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Original Article

Bundled management improves clinical outcome and reduces healthcare cost in multidrug-resistant bacterial infections: a retrospective study

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Abstract: Objective: To evaluate the effectiveness of a bundled management intervention for infection prevention, antibiotic use optimization, and clinical and economic outcomes for patients with multidrug-resistant bacterial infections. Methods: This retrospective study included 130 patients with multidrug-resistant bacterial infections. Data on knowledge awareness, hand hygiene compliance, infection incidence, clinical outcomes, antibiotic use, hospital stay, and costs were collected through questionnaires, observations, and medical records to evaluate the intervention's effectiveness. Results: The bundled management intervention significantly improved knowledge awareness, hand hygiene compliance, and adherence to infection control practices among patients, caregivers, and healthcare staff. It reduced MDR infection rates (3.07% vs. 15.38%), mortality (3.08% vs. 12.31%), and antibiotic overuse while lowering hospital costs and treatment duration compared to standard care ($P < 0.05$). Conclusion: The bundled management approach effectively enhanced infection prevention, optimized antibiotic use, improved clinical outcomes, and reduced healthcare costs, offering a robust strategy for managing MDR bacterial infections.

Keywords: Bundled management, multidrug-resistant bacterial infections, healthcare costs

Introduction

Multidrug-resistant bacterial infections have emerged as one of the most urgent issues in contemporary healthcare. They are likely to undermine decades of progress in the field of infection control and antimicrobial treatment [1]. These multidrug-resistant pathogens are associated with elevated morbidities, mortalities and prolonged hospitalization duration [2, 3]. This global rise in multidrug-resistant organisms (MDROs) is driven by excessive and improper antibiotic use, ineffective infection control measures, and the intra-facility transmission of resistant strains [4]. Current infection control measures are increasingly insufficient to curb this public health threat, with an urgent need for novel and effective strategies.

Bundled management has emerged as a promising model in response to this challenge. It integrates multiple evidence-based measures into a unified program to address the burden of MDROs [5-9]. In contrast to isolated interventions, such as antimicrobial stewardship or environmental decontamination alone, bundled management addresses the multifactorial mechanisms underlying MDRO transmission and infection [10, 11]. Evidence has shown that, when appropriately implemented, the bundled method significantly reduces infection rates and improves clinical outcomes, particularly in high-risk settings like the ICU [12-16]. Nonetheless, despite these advances, the optimal design and application of bundled management remain inadequately defined, and most of the available protocols overlook the heteroge-

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neity in pathogen distribution, healthcare resources, and patient populations.

This study aimed to address these limitations by evaluating a customized bundled management protocol tailored to the epidemiologic and clinical characteristics of our single-center setting. Using real-time monitoring data and microbial resistance patterns, intervention plans were dynamically adjusted to maximize protocol effectiveness in our healthcare center.

Materials and methods

Case selection

This retrospective study included 130 patients diagnosed with multidrug-resistant (MDR) bacterial infections at Fengcheng Hospital between January 2022 and December 2024. Patients were stratified into two groups according to the intervention they received. The control group (n = 65 cases) received standard medical care and routine nursing interventions, whereas the experimental group (n = 65 cases) received a bundled management protocol in addition to standard care. The study was approved by the Ethics Committee of Fengcheng Hospital.

To minimize possible confounding effects, baseline characteristics of patients were carefully evaluated, including season of admission, age, body weight, as they may affect infection outcomes and antibiotic use. No significant differences were observed in these variables between the two groups (all $P > 0.05$), ensuring adequate baseline comparability.

Inclusion criteria: (1) Patients aged ≥ 18 years who were diagnosed with, or at risk of developing, MDR bacterial infections confirmed by clinical and microbiological examination [17]. MDR infection was defined as infection caused by bacterial pathogens resistant to at least one agent in three or more antimicrobial classes, including carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and extended-spectrum β-lactamase (ESBL)-producing organisms; (2) Hospitalization for at least 7 days; (3) Patients or their families who were willing and able to attend education sessions and comply with the bundled management guidelines.

Exclusion criteria: (1) Presence of immunosuppressive conditions, such as advanced malignancies or organ transplantation, which might interfere with the results of the infection control program; (2) Incomplete medical records or insufficient data for analysis; (3) Discharge or transfer to another facility during the intervention period; and (4) Inability or unwillingness to comply with the intervention protocols, including follow-up assessments.

