Implementation and outcomes of an advanced antimicrobial stewardship program at a quaternary care hospital in the United Arab Emirates

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Purpose: The implementation of an advanced antimicrobial stewardship program (ASP) at a quaternary care hospital in the United Arab Emirates is described, including a report on the implementation and outcomes of the program.

Methods: This was a single-center quasi-experimental study to assess the impact of the ASP on antimicrobial use measures, ASP interventions performed, and clinical outcomes by comparing the data collected at baseline, from the third quarter (Q3) 1 July 2015 to the fourth quarter (Q4) of 31 December 2017, approximately 2 years following program implementation.

Results: From 1 July 2015 until 31 December 2017, the program reported a total direct cost savings estimated at $1,339,499, despite a significant increase in patient discharges and total patient-days. The antimicrobial cost per inpatient-day decreased by 32% from $47.2 to $32.3. Usage of monitored antimicrobials decreased despite an increase in patient census since hospital opening. Hospital-onset Clostridioides difficile infection (CDI) rates decreased from 0.46 cases per 1000 patient days in 2015 to 0.12 cases per 1000 patient days in 2017 (P = 0.035, 95% CI 0.08 to 0.91). Hospital-onset infections due to multidrug-resistant organisms (MDROs) decreased from 2.39 cases per 1000 patient days in 2015 to 0.38 cases per 1000 patient days in 2017 (P = 0.05, 95% CI 0.09 to 0.28). Overall, the number of ASP interventions amounted to a total of 4123 interventions, with an acceptance rate of 91%.

Conclusion: The implementation of an advanced ASP at a quaternary care hospital in the United Arab Emirates was associated with a decrease in antimicrobial utilization, antimicrobial expenditure, and a reduction in hospital-onset CDI and MDRO rates. To our knowledge, this is the first report describing the outcomes of an advanced ASP program at a quaternary care hospital utilizing real-time surveillance software and CDSS in the Middle East.

Keywords
antimicrobial stewardship, clinical decision support systems, electronic health records, United Arab Emirates

Antimicrobial stewardship programs (ASPs) are pivotal in health care facilities to curb antimicrobial resistance, improve patient outcomes, and decrease health care costs.1 Having an ASP is now a requirement for hospitals to be accredited through The Joint Commission and Joint Commission International (JCI).2,3 Various strategies for implementing antimicrobial stewardship in hospital settings have been described in the literature.4-6 One such strategy is by incorporating clinical decision support technology and computerized...
surveillance systems into ASPs. Joint guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America for Antimicrobial Stewardship recommend incorporating such computerized systems and technologies into ASPs to streamline the work of ASPs by guiding physicians prescribing at the point of order entry and identifying opportunities for interventions.5

The use of the electronic medical record (EMR) and clinical decision support systems (CDSS) for antimicrobial stewardship has been reported widely in the United States and the international setting, and outcomes of such systems are well documented in the literature.7-13 A recent survey conducted by the American Society of Health-System Pharmacists (ASHP) showed that 95% of hospitals have computerized prescriber-order-entry (CPOE) systems and of those, 39% of hospitals utilize clinical decision support for their ASPs.14 There is a lack of literature documenting the use of CDSS and computerized surveillance systems for ASP in the Middle East. In a recent survey documenting ASP strategies in the Gulf Cooperation Council (GCC) member states, active ASP was reported in 62% of institutions responding to the survey, and active ASP rounds were performed in only half of these institutions. The use of the EMR was reported by 75% of respondents in this survey. Barriers to implementation of ASP were attributed to lack of funding and limited personnel.15 A systematic literature review was conducted demonstrating that ASPs are still in their infancy in the Middle East with very few institutions conducting prospective audits with intervention and feedback. There was a lack of information on whether the use of EMR and CDSS played a role in any of those programs.16 A more recent review on the degree of adoption of ASPs in the GCC countries was conducted which highlighted the barriers for implementation including the lack of leadership support for ASPs, the lack of infectious diseases (ID) consultants and microbiologists, limited information technology (IT) infrastructure, and limited involvement of ID pharmacists in ASP.17 Although this recent review demonstrated that a few institutions in the GCC countries are implementing the core strategies of ASP, namely prospective audit with intervention and feedback and prior authorization of antimicrobials, it was evident from this review that the adoption of CDSS is still limited in this region.17 Adoption of CDSS and computerized surveillance systems is imperative to further enhance the efficiency of ASPs, particularly in the setting of limited personnel support.

