		
Time from onset to admission, days [Median (IQR)]		21.5 (9.0 to 45.0)
Etiology, n (%)	Hypertriglyceridemia	127 (36.7%)
	Biliary	157 (45.4%)
	Alcohol	43 (12.4%)
	Others	19 (5.5%)
RAC, n (%)	MSAP	143 (41.3%)
	SAP	203 (58.7%)
Referred patient, n (%)	No	141 (40.8%)
	Yes	205 (59.3%)
Prophylactic antimicrobial usage, n (%)	No	89 (25.7%)
	Yes	257 (74.3%)
Time from onset to first surgical intervention, days [Median (IQR)]		22.0 (14.0 to 33.0)
Step up, n (%)	No	42 (12.1%)
	Yes	304 (87.9%)
OPN, n (%)	No	283 (81.8%)
	Yes	63 (18.2%)
Surgical interventions, n [Median (IQR)]		4.0 (2.0 to 6.0)
ICU stays, days [Median (IQR)]		10.0 (0.0 to 23.0)
Hospital stays, days [Median (IQR)]		56.0 (37.0 to 75.0)
Death	No	270 (78.0%)
	Yes	76 (22.0%)
Major complications, n (%)		
Hemorrhage	No	297 (85.8%)
	Yes	49 (14.2%)
Intestinal leakage	No	271 (78.3%)
	Yes	75 (21.7%)
Pancreatic fistula	No	203 (58.7%)
	Yes	143 (41.3%)
MDRO infection, n (%)	No	138 (39.89%)
	Yes	208 (60.1%)

Notes: Data are presented as n (%), where n indicates the number of patients/events.
Abbreviations: DM, diabetes mellitus; RAC, revised Atlanta classification; MSAP, moderately severe acute pancreatitis; SAP, severe acute pancreatitis; OPN, open pancreatic necrosectomy; MDRO, multidrug-resistant organism.

Trends of MDRO Infection

The proportion of MDRO infection exhibited an upward trend from 2016 to 2019, peaking at 85.1% in 2018. Beginning from 2020, the proportion declined abruptly, reaching the lowest point in 2021, followed by a slow rise from 2022 to 2024 (Figure 1A). A total of 616 microbial isolates were cultured from samples of the pancreatic collection, of which 231 (37.5%) were classified as MDROs. The predominant MDROs were CRKPs, accounting for 39.8% (92 isolates), followed by CRABs, which were identified in 72 isolates (31.2%). Figure 1B delineated the temporal trends of the proportions of the predominant MDROs.

During the pandemic, the incidence of MDRO infection decreased compared to pre-pandemic levels (44.8% vs 81.1%, *P*<0.001), accompanied with reduced prophylactic antimicrobial usage (64.8% vs 85.1%, *P*<0.001), shorten ICU stays (6.0 days vs 15.0 days, *P*<0.001), and hospital stays (54.0 days vs 62.5 days, *P*=0.021) (Table 2).

The incidence of MDRO infection showed no significant difference between the pandemic and post-pandemic groups (44.8% vs 44.1%, *P*=0.924). There was also no significant difference in the prophylactic antimicrobial usage and ICU stays, with P-values of 0.658 and 0.973, respectively. However, the post-pandemic group showed a greater proportion of SAP and more surgical interventions compared to the pandemic group (Table 2).

