

The Impact of Clinical Pharmacist Consultation on the Treatment of Multi-Drug Resistant Organisms (MDRO) Infections: A Retrospective Observational Study

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Purpose: Multidrug-resistant organisms (MDROs) infections are associated with high mortality in hospitalized patients. Clinical pharmacists play a crucial role in optimizing anti-infection treatment strategies. This study aimed to evaluate the impact of clinical pharmacist consultation on the treatment of inpatients with MDRO infections.

Methods: Patients infected with MDROs who received clinical pharmacist consultation between June 2020 and June 2023 were enrolled. The adoption rate and effectiveness rate of consultation were calculated. Univariate and multivariate logistic regression analyses were conducted to identify factors influencing the effectiveness rate of consultation. Cox regression analysis was employed to estimate the 30-day survival rate post-consultation for patients infected with MDROs, comparing those who adopting pharmacists' suggestions with those who did not.

Results: A total of 620 patients were included. More patients were from the surgical system, especially neurosurgery. The top 3 infection sites were respiratory tract, urinary tract and blood, with prevalent MDROs including Carbapenem-resistant *Klebsiella pneumoniae* (CRKP), Carbapenem-resistant *Acinetobacter baumannii* (CRAB), and Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). Following the implementation of consultation recommendations, patients exhibited significant reductions in temperatures, inflammatory markers, and Sequential Organ Failure Assessment (SOFA) scores. The adoption and effectiveness rate of consultation were 89.67% and 58.71%, respectively. Multivariate analysis showed that there were significant association of liver dysfunction (adjusted OR = 0.331, 95% CI: 0.217–0.504), severity of infection (adjusted OR = 0.292, 95% CI: 0.151–0.562) and adopting pharmacists' suggestions (adjusted OR = 1.987, 95% CI: 1.126–3.507) with the effectiveness rate of consultation. Cox regression analysis revealed a significant difference in the 30-day survival rate between MDRO patients who received pharmacist recommendations and those who did not (HR = 0.422, 95% CI: 0.185–0.963, P = 0.04).

Conclusion: Our research indicated that the involvement of clinical pharmacists could be advantageous for patients afflicted with MDRO infections.

Keywords: multidrug-resistant organisms, infectious diseases, clinical pharmacists, consultations

Introduction

Antimicrobial resistance (AMR) poses a significant threat to human health. According to a recent study published in *The Lancet* in 2022, the Global Antibiotic Resistance Initiative estimated that 4.95 million deaths occurred worldwide in 2019 as a result of antibiotic resistance, including 1.27 million that were directly attributable to the drug.¹ Furthermore, the United States Centers for Disease Control and Prevention (US-CDC) found that the COVID-19 presented one of the greatest threats of the century and exacerbated the “silent pandemic” of AMR.^{2,3} Multi-drug resistant organisms (MDROs) play a key role in spreading various AMR genes and present a substantial challenge in clinical medicine.⁴ With the widespread use and even misuse of antibiotics, the emergence of MDROs has been steadily increasing. The

widespread and often inappropriate use of antibiotics has led to a steady increase in the emergence of MDROs, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and multidrug-resistant Gram-negative bacilli (eg, carbapenemase-producing Enterobacteriaceae).⁵ Patients infected with these MDROs often present with more severe conditions, have limited treatment options, and face higher mortality rates.

In hospital settings, effective treatment strategies are crucial for improving the prognosis of patients with MDRO infections.⁶ Under traditional healthcare models, physicians primarily rely on their clinical experience and limited antimicrobial susceptibility testing data to formulate anti-infective treatment plans. However, factors such as drug–drug interactions, individual patient variability (eg, renal function, liver function, age, and other factors affecting drug metabolism), and the complex resistance mechanisms of MDROs can limit the effectiveness of therapy. Clinical pharmacists, as integral members of the healthcare team, possess unique expertise in medication therapy management.⁷

In recent years, several Chinese policy documents have emphasized that clinical pharmacists should participate in the consultations for complex cases to provide treatment options or adjusting the drug regimen and share responsibility with physicians for medication.⁸ Previous literature has indicated that pharmacists' involvement in multidisciplinary teams (MDT) has become an emerging trend. This enables them to offer pharmaceutical expertise in clinical medication advice across various disciplines, including anti-infection, anticoagulation, gastroenterology, nutrition, and oncology.^{2,3,9,10} In particular, clinical pharmacists were required to provide individualized recommendations in anti-infection consultation, which has become an integral part of clinical pharmacist consultation.¹¹ However, there is limited research on this topic. Existing studies primarily focus on the clinical pharmacists' anti-infection experience in the field of obstetrics and gynecology.¹² Therefore, conducting a systematic retrospective observational study to explore the impact of clinical pharmacists' consultations on the treatment of MDRO infections and the factors influencing the effectiveness of consultations is of great practical significance for clarifying the role of clinical pharmacists within the MDRO infection treatment team and providing a scientific basis for clinical practice.

This single-center retrospective study aims to evaluate the impact of clinical pharmacists' involvement in infectious disease consultations and to identify factors influencing the effectiveness of these consultations. The findings of this research may serve as a valuable reference for clinical pharmacists seeking to enhance their practice in the field of pharmaceutical care.

Methods

We followed the STROBE Statement for cohort studies to conduct this study.

