World Journal of
Experimental Biosciences

Volume 14, Number 01: 10 – 15
P-ISSN: 2313-3937, e-ISSN: 3070-0647
2026

Research article

Controlling Imipenem-Resistant *Pseudomonas aeruginosa* in Hospitals: Effect of Improved Infection Control Measures from an Interrupted Time-Series Study

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ABSTRACT

Imipenem-resistant *Pseudomonas aeruginosa* (IRPA) causes serious healthcare-associated infections and negatively affects clinical outcomes. This study aims to determine if a structured bundle of enhanced infection-control measures can effectively reduce hospital-acquired IRPA cases at a tertiary care hospital. A retrospective interrupted time series analysis was conducted over two consecutive twelve-month periods: (1) 2023 served as the baseline period; (2) 2024 as the enhanced intervention period. The interventions included weekly active surveillance, prompt notification to physicians after positive culture results, structured on-site audits with a standardized checklist for isolating multidrug-resistant organisms, and monthly departmental performance reports. A total of 850 clinical isolates were analyzed. The main outcomes measured were the overall IRPA incidence, hospital-acquired IRPA infection rates, adherence to contact precautions for IRPA patients, and total Imipenem use, each expressed as a rate per 1,000 patient-days. Segmented linear regression was used for the interrupted time series analysis. IRPA incidence decreased from 1.842 to 0.963 cases per 1,000 patient-days ($p < 0.001$), and hospital-acquired IRPA infection rates dropped from 0.214 to 0.088 per 1,000 patient-days ($p = 0.001$). Contact isolation compliance increased from 31.4% to 76.2% ($p < 0.001$). Imipenem use rose to 1.183 defined daily doses per 1,000 patient-days per quarter ($p = 0.002$), with no significant change in this trend due to the intervention ($p = 0.112$). The implementation of a structured infection control bundle focusing on weekly surveillance and real-time notification led to a significant clinical and statistical reduction in hospital-acquired IRPA, despite increased Imipenem use. These findings offer practical evidence for resource-limited tertiary care settings.

Keywords: Active surveillance; Antimicrobial resistance, Hospital-acquired infection; Infection prevention and control; Imipenem-resistant *Pseudomonas aeruginosa*

Citation: Bhusal CK, Rasheed HJ (2026) Controlling Imipenem-Resistant *Pseudomonas aeruginosa* in Hospitals: Effect of Improved Infection Control Measures from an Interrupted Time-Series Study. *World J Exp Biosci* 14:10-15. doi: 10.65329/wjeb.v14.01.03

Received January 20, 2026; Revised February 28, 2026; Accepted: April 2, 2026; Published: April 9, 2026

1. INTRODUCTION

Healthcare-associated infections remain among the most consequential complications of inpatient care globally. They prolong hospital stays, increase mortality, and impose enormous costs on health systems operating with finite resources [1,2]. Of all the pathogens that drive nosocomial morbidity, Imipenem -resistant Gram-negative organisms have attracted the most urgent attention in recent years, and for good reason. When Imipenem fails, the therapeutic options that remain are few, toxic

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and often suboptimal [3]. *Pseudomonas aeruginosa* sits at the top of every clinician's list of difficult hospital pathogens. It thrives in moist environments, colonizes indwelling devices with remarkable efficiency, and causes devastating infections in immunocompromised patients and those managed in intensive care units [4]. What makes Carbapenem-resistant *P. aeruginosa* (CRPA) especially Imipenem-Resistant *P. aeruginosa* (IRPA) particularly alarming is the breadth of its resistance machinery: efflux pump overexpression, outer membrane porin loss, upregulation of chromosomally encoded AmpC beta-lactamase, and, in an increasing proportion of isolates, the acquisition of mobile Imipenemases including metallo-beta-lactamases (MBLs) such as VIM and IMP [5,6]. High-risk international clones, notably sequence types ST175 and ST235, have demonstrated the capacity to spread across hospital networks and across national borders, further compounding the threat [7].

The 2024 WHO bacterial priority pathogens list reaffirmed CRPA as a critical-priority organism requiring urgent research and intervention [8]. Global burden analyses have attributed well over 200,000 annual deaths to CRPA-related antimicrobial resistance, a figure that is almost certainly an underestimate given the challenges of ascertainment of attributable mortality in resource-limited settings [9]. Yet despite this burden, the evidence base specifically guiding CRPA prevention in routine clinical practice remains thinner than that for comparable organisms, such as imipenem-resistant *Klebsiella pneumoniae* or *Acinetobacter baumannii* [10].

