OPEN

Multifaceted Control Interventions for Healthcare-associated Infections in a Kidney Transplant Intensive Care Unit: Clinical Outcome Improvement and Bundle Adherence

Luana Oliveira Calegari, MD,[1,2] Maria Bethânia Peruzzo, MD,[1,2] Renato Demarchi Foresto, MD, PhD,[1,2] Helio Tedesco-Silva, MD, PhD,[1,2] José Medina Pestana, MD, PhD,[1,2] and Lúcio R. Requião-Moura, MD, PhD[1,2]

Background. Healthcare-associated infections (HAIs) are preventable complications that overwhelm the healthcare system. The implementation of multifaceted control intervention actions in the intensive care setting modifies clinical outcomes, but its effectiveness has not been specifically investigated for high-risk patients, such as kidney transplant recipients (KTRs). **Methods.** This observational retrospective natural experiment evaluated the effectiveness of multifaceted control interventions (bundles) in reducing HAIs in a KTR intensive care unit. We also measured the bundle adherence rate during 16 mo in the after era. **Results.** We included 1257 KTRs, 684 before and 573 in the postintervention period. After the bundle implementation, the incidence density of device-associated HAIs decreased from 8.5 to 3.9 per 1000 patient-days (relative risk [RR] = 0.46; 95% confidence interval [CI], 0.25-0.85; $P = 0.01$), primarily because of the reduction in central line-associated bloodstream infection from 8.0 to 3.4 events per 1000 catheter-days (RR = 0.43; 95% CI, 0.22-0.83; $P = 0.012$). Reductions in catheter-associated urinary tract infection (2.5 versus 0.6 per 1000 catheter-days; RR = 0.22; 95% CI, 0.03-1.92; $P = 0.17$) and ventilator-associated pneumonia (3.4 versus 1.0 per 1000 ventilator-days; RR = 0.29; 95% CI, 0.03-2.63; $P = 0.27$) were not significant. Central venous ($P = 0.53$) and urinary catheter ($P = 0.47$) insertion adherence were stable during 16 mo, whereas central venous ($P < 0.001$) and urinary catheter ($P = 0.004$) maintenance gradually increased. Finally, ventilator-associated pneumonia prevention bundle adherence slightly decreased over time ($P = 0.06$). **Conclusions.** The implementation of comprehensive multifaceted control intervention actions in an intensive care unit dedicated to KTR care was effective in significantly reducing device-associated infections. The impact was in line with the reductions observed in populations that have not undergone transplantation, underscoring the effectiveness of these interventions across different patient groups.

(*Transplantation Direct* 2024;10: e1718; doi: 10.1097/TXD.0000000000001718.)

Received 17 July 2024. Revision received 23 August 2024.

Accepted 26 August 2024.

[1] *Hospital do Rim, Fundação Oswaldo Ramos, São Paulo, Brazil.*

[2] *Nephrology Division, Universidade Federal de São Paulo, São Paulo, Brazil.*

This study was supported by Fundacão Oswaldo Ramos.

The authors declare no conflicts of interest.

L.O.C. and L.R.M. participated in research design, performing the research, data analysis, and approved the article. M.B.P. participated in research design, performing the research, in data analysis, and wrote and approved the article. R.D.F., H.T.S., and J.M.P. participated in research design and approved the article.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

Correspondence: Lúcio R. Requião-Moura, MD, PhD, Rua Borges Lagoa, 960 São Paulo 04038-032, Brazil. (lucio.requiao@gmail.com).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001718

Healthcare-associated infections (HAIs) are widely recognized as preventable, yet they remain among the most significant global public health challenges, as identified by the World Health Organization.[1-4] An epidemiological study in 2002 estimated that there were nearly 1.7 million cases of HAIs in American healthcare facilities, resulting in approximately 100 000 deaths.[5] This death toll surpasses that of any other notifiable disease. Even in high-income countries, about 30% of patients in intensive care units (ICUs) acquire at least 1 HAI, primarily because of invasive devices such as central line catheters, urinary catheters (UCs), or mechanical ventilation (MV).[6-9]

HAIs not only lead to preventable deaths but also impose substantial financial burdens, adding between $24 and $45 billion annually to healthcare costs.[10] In response to the critical need to control HAIs, the Institute for Healthcare Improvement (IHI) and the Centers for Disease Control and Prevention have implemented multifaceted control intervention actions.[11-14] These include standardization of procedures, extensive training, educational initiatives, meticulous outcome monitoring, and timely feedback involving all healthcare personnel. These coordinated efforts, globally recognized

as HAI prevention bundles, are endorsed by the World Health Organization and supported by various governmental and nongovernmental organizations. A meta-analysis covering 144 studies showed that these interventions reduced HAI rates by 35% to 55%, with consistent results across different economic regions.[15]

Despite these advances, the specific impact of HAI prevention bundles on vulnerable patient groups, such as kidney transplant recipients (KTRs), needs to be better elucidated. KTRs face heightened risks of severe infections because of their need for immunosuppressive medication and their generally higher comorbidity burden. This study focuses on the effects of HAI prevention bundles in an ICU specialized in KTR management within a teaching tertiary hospital. It offers a unique opportunity to assess adherence to these bundles and their clinical outcomes in a vulnerable group.