Study Design and Setting

This study was conducted at Tongji University Affiliated East Hospital, a 2000-bed comprehensive hospital located in Shanghai, China. In accordance with the ethical standards of the Helsinki Declaration, the Medical Ethics Committee of Tongji University Affiliated East Hospital approved this study design with approval number 2020173. It was a retrospective cohort study with an informed consent exemption. This study did not involve sensitive data, including personal information, privacy concerns, biological samples, or any elements that could pose risk or harm to the subjects. Consequently, the ethics committee determined that obtaining informed consent from participants was not necessary. For humanitarian reasons, clinical pharmacists fulfilled all consultation requests sent by clinicians; therefore, this study did not set the control group.

Participants

In this study, patients with infection who were consulted by clinical pharmacists from June 2020 to June 2023 were included. The exclusion criteria were as follows: (1) patients with non-MDRO infections; (2) patients received multidisciplinary consultations for complex cases; (3) patients for whom physicians requested consultation for the use of special antibiotics (eg, Carbapenems, Vancomycin, Tigecycline); and (4) patients discharged or died within 3 days after application of the clinical pharmacist's treatment plan.

Clinical Pharmacists' Consultation Intervention

The study consultation intervention was described as follows: (1) Physicians sent consultation requests for MDRO infections to the clinical pharmacy department through the workstation; (2) Clinical pharmacists on the schedule were responsible for these consultations, and all clinical pharmacists had undergone national standardized training and had been engaged in clinical work for more than 5 years; (3) Clinical pharmacists made a comprehensive assessment of the infection status of the patient according to the clinical symptoms, laboratory examination, etiology examination and imaging examination results. Treatment recommendations were given based on patient characteristics (such as age, gender, liver and kidney function, underlying diseases, etc.), current best clinical evidence (evidence-based guidelines) and drug characteristics (antimicrobial profile, pharmacokinetics/pharmacodynamic characteristics, adverse reactions, drug interactions, antimicrobial variety, dose, frequency of administration and course of treatment); (4) Physicians made the final decision on whether or not to adopt and implement these recommendations.

Physicians would evaluate the recommendations based on their own clinical judgment, the patient's overall condition, and any other relevant factors specific to the case. In some instances, if there were concerns about the feasibility or safety of the proposed treatment, or if there were alternative treatment options that the physicians deemed more appropriate, they might choose not to follow the pharmacist's recommendations.

Variables and Outcomes

In this investigation, the exposure factors under consideration were the extent to which physicians implemented the consultation recommendations and adhered to the anti-MDRO infection protocols proposed by clinical pharmacists. The treatment regimens outlined in the consultation documents were cross-referenced with what physicians actually prescribed, and instances of full or partial concordance were deemed indicative of acceptance of the consultation recommendations. The adoption rate was calculated as the proportion of accepted recommendations to the total requests made. The primary outcome was the proportion of patients who were effectively treated for anti-MDRO infection after physicians adopting consultation suggestions from pharmacists, which were regarded as effectiveness rate. The efficacy was evaluated 3 to 7 days after starting the recommended anti-infection regimen, with a 30-day follow-up period after consultation.

We evaluated the therapeutic efficacy following the Guiding Principles for the Clinical Application of Antimicrobial Agents (2015 edition).¹³ Effectiveness was operationally defined as the recovery or improvement in patients' symptoms, signs, laboratory findings, and imaging results, with the bacteria transitioning to colonization and asymptomatic status. Any lack of improvement or worsening within 72 hours after treatment was deemed invalid. The severity of infection and sepsis were determined on the basis of physicians' clinical judgment.

Data Collection and Management

The researchers constructed a comprehensive database to document pertinent information, including patients' demographic characteristics (age, sex), medical history (diagnosis, comorbidities), organ function (liver and kidney), laboratory parameters (temperature, infection indicators like WBC, CRP, PCT), pre- and post-treatment imaging findings, infection sites, bacterial culture results, drug susceptibility testing, distribution of patients across departments, infection severity, consultation duration, and clinical pharmacists' specialties. The data were extracted from inpatient electronic records and Hospital Information System (HIS). All procedures were performed independently by two pharmacists, and the validity and reliability of the assessments were confirmed by the third pharmacist.

Statistical Analysis

Statistical analysis was conducted using SPSS 25.0 software (SPSS Inc., Chicago, IL, USA) for Windows. Pareto charts were used to demonstrate the most common distribution of infection sites and MDROs in this study. Quantitative data were presented as mean \pm standard deviation (SD), and qualitative data was given as number and percentage. To compare patient groups before and after treatments, *T*-test was used. Frequency, rate, or proportion was utilized to count data, which were then analyzed by a chi-square test. Kaplan–Meier survival curves were employed to analyze the survival status of the patients with CRKP, CRAB, CRPA, MRSA, and VRE infection. Cox proportional hazards regression analysis was performed to assess survival outcomes.

Logistic regression analysis was conducted to investigate the association of the adherence to consultation advice and the effectiveness rate of anti-infection treatment, after adjustment for probable causes of both exposure and outcome. The covariates considered included age, sex, comorbidity, kidney and liver function, hypoproteinemia, type of departments, severity of infection and major of clinical pharmacists. Given the high correlation between patients' temperatures, inflammatory markers, site of infection, number of infection sites, and disease severity with the severity of infection, we exclusively incorporated the severity of infection into the multivariate analysis model. All statistical tests were two-sided and performed at the 0.05 level of significance.