Data collection

Demographic characteristics, clinical information, infection-related records, and cost data were extracted from medical charts and hospital information systems. In addition, patients and caregivers were interviewed using structured questionnaires to assess their knowledge of MDR bacterial infections and hand hygiene practices. Hand hygiene adherence among patients and caregivers was evaluated by direct observation; the hand hygiene compliance rate was calculated as the proportion of correctly performed hand hygiene actions (e.g., handwashing with soap or use of alcohol-based hand rub) at indicated moments (e.g., before and after patient contact or contact with potentially contaminated objects) divided by the total number of observed opportunities, expressed as a percentage.

To evaluate the bundled management strategy, information related to the intervention process was also documented, including: (1) Education exposure (education provided to patients and caregivers regarding MDR infection, infection-control measures, and correct hand hygiene); (2) Hand hygiene reinforcement (follow-up reminders and supervision to promote correct hand hygiene behaviors); (3) Antibiotic stewardship practices (evidence-based antibiotic selection and duration, with preference for narrow-spectrum agents when appropriate, supported by periodic review of prescriptions); and (4) Infection-control implementation by healthcare staff (personal protective equipment (PPE) use, environmental cleaning, and patient isolation procedures, supported by training and supervision).

Study outcomes were predefined. The primary outcome was the occurrence of MDR bacterial infection, confirmed using clinical and microbi-

Table 1. Comparison of baseline characteristics between the control group and observation group

	Control group	Observation group	t/X^2	p
Age, years (mean ± SD)	64.00 ± 26.89	58.89 ± 34.89	0.935	0.352
Male sex, n (%)	39 (60.0)	41 (63.1)	0.130	0.718
Body mass index, kg/m^2 (mean ± SD)	23.77 ± 2.95	24.05 ± 2.13	0.620	0.536
Smoking history, n (%)	21 (32.3)	24 (36.9)	0.306	0.580
Alcohol consumption, n (%)	18 (27.7)	20 (30.8)	0.149	0.700
Hypertension, n (%)	29 (44.6)	31 (47.7)	0.124	0.725
Diabetes mellitus, n (%)	22 (33.8)	24 (36.9)	0.135	0.714
Chronic kidney disease, n (%)	12 (18.5)	10 (15.4)	0.219	0.640
Chronic obstructive pulmonary disease, n (%)	15 (23.1)	17 (26.2)	0.166	0.684
Cardiovascular disease, n (%)	19 (29.2)	21 (32.3)	0.144	0.704
Immunosuppression, n (%)	9 (13.8)	11 (16.9)	0.236	0.627

ological evidence, and categorized by pathogen type, including carbapenem-resistant CRE, vancomycin-resistant VRE, methicillin-resistant MRSA, and ESBL-producing bacteria. Secondary indicators included (I) clinical outcomes (favorable outcome and mortality); (II) behavioral and process indicators (patient/caregiver knowledge and hand hygiene compliance, and staff compliance with infection-control measures such as hand hygiene, PPE use, and environmental cleaning); (III) antibiotic utilization indicators (average daily antibiotic use, the proportion of narrow- vs. broad-spectrum antibiotic use, and average duration of antibiotic treatment); and (IV) economic indicators (average daily hospital cost, total treatment cost, and antibiotic cost). These data collectively enabled a comprehensive assessment of the bundled management approach across clinical, behavioral, antimicrobial stewardship, and economic domains.

Statistical methods

All statistical analyses were performed using SPSS version 26.0. Continuous variables, such as average hospital stay and daily antibiotic use, were expressed as mean ± standard deviation and compared using independent-samples t-tests. Categorical variables, such as hand hygiene compliance rates and infection incidence, were expressed as frequencies and percentages and compared using the chi-square test (χ^2). For multiple comparisons, Bonferroni corrections were applied to control for type I error. A *P*-value of less than 0.05 was considered significant.

Results

Comparison of clinical baseline characteristics between the two groups

The baseline demographic and clinical characteristics were well balanced between the two groups (**Table 1**). The mean age was 64.00 ± 26.89 years in the control group and 58.89 ± 34.89 years in the observation group ($P = 0.352$). Male patients accounted for 60.0% and 63.1% of the control and observation groups, respectively ($P = 0.718$). There were no significant differences between groups with respect to body mass index, smoking history, or alcohol consumption (all $P > 0.05$). Similarly, the prevalence of comorbidities - including hypertension, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, cardiovascular disease, and immunosuppression - did not differ significantly between the two groups (all $P > 0.05$).