Infection prevention and control guidelines consistently advocate hand hygiene, contact precautions, environmental cleaning, and active surveillance as the cornerstones of containment [11]. In practice, however, compliance with these measures in busy clinical wards frequently falls short of recommended thresholds, and real-world evidence of their effectiveness against IRPA, in particular, continues to accumulate slowly. This gap is wider in resource-limited settings, where staffing shortages, structural barriers, and the absence of single-room isolation infrastructure compound the challenge [12].

In our healthcare facilities, it is uncommon for patients with antibiotic-resistant *P. aeruginosa* infections to be isolated only after a physician orders it in the medical records, often days after the lab results are released. Adherence to this procedure was not monitored, nor were medical teams informed. Our Infection Control and Prevention (ICP) team introduced an improved, structured four-part procedure: weekly active surveillance, real-time physician notification, field audits with immediate feedback, and monthly performance reports. The present study aims to evaluate the effectiveness of a structured bundle of enhanced infection-control measures in reducing the incidence of hospital-acquired IRPA infections at a tertiary care hospital in Baghdad, Iraq.

2. MATERIALS AND METHODS

2.1. Study setting and design

This was a retrospective, single-center, interrupted time-series study conducted at Different Teaching Hospitals, public tertiary care institutions in Baghdad and Wasit, Iraq, with a combined bed capacity of approximately 920. The study period was divided into two consecutive twelve-month intervals: Period 1 (January 1 – December 31, 2023), which served as the pre-intervention baseline, and Period 2 (January 1, 2024 – January 1, 2025), which represented the intervention period. A total of 850 clinical isolates of *P.* aeruginosa were included across both periods.

2.2. Baseline period (Period 1)

During the baseline year, contact isolation for IRPA-positive patients was physician-initiated and order-dependent, with no standardized active surveillance program and no formal mechanism to monitor compliance or provide feedback to clinical teams. Routine infection-prevention practices, hand hygiene protocols, and environmental disinfection were carried out per standard operating procedures but without structured auditing.

2.3. Enhanced infection control intervention (Period 2)

Beginning January 1, 2024, A four-component IPC bundle was implemented, including active surveillance, rapid physician notification, weekly audit with feedback, and monthly performance reporting to improve IRPA isolation and infection control compliance.

2.4. Case definitions and outcome measures

IRPA incidence was defined as the detection of *P. aeruginosa* resistant to imipenem in any clinical specimen, regardless of whether the patient met clinical criteria for infection. For each patient, only the earliest positive specimen per anatomical site was counted; screening specimens were excluded. Hospital-acquired IRPA events were defined as culture-confirmed infections occurring more than 48 hours after admission, jointly verified by the attending physician and IPC staff; only the first episode per patient was recorded. Contact isolation compliance was calculated as the proportion of IRPA-positive inpatients, excluding those discharged before the report date and those already under isolation for other reasons, with an active contact isolation order in the long-term medical instructions. Imipenem consumption (meropenem, imipenem/cilastatin, and doripenem combined) was expressed as defined daily doses (DDD) per 1,000 patient-days.

2.5. Laboratory methods

All *P. aeruginosa* isolates were identified using biochemical tests (oxidase and catalase) and colonies' morphological features on MacConkey agar and cetrimide agar. The VITEK 2 Compact automated system (bioMérieux, France). Antimicrobial susceptibility testing was performed using the VITEK 2 AST-N391 card, and results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) M100, 33rd edition (2023) breakpoints [13]. Isolates demonstrating resistance to imipenem were classified as Imipenem-resistant.

2.6. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 29.0. An interrupted time-series analysis using segmented linear regression was applied to assess intervention effects on all primary outcomes, according to the model:

$$Y = \beta0 + \beta1 \times time + \beta2 \times intervention + \beta3 \times time_after + \varepsilon$$

In this model, Y is the outcome at each quarterly time point; time is a continuous quarterly counter; intervention is a binary variable (0 = Period 1, 1 = Period 2); and time_after counts quarters elapsed since intervention start. β1 captures the pre-intervention trend slope, β2 represents the immediate level change at the intervention point, and β3 captures the change in post-intervention slope. Autocorrelation was assessed using the Durbin–Watson statistic. All tests were two-sided, with a significance threshold of $p < 0.05$.

3. RESULTS

3.1. Study population and sample characteristics

In the current study, 850 clinical isolates were analyzed. 512 were collected during Period 1 and 338 during Period 2. Total patient-days were 274,320 in Period 1 and 258,740 in Period 2. The most frequent specimen sources were sputum (43.7%), wound swabs (21.2%), urine (18.9%), blood cultures (10.1%), and bronchoalveolar lavage or drain fluid (6.1%). Table 1 summarizes baseline characteristics and between-period comparisons.