Results

Characteristics

A total of 1298 patients received anti-infection consultations between June 2020 and June 2023. After applying the inclusion and exclusion criteria, 620 patients infected with MDROs were enrolled in the final analysis (Figure 1). The characteristics of consultations and patients infected with MDROs were shown in Table 1. Most of the enrolled patients were over 65 years old (63.87%), and less than half of them were male (46.29%). About 85.81% of patients received consultation 7 days after admission, and 21.94% received consultations from professional pharmacists. Patients with abnormal kidney function and liver function accounted for 30.81% and 30.97%, respectively. The proportion of patients with complications was 81.61%, and with hypoalbuminemia was 86.13%.

Clinically, 40.48% of the patients were with fever symptoms, 90.65% with increased inflammatory indicators (eg, WBC count, CRP, PCT), 67.74% with imaging examination results (such as X-ray examination report, CT examination report, B ultrasound examination report, etc.), and 96.45% with etiological evidence (ie, culture of pathogenic microorganisms and drug sensitivity test). In addition, 20.65% of the patients had multiple site infection. As for the severity of infection, sepsis and septic shock accounted for less than 10%.

Adoption Rate and Effectiveness Rate of Consultation

Among 620 MDRO infection consultations, physicians fully adopted clinical pharmacists' recommendations in 526 cases and partially adopted them in 30 cases, resulting in an overall adoption rate of 89.67% (556/620 cases). According to our definition of effectiveness, 364 cases were effective; hence, the total effectiveness rate was 58.71% (364/620 cases), as detailed in Table 1.

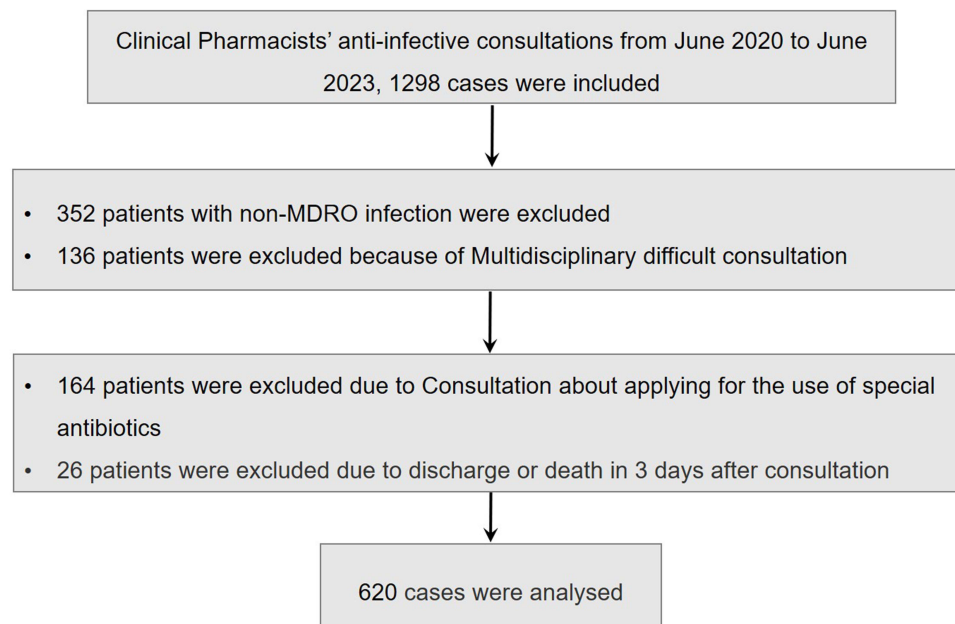


Figure 1 The flow chart of the study.

Table 1 Analysis of the Factors That Impact the Efficacy of Anti-Infection Treatment in Post-Consultation (N = 620)

Variable	Total (n = 620)		
	Effective Group, n (%) (n = 394)	Ineffective Group, n (%) (n = 226)	P value
Sex			0.347
Female	206(52.28)	127(56.19)	
Male	188(47.72)	99(43.81)	
Age (mean ± SD, y)			0.094
<65	152(38.58)	72(31.86)	
≥65	242(61.42)	154(68.14)	
Time of consultation			0.239
Within 7 days of admission	51(12.94)	37(16.37)	
More than 7 days of admission	343(87.06)	189(83.63)	
Type of departments*			0.035
Internal medicine system	106(26.90)	75(33.19)	
Intensive care unit system	103(26.14)	69(30.53)	
Surgery system	185(46.95)	82(36.28)	
Major of clinical pharmacists			0.471
Anti-infection	90(22.84)	46(20.35)	
Non- anti-infection	304(77.16)	180(79.65)	
With comorbidity	317(80.46)	189(83.63)	0.327
Kidney dysfunction	116(29.44)	75(33.19)	0.331
Liver dysfunction*	97(24.62)	95(42.04)	0.000
Hypoalbuminemia	334(84.77)	200(88.50)	0.198
With fever symptoms	169(42.89)	82(36.28)	0.107
With elevated inflammatory markers	364(92.39)	198(87.61)	0.051
With imaging examination results	264(67.01)	156(69.03)	0.604
With etiological evidence	383(97.21)	215(95.13)	0.184
Number of infection site			0.170
<2	306(77.66)	186(82.30)	
≥2	88(22.34)	40(17.70)	
Severity of the infection *			0.000
Non-sepsis	376(95.43)	191(86.73)	
Sepsis/ Septic shock ^a	18(4.57)	35(13.27)	
Adopting consultation suggestions*			0.004
Yes	364 (92.39)	192 (84.96)	
No	30 (7.61)	34 (15.04)	

Notes: * indicated $P \leq 0.05$. ^a indicated that 3 shock patients in sepsis/septic shock group Total exceeds or fall short of 100% where rounding of decimal fractions occurred.

