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Research article

# Novel preventive bundle for multidrug-resistant organisms in intensive care setting; tertiary care experience

Majid M. Alshamrani[a,b,c,*], Aiman El-Saed[a,b,c,d], Mohammed Al Zunitan[a,b,c], Mohammed Abalkhail[c,e], Doris Abagguey[a], Fayssal M. Farahat[a,b,c]

[a] Infection Prevention and Control Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia
[b] King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[c] King Abdullah International Medical Research Center, Riyadh, Saudi Arabia
[d] Community Medicine Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt
[e] Infection Prevention and Control Department, King Abdullah Specialist Children Hospital, Riyadh, Saudi Arabia

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ABSTRACT

*Background:* A widely-accepted standardized preventive bundle targeting multidrug-resistant organisms (MDROs) is lacking. The objective was to describe the components, implementation, compliance, and impact of a novel MDROs bundle in intensive care units (ICUs).

*Methods:* Cohort study of surveillance activities on the components of MDROs bundle (July 2019 to June 2022) and the incidence of MDROs (April 2016 to June 2022). The implementation of MDROs bundle were preceded by ICPs-led education of the staff working in target ICUs about the importance and components of the MDROs bundle. These included the overall use of antimicrobials, appropriate environmental cleaning, appropriate contact precautions, and hand hygiene compliance.

*Results:* During implementation, the overall use of antimicrobials was 57.8 days of therapy per 100 patient-days (44,492/76,933). It was higher in adult compared with pediatric/neonatal ICUs ($p < 0.001$). Appropriate environmental cleaning was 74.8% (12,409/16,582), appropriate contact precautions was 83.8% (10,467/12,497), and hand hygiene compliance was 86.9% (27,023/31,096). The three components were significantly higher in pediatric/neonatal compared with adult ICUs ($p = 0.027$, $p < 0.001$, $p = 0.006$, respectively). The MDROs rates per 10,000 patient-days were 71.8 before (April 2016 to June 2019) and 62.0 during (July 2019 to June 2022) the bundle implementation (858/119,565 versus 891/143,649 $p = 0.002$). The reduction in MDROs rates were replicated in adult ($p = 0.001$) but not pediatric/neonatal ICUs ($p = 0.530$).

*Conclusions:* The finding of this study indicate that the implementation of the current bundle was associated with a modest decrease in MDROs rates in adult ICUs. The provided detailed definitions and methodology will facilitate its use by other healthcare facilities.

* Corresponding author. Infection Prevention and Control, King Abdualziz Medical city , Adult Infectious Disease, King Saud bin Abdulaziz University for Health Sciences Riyadh, Saudi ArabiaP.O. Box 22490, Riyadh, 11426, Kingdom of Saudi Arabia.

*E-mail addresses:* Dr_shomrani@yahoo.com, Alshamranima2@ngha.med.sa (M.M. Alshamrani).

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## 1. Introduction

Approximately one-third of hospital infections are caused by multidrug-resistant organisms (MDROs) [1,2]. Infections caused by MDROs are associated with increased mortality, length of hospital stay, and healthcare costs compared with infections caused by susceptible organisms [3,4]. Antimicrobial resistance including MDROs are thought to be responsible for almost 5 million deaths and 2.3 million years of disability every year [5]. The negative impacts of MDROs have been observed in both healthcare- and community-associated infection [6], and in both developing and developed countries [4,6]. When the MDROs burden is combined with that of background healthcare-associated infections, the impacts on the patient and healthcare system are mounted and the prevention programs are further challenged [7–9].