3.2. IRPA incidence trends

During the pre-intervention period, IRPA incidence was not only high but trending upward, rising by 0.092 cases per 1,000 patient-days per quarter (95% CI: 0.011–0.173, $p = 0.031$). Post the intervention bundle was introduced, that trajectory reversed sharply: the post-intervention slope represented a quarterly decline of 0.162 cases/1,000 patient-days (95% CI: −0.291 to −0.034, $p = 0.017$). The Durbin–Watson statistic was 1.814 ($p = 0.611$), showing no statistically significant autocorrelation.

3.3. Hospital-acquired IRPA events

The rate of hospital-acquired IRPA infection fell from 0.214 per 1,000 patient-days in Period 1 to 0.088 per 1,000 patient-days in Period 2 ($p = 0.001$). The pre-intervention quarterly slope showed a rising trend of 0.019 cases per 1,000 patient-days per quarter (95% CI: 0.007–0.031, $p = 0.004$); following the intervention, this reversed to −0.031 per 1,000 patient-days per quarter (95% CI: −0.048 to −0.014, $p = 0.002$). The Durbin–Watson statistic was 2.163 ($p = 0.782$).

3.4. Contact isolation compliance

The rate of compliance with contact isolation increased from 31.4% in Period 1 to 76.2% in Period 2 ($p < 0.001$), reflecting an immediate 42.7-percentage-point step change at the point of intervention ($\beta 2 = 42.7$, $p < 0.001$). However, the slope of the within-Period 2 data points no longer statistically rose ($\beta 3 = +1.94$ percentage points per quarter, $p = 0.216$), suggesting that the 42.7 percentage point increase was achieved quickly through a sudden change in compliance rather than as a series of incremental changes over time — an observation that

indicates a significant structural behavioural change rather than a gradual cultural shift.

3.5. Imipenem consumption

Imipenem usage increased steadily over both timepoints by 1.183 DDD per 1,000 patient-days per quarter (95% CI: 0.493 – 1.872; $p = 0.002$). No statistical significance was found in modifying this trend following the intervention ($p = 0.112$), which lends support to the notion that the IPC bundle had no effect on changing the rate of prescribing. Despite the ongoing increase in pressure from antibiotics to cause hospital-acquired IRPA infections; IRPA rates dropped significantly in Period 2, a significant disconnect that is crucial for understanding our results.

4. DISCUSSION

Carbapenem-resistant *P. aeruginosa* (CRPA), especially imipenem-resistant *P. aeruginosa* (IRPA), poses a major threat to global public health and necessitates significant changes in clinical practice, particularly in critical care units [14]. The first observation from this research project is that a bundle consisting of improved infection prevention/control had a substantial and statistically significant decrease in the rates of IRPA infections that were acquired during hospitalization at a large tertiary hospital in Baghdad, Iraq. Further, this decrease was observed despite a general increase in Imipenem consumption. This is an important fact and serves as an important lesson. It demonstrates that the interruption of nosocomial infection transmission through non-pharmacological means is possible despite the changes in the antibiotic resistance environment continuing to favor resistant organisms and that these two aspects of antimicrobial resistance control (i.e., stewardship and prevention) are generally complementary, rather than interchangeable.

The literary representation of the process through which the four components of the intervention created the observed outcomes is illustrated in Figure 1. The pathway extends from early implementation of contact precaution procedures and subsequent improvement in adherence, through reduction of patient-to-patient transmission, to continued late decreases in the rates of IRPA infections acquired during hospitalization, while the pressure from the drug Imipenem was continued to increase unabated.

Imipenem use has increased for the duration of our study (about 1,183 DDD/1,000 Patient Days/per Quarter) as has been repor-

Table 1. Baseline characteristics and overall outcome comparisons between Period 1 (2023) and Period 2 (2024). *IRPA= Imipenem -resistant Pseudomonas aeruginosa; DDD = defined daily doses; CI = confidence interval.*

Variable	Period 1 (2023)	Period 2 (2024)	p-value
Total isolates, n	512	338	—
Total patient-days	274,320	258,740	—
IRPA incidence (per 1,000 patient-days)	1.842 (95% CI: 1.563–2.114)	0.963 (95% CI: 0.752–1.198)	< 0.001
Hospital-acquired IRPA rate (per 1,000 patient-days)	0.214 (95% CI: 0.148–0.312)	0.088 (95% CI: 0.051–0.141)	0.001
Contact isolation compliance (%)	31.4% (95% CI: 26.1–37.2%)	76.2% (95% CI: 71.3–81.1%)	< 0.001
Imipenem use (DDD per 1,000 patient-days)	32.47 (95% CI: 24.31–40.88)	41.62 (95% CI: 36.77–46.81)	0.062