MATERIALS AND METHODS

Study Design

This retrospective cohort study included KTRs treated at the Hospital do Rim in São Paulo, Brazil, and admitted to the ICU from March 2016 to June 2019. Hospital do Rim is a tertiary hospital dedicated to kidney transplants with 151 beds, including a 16-bed ICU. The center usually performs almost 1000 KTRs yearly, 85% from deceased donors and supported by the Brazilian Public Health System. As of June 2019, the center had 11 875 KTRs on follow-up in the local outpatient clinic. Following a 3-mo intensive training program supported by the National Health Ministry, a comprehensive suite of multifaceted control interventions was fully implemented in the ICU starting in December 2017. This implementation created a natural experiment opportunity, allowing the study to adopt a before-and-after design to assess the impact of these interventions on the incidence rates of HAIs. For this analysis, the 3 mo before implementation (September 2017 to December 2017) were designated as the training and implementation phase, and the subsequent 3 mo (December 2017 to March 2018) were considered an adaptation period. Consequently, this 6-mo window was excluded from the analysis to avoid confounding effects during these transitional phases. The natural experiment temporal design is depicted in **Figure S1** (**SDC,** http://links.lww.com/TXD/A706).

Moreover, like all human endeavors, achieving high adherence rates to HAI prevention bundles critically depends on the engagement of healthcare practitioners, in addition to the necessary training and implementation processes. Therefore, the evaluation of adherence to the implemented interventions focused exclusively on the period after this adjustment phase.

The study was approved by the Ethics Committee at the Federal University of São Paulo (identification number CAEE 4063120.8.0000.5505 and approval number 4.228.520). The informed consent form was waived.

Inclusion and Exclusion Criteria

We included all adult KTRs older than 18 y with a functioning graft, admitted to the ICU for any reason, and on any immunosuppressive therapy. The exclusion criteria were as follows: patients who had lost their graft before hospital admission; patients with simultaneous or sequential multiorgan transplants (including pancreas, liver, or others); patients transferred from other hospital units, likely already using device support without the implemented bundles; and patients admitted to the ICU during the transition period, precisely 3 mo before and after the start of the natural experiment (**Figure S1, SDC,** http://links.lww.com/TXD/A706). As the center has a dedicated unit for the immediate postoperative recovery of transplant patients, only recipients who are hemodynamically unstable or have high cardiovascular risk are transferred to the ICU, resulting in the majority of recipients in the immediate postoperative phase not being transferred to the ICU. Therefore, these patients were also excluded.

Multifaceted Control Interventions Actions and Adherence Monitoring Plan

The multifaceted control intervention actions implemented in December 2017 evolved all types of HAIs, but we detailed the bundles for device-associated HAIs for this analysis. As mentioned, the ICU practitioners underwent a 3-mo intensive training program on a comprehensive suite of multifaceted control interventions, fully implemented in December 2017. Aligned with the recommendations from the IHI and the Centers for Disease Control and Prevention, this program adheres to guidelines set by the Brazilian Health Regulatory Agency (ANVISA). The interventions addressed various types of HAIs. However, for this analysis, we focused specifically on the bundles related to device-associated HAIs, including central line-associated bloodstream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), and ventilator-associated pneumonia (VAP). Details of these multifaceted control interventions are provided in **Tables S1–S3** (**SDC,** http://links.lww.com/TXD/A706).

To execute the training program for the multidisciplinary teams, the leaders who received training supported by the National Health Ministry formed a group responsible for replicating the concepts to the other team members. This group consisted of 2 physicians, 3 nurses, a physiotherapist, and an administrative assistant. They developed the teaching and learning strategies in collaboration with the institution's corporate education team. The initial approach involved lecture-based sessions to demonstrate the negative impacts of HAIs on patient outcomes and to introduce the concept of preventable events. Subsequently, specific information about the bundles was shared with the team members for study, replicating material provided by the National Health Ministry and ANVISA. During the 3 mo of training preceding the full implementation (December 2017), the multidisciplinary team members were trained on each item described in **Tables S1–S3** (**SDC,** http://links.lww.com/TXD/A706) through realistic simulations, followed by individual bedside validation.

The adherence monitoring plan for the prevention bundles (**Tables S1–S3, SDC,** http://links.lww.com/TXD/A706) was tailored to the dynamics of the local ICU, specialized in KTR care, following protocols from ANVISA and IHI. Adherence was observationally measured using checklists that itemized the required device insertion and maintenance actions.

The adherence measures for the insertion of a central venous catheter (CVC) and UC were meticulously recorded on a checklist at the time of device insertion. These observations were carried out by trained nursing technicians or nurses during the procedure. For the maintenance items of CVC, UC, and MV, adherence measures were captured by a single professional each month, 3 times per week, covering all shifts and varying times, to capture a representative sample of device use

and maintenance practices. Eight hours of direct observation were conducted weekly, with 2 h allocated to each shift on alternate days and times to ensure that different moments of care were covered. All information was recorded on specific spreadsheets. Daily inquiries during multiprofessional visits recorded information on device use duration. Feedback was provided to the care teams based on the adherence data collected, with targeted educational interventions developed for areas of low adherence. Active learning methodologies were used to enhance team engagement, promoting an educational strategy where "everyone teaches, and everyone learns."

Outcomes and Definitions

The primary outcome was the incidence rate of device-associated HAIs, such as CLABSI, CAUTI, and VAP. These were analyzed as aggregated data and stratified by device type, comparing the incidence rates before and after implementing multifaceted control interventions. We assessed the adherence rates to bundle items postintervention and responses to educational interventions as an exploratory outcome.

The Hospital Infection Control Service identified and reported device-associated HAIs following ANVISA guidelines, incorporating recommendations from the IHI and the Centers for Disease Control and Prevention. A comprehensive review of all HAI events was conducted during data collection. Adherence was evaluated using an "all-or-nothing" approach, where any missing preventive measure at the time of observation was recorded as nonadherence. Details of the measured items are provided in **Tables S1–S3** (**SDC,** http://links.lww.com/TXD/A706).