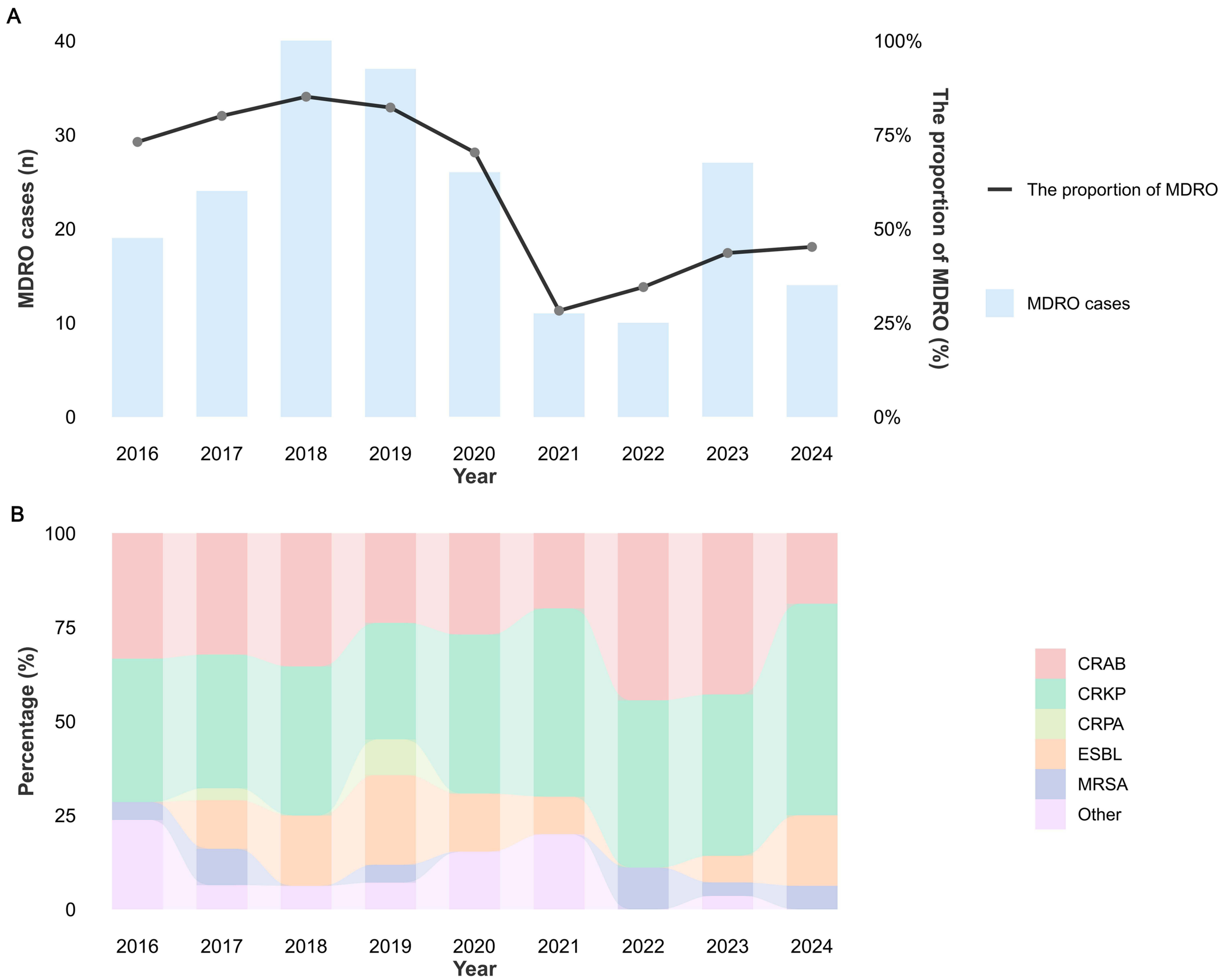

Figure 1 (**A**) The trend of MDRO infection in IPN from 2016–2024. (**B**) Annual trend of proportion of MDRO infection in IPN from 2016–2024.

Logistic Regression Analysis of MDRO Infection

MDRO infection was significantly associated with prophylactic antimicrobial usage, prolonged ICU stays, and the COVID-19 pandemic ($P<0.001$). The patients with MDRO infection exhibited higher incidence of intestinal leakage

Table 2 Comparison of Baseline Demographic and Clinical Characteristics Across Three Time Periods According to Different IPC Policies on the Pandemic in IPN Patients

Variable		Pre-Pandemic 2016–2019 (N=148)	Pandemic 2020–2022 (N=105)	Post-Pandemic 2023–2024 (N=93)	P^a	P^b	P^c
Gender, n (%)	Male	108 (73%)	75 (71.4%)	76 (81.7%)	0.196		
	Female	40 (27%)	30 (28.6%)	17 (18.3%)			
Age, years (Mean ± SD)		47.09 ± 12.34	45.72 ± 13.08	46.82 ± 13.83	0.698		
Time from onset to admission, days [Median (IQR)]		22.00 (10.00 to 46.50)	21.00 (8.00 to 40.00)	21.00 (7.00 to 47.00)	0.665		
Etiology, n (%)	Hypertriglyceridemia	48 (32.4%)	40 (38.1%)	39 (41.9%)	0.146		
	Biliary	79 (53.4%)	39 (37.1%)	39 (41.9%)			
	Alcohol	15 (10.1%)	18 (17.1%)	10 (10.8%)			
	Others	6 (4.1%)	8 (7.6%)	5 (5.4%)			

(*Continued*)

Table 2 (Continued).