Audit and feedback on different infection control practices have been shown to considerably reduce infection rates [10]. The positive impact on infection rates has been replicated in different device-associated infections and surgical site infections [10]. The US Centers for Disease Control and Prevention (CDC) and the British National Health Service (NHS) suggested a number of preventive strategies and checklists to reduce the MDROs burden [11,12]. These included administrative measures, education and training, antimicrobial agents, surveillance, standard precautions including hand hygiene and use of personal protective equipment, and environmental measures. Attempts to establish MDROs bundles covering few of the above components have been suggested [13–16]. However, the suggested bundles were not consistent regarding the set of components included. Additionally, the data on the bundle implementation and effectiveness were either limited or never been published in full report [15,16]. Moreover, some MDROs preventive bundles focused only on a specific type of bacterial resistance and/or specific patients [17,18]. The objective of the current study was to describe the components, implementation, and compliance of a novel MDROs bundle in both pediatric and adult intensive care setting. Additionally, to examine the bundle impact on the rate of MDROs.

## 2. Methods

**Setting:** The current study was conducted at ten adult and four pediatric/neonatal intensive care units (ICUs) at King Abdulaziz Medical City at Riyadh (KAMC-R), Saudi Arabia. KAMC-R is an approximately 1488-bed tertiary care facility composed of two hospitals. It had a total 172 (11.6%) ICU beds and 168 (11.3%) emergency beds. KAMC-R provides healthcare services for almost 1.15 million eligible Saudi National Guard soldiers, employees and their families. The facility is accredited by Joint Commission International (JCI). According to local hospital statistics at the start of bundle implementation (2019), KAMC-R received 55,025 admissions per year.

**Infection prevention and control (IPC) program:** IPC department and program are well-established and run by 21 infection control professionals (ICPs). This represents approximately 1.4 ICPs per 100 beds, with almost half of the ICPs had CIBC certification. The surveillance activities are done according to the recommendations of the US National Healthcare Safety Network (NHSN). They cover device-associated infections, surgical site infections, preventive bundles, MDROs, and antimicrobial use.

**Design:** Prospective/retrospective cohort study of surveillance activities was conducted in adult and pediatric/neonatal ICUs. Prospective data collection was done for the implementation of the components of MDROs bundle and the concurrent incidence of MDROs between July 2019 and June 2022. Retrospective data collection was done for the pre-implementation incidence of MDROs between April 2016 and June 2019.

**Data collection:** The data were collected by ICPs working in IPC department using standard surveillance forms. Antimicrobials use data were abstracted daily from the electronic pharmacy records. Compliance with environmental cleaning, contact precautions, and hand hygiene were assessed by direct observation of the respective units/staff by ICPs during daily rounds. The incidence of MDROs was confirmed using the daily microbiological laboratory reports. ICPs ensured that all required data are concomitantly collected in target ICUs. Collected data were then aggregated per quarter and year in an Excel file.

**Intervention:** ICPs provided education of the staff working in target ICUs about the importance and components of the MDROs bundle before implementation. Additionally, ICPs provided periodic auditing, training, and feedback during daily rounds during the implementation period. The components of the MDROs bundle included overall use of antimicrobials, appropriate environmental cleaning, appropriate contact precautions, and hand hygiene compliance.

***Overall use of antimicrobials*** was expressed as antimicrobial days of therapy (DOTs) per 100 patient-days in a specific unit and period. Antimicrobial DOTs were defined as calendar days in which the patient received any amount of a specific antimicrobial agent. The agents included aminoglycosides, carbapenems, third-generation cephalosporins, fluoroquinolones, piperacillin/tazobactam, vancomycin, tigecycline, and colistin. The routes of administration included intravenous, intramuscular, and oral routes. The data were abstracted daily from the electronic pharmacy records. In case of polymicrobial therapy, a single patient may contribute two or more antimicrobial DOTs to the same unit during a single calendar day. In case of unit transfer, a single patient may contribute one DOT to each unit during a single calendar day. The denominator was collected as the sum of daily number of patients who were present for any portion of the day in a specific unit and period. A single patient may not contribute more than one patient-day to any specific unit during the same calendar day. In case of transfer, the patient may contribute one patient-day for each unit on the same calendar day.