Statistical Analysis

Data were collected from the institution's database and electronic medical records, included on the RedCap platform, anonymized, and deidentified before statistical analysis. After a nonnormal distribution confirmed by the Kolmogorov-Smirnov normality test, continuous variables were presented as medians with interquartile ranges (IQRs). Categorical variables were expressed as frequencies and percentages. The populations were stratified by era—before and after the implementation—with numerical variables compared using the Mann-Whitney *U* test and categorical variables using the chi-square test.

The incidence rates were calculated as the frequency of patients who met the diagnostic criteria for each type of infection relative to the total number of patients at risk per day in the ICU for all HAIs and per device-day for specific device-associated HAIs. The effects of the era on HAIs rate (accounting tighter or by type) were evaluated using a Poisson regression model considering the exposure. An additional model adjusted by the patients' severity (using Sequential Sepsis-related Organ Failure Assessment [SOFA] and Simplified Acute Physiology Score III [SAPS III]) was also performed. The results were summarized as relative risk (RR) and 95% confidence interval (CI).

For adherence metrics, we considered absolute numbers of observations, medians, and IQRs of adherence percentages in the months after the bundle implementations. The pattern of the time series was evaluated using Joinpoint regression models, which allow for the analysis of both significant trends and inflection points (the joinpoints), moments when a change in trend occurs over time. The Joinpoint regression model assumes that the time series is formed by a set of segments with different slopes, connected by change points (inflection points). The regression was estimated using an algorithm that checked whether a multisegment line was significantly better than a straight line or a line with fewer segments. In each segment of the final model, the monthly percentage change (MPC) was presented.

All statistical analyses were performed using SPSS software version 29 (IBM Corp, Armonk, NY), Joinpoint Regression Program version 4.9.1 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute), and Stata 17 (College Station, TX. StataCorp LLC). A 2-sided *P* value of <0.05 was considered statistically significant, with a 95% CI.

RESULTS

Population Disposition

The population flowchart is detailed in Figure 1. From March 2016 to June 2019, 2025 patients were admitted to the ICU, of whom 1864 were adult KTRs. The training, implementation, and adaptation period was from September 2017 to March 2018, as detailed before and depicted in **Figure S1** (**SDC,** http://links.lww.com/TXD/A706), with 303 patients excluded because they were admitted in this period. Other 304 patients were also excluded: 81 in the immediate postoperative period of a kidney transplant, 78 recipients of a simultaneous transplant of a kidney with another solid organ, and 145 who no longer had a functioning renal graft. Thus, a total of 1257 KTRs were included, 684 (54.4%) comprising the before era implementation of infection prevention bundles and 573 (45.6%) the after era.

Baseline Characteristics by Era

The baseline characteristics and clinical events before ICU admission, stratified by eras, are summarized in Table 1. The time between the transplant and ICU admission was longer in the after era (54.5 versus 65.1 mo, $P < 0.001$). There was a difference in the frequency of the type of maintenance immunosuppression, according to the eras. However, in both eras, the combination of calcineurin inhibitors with mycophenolate acid (MPA) predominated. There were no differences regarding the reason for ICU admission. However, patients admitted in the before era presented slightly higher SOFA and SAPS III scores: 5.0 versus 4.0 points, $P < 0.001$ for SOFA, and 49.5 versus 48.0 points, $P = 0.009$, for SAPS III. In the same era, a lower estimated glomerular filtration rate at ICU admission was observed (23.6 versus 25.3 mL/min/1.73 m^2, $P = 0.019$).

Clinical Events After ICU Admission and Rates of Device Usage

Table 2 shows the main clinical events and the device usage rate by era. The incidence of acute kidney injury was higher in the before era (73.1% versus 67.2%, $P = 0.02$), as was the need for renal replacement therapy (37.6% versus 32.5%, $P = 0.05$). Other advanced life support measures, such as amine vasoactive, parenteral nutrition, and blood transfusions, remained similar across eras. Regarding the devices, although there was a trend toward reduced use of UC in the after era (47.2% versus 42.1%, $P = 0.06$), no significant differences were observed in the frequency of CVC and MV between the eras.

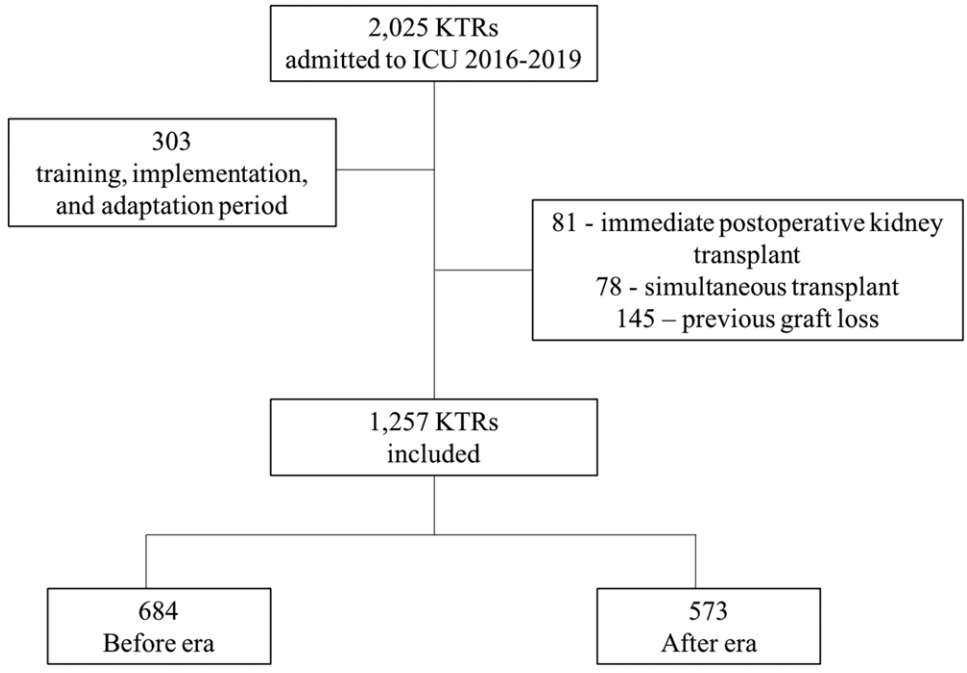

FIGURE 1. Population flowchart. ICU, intensive care unit; KTR, kidney transplant recipient.