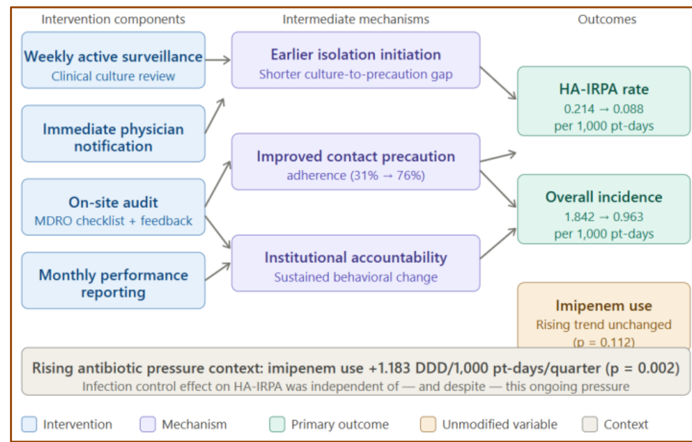

Fig 1. Mechanistic pathway linking the enhanced IPC bundle to reduced hospital-acquired IRPA. Conceptual framework illustrating the hypothesized causal pathways between the four IPC intervention components and observed outcomes. Arrows indicate proposed causal relationships. Imipenem use

ted across many Healthcare Systems worldwide [15]. Continuing (or even increasing) levels of Imipenem-Exposed Patients in clinical practice create selective pressure that you would expect to maintain or increase the rate of imipenem-resistant organisms (IRPA). However, in our study, the observed decline in the number of cases of indigenously acquired infection in our institution was consistent with the results of a study by Li et al. in a similar multicampus intervention in China where they utilized enhanced infection prevention/control (IPC) measures to significantly reduce hospital-acquired imipenem resistant organisms, even though total use of antibiotics were increasing in the institution [16]. This suggests that there is a strong possibility that the relationship between antibiotic pressure/infection rates caused by acquired infection is not causal, and that effective methods/techniques for preventing infection through behavioral infection prevention/control can greatly reduce or eliminate any of the expected increases in hospital-acquired antibiotic-resistant organisms.

Contact isolation compliance is one of the most heavily studied intermediate outcomes in hospital infection control. Low compliance is consistently associated with higher rates of transmission of drug-resistant organisms [17], and our baseline figure of 31.4% placed us in a poor position relative to benchmarks from comparable institutions. The improvement to 76.2% following the intervention, a 44.8 percentage point increase, was the largest single shift we observed, and it manifested primarily as a step-change rather than a gradual quarterly improvement. This pattern suggests that the structural elements introduced at the start of Period 2, particularly the weekly surveillance loop and the immediate notification pathway, triggered a rapid behavioral adjustment rather than a slow cultural evolution. Such step-change dynamics are well described in behavior change science: direct feedback and visible accountability tend to produce faster and more pronounced responses than educational interventions delivered without contemporaneous monitoring [18].

One aspect of our setting deserves particular attention. Like most tertiary care hospitals in Iraq and across the broader Middle East, Al-Yarmouk operates multi-bed open wards rather than single-occupancy isolation rooms. Physical cohorting of IRPA-positive patients is therefore rarely feasible in practice. Our intervention was designed around this constraint: instead of attempting to spatially isolate patients, we focused on shortening the time from culture positivity to the initiation of bedside contact precautions and on making adherence to those precautions visible and accountable. A prior mathematical modeling study estimated that under standard contact precautions, a susceptible patient sustains roughly 4.8 daily contacts with Imipenem -resistant organism-positive individuals within the same ward environment [19]. Our intervention directly targeted the window during which those contacts occurred unprotected, the gap between the laboratory report and the isolation order, and the quality of protection once isolation was in place.

The lack of any significant change in Imipenem consumption trends was not unexpected. Our intervention was IPC-focused, not stewardship-focused, and the two address different aspects of the resistance equation. Antibiotic prescribing in tertiary care hospitals reflects patient acuity, clinical culture, formulary policies, and the prevalence of severe infections — none of which were directly targeted by our bundle. The continued rise in Imipenem use may reflect increasing patient complexity, formulary gaps favoring broad-spectrum agents, or institutional stewardship practices that were not part of this study's remit. Future work examining the combined or synergistic effect of simultaneous stewardship intensification and enhanced IPC is warranted, particularly in settings where Imipenem use is rising and IRPA endemicity is established [20].