***Appropriate environmental cleaning*** was expressed as percentage. It was defined as the number of surfaces appropriately cleaned in a specific unit and period relative to the total number of surfaces evaluated in the same unit and period. Assessment was done by direct observation of environmental cleaning in the respective unit/staff during daily rounds. Targeted surfaces included high touch surfaces group I (bed rails, tray table, and IV pole), high touch surfaces group II (button call bell, button telephone, and bedside table handle), high touch surfaces group III (chair, room sink, room light switch, room inner doorknob), bathroom surfaces (bathroom inner door knob, bathroom light switch, bathroom hand rails, bathroom sink, toilet seat, toilet flush handle, and toilet bedpan cleaner), and equipment surfaces (IV pump control, monitor controls, monitor touch screen, monitor cables, ventilator panel, and continuous renal replacement therapy "CRRT").

***Appropriate contact precautions*** were expressed as percentage. They were defined as the number of contact precautions opportunities appropriately followed in a specific unit and period relative to the total number of contact precautions opportunities evaluated in the same specific unit and period. Assessment was done by direct observation of contact precautions in the respective unit/staff during daily rounds. The compliance data were collected separately for physicians, nurses, and other healthcare workers. Contact precautions opportunities included hand hygiene before entering the room, gown before entering the room, gloves before entering the room, hand hygiene before and after tasks/procedures done in patient room, gloves removed before leaving the room, gown removed before leaving the room, and hand hygiene outside the patient room.

***Hand hygiene compliance*** was expressed as percentage and was defined as the number of WHO hand hygiene opportunities with hand hygiene appropriately done (hand wash or use of alcohol-based handrub) in a specific unit and period relative to the total number of WHO hand hygiene opportunities evaluated in the same specific unit and period. Assessment was done by direct observation of hand hygiene compliance in the respective staff during daily rounds. The compliance data were collected separately for physicians, nurses, and other healthcare workers. The five WHO hand hygiene opportunities included before touching a patient, before clean/aseptic procedures, after body fluid exposure/risk, after touching a patient, and after touching patient surroundings.

**Study outcome:** It was the overall MDROs rate per 10,000 patient-days in a specific unit and period. MDROs definition was following the NHSN manual [19] and reports [20,21]. Accordingly, MDROs included the following seven types of resistant bacteria; methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), cephalosporin-resistant *Klebsiella*, carbapenem-resistant *Enterobacteriaceae* (CRE), and multidrug-resistant (MDR) *Acinetobacter*, *Pseudomonas*, and *Klebsiella*. MDR gram-negative pathogens were tested non-susceptible (resistant or intermediate) to at least one agent in at least three antimicrobial classes. MDROs data were derived from clinical cultures with no surveillance cultures included. Microbiological examination was done in the main hospital laboratory. Bacterial identification and antibiotic susceptibility were done using Vitek 2 compact automated system (Biomérieux). Minimum inhibitory concentration (MIC) and susceptibility results were interpreted according to the Clinical Laboratory Standards Institute (CLSI) guidelines.

**Statistical methods:** Overall use of antimicrobials was expressed as antimicrobial DOTs per 100 patient-days. Appropriate environmental cleaning, appropriate contact precautions, and hand hygiene compliance were expressed as percentages of compliant opportunities relative to the total number of opportunities evaluated. MDROs rates were expressed as MDROs per 10,000 patient-days. To examine the impact of the MDROs bundle, the rate of MDROs during the bundle implementation (July 2019 to June 2022) was compared with the rate of MDROs in the preceding years (April 2016 to June 2019). Differences before and during bundle implementation and between adult and pediatric/neonatal ICUs were compared using Chi-square for proportions and Z-test for person-time data. SPSS (Version 25.0. Armonk, NY: IBM Corp) and OpenEpi (Version 3.01) were was used for all statistical analyses.