Factors Associated with the Effectiveness Rate of Consultations

To explore factors influencing the effectiveness of anti-infection treatment in patients after consultation, effective group (n = 394) were compared to ineffective group (n = 226). Both univariate analysis and subgroup analyses of the non-sepsis group and sepsis/septic shock group showed no statistically significant differences ($P > 0.05$) in sex, age, time of consultation, major of clinical pharmacists, comorbidities, kidney dysfunction, hypoalbuminemia, fever symptoms, elevated inflammatory markers, imaging examination results or etiological evidence between the effective and ineffective groups ($P > 0.05$) (Tables 1 and S1). The type of department showed a statistically significant difference in the overall analysis ($P = 0.035$), with disparities in the distribution of internal medicine system, intensive care unit (ICU), and surgery systems between effective and ineffective groups, though no significant differences were observed in subgroup analyses ($P > 0.05$) (Tables 1 and S1).

Liver dysfunction demonstrated statistically significant differences between effective and ineffective groups in the non-sepsis group ($P = 0.000$), sepsis/septic shock group ($P = 0.000$), and overall analysis ($P = 0.000$), with a higher proportion of treatment failure in patients with liver dysfunction. Infection severity was significantly associated with treatment outcomes in the overall analysis ($P = 0.000$), as sepsis/septic shock patients had a higher rate of treatment failure compared to non-sepsis patients. Adoption of consultation suggestions showed statistically significant differences in the non-sepsis group ($P = 0.000$), sepsis/septic shock group ($P = 0.043$), and overall analysis ($P = 0.004$), with higher treatment efficacy in patients treated by physicians who adopted the consultation suggestions (Tables 1 and S1).

On multivariate analysis, liver dysfunction, severity of infection, and adopting consultation suggestions were associated with the effectiveness rate of consultations ($p < 0.05$). Liver dysfunction (adjusted OR = 0.331, 95% CI: 0.217–0.504) and severe infection (adjusted OR = 0.292, 95% CI: 0.151–0.562) had a negative effect on the treatment outcome of patients with MDRO infections, while adopting consultation suggestions could improve the prognosis of patients (adjusted OR = 1.987, 95% CI: 1.126–3.507), as detailed in Table 2.

Departments of Patients Infected with MDROs

As shown in Figure 2, patients infected with MDROs who received consultation were from 27 clinical departments, of which neurosurgery patients were the highest proportion (104, 16.77%), followed by central intensive care unit (97, 15.65%) and oncology (49, 7.90%). Furthermore, more patients came from the surgery system (267, 43.06%) as compared to the internal medicine system (181, 29.19%) and intensive care unit system (172, 27.74%).

Distribution of Infection Sites and MDROs

As shown in Figure 3A, the patients with respiratory tract infection accounted for nearly half (374, 48.57%), followed by those with urinary tract infection (162, 21.04%), blood infection (94, 12.21%). The top remaining sites for infection were abdominal infection (34, 4.42%), skin or soft tissue infection (26, 3.38%) and intracranial infection (26, 3.38%).

Regarding the composition of the MDROs in Figure 3B, a total of 620 MDROs isolates were detected, the top 3 concerns CRKP (296, 47.74%), CRAB (150, 24.19%) and CRPA (70, 11.29%), all of which were carbapenem-resistant Gram-negative bacilli. Additionally, the most common multidrug-resistant positive bacteria were related to MRSA (44, 7.1%) and VRE (10, 1.61%).

Inflammatory Indicators and SOFA Score

As for the inflammatory measures and SOFA scores, Table 3 showed them. After consultation suggestions regarding treatment regimen were adopted and implemented for 3 days, the temperatures, inflammatory indicators (ie, WBC counts, CRP, PCT) and SOFA scores of patients were significantly lower than those before consultation ($p < 0.01$). Moreover, the number of patients with normal temperatures, WBC counts, CRP and PCT after 3 days of treatment was significantly increased (<0.01).

Table 2 Multivariate Analysis for the Factors Influencing the Effective Rate of Consultations

Variables	Adjusted OR	95% CI	P-value
Type of departments			0.296
Intensive care unit system vs Internal medicine system ^a	1.017	[0.641, 1.616]	
Surgery system vs Internal medicine system ^a	1.359	[0.886, 2.082]	
Liver dysfunction*			
Yes vs No ^a	0.331	[0.217, 0.504]	0.000
Severity of infection*			
Sepsis vs Non-sepsis ^a	0.292	[0.151, 0.562]	0.000
Adopting consultation suggestions*			
Yes vs No ^a	1.987	[1.126, 3.507]	0.018

Notes: * indicated $P \leq 0.05$. ^a Reference group.