The 2024 IDSA guidance on antimicrobial-resistant Gram-negative infections reinforces the importance of infection control as a complement to, rather than a replacement for, appropriate antibiotic therapy, noting that preventing IRPA transmission is foundational to limiting this pathogen's clinical impact [21]. Similarly, the 2025 systematic review of outbreak investigations for Imipenemase-producing *P. aeruginosa* underscores the critical role of timely environmental and patient screening in identifying transmission chains [22]. Our study provides a real-world demonstration from a resource-limited setting that structured surveillance and accountability reporting can achieve meaningful gains without requiring the infrastructure found in higher-income healthcare systems.

Table 2. Interrupted time-series analysis results for key outcome variables. *DDD = defined daily doses; IRPA= Imipenem -resistant Pseudomonas aeruginosa.*

Outcome	Pre-intervention slope (β1)	Immediate effect (β2)	Post-intervention slope change (β3)	p-value (β3)
IRPA incidence (per 1,000 patient-days)	+0.092 (p = 0.031)	−0.341 (p = 0.048)	−0.162	0.017
Hospital-acquired IRPA rate (per 1,000 patient-days)	+0.019 (p = 0.004)	−0.107 (p = 0.039)	−0.031	0.002
Contact isolation compliance (%)	−2.81 (p = 0.043)	+42.7 (p < 0.001)	+1.94	0.216
Imipenem use (DDD per 1,000 patient-days)	+1.183 (p = 0.002)	+3.41 (p = 0.219)	+0.621	0.112

Several limitations must be acknowledged. This is a single-center study from one institution in Iraq, and the generalizability of our findings to other clinical environments cannot be assumed. The interrupted time-series design lacks a concurrent control group, and although segmented regression accounts for pre-existing trends, residual confounding due to secular trends, seasonal variation, or unmeasured concurrent changes in clinical practice cannot be fully excluded. The twelve-month intervention period is relatively short, and whether the gains in compliance and infection rates are sustained beyond that window remains to be demonstrated. We did not stratify IRPA cases by site of infection or resistance mechanism, which would have provided additional granularity regarding transmission dynamics. Most importantly, the absence of whole-genome sequencing data means we cannot confirm the interruption of specific nosocomial transmission chains or exclude the possibility that some of the decline in hospital-acquired infections reflected changes in patient case-mix rather than interrupted cross-transmission. Finally, this study focused exclusively on IRPA and did not examine the effect of the same intervention on other imipenem-resistant organisms circulating in our institution.

5. CONCLUSION

We implemented a structured 'Infection Control Bundle', which included weekly active surveillance (tracking known & unknown microbes), immediate notification to the doctor, a structured on-site audit of the infection control processes used, & monthly accountability reports to identify areas of infection control non-compliance. There was a dramatic and clinically relevant decrease in the number of Institutional Resistance Pathway-associated (IRPA) infections in our facility following the implementation of the infection control bundle (controlling for the continuous increase in imipenem use), indicating that infection control practices substantially reduce nosocomial (hospital-acquired) infections, even with continued antibiotic use being used against resistant organisms. The significant improvement in contact isolation compliance at our facility is due largely to the 'step change' approach to the infection control bundle, rather than through gradual cultural change, further establishing the value of real-time feedback from active surveillance in the timely alteration of clinical behavior. These results support the use of structured infection control programs as a low-cost, practical model for tertiary hospitals that cannot isolate patients in single rooms. Future research should examine the long-term sustainability of infection control bundles, the value of implementing a concurrent antimicrobial stewardship program with an infection control bundle, and how the development and use of whole-genome sequencing provide mechanistic verification that transmission has been interrupted.

Acknowledgments

We would like to thank the staff of the Department of Biology, College of Science, University of Baghdad, for their support and advice.

Funding information

This work received no specific grant from any funding agency.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could be perceived as influencing the work reported in this paper.

Ethical Approval

Ministry of Health, Baghdad, Iraq (MoH, 12042; 12/10/2022).

CRediT authorship contribution statement

Bhusal CK: Formal analysis; Writing – Review & Editing; Validation.
Rasheed HJ: Conceptualization; Investigation; Data curation; Formal analysis; Methodology; Project administration; Resources; Supervision; Writing – Original Draft; Visualization.
All authors have read and agreed to the published version.

Availability of data and materials

All information used is available in the cited literature.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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