Primary Outcome

Figure 2 shows the incidence rates of device-associated HAIs. Analyzing the grouped data for the 3 event types, there was a significant reduction in the overall rate from 8.50 to 3.90 per 1000 device-days, representing a risk reduction of 54% (RR = 0.46; 95% CI, 0.25-0.85, $P = 0.01$). Specifically, the incidence rates of CLABSI decreased from 8.00 to 3.40 events per 1000 CVC-days, corresponding to a risk reduction of 57% (RR = 0.43; 95% CI, 0.22-0.83; $P = 0.012$). Although there were decreases in other types of device-associated HAIs, these were not statistically significant: the rate of CAUTI dropped from 2.50 to 0.60 per 1000 catheter-days (RR = 0.22; 95% CI, 0.03-1.92; $P = 0.17$), and the rate of VAP declined from 3.40 to 1.00 per 1000 ventilator-days (RR = 0.29; 95% CI, 0.03-2.63; $P = 0.27$). The effect of the era on the infection rate was also analyzed in a model adjusted for patient severity (SOFA and SAPS III), and the results were similar to those of the unadjusted model (Table 3).

Adherence Analysis

For the analysis of adherence rates, the elements of each bundle were categorized into insertion and maintenance items for CVC and UC, as well as the bundle for MV (detailed in **Tables S1–S3, SDC,** http://links.lww.com/TXD/A706). From March 2018 to June 2019, corresponding to the after era, a total of 2872 observations were gathered. The results are summarized in Table 4, illustrated month-by-month in Figure 3, and detailed per item in **Tables S4–S8** (**SDC,** http://links.lww.com/TXD/A706). In addition, the Joinpoint model analysis is shown in Table 5.

In the case of CVC insertion items (Figure 3A), a consistent stability trend was noted, with a median adherence rate of 100% (IQR, 96.9–100) and an MPC of –0.09 (95% CI= –0.40 to 0.22, $P = 0.53$) across 663 observations. There was a gradual (MPC = 4.06; 95% CI, 2.51-5.63) and significant ($P < 0.001$) increase in adherence to maintenance tasks, achieving a median rate of 64.2% (IQR, 46.5–71.4) in 678 observations (Figure 3A).

For UC insertion, 283 observations were recorded throughout the period, maintaining a stable adherence rate (MPC = –0.05; 95% CI= –0.19 to 0.09; $P = 0.47$) of 100% over time (Figure 3B). For maintenance tasks, 470 observations indicated a significantly upward trend in adherence (Figure 3B), with an MPC of 3.92 (95% CI, 1.44-6.45; $P = 0.004$), achieving a median rate of 49.5% (IQR, 39.3–63.8). Finally, for the VAP prevention bundle, 778 observations were analyzed, showing a slight decrease in adherence over time (Figure 3C; MPC = –1.11; 95% CI, –2.25 to 0.05; $P = 0.06$), with a median adherence rate of 80.8% (IQR, 76.2–85.4).

DISCUSSION

In the last 2 decades, there has been a global movement for the control and prevention of HAIs, with the adoption of multifaceted control intervention actions. These measures have consistently reduced the occurrence of HAIs by about 35% to 55% when the populations studied are not stratified for different epidemiological contexts.[15-20] The population of KTRs is highly vulnerable to infections, notably because of the unavoidable use of immunosuppressive agents and a cumulative number of comorbidities. To our knowledge, this is the first study to evaluate the impact of implementing these measures in KTRs requiring ICU admission, and interestingly, the magnitude of the reduction in device-associated HAIs was similar to that previously published in general populations. Notably, we started from low incidences of HAIs, and even in an ecosystem with low densities of certain types of device-associated HAIs, the implementation of these strategies showed clinically significant results. Additionally, we assessed adherence to care bundles, uncovering patterns that underscore the importance of continually fostering a safety culture among all healthcare personnel involved in managing high-risk patients.

TABLE 1.