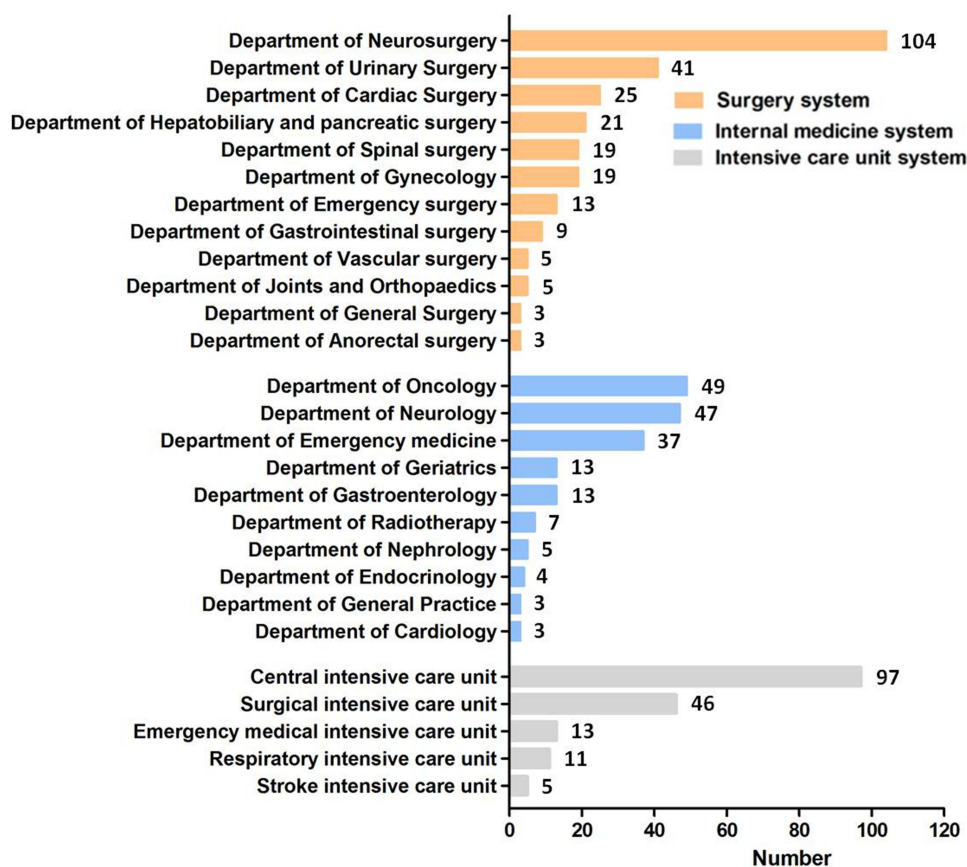


Figure 2 Departments of patients infected with MDROs in clinical pharmacists' consultation cases (N = 620).

Survival Analysis of the Patients Infected with MDROs

A total of 516 patients with MDRO infections were analyzed (Figure 4). There were 296, 150, 70, 44 and 10 patients with CRKP, CRAB, CRPA, MRSA and VRE infection, respectively. The study found that CRKP infection had impact on patients' short-term survival, with survival rates at 4 days, 15 days, and 30 days being 97.7%, 93.6%, and 92.9%, respectively. Similarly, CRAB-infected patients with survival rates at 4 days, 15 days, and 30 days were 99.3%, 94%, and 93.3%, respectively. The 4-, 15-, 30-day survival rates were 98.6%, 91.4% and 91.4% for CRPA-infected patients. For the MRSA and VRE-infected patients, the survival rates at 4 days, 15 days, and 30 days were 100%, 90.24%, 90.24%, and 100%, 90.91%, 90.91%, respectively. No significant difference was found in 4-day, 15-day, and 30-day survival rates among 5 groups (Figure 4A). Our study showed that the survival rates for ICU patients where pharmacist recommendations were accepted and rejected at 4 days, 15 days, and 30 days were 93.3%, 84%, 82.7%, and 100%, 81.8%, 72.7%, respectively (Figure 4B). Additionally, the survival rates for MDRO-infected patients whose cases had pharmacist recommendations that were either accepted or rejected at 4 days, 15 days, and 30 days were 95.71%, 90.71%, 87.50%, and 90%, 76.67%, 70.00%, respectively (Figure 4C).

Cox risk model analysis showed that ICU admission (HR = 2.439, 95% CI: 1.292–4.605, $p = 0.006$) and adherence to pharmacists' recommendations (HR = 0.422, 95% CI: 0.185–0.963, $p = 0.04$) were significantly associated with 30-day survival, while age (below or above 65 years) (HR = 0.824, 95% CI: 0.416–1.634, $p = 0.579$) and comorbidities (with/without) (HR = 1.176, 95% CI: 0.531–2.604, $p = 0.689$) did not show a significant effect on survival in this study (Table 4).