Variable		Pre-Pandemic 2016–2019 (N=148)	Pandemic 2020–2022 (N=105)	Post-Pandemic 2023–2024 (N=93)	P^a	P^b	P^c
RAC, n (%)	MSAP	59 (39.9%)	61 (58.1%)	23 (24.7%)	**<0.001**	0.632	**<0.001**
	SAP	89 (60.1%)	44 (41.9%)	70 (75.3%)			
Referred patient, n (%)	No	70 (47.3%)	35 (33.3%)	36 (38.7%)	0.075		
	Yes	78 (52.7%)	70 (66.7%)	57 (61.3%)			
Prophylactic antimicrobial usage, n (%)	No	22 (14.9%)	37 (35.2%)	30 (32.3%)	**<0.001**	**<0.001**	0.658
	Yes	126 (85.1%)	68 (64.8%)	63 (67.7%)			
Time from onset to first surgical intervention, days [Median (IQR)]		22.0 (15.0 to 33.0)	24.0 (14.0 to 34.0)	20.0 (14.0 to 28.0)	0.273		
Step up, n (%)	No	23 (15.5%)	12 (11.4%)	7 (7.5%)	0.173		
	Yes	125 (84.5%)	93 (88.6%)	86 (92.5%)			
OPN, n (%)	No	123 (83.1%)	78 (74.3%)	82 (88.2%)	**0.035**	0.583	**0.013**
	Yes	25 (16.9%)	27 (25.7%)	11 (11.8%)			
Surgical interventions, n [Median (IQR)]		3.0 (2.0 to 5.0)	3.00 (2.0 to 5.0)	5.0 (3.0 to 8.0)	**<0.001**	0.937	**<0.001**
ICU stays, days [Median (IQR)]		15.0 (6.5 to 31.0)	6.0 (0.0 to 18.0)	5.0 (0.0 to 17.0)	**<0.001**	**<0.001**	0.973
Hospital stays, days [Median (IQR)]		62.5 (46.5 to 88.5)	54.0 (34.0 to 76.0)	48.0 (29.0 to 67.0)	**<0.001**	**0.021**	0.101
Death	No	111 (75%)	82 (78.1%)	77 (82.8%)	0.363		
	Yes	37 (25%)	23 (21.9%)	16 (17.2%)			
Major complications, n (%)							
Hemorrhage	No	124 (83.8%)	94 (89.5%)	79 (84.9%)	0.417		
	Yes	24 (16.2%)	11 (10.5%)	14 (15.1%)			
Intestinal leakage	No	105 (70.9%)	90 (85.7%)	76 (81.7%)	0.417		
	Yes	43 (29.1%)	15 (14.3%)	17 (18.3%)			
Pancreatic fistula	No	76 (51.4%)	54 (51.4%)	73 (78.5%)	**<0.001**	0.017	**<0.001**
	Yes	72 (48.6%)	51 (48.6%)	20 (21.5%)			
MDRO infection, n (%)	No	28 (18.9%)	58 (55.2%)	52 (55.9%)	**<0.001**	**<0.001**	0.924
	Yes	120 (81.1%)	47 (44.8%)	41 (44.1%)			

Notes: Data are presented as n (%), where n indicates the number of patients/events. [a]$P < 0.05$ indicated that there was a statistical difference among the three groups. Post-hoc multiple comparisons were needed to explore which two groups are statistically significant. After the non-parametric test, a Nemenyi multiple comparison correction was used. The chi-square segmentation method was used for pairwise comparison after establishing the meaningfulness of the chi-square test. [b]Group Pre-pandemic period vs Group Pandemic period. [c]Group Pandemic period vs Group Post-pandemic period. Bold values indicate statistically significant differences.

Abbreviations: DM, diabetes mellitus; RAC, revised Atlanta classification; MSAP, moderately severe acute pancreatitis; SAP, severe acute pancreatitis; OPN, open pancreatic necrosectomy; MDRO, multidrug-resistant organism.

(30.3% vs 8.7%; *P*<0.001), longer hospital stays (median: 62.00 days vs 52.00 days, *P*< 0.001), and higher mortality (30.8% vs 8.7%; *P*<0.001), with more surgical interventions (*P*=0.002) (Table 3).

Multi-factor logistic regression identified prophylactic antimicrobial usage (OR 17.28, 95% CI 7.81–38.24, *P* < 0.001), ICU stays (OR 1.07, 95% CI 1.04–1.10, *P* <0.001), and the COVID-19 pandemic (OR 0.21, 95% CI 0.11–0.40, *P* <0.001) as independent factors associated with MDRO infection (Table S1).