Demographic characteristics and baseline ICU admission stratified by era

Variable	Total (N = 1257)	Before (N = 684)	After (N = 573)	*P*
Age at ICU admission	58.5 (48.0-65.7)	58.7 (48.6-65.6)	58.3 (46.8-66.0)	0.74
Sex (male), n (%)	768 (61.1)	422 (61.7)	346 (60.4)	0.63
Ethnicity, n (%)				0.94
White	795 (63.2)	429 (62.7)	366 (63.9)	
Afro-Brazilian	429 (34.1)	236 (34.5)	193 (33.7)	
Others	33 (2.7)	19 (2.8)	14 (2.4)	
Time after transplantation, mo	61.2 (9.0-112.2)	54.5 (3.1-109.8)	65.1 (21.5-115.7)	<0.001
Immunosuppression,[a] n (%)				<0.001
CNI + AZA	337 (26,8)	169 (24.7)	*167 (29.1)*	
CNI + MPA	560 (44,6)	312 (45.6)	*248 (43.3)*	
CNI + imTOR	94 (7,5)	65 (9.5)	*29 (5.1)*	
Others	267 (21,2)	138 (20,2)	*129 (22,5)*	
Cancer after transplantation,[b] n (%)	198 (15.8)	103 (15.2)	95 (16.6)	0.49
Referring unit, n (%)				0.44
Ward	541 (43.0)	286 (41.8)	*255 (44.5)*	
Emergency room	493 (39.2)	266 (38.9)	*227 (39.6)*	
Surgery room	220 (17.5)	130 (19.0)	*90 (15.7)*	
Outpatient unit	3 (0.2)	2 (0.3)	*1 (0.2)*	
Reason for ICU admission, n (%)				0.52
Sepsis	271 (21.6)	151 (22.1)	*120 (20.9)*	
Respiratory failure	228 (18.1)	117 (17.1)	*111 (19.4)*	
Cardiovascular event	205 (16.3)	120 (17.5)	*85 (14.8)*	
Postoperative (nontransplant)	193 (15.4)	112 (16.4)	*81 (14.1)*	
Neurologic event	157 (12.5)	79 (11.5)	*78 (13.6)*	
Bleeding	51 (4.1)	27 (3.9)	*24 (4.2)*	
Others	152 (12.1)	*78 (11.4)*	*74 (12.9)*	
Charlson, points	5.0 (4.0-7.0)	5.0 (4.0-7.0)	5.0 (3.5-7.0)	0.14
SOFA, points	5.0 (3.0-7.0)	5.0 (3.0-8.0)	4.0 (3.0-7.0)	<0.001
SAPS III, points	49.0 (41.0-58.0)	49.5 (42.0-59.0)	48.0 (40.5-56.0)	0.009
Glasgow, points	15.0 (14.0-15.0)	15.0 (14.0-15.0)	15.0 (14.0-15.0)	0.11
eGFR,[b] mL/min/1.73 m^2	24.1 (12.7-42.8)	23.6 (11.0-40.6)	25.3 (13.5-44.7)	0.02

[a]All patients were undergoing prednisone associated with each combination described in this table. Details on the standard immunosuppression used in the center is presented in the **Supplemental Digital Content** (**SDC**, http://links.lww.com/TXD/A706).
[b]Missing values: neoplasia after transplantation, 5; eGFR, 2.
AZA, azathioprine; CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; imTOR, inhibitor of the mammalian target of rapamycin; MPA, mycophenolate acid; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Sepsis-related Organ Failure Assessment.

TABLE 2.

Clinical events after ICU admission and the device usage rate by era

Variable	Total (N = 1257)	Before (N = 684)	After (N = 573)	*P*
Vasopressors use, n (%)	402 (32.0)	228 (33.3)	174 (30.4)	0.26
Acute kidney injury, n (%)	885 (70.4)	500 (73.1)	385 (67.2)	0.02
Renal replacement therapy, n (%)	443 (35.2)	257 (37.6)	186 (32.5)	0.05
Parenteral nutrition, n (%)	39 (3.1)	21 (3.1)	18 (3.1)	0.94
Central line catheter, n (%)	657 (52.3)	353 (51.6)	304 (53.1)	0.60
Urinary catheter, n (%)	564 (44.9)	323 (47.2)	241 (42.1)	0.06
Mechanical ventilation, n (%)	362 (28.8)	196 (28.7)	166 (29.0)	0.90

ICU, intensive care unit.

Aligned with results from previous studies, implementing multifaceted control intervention actions in our study markedly decreased the incidence of HAIs. Breaking down the data, in terms of RR, there was a 57% reduction in CLABSI, 78% in CAUTI, and 71% in VAP. Although all 3 types of HAIs showed notable relative reductions, only the decrease in CLABSI was statistically significant when examined independently. A meta-analysis encompassing data from 114 studies on the proportion of preventable infections indicated that comprehensive control interventions lowered the risk of CLABSI by 46%.[15] No studies have specifically targeted the population of KTRs. In a study conducted at our service in 2010 involving 185 KTRs, with bloodstream infection associated or not with CVC, the primary infection source was identified as urinary