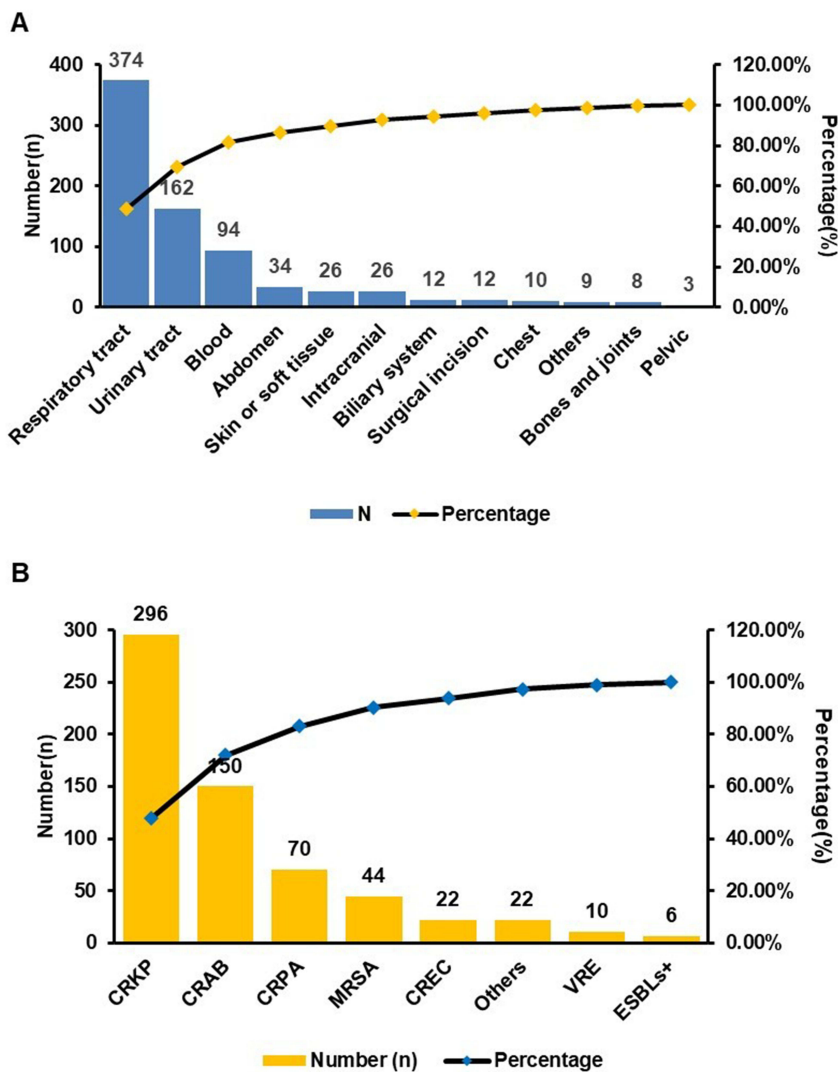


Figure 3 Pareto diagram of infection site (N = 770) and MDROs distribution (N = 620). **(A)** Pareto diagram of infection site distribution. **(B)** Pareto diagram of MDROs distribution.
Abbreviations: CRKP, Carbapenem-resistant Klebsiella pneumoniae; CRAB, Carbapenem-resistant Acinetobacter baumannii; CRPA, Carbapenem-resistant Pseudomonas aeruginosa; MRSA, Methicillin-resistant Staphylococcus aureus; CREC, Carbapenem-resistant E. coli; ESBLs+, Extended spectrum beta-lactamases positive; VRE, Vancomycin resistant enterococcus.

Discussion

Pharmacist consultation serves as a pivotal component of multidisciplinary care, enabling clinical pharmacists to optimize antimicrobial therapy through evidence-based recommendations.^{14,15} Prior studies have shown that pharmacist intervention can improve the treatment outcomes,^{16–19} reduce the incidence of adverse reactions and drug - related problems,^{20,21} and lower

Table 3 Inflammatory Indicators and SOFA Score of the Consultation Patients

	Before Treatment	3d After Treatment	P-value
Temperature (°C, n = 620)			
Normal	369(59.52%)	419(67.58%)	0.003
Abnormal	251(40.48%)	201(32.42%)	
Mean ± SD	37.77 ± 1.15	37.15 ± 0.66	0.000

(Continued)

Table 3 (Continued).

	Before Treatment	3d After Treatment	P-value
WBC ($\times 10^9/L$, n = 620)			
Normal	173(27.90%)	263(42.42%)	0.000
Abnormal	447(72.10%)	357(57.58%)	
Mean \pm SD	13.11 \pm 5.71	10.06 \pm 3.75	0.000
CRP (mg/L, n = 603)			
Normal	52(8.62%)	99(16.42%)	0.000
Abnormal	551(91.38%)	504(83.58%)	
Mean \pm SD	92.58 \pm 55.79	64.54 \pm 45.0	0.000
PCT (mg/mL, n = 571)			
Normal	31(5.43%)	57(9.98%)	0.004
Abnormal	540(94.57%)	514(90.02%)	
Mean \pm SD	2.30 \pm 2.13	1.01 \pm 0.75	0.000
SOFA Score, (mean \pm SD, n = 172)	2.65 \pm 1.63	1.90 \pm 1.22	0.000

Abbreviations: WBC, white blood cell counts; CRP, C-reactive protein; PCT, procalcitonin; SOFA, Sequential organ failure assessment.

healthcare costs.^{22,23} However, some studies have indicated that the benefits of pharmacist intervention were not obvious.^{24,25} In this retrospective study, we evaluated the impact of clinical pharmacist consultation intervention involved in the treatment of MDRO infections, and investigated the variables influencing the success of such consultations.