## 3. Results

Table 1 and Fig. 1 show the components of MDROs bundle by the type of ICU. During the implementation of MDROs bundle, 44,492 DOTs were recorded in 76,933 patient-days of surveillance, representing a rate of 57.8 DOTs per 100 patient-days. The rate of antimicrobial use was significantly higher (almost double) in adult ICUs compared with pediatric/neonatal ICUs (69.5 versus 35.8, $p < 0.001$). Out of 16,582 observed environmental cleaning opportunities, 12,409 surfaces were appropriately cleaned, which represents a prevalence of 74.8%. The prevalence of appropriate environmental cleaning was slightly but significantly higher in pediatric/neonatal ICUs compare with adult ICUs (76.2% versus 74.4%, $p = 0.027$). Out of 12,497 observed contact precautions opportunities, 10,467

**Table 1**
Components and outcome of multidrug-resistant organisms (MDROs) bundle by type of intensive care unit (ICU) between July 2019 and June 2022.

| | Adult ICUs | Pediatric/neonatal ICUs | All ICUs | *P*-value |
|---|---|---|---|---|
| **Overall use of antimicrobials** | | | | |
| Days of therapy | 34,972 | 9520 | 44,492 | <0.001 |
| Patient days | 50,323 | 26,610 | 76,933 | – |
| **Appropriate environmental cleaning** | | | | |
| Surfaces appropriately cleaned | 9646 | 2763 | 12,409 | 0.027 |
| Surfaces evaluated | 12,958 | 3624 | 16,582 | – |
| **Appropriate contact precautions** | | | | |
| Opportunities appropriately done | 5555 | 4912 | 10,467 | <0.001 |
| Opportunities observed | 6858 | 5639 | 12,497 | – |
| **Hand hygiene compliance** | | | | |
| Opportunities appropriately done | 19,006 | 8017 | 27,023 | 0.006 |
| Opportunities observed | 21,956 | 9140 | 31,096 | – |
| **MDROs** | | | | |
| Gram-negative organisms | 572 | 56 | 628 | <0.001 |
| Gram-positive organisms | 231 | 32 | 263 | <0.001 |
| All organisms | 803 | 88 | 891 | <0.001 |
| Patient days | 81,755 | 61,894 | 143,649 | – |

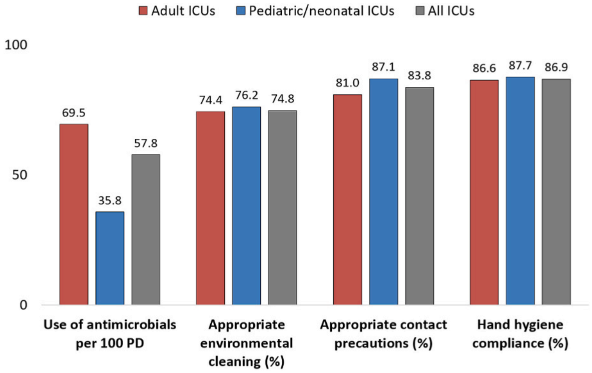


**Fig. 1.** Levels of the components of MDROs bundle by the type of ICU during the implementation of MDROs bundle (July 2019 to June 2022).

opportunities were appropriately followed, which represents a prevalence of 83.8%. The prevalence of appropriate contact precautions was significantly higher in pediatric/neonatal ICUs compared with adult ICUs (87.1% versus 81.0%, $p < 0.001$). Out of 31,096 observed hand hygiene opportunities, 27,023 opportunities were appropriately done, which represents a prevalence of 86.9%. The prevalence of hand hygiene compliance was slightly but significantly higher in pediatric/neonatal ICUs compare with adult ICUs (87.7% versus 86.6%, $p = 0.006$).

Fig. 2 shows the trends of the levels of the components of the MDROs bundle by the type of ICU. Irrespective of ICU type, the trends of appropriate contact precautions and hand hygiene compliance were relatively stable over the period of the study (Fig. 2A–C). On the other hand, the rate of antimicrobial use had bigger fluctuations over the period of the study, with a clearly lower rate and bigger