In this article we report on the outcomes of an advanced ASP at the Cleveland Clinic Abu Dhabi (CCAD), a recently activated quaternary care hospital in the United Arab Emirates (UAE), where CDSS and computerized surveillance system were used.

1 | SETTING

An ASP was developed at CCAD, a multispecialty quaternary-care hospital in the UAE that was activated in May 2015 and licensed to operate 364 beds including 288 beds in general medical surgical floors and 72 medical-surgical intensive care unit beds. The hospital is owned by Mubadala Development Company and managed and operated by the US-based Cleveland Clinic in Ohio. This partnership between these two enterprises represents the first extension of its kind for the Cleveland Clinic model of care in the international setting. This partnership allowed for the alignment of standards of practice with Cleveland Clinic Ohio and facilitated sharing of best practices in antimicrobial stewardship between the two institutions.

At the time of the study, the hospital operated an average of 360 beds daily each year (patient volume statistics for 2015, 2016, and 2017 are shown in Table 1). The Department of Pharmacy Services is operational 24 hours per day, 7 days a week. During this study period, the Department of Pharmacy Services was staffed by 47 full-time pharmacists including 15 inpatient pharmacists, 9 pharmacotherapy specialists, and 23 Ambulatory pharmacists. Inpatient pharmacists rotate through both distributive and clinical duties. Thirty percent of pharmacists are board-certified through the US Board of Pharmacy Specialties and 18% are residency trained through ASHP-accredited postgraduate year one and postgraduate year two (PGY2) residency programs. The ASP is supported by a US trained pharmacist with PGY2 ID residency training. The program was supported by four US-trained and board-certified ID physicians. Full-time equivalents (FTE) dedicated to ASP included 0.25 ID physician FTE and 0.5 ID pharmacist FTE. The ASP team was also supported by a team of five pharmacy informaticists who dedicated 0.2 FTE to implement various ASP projects.

2 | PROGRAM DEVELOPMENT AND IMPLEMENTATION

2.1 | Program structure and ASP strategies

The ASP was implemented in April 2015. Various tools and resources were implemented prior to hospital opening, including antimicrobial order sets, a computerized surveillance system (RL Solutions, Toronto, CA) and facility specific guidelines and policies. The ASP subcommittee included representation from various teams including ID, hospitalists, Respiratory and Critical Care Medicine, Infection Prevention and Control, Clinical Microbiology, Pharmacy, and Nursing. Post-hospital opening, additional resources and tools in the EMR, as well as policies, procedures, and guidelines to support the ASP were developed. Inpatient pharmacists and pharmacotherapy specialists were trained in antimicrobial stewardship principles through departmental training modules and formal certification. All pharmacists were tasked with
performing antimicrobial stewardship activities at various levels and the core ASP team consisting of the ASP pharmacist and ASP ID physician performed rounds three times per week to follow-up on complex ID cases and formulate various ASP strategies. This step-wise approach ensured that antimicrobial stewardship activities were performed routinely throughout the hospital and allowed the core ASP team to focus on more complex issues that required a higher level of expertise (Figure 1).

### 2.2 Integration of ASP into the EMR

Various ASP strategies were implemented into the EMR system (Epic Systems Corporation, Verona, Wisconsin), which allowed for streamlining of workflows and afforded greater efficiency in day-to-day activities. These included mandatory documentation of indications when ordering restricted and monitored antimicrobials, developing specific intervention categories for ASP interventions for ease of documentation in the EMR, and developing an EMR generated real-time list displaying patients on antimicrobials that met criteria for intravenous to oral (i.v.-to-p.o.) therapy conversion. A real-time computerized surveillance system (RL Solutions, Toronto, CA) was integrated into the EMR, which provided a daily list of patients actively receiving broad-spectrum antimicrobials, a list of patients who met criteria for de-escalation, as well as patients with discordant therapy based on culture results. A real-time ASP dashboard to monitor program metrics was developed in addition to an ASP repository in the EMR for policies, procedures, and guidelines. Order panels for extended-infusion beta-lactams and restricted antimicrobials as well as various antimicrobial order sets for the most common ID cases observed were built into the EMR. In December 2016, the hospital implemented a rapid, multiplex polymerase chain reaction (PCR)-based blood culture identification panel (BioFire Film Array, bioMérieux, Incorporated, Durham, North Carolina) which was integrated into the real-time computerized surveillance system. This integration triggered e-mail notification to the ASP team whenever blood cultures were positive for specific bacterial and some fungal pathogens allowing for prompt initiation or de-escalation of antimicrobial therapy based on multiplex PCR results. When ASP interventions were integrated into the EMR, we ensured the alerts were indeed actionable and did not result in alert fatigue.