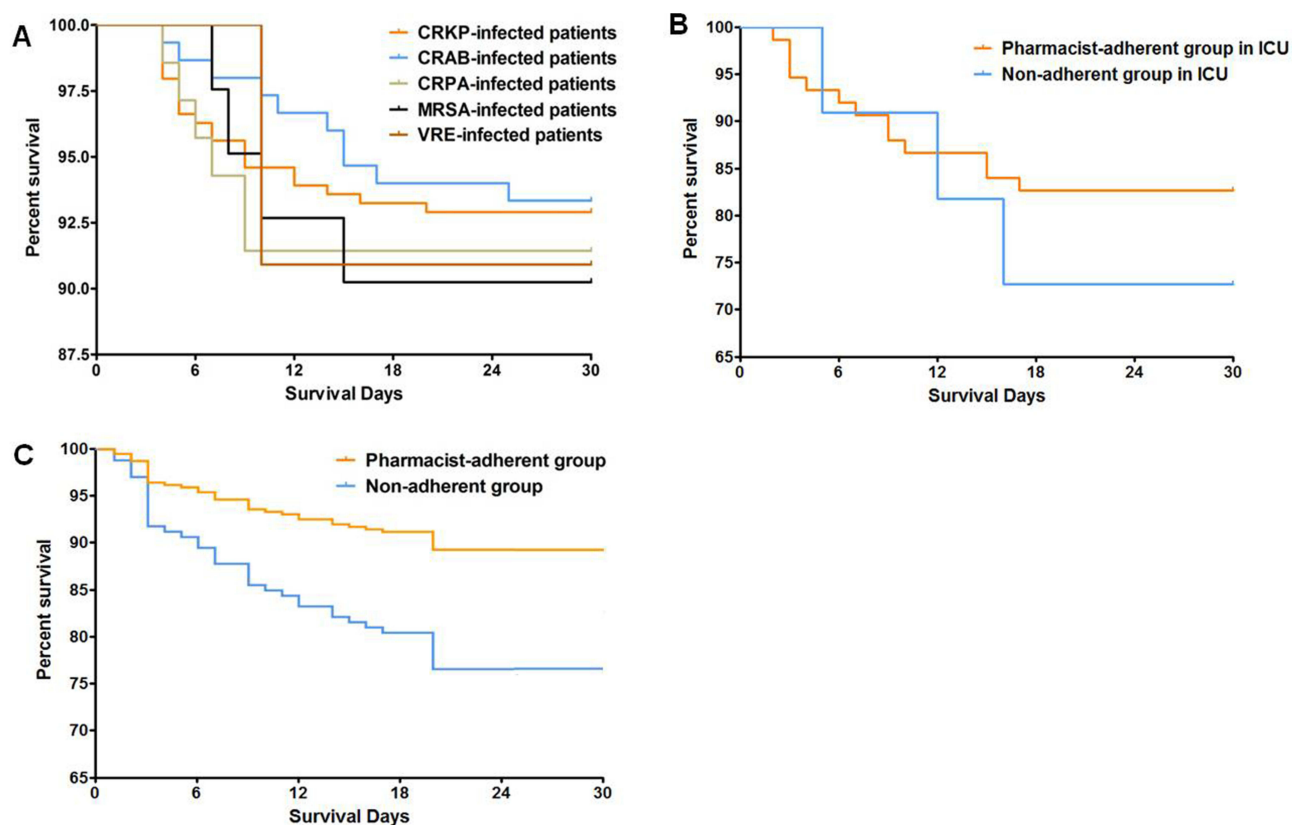


Figure 4 Survival curves within 30-day were analyzed for patients infected with MDROs among the consultation patients. **(A)** Survival curves within 30-day were analyzed for patients infected with the CRKP, CRAB, CRPA, MRSA, and VRE among the consultation patients. **(B)** 30-day survival curves were analyzed for ICU patients based on whether pharmacist recommendations were accepted or rejected. **(C)** Comparison of 30-day survival curves between MDRO-infected patients whose cases had pharmacist recommendations that were either accepted or rejected.

Table 4 Risk Factors for Survival in Cox Model Analysis

	HR	95% CI	p value
Age (below or above 65 years)	0.824	0.416–1.634	0.579
Co-morbidities (with /without)	1.176	0.531–2.604	0.689
ICU status (Yes / No)	2.439	1.292–4.605	0.006
Pharmacist-adherent group (Yes / No)	0.422	0.185–0.963	0.04

Abbreviations: CI, confidence interval; HR, hazard ratio.

MDRO infections remain a critical challenge in hospitals, particularly in intensive care units (ICUs), where prevalence rates can exceed 50%.²⁶ This study revealed that more patients infected with MDROs receiving consultations by the clinical pharmacist were from the Department of Neurosurgery (16.77%), followed by ICU (15.65%) and oncology (7.90%) (Figure 2). Furthermore, the surgery system accounted for the highest proportion of patients at 43.06% (Figure 2). This discrepancy may reflect the complex clinical profiles of neurosurgical patients, including prolonged antibiotic exposure, invasive procedures, and suboptimal postoperative antimicrobial stewardship.²⁷ Consistent with global trends, respiratory tract infections (48.57%) dominated MDRO cases (Figure 3A), with CRKP, CARB, CRPA, MRSA, and VRE being the most prevalent pathogens (Figure 3B).^{28,29} Inflammatory markers such as WBC, CRP, and PCT are widely used to monitor infection severity and therapeutic response.³⁰ Our data demonstrated significant reductions in these biomarkers post-treatment (Table 3), aligning with studies reporting declines within 3–7 days of anti-infective therapy.¹² However, Schutz et al observed no significant differences in inflammatory markers between antibiotic-treated and untreated cohorts,³¹ underscoring the complexity of biomarker interpretation in heterogeneous patient populations. Additionally, improvements in SOFA scores (2.65 ± 1.63 vs 1.90 ± 1.22 , $p < 0.001$) and temperature normalization (59.52% vs 67.58%, $p = 0.003$) post-treatment suggested the alleviation of infectious symptoms (Table 3). Meanwhile, the results suggested that effective clinical interventions (eg, timely empirical or targeted antimicrobial therapy) may have mitigated the immediate mortality risk associated with these resistant organisms. Additionally, the host factors including comorbidities, infection site, and severity may play a more dominant role in short-term outcomes than resistance profiles alone. Furthermore, although the survival rate was higher in the pharmacist-adherent group compared to the non-adherent group for ICU patients, no statistically significant difference was observed between the two groups ($P > 0.05$) (Figure 4B). The observed trend of higher survival rates in ICU patients receiving pharmacist-adherent care raised important considerations for antimicrobial stewardship in critical care settings. Notably, this is similar to the findings of J Zhang et al demonstrating pharmacist interventions reduced MDRO mortality in ventilated patients.³² Cox proportional hazards regression demonstrated that receiving pharmacist advice was significantly associated with reduced mortality risk ($p = 0.04$) (Figure 4C). Additionally, we incorporated age (below or above 65 years), presence or absence of comorbidities, and ICU status (Yes/No) as dichotomous variables into a univariate Cox proportional hazards model (Table 4). The results indicated that only ICU status (Yes/No) was an important risk factor for patient survival. ($p = 0.000$). This finding contextualizes our earlier subgroup analysis: The non-significant survival trend in ICU patients (Figure 4B) likely reflects competing risks inherent to critical illness. And the overwhelming impact of organ dysfunction in ICU settings may attenuate the measurable benefit of pharmaceutical interventions. This dichotomy underscores the necessity of early pharmacist involvement before progression to multiorgan failure. Additionally, the non-significance of age and comorbidities may be due to insufficient sample size and unadjusted confounders, such as specific disease types.