Table 3 Comparison of Baseline Characteristics and Outcomes Between Patients with and without MDRO Infection

Variable		Non-MDRO Infection Group (N=138)	MDRO Infection Group (N=208)	*P*
Gender, n (%)	Male	101 (73.2%)	158 (76%)	0.649
	Female	37 (26.8%)	50 (24%)	
Age, years (Mean ± SD)		46.5 ± 13.1	46.7 ± 12.9	0.883
Time from onset to admission, days [Median (IQR)]		20.0 (7.0 to 50.0)	22.5 (10.0 to 40.0)	0.900
DM, n (%)	No	102 (73.9%)	165 (79.3%)	0.296
	Yes	36 (26.1%)	43 (20.7%)	
Etiology, n (%)	Hypertriglyceridemia	52 (37.7%)	75 (36.1%)	0.133
	Biliary	54 (39.1%)	103 (49.5%)	
	Alcohol	22 (15.9%)	21 (10.1%)	
	Others	10 (7.2%)	9 (4.3%)	

(*Continued*)

Table 3 (Continued).

Variable		Non-MDRO Infection Group (N=138)	MDRO Infection Group (N=208)	*P*
RAC, n (%)	MSAP	77 (55.8%)	66 (31.7%)	**<0.001**
	SAP	61 (44.2%)	142 (68.3%)	
Referred patient, n (%)	No	54 (39.1%)	87 (41.8%)	0.698
	Yes	84 (60.9%)	121 (58.2%)	
Prophylactic antimicrobial usage, n (%)	No	76 (55.1%)	13 (6.2%)	**<0.001**
	Yes	62 (44.9%)	195 (93.8%)	
Time from onset to first surgical intervention, days [Median (IQR)]		22.0 (13.0 to 34.0)	22.0 (15.0 to 31.5)	0.989
Step up, n (%)	Yes	126 (91.3%)	178 (85.6%)	0.153
	No	12 (8.7%)	30 (14.4%)	
OPN, n (%)	No	121 (87.7%)	162 (77.9%)	0.030
	Yes	17 (12.3%)	46 (22.1%)	
Surgical interventions, n [Median (IQR)]		3.0 (2.0 to 6.0)	4.0 (3.0 to 6.0)	0.062
ICU stays, days [Median (IQR)]		1.5 (0.0 to 10.0)	18.0 (8.0 to 32.5)	**<0.001**
Hospital stays, days [Median (IQR)]		52.0 (33.0 to 67.0)	62.0 (43.0 to 85.0)	**<0.001**
Death	No	126 (91.3%)	144 (69.2%)	**<0.001**
	Yes	12 (8.7%)	64 (30.8%)	
Major complications, n (%)				
Hemorrhage	No	122 (88.4%)	175 (84.1%)	0.338
	Yes	16 (11.6%)	33 (15.9%)	
Intestinal leakage	No	126 (91.3%)	145 (69.7%)	**<0.001**
	Yes	12 (8.7%)	63 (30.3%)	
Pancreatic fistula	No	80 (58%)	123 (59.1%)	0.917
	Yes	58 (42%)	85 (40.9%)	
COVID-19 pandemic	No	28 (20.3%)	120 (57.7%)	**<0.001**
	Yes	110 (79.7%)	88 (42.3%)	

Notes: Data are presented as n (%), where n indicates the number of patients/events. Bold values indicate statistically significant differences.
Abbreviations: MDRO, multidrug-resistant organism; DM, diabetes mellitus; RAC, revised Atlanta classification; MSAP, moderately severe acute pancreatitis; SAP, severe acute pancreatitis; OPN, open pancreatic necrosectomy.

ITSA

To evaluate the impact of the pandemic on the longitudinal trend of MDRO infection, prophylactic antimicrobial usage and ICU stays, a multi-segment ITSA design was employed. There was a significant decrease in the trend during the pandemic period compared to the pre-pandemic period, with a decrease of approximately 4.7% per quarter ($P = 0.006$) (Figure 2A and Table 4). During the post-pandemic period, a significant immediate level increase in MDRO infection was observed compared to the pandemic (β=0.308, P=0.040). The trend of MDRO infection increased slightly, but the difference was not statistically significant between the pandemic and post-pandemic period (Figure 2A and Table 4). Similar trend variations were observed in the proportion of prophylactic antimicrobial usage, with a decrease in the trend at approximately 3.0% per quarter during the pandemic compared to pre-pandemic period ($P = 0.10$) (Figure 2B and Table S2). The changes in ICU stays across the three time periods were not statistically significant (Figure 2C and Table S3).

Discussion

To our knowledge, this is the first interrupted time-series analysis evaluating trends of MDRO infection in AP across three time periods according to the pandemic-related IPC policies. The present study reveals a dynamic relationship between the COVID-19 pandemic and MDRO infection, with three important findings: (1) A significant reduction in MDRO infection during the pandemic, maintaining at a lower level during the post-pandemic period; (2) A transient rebound in MDRO incidence immediately following the relaxation of COVID-19 restrictions, though not reaching pre-pandemic levels; (3) Sustained reductions in prophylactic antimicrobial usage and ICU stays as key modifiable factors associated with MDRO infection. These findings provide critical insights into effective strategies to control MDRO infection in AP patients and the complex interplay between public health policies and nosocomial infection dynamics.