Comparison of knowledge awareness between the two groups

For patients, awareness of MDR bacterial infection (49.23% vs. 31.47%; $P < 0.05$) and proper hand hygiene (72.31% vs. 46.15%; $P < 0.05$) was significantly higher in the observation group than in the control group (**Table 2**).

Among family members or caregivers, the observation group also demonstrated significantly better awareness of MDR bacterial infection (93.84% vs. 73.85%; $P < 0.05$) and hand hygiene (98.46% vs. 84.62%; $P < 0.05$) (**Table 2**).

Table 2. Comparison of knowledge awareness between the two groups

Group	Sample Size	Patients' Awareness of MDR Resistance	Patients' Awareness of Hand Hygiene	Caregivers' Awareness of MDR Resistance	Caregivers' Awareness of Hand Hygiene
Observation Group	65	32 (49.23%)	47 (72.31%)	61 (93.84%)	64 (98.46%)
Control Group	65	20 (31.47%)	30 (46.15%)	48 (73.85%)	55 (84.62%)
χ^2	-	4.615	9.206	9.598	8.044
P Value	-	0.032	0.002	0.002	0.005

Table 3. Comparison of hand hygiene performance rate between the two groups

Group	Sample Size	Patients' Hand Hygiene Execution Rate	Caregivers' Hand Hygiene Execution Rate
Observation Group	65	42 (64.62%)	57 (87.69%)
Control Group	65	29 (44.62%)	41 (63.08%)
χ^2	-	5.245	10.612
P Value	-	0.022	0.001

Table 4. Comparison of the incidence and outcome of multidrug-resistant bacterial infections between the two groups

Group	Sample Size	Incidence of MDR Infection	Mortality	Favorable Outcome
Observation Group	65	2 (3.07%)	2 (3.08%)	10 (15.38%)
Control Group	65	10 (15.38%)	8 (12.31%)	3 (4.62%)
χ^2	-	5.876	3.900	4.188
P Value	-	0.015	0.048	0.041

Comparison of hand hygiene performance rate between the two groups

In the observation group, the hand hygiene performance rate among patients was 64.62% (42/65), significantly higher than the 44.62% (29/65) observed in the control group (P < 0.05) (**Table 3**). Similarly, caregivers in the observation group exhibited a significantly higher hand hygiene performance rate of 87.69% (57/65), compared to 63.08% (41/65) in the control group (P < 0.05) (**Table 3**).

Comparison of incidence and outcomes of MDR bacterial infections between the two groups

The incidence and outcomes of MDR bacterial infections differed significantly between the two groups (**Table 4**). The incidence of MDR infection was 3.07% (2/65) in the observation group, significantly lower than 15.38% (10/65) in the control group (P = 0.015). The mortality rate was also significantly lower in the observation group compared to the control group (3.08% vs. 12.31%; P = 0.048). In addition, the proportion of favorable outcomes was higher in the observation group (10/65, 15.38%) than in the control group (3/65, 4.62%) (P = 0.041).

Comparison of types of MDR bacterial infections between the two groups

As shown in **Table 5**, the pathogen-specific distribution of MDR infection rates differed between the two groups, with consistently lower infection rates in the observation group. Specifically, the observation group had significantly reduced rates of CRE (3.07% vs. 18.46%, P = 0.005), MRSA (4.62% vs. 15.38%, P = 0.041), and VRE (4.62% vs. 18.46%, P = 0.013) compared to the control group. Although the incidence of ESBL-producing bacteria was also lower in the observation group (10.77% vs. 21.54%), this difference was not statistically significant (P = 0.095). Taken together, these reductions contributed to a markedly lower overall MDR infection rate in the observation group (23.08% vs. 73.85%, P < 0.001).

Comparison of length of hospital stay and clinical care satisfaction scores between the two groups

The observation group demonstrated a significantly shorter length of hospital stay (10.12 ± 2.57 days vs. 15.40 ± 3.64 days; P < 0.001) compared to the control group. In addition, clin-

Table 5. Comparison of types of multidrug-resistant bacterial infections between the two groups

Type of Bacteria	Observation Group (n = 65)	Control Group (n = 65)	χ^2	p
Carbapenem-resistant Enterobacteriaceae (CRE)	2 (3.07%)	12 (18.46%)	8.005	0.005
Methicillin-resistant Staphylococcus aureus (MRSA)	3 (4.62%)	10 (15.38%)	4.188	0.041
Vancomycin-resistant Enterococcus (VRE)	3 (4.62%)	12 (18.46%)	6.104	0.013
Extended-spectrum β-lactamase (ESBL)-producing bacteria	7 (10.77%)	14 (21.54%)	2.783	0.095
Total Infections	15 (23.08%)	48 (73.85%)	33.539	< 0.001