### 3 METHODS

We conducted a single-center quasi-experimental study to assess the impact of the ASP on antimicrobial use measures, ASP interventions performed, and clinical outcomes by comparing the data collected at baseline, from 1 July 2015 to 31 December 2017, and approximately 2 years following program implementation. The ASP began in April of 2015. Metrics monitored in the program included days of therapy per 1000 patient days, antimicrobial cost savings based on antimicrobial administered to patients, ASP recommendations and acceptance rates, rates of hospital-onset Clostridioides difficile infections (CDI), rates of hospital-onset multidrug-resistant organisms (MDROs) including Carbapenem-resistant Enterobacteriaceae (CRE), vancomycin-resistant enterococci (VRE), Acinetobacter baumannii, and methicillin-resistant Staphylococcus aureus (MRSA).

### 3.1 Antimicrobial use measures

Barcode medication administration was implemented at hospital opening which allowed any change in antimicrobial consumption rates to be measured using days of therapy per 1000 patient days (DOT/1000 PD). The computerized surveillance system was used to extract this data and data was visualized using data analytics software (Tableau Software, Seattle, Washington). Antimicrobial consumption data was analyzed quarterly comparing the period of 1 July 2015 to 31 December 2017. All antimicrobial agents were included in this analysis, with the exception of rifaximin, demeclocycline, antimycobacterial agents, and antiretrovirals as they were used over the study period almost exclusively for the treatment of hepatic encephalopathy, the syndrome of inappropriate antidiuretic hormone (SIADH) syndrome.

### FIGURE 1

Integration of ASP activities into daily pharmacists activities at our institution. ASP, antimicrobial stewardship program; ID, infectious diseases

| Inpatient Pharmacists |
|-----------------------|
| Basic ASP activities  |
| (e.g., renal dose adjustments, intravenous to oral therapy conversion) |

| Pharmacotherapy Specialists |
|----------------------------|
| Advanced ASP activities    |
| (e.g., prospective audit with intervention and feedback, dose optimization, de-escalation, therapeutic drug monitoring) |

| ASP team (ID Pharmacist and ID Physician) |
|------------------------------------------|
| Complex ASP activities                  |
| Formal ID training                      |
| -Formulating ASP strategies             |
| -ASP rounds (prospective audit with intervention and feedback, dose optimization, de-escalation) |
hormone, treatment of *Mycobacterium tuberculosis*, and post-
exposure prophylaxis, respectively. Monitored antimicrobials
included restricted antimicrobials that needed additional require-
ments for ordering per hospital policy. There were no reported
changes in the acquisition price of any of the antimicrobials ana-
alyzed during the study period.

### 3.2 Economic outcomes

Antimicrobial cost data was generated based on acquisition cost of
antimicrobials administered to patients normalized to 1000 patient
days. Antimicrobial cost data were based on antimicrobial therapy
administered to patients as generated through the EMR. Cost savings
were generated by calculating the delta in antimicrobial acquisition
cost per 1000 patient days between the baseline quarter (ie, 1 July
2015 to 30 September 2015) and each subsequent quarter thereafter,
then adding this delta from each quarter to arrive at a total cost saving
for the entire study period. Rifaximin, demeclocycline, antimycobac-
terial agents, and antiretrovirals were excluded for the reasons stated
earlier.

### 3.3 Antimicrobial stewardship interventions

The number and type of antimicrobial stewardship interventions made
and the percentage accepted were determined. Data was included for
2016 and 2017 as there was no specific category for ASP interven-
tions built in our EMR prior to that. Interventions that were document-
ted as accepted were enacted in the EMR by the prescriber.