Most clinical pharmacists in China primarily manage clinical anti-infective treatment, yet the impact of pharmacist intervention in treating MDRO infections remains underexplored.³³ In our study, the consultation adoption rate (89.67%, 556/620) exceeded rates reported in earlier infectious disease studies,^{34,35} likely due to heightened MDRO complexity necessitating multidisciplinary input. However, the effectiveness rate (58.71%, 364/620) was comparatively lower, potentially reflecting the enrollment of refractory cases with prolonged hospitalization, polymicrobial infections, and organ dysfunction.^{36,37} The discrepancy in efficacy rates underscores the need for standardized outcome metrics in pharmacist intervention research.

Multivariate regression analysis identified liver dysfunction, severity of infection, and adherence to recommendations were independent variables influencing the efficacy of consultation in the treatment of patients with MDRO infections

(Table 2). These results were consistent with previous research findings.³⁸ The efficacy of therapy was influenced by multiple factors, primarily encompassing the pharmacological properties of the drug, the physiological and pathological condition of the patient, and the susceptibility of the pathogens to the medication.³⁹ In our study, it was observed that patients with liver dysfunction exhibited a diminished response to anti-infection treatment (adjusted OR = 0.331, 95% CI: 0.217–0.504). Liver impairment compromises antibiotic metabolism (eg, β -lactams, vancomycin), necessitating dose adjustments to avoid toxicity or subtherapeutic levels.⁴⁰ Previous studies has shown that the severity of infection was related to the prognosis of patients, and patients with severe infection had worse outcome.^{41,42} Sepsis severity, a well-established prognostic marker, likely reflects cumulative organ damage and immunoparalysis.^{43,44} The low proportion of sepsis/septic shock cases (8.5%) in our study may limit the comprehensive evaluation of consultation efficacy in critically ill patients. Although subgroup analyses demonstrated a significant association between infection severity and treatment outcomes, the small sample size likely reduced statistical power. Future multicenter studies with larger cohorts are needed to validate the specific impact of clinical pharmacists' interventions in critically ill populations. The significance of department type observed in the univariate analysis did not translate to a significant impact on consultation effectiveness in the multivariate model and subgroup analyses. This discrepancy may be explained by the homogeneity of the consulted cases, all of whom were patients with severe infections.

In the course of our study, the implementation of consultation recommendations resulted in a 1.987-fold increase in the efficacy of anti-infective treatment (Table 2). This finding underscored the significance of clinical pharmacist consultation for patients infected with MDROs. The incidence of MDRO infections has been linked to inappropriate or unnecessary antibiotic use in clinical settings.^{45,46} Nevertheless, clinical pharmacist intervention has shown promise in curbing antibiotic usage and encouraging judicious prescribing practices. Numerous studies have shown that clinical pharmacists were essential members of the antimicrobial team, contributing to guideline development, prescription management, program evaluations, patient reviews, and optimizing antimicrobial therapy.^{47–51} This highlights the vital importance of clinical pharmacists in managing infectious diseases, particularly in providing care to MDRO infected patients.

Limitations

There were some limitations in our study as follows: First of all, this was a single-center, retrospective study, which may have led to selective bias. However, our hospital is a comprehensive tertiary hospital in China, and patients from all over the country seek their medical services. Secondly, the lack of strict control for baseline balance between the exposed and control groups may have biased the study results. Finally, the results were still preliminary due to the small sample size for clinical pharmacist consultation intervention on treatment outcomes. Therefore, large-scale, multicenter prospective studies are needed to expand the sample size, especially in critically ill patients, and to include additional clinical outcome measures (eg, length of stay in the ICU, need for organ support) to more fully evaluate consultation outcomes.

Conclusions

Our study evaluated the effectiveness of clinical pharmacist consultations in the management of MDRO infections and investigated the factors impacting the success rate of these consultations. Our findings demonstrated a correlation between consultation effectiveness and patients' liver dysfunction, infection severity, and adherence to consultation recommendations by clinicians. These results suggested that clinical pharmacist interventions through consultations could be advantageous for patients with MDRO infections.

Acknowledgments

The authors wish to thank the staff of the Pharmacy Department for supporting the study.

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

No funding sources.

Disclosure

The authors declare no conflicts of interest in this work.

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