Table 6. Comparison of hospital stay and clinical care satisfaction scores between the two groups

Group	Average Length of Hospital Stay (days)	Clinical Care Satisfaction Score
Observation Group (n = 65)	10.12 ± 2.57	91.85 ± 4.08
Control Group (n = 65)	15.40 ± 3.64	84.32 ± 5.05
t	9.541	9.344
P	< 0.001	< 0.001

ical care satisfaction scores were significantly higher in the observation group compared to the control group (P < 0.001) (**Table 6**).

Comparison of compliance of healthcare staff with infection control practices between the two groups

As shown in **Table 7**, the observation group exhibited significantly higher compliance rate with infection control practices than the control group. Hand hygiene, proper PPE use, and adherence to environmental cleaning protocols were all markedly improved (all P < 0.05). Overall compliance was also substantially higher in the observation group (94.62% vs. 79.23%, P = 0.008) compared to the control group.

Compliance of antibiotic use between the two groups

As summarized in **Table 8**, the observation group demonstrated significantly better antibiotic stewardship than the control group. Overall antibiotic exposure was reduced, with a significantly lower average daily antibiotic use (P < 0.001), and the prescribing pattern shifted toward more appropriate coverage, reflected by a higher use of narrow-spectrum agents and a lower use of broad-spectrum agents (both P = 0.002). In addition, the average duration of antibiotic treatment was significantly shorter in the observation group (P < 0.001).

Comparison of compliance with antibiotic stewardship guidelines

As summarized in **Table 9**, stewardship performance differed significantly between groups, favoring the observation group. Patients managed under the bundled approach were more likely to receive appropriate initial antibiotic therapy (P < 0.05) and more likely to undergo antibiotic de-escalation when indicated (P < 0.05) than those in the control group.

Comparison of cost analysis between the two groups

As shown in **Table 10**, the observation group demonstrated a clear economic advantage over the control group. Both the average daily hospitalization cost and the total treatment cost per patient were significantly lower in the observation group (both P < 0.001). Notably, antibiotic-related expenditure was also markedly decreased in the observation group (P < 0.001).

Discussion

This paper provides several original contributions to MDR bacterial infection management. First, while previous studies had examined individual or partial strategies such as education programs, hand hygiene promotion, antibiotic stewardship, or enhanced infection control protocols, the present study integrated these strategies into a comprehensive and coordinated intervention. Second, this study demonstrated the clinical effectiveness of the bundled management protocol by significantly reducing MDR infection incidence, while yielding measurable economic benefits. These findings support the relevance of bundled interventions to

Table 7. Comparison of compliance of healthcare staff with infection control practices between the two groups

Practice Type	Observation Group (n = 65)	Control Group (n = 65)	χ^2	*P* Value
Hand Hygiene Compliance	62 (95.38%)	51 (78.46%)	8.188	0.004
Proper Use of PPE	60 (92.31%)	50 (76.92%)	5.909	0.015
Adherence to Environmental Cleaning Protocols	61 (93.85%)	52 (80.00%)	5.482	0.019
Overall Compliance Rate	94.62%	79.23%	7.127	0.008

Note: PPE: Personal Protective Equipment.

Table 8. Comparison of antibiotic use between the two groups

Group	Sample Size	Average Daily Antibiotic Use (mg)	Percentage of Narrow-Spectrum Antibiotics Used	Percentage of Broad-Spectrum Antibiotics Used	Average Duration of Antibiotic Treatment (days)
Observation Group	65	347.81 ± 50.97	80.0%	20.0%	7.15 ± 1.65
Control Group	65	500.64 ± 70.68	60.0%	40.0%	10.71 ± 1.92
t/χ^2		14.139	9.524	9.525	11.321
P	-	< 0.001	0.002	0.002	< 0.001

Table 9. Comparison of compliance with antibiotic stewardship guidelines

Group	Sample Size	Proportion of Patients Receiving Initial Appropriate Therapy	Proportion of Cases with Antibiotic De-escalation
Observation Group	65	57 (87.69%)	52 (80.00%)
Control Group	65	45 (69.23%)	38 (58.46%)
χ^2	-	9.555	7.078
P	-	0.010	0.008

Table 10. Comparison of cost analysis between the two groups

Group	Sample Size	Average Daily Hospital Cost (USD)	Total Cost of Treatment per Patient (USD)	Cost of Antibiotics per Patient (USD)
Observation Group	65	251.29 ± 32.21	2957.80 ± 511.82	243.97 ± 32.09
Control Group	65	323.28 ± 37.23	4,508.66 ± 590.54	787.49 ± 97.94
t	-	11.789	16.000	42.519
P	-	< 0.001	< 0.001	< 0.001

MDR infection management, especially in settings with a high burden of antimicrobial resistance.