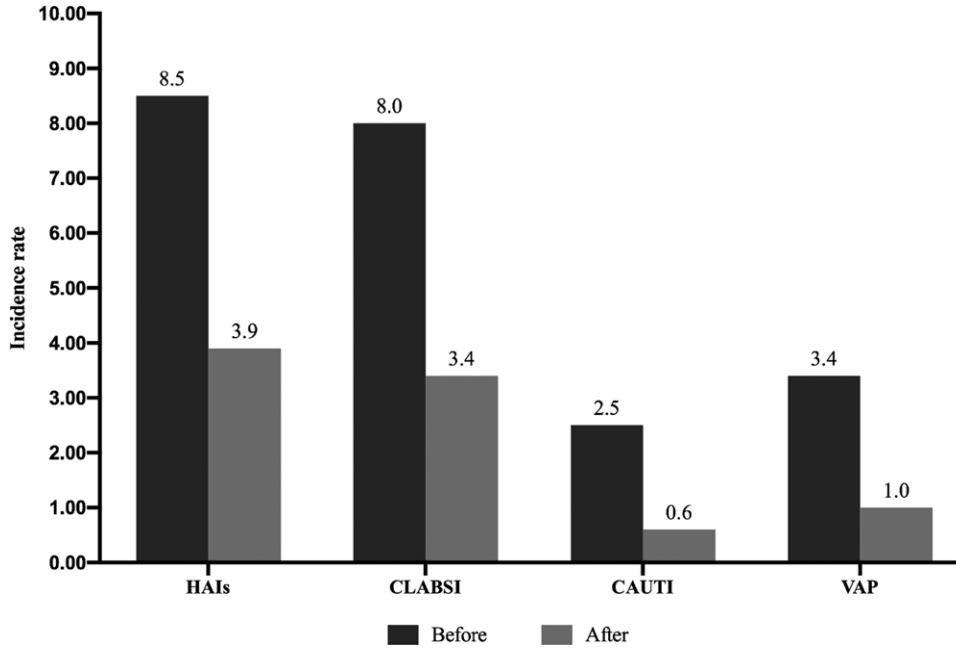

FIGURE 2. HAIs incidence rate stratified by era and by devices. The devices HAIs are expressed in infections per patients-day and stratified by the device in infections per device-day: CLASBI, per 1000 catheter-day; CAUTI, per 1000 catheter-day; VAP, per 1000 mechanical ventilation-day. CAUTI, catheter-associated urinary tract infection; CLASBI, central line-associated bloodstream infection; HAI, devices healthcare-associated infection; VAP, ventilator-associated pneumonia.

TABLE 3.

Unadjusted and adjusted Poisson model for risk of infection by era and device

	Before		After		Unadjusted model		Adjusted model	
Infections	**Incidence rate**	**N**	**Incidence rate**	**N**	**RR (95% CI)**	***P***	**RR (95% CI)**	***P***
HAIs	8.5	449	3.9	349	0.46 (0.25-0.85)	0.013	0.46 (0.25-0.86)	0.015
CLASBI	8.0	353	3.4	304	0.43 (0.22-0.83)	0.012	0.47 (0.24-0.93)	0.030
CAUTI	2.5	323	0.6	241	0.22 (0.03-1.92)	0.172	0.17 (0.02-1.52)	0.113
VAP	3.4	196	1.0	166	0.29 (0.03-2.63)	0.273	0.31 (0.03-2.94)	0.309

The devices HAIs are expressed in infections per patients-day and stratified by the device in infections per device-day: CLASBI, per 1000 catheter-day; CAUTI, per 1000 catheter-day; VAP, per 1000 mechanical ventilation-day.
The Poisson regression model was adjusted by patients' severity (SOFA and SAPS III).
CAUTI, catheter-associated urinary tract infection; CI, confidence interval; CLASBI, central line-associated bloodstream infection; HAI, healthcare-associated infection; RR, relative risk; VAP, ventilator-associated pneumonia.

TABLE 4.

Number of observations and bundles' adherence rates

Items for prevention actions	No. of observations	Rates of adherence (medians of %)
Insertion items for CVC	663	100.0 (IQR, 96.9–100.0)
Maintenance items for CVC	678	64.2 (IQR, 46.5–71.4)
Insertion items for UC	283	100.0 (IQR, 100.0–100.0)
Maintenance items for UC	470	49.5 (IQR, 39.3–63.8)
Bundle for VAP prevention	778	80.8 (IQR, 76.2–85.4)

The details about each item compound the insertion and maintenance (for CVC and UC) and for the VAP prevention ins presented in **Tables S4–S8** (**SDC,** http://links.lww.com/TXD/A706).
CVC, central venous catheter; IQR, interquartile range; UC, urinary catheter; VAP, ventilator-associated pneumonia.

tract infections, constituting 37.8% of cases.[21] No existing research has specifically addressed this infection type within this demographic in ICU settings that necessitate advanced life care. In a single-center prospective ICU cohort in Taiwan, the targeted HAI control measures reduced the incidence density of CLABSIs from 7.4 to 3.9 infections per 1000 catheter-days, achieving a relative reduction of 47.3%, with 32.6% of patients suffering from chronic kidney disease; however, only 5.5% were immunosuppressed.[22] Our findings affirm that even in a highly vulnerable patient group, implementing infection control strategies effectively reduces infection rates.

Despite CAUTI and VAP achieving higher relative reductions than CLABSI, these reductions did not reach statistical significance. Stratified by the income level of the country where the studies were conducted, the implementation of measures to reduce CAUTI ranged from 47% to 59%.[15] A pioneering study in Brazil demonstrated in the early 2010s a reduction from 7.6 to 5.0 CAUTI per 1000 catheter-days with the implementation of prevention measures.[23] Notably, these results were observed in a private tertiary hospital in the same city as our service. Comparing both eras, some results suggested that patients in the preimplementation era were sicker than those in the postimplementation era, as indicated by higher SOFA and SAPS III scores and a higher incidence of acute kidney injury. Despite this, what is most

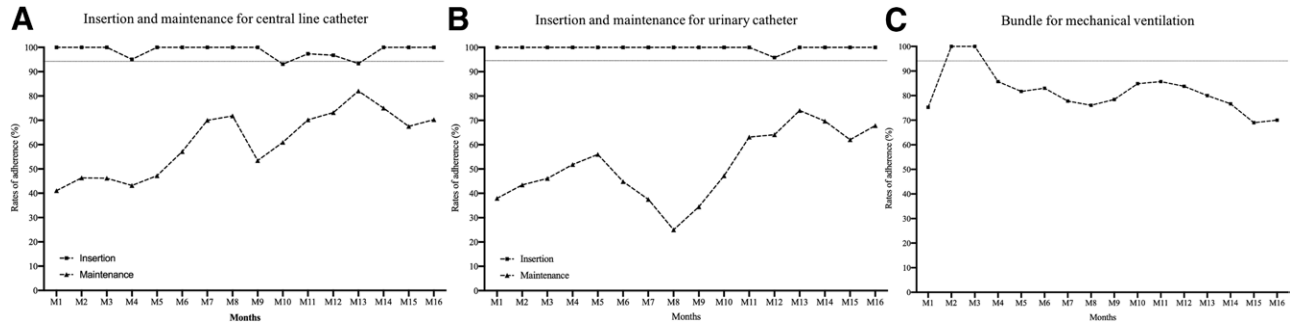

FIGURE 3. The bundle adherence over time. M1 represents March 2018, and M16 represents June 2019. The month-to-month values are the median of all measurements captured by the observer, considering the approach of "all or nothing." The solid grey line at 95% represents the ideal goal standardized by IHI. IHI, Institute for Healthcare Improvement.