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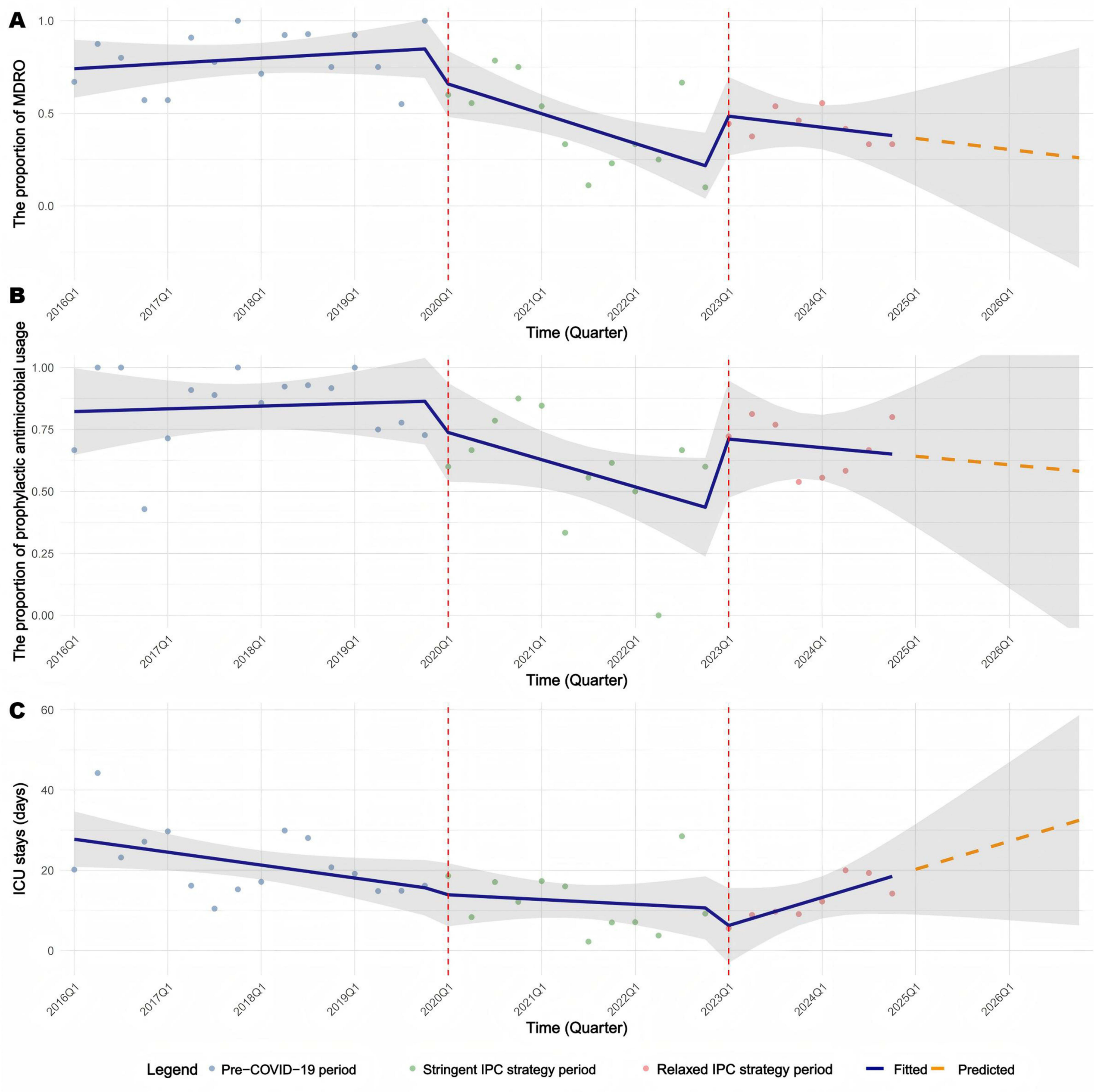

Figure 2 Interrupted time-series analysis of (**A**) MDRO infection, (**B**) prophylactic antimicrobial usage and (**C**) ICU stays in IPN patients.