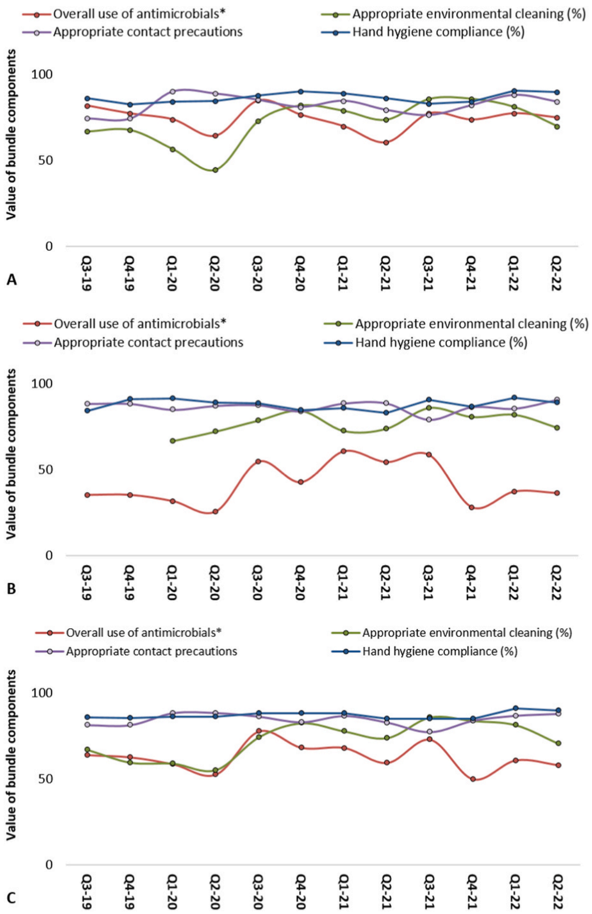


**Fig. 2.** Trends of the components of MDROs bundle in adult (A), pediatric/neonatal (B), and all intensive care units (C) during the implementation of MDROs bundle (July 2019 to June 2022).

fluctuations in pediatric/neonatal ICUs (Fig. 2B) compared with adult ICUs (Fig. 2A). In adult ICUs (Fig. 2A) and all ICUs (combined adult/pediatric/neonatal ICUs, Fig. 2C), there was a slight (8%–9%) decrease in the antimicrobial use by the end of the study. Appropriate environmental cleaning had a drop during the first year of the study followed by relatively stable improvement.

As shown in Table 2, 858 MDROs were detected before and 891 MDROs were detected during the implementation of MDROs bundle. Gram-negative organisms represented approximately 70% of all MDROs. The MDROs rate was almost seven-folds higher in adult ICUs compared with pediatric/neonatal ICUs (106.4 versus 14.9, $p < 0.001$). As shown in Table 2 and Fig. 3A, there was a significant reduction in the overall MDROs rates during the implementation of the MDROs bundle in adult ICUs (116.5–98.2, $p = 0.001$) and all ICUs (71.8–62.0, $p = 0.002$). The up fluctuations tend to be fewer in adult ICUs during the implementation of the MDROs bundle (Fig. 3B). On the other hand, there was no significant reduction in the overall MDROs rates during the implementation of the MDROs bundle in pediatric/neonatal ICUs (15.7–14.2, $p = 0.530$, Fig. 3A). The reduction in MDROs rates in all ICUs during the implementation of the MDROs bundle was observed in Gram-negative but not Gram-positive MDROs ($p < 0.001$ and $p = 0.159$, respectively). The reduction in rates of Gram-negative MDROs was apparent in *Pseudomonas aeruginosa*, *Acinetobacter* spp., and *Escherichia coli.*

## 4. Discussion

The current report describes a novel MDROs bundle already implemented for three years in the ICUs of a tertiary care hospital system in Riyadh, Saudi Arabia. The novelty is claimed due to the shared standard definitions, methodology, data collection, and implementation of four components of the MDROs bundle combined with the bundle outcome; the MDROs rate. The components of the MDROs bundle were the ones that have been recommended by international institutions [11,12], and have been used separately or in different combinations to effectively reduce MDROs rates [22–24]. For example, it has been reported that a four-component strategy composed of antimicrobial stewardship program (ASP), environmental cleaning, source control, and standard care, was associated with a very effective reduction of MDROs rates [24]. It is believed that the implementation and effectiveness of preventive bundles can be enhanced when the bundle focuses on a few (four or five) components [25] rather than a long list of preventive strategies [11].