The observed improvements in knowledge awareness and hand hygiene compliance are consistent with previous research emphasizing the importance of education and behavioral interventions for preventing MDR pathogen transmission. Ciccacci et al. [18] reported that multi-modal hand hygiene promotion strategies greatly reduce healthcare-associated infections worldwide. Consistently, our result showed significantly higher awareness about MDR resistance and hand hygiene practices among patients and caregivers in the observation group, with the increased rates of 20% and 24%, respectively. Moreover, the lower incidence of MDR infections observed in the observation group is consistent with the findings of Rizk et al. [19], who reported that combining infection control measures with antimicrobial stewardship led to reduced MDR organism transmission. In this study, the incidence of MDR infections was significantly lower in the observation group than the control group, with marked reductions in infections caused by high-risk pathogens such as CRE and VRE. These

results prove that bundle management is effective at breaking the cycle of MDR bacteria spread in hospitals.

The effectiveness of the bundled management protocol likely stems from its comprehensive design, dealing with various parts of infection prevention and control simultaneously [20]. First, patient and caregiver education likely enhanced their adherence to preventive measures, especially proper hand hygiene [21]. Pittet et al. emphasized that hand hygiene remains a cornerstone of MDR transmission prevention [22]. In our study, the hand hygiene performance rate in healthcare workers of the observation group was significantly higher than that of the control group, which may have contributed to fewer MDR infection rates observed in the observation group. Second, the inclusion of antibiotic stewardship principles within the protocol significantly reduced unnecessary antibiotic use, thereby decreasing selective pressure for resistance development [23]. This finding corroborates the conclusions of Farhat et al. [24], who reported that antimicrobial stewardship programs are associated with reduced antimicrobial resistance and improved clinical outcomes. Lastly, improvements in environment cleaning and PPE use likely reduced environmental reservoirs for MDR pathogens and therefore decreased the opportunities for transmission. As mentioned by Banerjee et al. [25], environmental hygiene is essential for controlling MDR bacteria, especially in high risk places such as ICUs.

The findings in this study have important clinical implications. First, they support the implementation of comprehensive, bundled interventions rather than isolated to respond to effectively address MDR bacterial infections [26, 27]. Bundled protocols may produce synergistic effects by simultaneously addressing multiple factors in infection prevention [28]. Second, this study highlights the necessity of engagement of both patients and their caregivers in infection prevention [29]. The high-level awareness of caregivers about MDR resistance (93.84%) and hand hygiene awareness (98.46%) observed in the observation group underscore their potential contribution to reducing MDR transmission, particularly during extended hospital stays [30]. Finally, the economic gains attained in this study further support the adoption of bundled management interventions [31]. Consistent with the findings by Hurtado et al. [32], antimicrobial stewardship programs were associated with reduced use of broad-spectrum antibiotics and shorter hospital stays, translating into significant cost saving.

Despite these strengths, several limitations should be acknowledged. First, the single-center study may limit the generalizability of the findings. Multicenter studies are needed to validate the effectiveness of bundled management across different healthcare settings. Second, although short-term improvements in compliance and clinical outcomes were observed, the long-term effects of bundled management remains uncertain. Behavioral adherence, such as hand hygiene practices, may decline over time, highlighting the need for sustained interventions. Third, this study focused on selected MDR pathogens, including CRE, VRE, MRSA and ESBL-producing organisms. However, given the evolving landscape of antimicrobial resistance, such as colistin-resistant bacteria and carbapenemase-producing organisms, future studies should assess the effectiveness of bundled intervention against newly emerging MDR pathogens.

Conclusion

This study provided robust evidence supporting the effectiveness of bundled management interventions in reducing MDR bacterial infections. The success of this bundled strategy underscores the necessity of multifaceted approaches to address the complex challenge of antimicrobial resistance. By simultaneously targeting behavioral, clinical, and economic aspects, bundled management may substantially enhance patient outcomes and represent a valuable component of global initiatives to combat the growing threat of MDR bacterial infections.

Disclosure of conflict of interest

None.

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