It is estimated that AMR causes at least 1.27 million deaths worldwide annually, posing a severe threat to individual lives, community health, and national security.[9,10] The global burden of antimicrobial resistance is immense and continues to grow as pathogens become resistant to available antibiotics. The long-term consequences of AMR are profound, with potential increases in mortality and morbidity from infections that were previously treatable The COVID-19 pandemic has significantly disrupted healthcare systems globally, further exacerbating the AMR crisis. The pandemic put tremendous pressure on healthcare resources, resulting in the prioritization of COVID-19 management over other critical health issues. However, the consequences of these disruptions have not been fully realized, especially with respect to the increase in AMR infections.

Overuse and misuse of antimicrobials have been major factors driving the dissemination of AMR during the pandemic.[11] More than 70% of hospitalized COVID-19 patients were prescribed antimicrobials, despite limited evidence supporting bacterial infections.[12] The indiscriminate use of antibiotics, especially in cases where viral infections predominated, may have contributed to the rise of MDROs. Additionally, surges in hospital admissions have led to shortages of PPE, insufficient medical staff, and

Table 4 Regression Model Parameters of Interrupted Time-Series Analysis on the Proportion of MDRO Infection

Term	Estimate (β)	Std. Error	95% CI	*t*	*P*
(Intercept)	0.734	0.084	(0.569, 0.899)	8.702	< 0.001
Time (pre-pandemic)	0.007	0.009	(−0.010, 0.024)	0.817	0.421
Stringent IPC period	−0.197	0.121	(−0.434, 0.040)	−1.620	0.116
Trend change (t1)	−0.047	0.016	(−0.079, −0.016)	−2.948	**0.006**
Relaxed IPC period	0.308	0.143	(0.016, 0.600)	2.145	**0.040**
Trend change (t2)	0.025	0.028	(−0.030, 0.080)	0.891	0.380

Notes: Stringent IPC period: Immediate level change during the stringent IPC strategy. Trend change (t1): Change in trend during the stringent IPC strategy period. Relaxed IPC period: Immediate level change during the relaxed IPC strategy. Trend change (t2): Change in trend during the relaxed IPC strategy period. Bold values indicate statistically significant differences.
Abbreviations: Std. Error, standard error.

critical care unit beds.[13] This shortage of resources has significantly hindered the ability of healthcare facilities to implement effective IPC measures. Such constraints have made it challenging to mitigate the spread of AMR within hospital settings.

However, the truth is not entirely this way.[3] IPC measures including hand hygiene and mask wearing could result in a reduction in the transmission rate of MRSA within hospitals.[14] Additionally, Smith et al employed a mathematical model demonstrating that policies dealing with COVID-19 were associated with a 28.2% reduction of MDRO colonization.[15] The IPC measures strictly adopted in hospital settings during the pandemic were effective in reducing HAIs.[16–20] With the lifting of COVID-19 related restrictions and the exhausting of medical resources, this may lead to a resurgence in MDRO transmission.

The study employed a multi-segment ITSA to assess the impact of the pandemic on the proportion of MDRO infections. During the pandemic which commenced the end of 2019, a significant downward trend in MDRO infection was observed. Following the relaxed IPC strategy in 2023, there was an immediate rise in MDRO infection. However, no significant ongoing change was observed thereafter. Although an increase in the proportion of SAP cases and a relatively higher rate of surgical interventions were observed during the post-pandemic period, the overall level of MDRO infection remained significantly lower than that prior to the pandemic. These findings suggested that COVID-19 and its associated IPC policies had significant impact on MDRO infection in patients with IPN.

MDRO infection is a serious threat to AP patients with increased morbidity and mortality. Previous study showed the percentage of MDRO infection in IPN increased from 16.7% in 2010 to 74.6% in 2019.[2] However, this study revealed that following the implementation of stringent IPC measures due to COVID-19, the MDRO infection rate among IPN patients decreased substantially from 80.6% to 44.8%, with concomitant reduced ICU stays and prophylactic antimicrobial usage. Prolonged ICU stays were associated with the development of MDRO infection.[17] The rate rose from 13.2% in the first week to 82.1% for patients who stayed longer than three weeks in ICU.[18] This suggested that the longer patients stayed in the ICU, the higher the risk of acquiring MDROs was. This might be due to factors such as prolonged exposure to invasive devices and inadequate adherence to IPC measures.[18] As hospitals faced an unprecedented surge of COVID-19 cases, many facilities had to reorganize their resources, which included reallocating ICU beds primarily for COVID-19 patients. This shift often resulted in shorter ICU or hospital stays for non-COVID patients, as they were either discharged earlier or had their elective procedures postponed or canceled due to the overwhelming demand for critical care resources.[19] This reduction in ICU admissions for non-COVID patients might have inadvertently lowered their exposure to the hospital environment, contributing to a decrease in MDRO infection.