The current bundle has been designed to be implemented in adult and pediatric/neonatal ICUs targeting all types of MDROs. Therefore, interventions with limited or conflicting efficacy such as screening for MRSA or VRE [26,27] and skin decolonization with chlorhexidine [22,23] were not included in the current bundle. Another reason for exclusion was the lack of standard implementation of these interventions in different units. For example, screening methodology may target all admissions versus only previously positive patients and/or admissions from other hospitals [27]. Similarly, it may target limited versus extended number of different MDROs [27]. Additionally, skin decolonization is recommended only in limited types of MDROs such as MRSA.

The overall use of antimicrobials was the first component of the current MDROs bundle. ASP practices and their associated reduced antimicrobial use have been shown to significantly reduce the MDROs rates, with or without other components [23,24,28]. The use of antimicrobials is probably the most important component of the MDROs bundle, specially when combined with hand hygiene [26]. Additionally, it is the single most important outcome of the ASP activities. It should reflect all underlying ASP activities, such as education, updating guidelines, antimicrobial restrictions, electronic monitoring, and auditing and feedback rounds in the bundle. Finally, antimicrobial DOTs rather than defined daily doses were used to allow more straightforward interpretation in

**Table 2**
Multidrug-resistant organisms (MDROs) before (April 2016 to June 2019) and during (July 2019 to June 2022) the implementation of MDROs bundle.

| | Before implementation | During implementation | Total | *P*-value |
|---|---|---|---|---|
| **Adult ICUs, overall** | | | | |
| MDROs | 775 | 803 | 1578 | 0.001 |
| Patient days | 66,535 | 81,755 | 148,290 | |
| Rate per 10,000 patient days | 116.5 | 98.2 | 106.4 | |
| **Pediatric/neonatal ICUs, overall** | | | | |
| MDROs | 83 | 88 | 171 | 0.530 |
| Patient days | 53,030 | 61,894 | 114,924 | |
| Rate | 15.7 | 14.2 | 14.9 | |
| **All ICUs, overall** | | | | |
| MDROs | 858 | 891 | 1749 | 0.002 |
| Patient days | 119,565 | 143,649 | 263,214 | |
| Rate | 71.8 | 62.0 | 66.4 | |
| **All ICUs, individual** | | | | |
| Gram-negative organisms | 56.2 | 44.1 | 49.6 | <0.001 |
| *Pseudomonas aeruginosa* | 13.9 | 7.7 | 10.5 | <0.001 |
| Acinetobacter spp | 19.9 | 13.7 | 16.5 | <0.001 |
| Enterobacter spp | 0.0 | 0.6 | 0.3 | 0.008 |
| *Escherichia coli* | 3.8 | 1.3 | 2.4 | <0.001 |
| Klebsiella spp | 18.4 | 20.6 | 19.6 | 0.217 |
| Gram-positive organisms | 15.9 | 18.2 | 17.2 | 0.159 |
| MRSA | 11.2 | 11.8 | 11.5 | 0.676 |
| VRE | 4.7 | 6.4 | 5.6 | 0.063 |

*Per 10,000 patient days.