TABLE 5.

Temporal trends on the adherence rates estimated by the Joinpoint model

Items	MPC (95% CI)	*P*
CVC insertion	−0.09 (−0.40 to 0.22)	0.532
CVC maintenance	4.06 (2.51 to 5.63)	<0.001
UC insertion	−0.05 (−0.19 to 0.09)	0.473
UC maintenance	3.92 (1.44 to 6.45)	0.004
Bundle for VAP prevention	−1.11 (−2.25 to 0.05)	0.060

CI, confidence interval; CVC, central venous catheter; MPC, monthly percentage change; UC, urinary catheter; VAP, ventilator-associated pneumonia.

striking in our data is a relatively low starting incidence in the era before the implementation of prevention measures (2.5 events per 1000 catheter-days). This could be explained by the peculiarities of the service, which, in addition to having a high volume of renal transplants performed annually, has an ICU that is highly specialized in the care of patients with urinary tract pathologies. Moreover, although tangential, we observed a reduced urinary device utilization rate. It is possible that the relative reduction in CAUTI did not reach levels of statistical significance because of limitations imposed by the number of patients included and the low incidence of events already observed before the implementation of the prevention measures.

The same pattern was observed in VAP, with a significant relative reduction from 3.4 to 1.0 VAP per 1000 patients in MV-days, in line with several other studies in countries with the same Brazilian income profile.[24-26] At the end of the 2000s, assessing the impact of changes in prevention routines at the same tertiary hospital in Brazil mentioned above, Marra et al[27] observed a reduction from 16.4 to 10.4 events per 1000 patients in MV-days. Again, our study started with a very low incidence density. Moreover, despite no reduction in the MV usage rate between the 2 eras (Table 3), our cohort had a low frequency of patients admitted because of respiratory failure and a relatively low severity index (Table 1). Moreover, it should be considered that the prevention measures for VAP were the only ones that showed a reduction in adherence over time, unlike what was observed by the pioneering Brazilian study, which achieved the impressive mark of zero VAP when adherence to interventions reached rates >95%.[27]

The effectiveness of multifaceted control intervention actions for HAIs heavily relies on the commitment of healthcare teams involved in direct patient care.[28] Establishing daily achievable goals, maintaining robust communication, and prioritizing continuous education are fundamental components of cultivating an environment of mutual collaboration supported by the efforts of a multidisciplinary team. Previous reports have indicated poor quality and a lack of knowledge regarding HAI controls among healthcare providers contribute to high infection rates.[1,29] Conversely, forming specialized teams focused on information dissemination, using ongoing education strategies, and fostering a safety culture are effective methods for engaging teams and improving healthcare outcomes, even in low- and middle-income countries.[30] For example, a recent study in Brazil highlighted the importance of monitoring adherence to infection control bundle protocols and identified a strong link between adherence rates to device-associated HAI bundle items and incidence density rates.[31]

Our study revealed high and stable adherence rates for insertion protocols and a progressive increase in maintenance adherence for CVC and UC. Notably, during the 16-mo observation period, the adherence rates for CVC insertion items fell below 100% only 5 times, and for UC, just once. Whenever these drops occurred, a swift recovery in adherence was observed. In the case of handling and maintenance protocols, we noted a gradual improvement in adherence rates over time. However, there were instances of temporary declines, which were quickly and consistently rectified. These findings highlight that safety culture was effectively implemented through strategic information sharing, educational interventions, and strong team engagement.[32] Recognized strategies facilitated this, including daily updates shared via a mobile communication system, real-time HAI data dissemination during shifts, displaying infection data on ICU panels, and monthly campaigns targeting protocols with low adherence.[33] Additionally, appointing guardians for each HAI type helped address team queries and promote best practices, whereas the use of engaging, playful learning methods with immediate feedback and involving patients and their families further reinforced this culture.

Although our study provides valuable insights from the scientific measurement of a successful clinical practice, it also has limitations that must be highlighted. The primary limitations arise from its retrospective nature, which introduces potential biases and confounding. The study was conducted at a single center, so the data might need to be more generalizable to other centers or populations. Our center has a high volume of kidney transplants, many patients in outpatient follow-up, a highly specialized team, an ICU dedicated to caring for KTRs,

and a multidisciplinary team with low turnover. These factors may not reflect the situation at most other centers, including in low- or middle-income countries that manage such patients. Finally, the number of observations for maintenance bundles was small considering the postintervention study period, which can be a weakness of the study.

CONCLUSIONS

This study demonstrated that multifaceted control intervention actions effectively reduce HAIs in highly vulnerable KTRs admitted to the ICU. Our study also revealed high and stable adherence rates for insertion protocols and a progressive increase in maintenance adherence for CVC and UC over time.