It was well recognized that early diagnosis of IPN was challenging, which might lead to antibiotic overuse and thus increase the selective pressure for MDROs. Timmerhuis et al found that the presence of MDROs in the initial pancreatic tissue sample was relatively low (15%), which was attributed to the restrictive antibiotic policies in the Netherlands. In fact, after the COVID-19 outbreak, the National Health Commission of China issued a series of regulations and announcements in 2020, aiming at improving infection control in hospitals and promoting the prudent use of antimicrobials.[20,21] Li et al reported a significant long-term decline in weekly AMR rates after the COVID-19 pandemic, particularly following the implementation of the national antibiotic management policy.[22] Our results aligned with these

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findings. Furthermore, NGS technology has been used in IPN diagnosis since 2019.[23] Our previous research showed that the rate of correct use of antibiotics would be improved from 18.6% to 81.4% if adjusted according to the mNGS results.[24] NGS might innovatively contribute to guiding precise antimicrobial therapy and reduce the use of broad-spectrum antibiotics in IPN patients during the pandemic. The lifting of strict prevention and control measures after the COVID-19 pandemic raised significant concerns regarding the potential increase in AMR.[25] The trend presented in this study supported this point. After the pandemic, the proportion of MDRO infection in IPN increased slightly. However, the overall proportion remained significantly lower than that prior to the pandemic. This indicated that the policies and measures related to the COVID-19 might continue to play a role.

Several limitations should be acknowledged in this study. First, the single-center raised concerned about generalizability. Second, while the post-hoc analysis of a prospective cohort provided longitudinal insights, the observational study nature limited causal inference. Third, heterogeneity in COVID-19 mitigation strategies—particularly regional disparities in resource allocation (eg, ICU bed availability, antimicrobial stewardship program intensity)—likely contributed to divergent AMR trajectories across healthcare systems. Future studies would focus on establishing standardized IPC protocols and AMR surveillance frameworks to validate our findings in multicenter cohorts of AP.

Conclusions

The incidence of MDRO infection in IPN patients significantly reduced in the COVID-19 pandemic, which was likely linked to pandemic-related changes such as reduced prophylactic antibiotic usage and shorter ICU stays, due to stringent infection control practices. This highlights the importance of optimizing IPC strategies to curb the spread of resistant infections. While the pandemic contributed to a decrease in MDRO transmission, sustained efforts in antimicrobial stewardship and infection control will be essential to keep these improvements.

Data Sharing Statement

The data supporting the findings of this study are available upon reasonable request from the corresponding author.

Ethics Approval

This study is a post-hoc analysis of a prospective database of patients with IPN, which was initiated in 2010 at Xiangya Hospital, Central South University. The study protocol was originally approved by the Ethics Committee of Xiangya Hospital on December 5, 2010 (Approval No. 201012067), and was amended and approved in 2021 to extend the study period from January 2011 to December 2027. The study has undergone continuous annual tracking review, with the most recent approval issued on April 21, 2025 (valid until April 21, 2026). Written informed consent was obtained from all participants or their legal representatives at the time of enrollment. A certified English translation of the relevant approval documents has been submitted with the manuscript. This study was conducted in accordance with the ethical standards of the institutional research committee and the principles of the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis 2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102–111. doi:10.1136/gutjnl-2012-302779