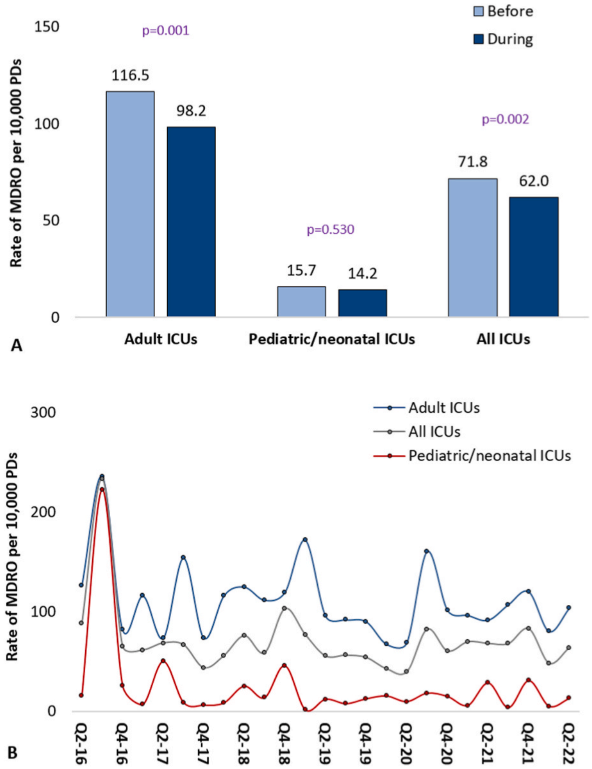


**Fig. 3.** Trends (A) and overall (B) rate of MDROs per 10,000 patient days before (April 2016 to June 2019) and during (July 2019 to June 2022) the implementation of MDROs bundle by the type of ICU.

pediatric/neonatal versus adult ICUs [29].

Implementing the current MDROs bundle resulted in approximately 15% reduction of the overall MDROs rates in adult but not pediatric/neonatal ICUs. Such implementation was preceded and accompanied by intense educational activities in the included units. Previous data showed effectiveness of the components included in the current bundle, separately or in different combinations, in reducing the burden of MDROs [22–24]. However, they did not differentiate between adult and pediatric/neonatal populations. The lack of bundle effectiveness in pediatric/neonatal ICUs in the current study may be related to the significantly lower baseline MDROs rates and overall antimicrobial use in pediatric/neonatal compared with adult ICUs. Gram-negative MDROs which were more represented in adult ICUs were the main drive for reduction of overall MDROs rates. As the COVID-19 pandemic was globally associated with limited ASP activities and higher MDROs rates [30,31], the coincidence of the COVID-19 pandemic with the implementation of the current bundle may have underestimated its positive impact. Finally, it is almost impossible to dissociate the antagonistic effects of enforced infection control practices in this study aiming to reduce MDROs rates in target units from MDROs received from the community, other hospitals, and other non-included units in the same hospital.

The current study has several strengths and some limitations. For example, it is bridging an explicit data limitation as regards the MDROs bundle. Data on MDROs rates and most of the current components of the MDROs bundle can be obtained from other routine surveillance activities. Additionally, the provided detailed definitions and methodology will facilitate the bundle use by other healthcare facilities. Nevertheless, not all included ICUs contributed data for the whole implementation period, which further complicate the interpretation. Hawthorn overestimation of hand hygiene compliance and may be appropriate environmental cleaning cannot be excluded. However, these limitations represent daily challenges in real infection control surveillance and are unlikely to impact the current study's findings.

In conclusion, we are reporting a four-component MDROs bundle for use in different ICU settings. They included the overall use of antimicrobials, appropriate environmental cleaning, appropriate contact precautions, and hand hygiene compliance. The bundle outcome was the overall MDROs rates. Implementing the current bundle was associated with a modest decrease in MDROs rates in adult ICUs. The provided detailed definitions and methodology may facilitate its use by other healthcare facilities.

## Ethics approval

The study obtained all required approvals from the IRB committee of King Abdullah International Medical Research Center (KAIMRC), Riyadh, Saudi Arabia. protocol number NRC22R/554/11.

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## Data availability statement

Data will be made available with reasonable request and after the permission of the IRB committee of the King Abdullah International Medical Research Center (KAIMRC).

## CRediT authorship contribution statement

**Majid M. Alshamrani:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Aiman El-Saed:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Mohammed Al Zunitan:** Writing – review & editing, Methodology. **Mohammed Abalkhail:** Writing – review & editing, Methodology. **Doris Abagguey:** Writing – review & editing, Methodology, Data curation. **Fayssal M. Farahat:** Writing – review & editing, Methodology.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.


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