REFERENCES

1. Haque M, Sartelli M, McKimm J, et al. Health care-associated infections—an overview. *Infect Drug Resist*. 2018;11:2321–2333.
2. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med*. 1991;324:370–376.
3. Haque M, McKimm J, Sartelli M, et al. Strategies to prevent healthcare-associated infections: a narrative overview. *Risk Manag Healthc Policy*. 2020;13:1765–1780.
4. Mayor S. Hospital acquired infections kill 5000 patients a year in England. *BMJ*. 2000;321:1370.
5. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep*. 2007;122:160–166.
6. Vincent JL. Nosocomial infections in adult intensive-care units. *Lancet*. 2003;361:2068–2077.
7. Richards MJ, Edwards JR, Culver DH, et al. Nosocomial infections in combined medical-surgical intensive care units in the United States. *Infect Control Hosp Epidemiol*. 2000;21:510–515.
8. Torres A, Aznar R, Gatell JM, et al. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. *Am Rev Respir Dis*. 1990;142:523–528.
9. Vincent JL, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA*. 1995;274:639–644.
10. Stone PW. Economic burden of healthcare-associated infections: an American perspective. *Expert Rev Pharmacoecon Outcomes Res*. 2009;9:417–422.
11. Lisboa T, Rello J. Towards zero rate in healthcare-associated infections: one size shall not fit all. *Crit Care*. 2013;17:139.
12. Burke JP. Infection control—a problem for patient safety. *N Engl J Med*. 2003;348:651–656.
13. Gerberding JL. Hospital-onset infections: a patient safety issue. *Ann Intern Med*. 2002;137:665–670.
14. Milne R, Munro A, Scott R, et al. A follow up study of 200 men after vasectomy. *Health Bull (Edinb)*. 1986;44:137–142.
15. Schreiber PW, Sax H, Wolfensberger A, et al; Swissnoso. The preventable proportion of healthcare-associated infections 2005-2016: systematic review and meta-analysis. *Infect Control Hosp Epidemiol*. 2018;39:1277–1295.
16. Allen GB, Miller V, Nicholas C, et al. A multitiered strategy of simulation training, kit consolidation, and electronic documentation is associated with a reduction in central line-associated bloodstream infections. *Am J Infect Control*. 2014;42:643–648.
17. Hewitt DB, Tannouri SS, Burkhart RA, et al. Reducing colorectal surgical site infections: a novel, resident-driven, quality initiative. *Am J Surg*. 2017;213:36–42.
18. Leblebicioglu H, Ozturk R, Rosenthal VD, et al. Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). *Ann Clin Microbiol Antimicrob*. 2013;12:10.
19. Mathur P, Tak V, Gunjiyal J, et al. Device-associated infections at a level-1 trauma centre of a developing nation: impact of automated surveillance, training and feedbacks. *Indian J Med Microbiol*. 2015;33:51–62.
20. Sutherland T, Beloff J, McGrath C, et al. A single-center multidisciplinary initiative to reduce catheter-associated urinary tract infection rates: quality and financial implications. *Health Care Manag (Frederick)*. 2015;34:218–224.
21. Silva M Jr, Marra AR, Pereira CA, et al. Bloodstream infection after kidney transplantation: epidemiology, microbiology, associated risk factors, and outcome. *Transplantation*. 2010;90:581–587.
22. Lin KY, Cheng A, Chang YC, et al. Central line-associated bloodstream infections among critically-ill patients in the era of bundle care. *J Microbiol Immunol Infect*. 2017;50:339–348.
23. Marra AR, Sampaio Camargo TZ, Goncalves P, et al. Preventing catheter-associated urinary tract infection in the zero-tolerance era. *Am J Infect Control*. 2011;39:817–822.
24. Abbasinia M, Bahrami N, Bakhtiari S, et al. The effect of a designed respiratory care program on the incidence of ventilator-associated pneumonia: a clinical trial. *J Caring Sci*. 2016;5:161–167.
25. Alsadat R, Al-Bardan H, Mazloum MN, et al. Use of ventilator associated pneumonia bundle and statistical process control chart to decrease VAP rate in Syria. *Avicenna J Med*. 2012;2:79–83.
26. Ban KO. The effectiveness of an evidence-based nursing care program to reduce ventilator-associated pneumonia in a Korean ICU. *Intensive Crit Care Nurs*. 2011;27:226–232.
27. Marra AR, Cal RG, Silva CV, et al. Successful prevention of ventilator-associated pneumonia in an intensive care setting. *Am J Infect Control*. 2009;37:619–625.
28. Al-Tawfiq JA, Abed MS, Al-Yami N, et al. Promoting and sustaining a hospital-wide, multifaceted hand hygiene program resulted in significant reduction in health care-associated infections. *Am J Infect Control*. 2013;41:482–486.
29. Blot S, Ruppe E, Harbarth S, et al. Healthcare-associated infections in adult intensive care unit patients: changes in epidemiology, diagnosis, prevention and contributions of new technologies. *Intensive Crit Care Nurs*. 2022;70:103227.
30. Storr J, Twyman A, Zingg W, et al; WHO Guidelines Development Group. Core components for effective infection prevention and control programmes: new WHO evidence-based recommendations. *Antimicrob Resist Infect Control*. 2017;6:6.
31. Tuma P, Vieira Junior JM, Ribas E, et al; Collaborative Study Group "Saúde em Nossas Mãos". A National Implementation Project to prevent healthcare-associated infections in intensive care units: a collaborative initiative using the breakthrough series model. *Open Forum Infect Dis*. 2023;10:ofad129.
32. Farokhzadian J, Dehghan Nayeri N, Borhani F. The long way ahead to achieve an effective patient safety culture: challenges perceived by nurses. *BMC Health Serv Res*. 2018;18:654.
33. Glowicz JB, Landon E, Sickbert-Bennett EE, et al. SHEA/IDSA/APIC practice recommendation: strategies to prevent healthcare-associated infections through hand hygiene: 2022 Update. *Infect Control Hosp Epidemiol*. 2023;44:355–376.