2. Ning C, Huang G, Shen D, et al. Adverse clinical outcomes associated with multidrug-resistant organisms in patients with infected pancreatic necrosis. *Pancreatology*. 2019;19(7):935–940. doi:10.1016/j.pan.2019.09.008
3. Langford BJ, Soucy JR, Leung V, et al. Antibiotic resistance associated with the COVID-19 pandemic: a systematic review and meta-analysis. *Clin Microbiol Infect*. 2023;29(3):302–309. doi:10.1016/j.cmi.2022.12.006
4. Ansari S, Hays JP, Kemp A, et al. The potential impact of the COVID-19 pandemic on global antimicrobial and biocide resistance: an AMR Insights global perspective. *JAC Antimicrob Resist*. 2021;3(2):dlab038. doi:10.1093/jacamr/dlab038
5. China TSCotPsRo. COVID-19 response further optimized with 10 new measures. Available from: https://www.gov.cn/xinwen/2022-12/07/content_5730443.htm. Accessed December 7, 2022.
6. Al Oweidat K, Toubasi AA, Khraisat FA, et al. The impact of COVID-19 on antibiotic resistance and clinical outcomes among critically ill patients. *Am J Infect Control*. 2024;52(5):546–551. doi:10.1016/j.ajic.2023.12.009
7. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Int J Surg*. 2014;12(12):1500–1524. doi:10.1016/j.ijsu.2014.07.014
8. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268–281. doi:10.1111/j.1469-0691.2011.03570.x
9. Craig M, Jernigan D, Laserson K, et al. Antimicrobial resistance at a crossroads: the cost of inaction. *Lancet*. 2024;404(10458):1083–1085. doi:10.1016/S0140-6736(24)01705-7
10. Collaborators GBDAR. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. *Lancet*. 2024;404(10459):1199–1226. doi:10.1016/S0140-6736(24)01867-1
11. Ortega-Paredes D, Larrea-Alvarez CM, Torres-Elizalde L, et al. Antibiotic resistance awareness among undergraduate students in Quito, Ecuador. *Antibiotics*. 2022;11(2):197. doi:10.3390/antibiotics11020197
12. Langford BJ, So M, Raybardhan S, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clin Microbiol Infect*. 2021;27(4):520–531. doi:10.1016/j.cmi.2020.12.018
13. Glance LG, Dick AW, Shippey E, et al. Association between the COVID-19 pandemic and insurance-based disparities in mortality after major surgery among US adults. *JAMA Network Open*. 2022;5(7):e2222360. doi:10.1001/jamanetworkopen.2022.22360
14. Madden G, Bielskas M, Kamruzzaman M, et al. 173. Deciphering COVID-19-Associated Effects on Hospital MRSA Transmission and Social Networks. *Open Forum Infect Dis*. 2021;8(Suppl 1):S104–S106.
15. Smith DRM, Shirreff G, Temime L, Opatowski L. Collateral impacts of pandemic COVID-19 drive the nosocomial spread of antibiotic resistance: a modelling study. *PLoS Med*. 2023;20(6):e1004240. doi:10.1371/journal.pmed.1004240
16. Lo SH, Lin CY, Hung CT, He JJ, Lu PL. The impact of universal face masking and enhanced hand hygiene for COVID-19 disease prevention on the incidence of hospital-acquired infections in a Taiwanese hospital. *Int J Infect Dis*. 2021;104:15–18. doi:10.1016/j.ijid.2020.12.072
17. Cheng G, Wang D, Zhu P, et al. Clinical characteristics of acute pancreatitis patients with multidrug-resistant bacterial infection. *Infect Drug Resist*. 2022;15:1439–1447. doi:10.2147/IDR.S354347
18. Ma X, Wu Y, Li L, et al. First multicenter study on multidrug resistant bacteria carriage in Chinese ICUs. *BMC Infect Dis*. 2015;15:358. doi:10.1186/s12879-015-1105-7
19. Au Yong PSA, Kwa CWX, Chan XHD. Anaesthetic considerations for rationalizing drug use in the operating theatre: strategies in a Singapore hospital during COVID-19. *SN Compr Clin Med*. 2020;2(7):871–873. doi:10.1007/s42399-020-00345-6
20. China TSCotPsRo. Circular of the general office of the national health commission on further strengthening the prevention and control of infections in medical institutions during the epidemic period 2020. Available from: http://www.nhc.gov.cn/yzygj/s7659/202003/0c85996bb762437581e98317365fa01c.shtml. Accessed March 13, 2020.
21. China TSCotPsRo. Circular of the general office of the national health commission on continuous management of the clinical application of antimicrobial agents 2020. Available from: http://www.nhc.gov.cn/yzygj/s3593/202007/8311bda4cf2443dfae4d719f1d0d72da.shtml. Accessed July 23, 2020.
22. Li W, Yang X, Liu C, et al. Multiple impacts of the COVID-19 pandemic and antimicrobial stewardship on antimicrobial resistance in nosocomial infections: an interrupted time series analysis. *Front Public Health*. 2024;12:1419344. doi:10.3389/fpubh.2024.1419344
23. Lin C, Bonsu A, Li J, et al. Application of metagenomic next-generation sequencing for suspected infected pancreatic necrosis. *Pancreatology*. 2022;22(7):864–870. doi:10.1016/j.pan.2022.07.006
24. Lin C, Li J, Liu B, et al. Metagenomic next-generation sequencing, instead of procalcitonin, could guide antibiotic usage in patients with febrile acute necrotizing pancreatitis: a multicenter, prospective cohort study. *Int J Surg*. 2024;110(5):2721–2729. doi:10.1097/JS9.0000000000001162
25. Cai J, Deng X, Yang J, et al. Modeling transmission of SARS-CoV-2 Omicron in China. *Nat Med*. 2022;28(7):1468–1475. doi:10.1038/s41591-022-01855-7