Table 2: ASP intervention classifications and recommendations during study period

| Classification                                      | No. of interventions January-December 2016 | No. of interventions January-December 2017 | Change (%) |
|-----------------------------------------------------|--------------------------------------------|--------------------------------------------|------------|
| Dose optimization                                   | 626                                        | 952                                        | +52%       |
| i.v. to p.o conversion                              | 26                                         | 217                                        | +734%      |
| Discontinuation of antimicrobials not indicated      | 314                                        | 340                                        | +8.2%      |
| Streamline to definitive therapy based on cultures  | 66                                         | 182                                        | +175%      |
| Broaden antimicrobial therapy                        | 336                                        | 282                                        | −16%       |
| Limit duration to specific stop date                | 74                                         | 144                                        | +94%       |
| Change therapy due to culture-treatment mismatch    | 29                                         | 71                                         | +144%      |
| Discontinue redundant therapy                        | 43                                         | 54                                         | +25%       |
| Total interventions                                 | 1514                                       | 2242                                       | +48%       |

**Abbreviations:** ASP, antimicrobial stewardship program; i.v., intravenous; p.o, oral.

*The change was calculated for 2016 data compared with 2017 data.*

### 3.4 Clinical outcomes

Hospital-onset CDI rates per 1000 patient days and hospital-onset
infections due to MDROs per 1000 patient days from 1 July 2015
until 31 December 2017 were assessed. Incidence rates for hospital-
onset CDI and hospital-onset MDROs were calculated based on
methods set forth by the National Healthcare Safety Network
(NHSN). The study was not designed to investigate the impact of
implementing the ASP on hospital length of stay, mortality, or 30-day
readmission rates.

### 4 Statistical analysis

Descriptive analysis was used for antimicrobial stewardship interven-
tion data. The Poisson rate ratio test was used to calculate confidence
intervals and *P* values for hospital-onset CDI and hospital-onset
MDRO incidence rates. Assuming the incidence of CDI is a Poisson
distribution, we used the RateRatio test method in the statistical soft-
ware, R (version 3.4.3, Free Software Foundation, Inc., Boston, Massa-
chusetts) to compare the incidence rates of hospital-onset CDI per
1000 patient days between 1 July 2015 and 31 December 2017 to
establish if there was a significant downward trend. The same method
was used for hospital-onset MDRO incidence rate. A proportion *z*-test
was used to calculate days of therapy per 1000 patient days and
acquisition cost of antimicrobials. The a priori level of significance was
set at 0.05 for a two-tailed test. Statistical calculations were per-
formed using R.

### 5 Results

All data reported was a comparison of the time period between 1 July
2015 to 31 December 2017. In total, direct cost savings attributed to
the ASP were estimated at $1 339 499 despite a significant increase
of patient discharges and total patient-days, an increase of 300% and
342%, respectively (Figure 2). The antimicrobial cost per inpatient day
decreased by 32% from $47.2 to $32.3. Usage of monitored anti-
microbials, which included high cost antimicrobials, decreased by 8%
from 359 DOT per 1000 patient days to 330 DOT per 1000 patient
days (*P* = 0.0081, 95% confidence interval [CI] −46 to −13.3). This
decrease in high cost antimicrobials could explain the significant cost-
savings realized since ASP implementation. Aggregate Antimicrobial
DOT per 1000 patient days (DOT/1000 PDs) decreased from 625
DOT/1000 PDs to 561 DOT/1000 PDs, a decrease of 10% (*P* < 0.05, 95% CI −46 to −13.3) (Figure 3). Carbapenem usage
decreased by 24% from 106 DOT/1000 PDs to 80 DOT/1000 PDs
(*P* = 0.01, 95% CI −36.8 to −16.1) (Figure 4). Anti-MRSA agents usage
decreased by 57% from 110 DOT/1000 PDs to 70 DOT/1000 PDs (P < 0.05, 95% CI −50.8 to −29.9) (Figure 5), anti-pseudomonal agent usage decreased by 6% from 182 DOT/1000 PDs to 170 DOT/1000 PDs (P = 0.08, 95% CI −25.4 to 0.08) which was not statistically significant (Figure 6).

Hospital-onset CDI rates decreased from 0.46 cases per 1000 patient days in 2015 to 0.12 cases per 1000 patient days in 2017 (P = 0.035, 95% CI 0.08 to 0.91). Hospital-onset infections due to MDROs decreased from 2.39 cases per 1000 patient days in 2015 to 0.38 cases per 1000 patient days in 2017 (P = 0.05, 95% CI 0.09 to 0.28) (Figures 7 and 8).

The rate of acceptance for ASP recommendations made was 91%. There were a total of 4123 recommendations made in 2016 and 2017, and 3756 recommendations were included in the accepted calculation. Automatic i.v.-to-oral conversions increased from 26 to 217 which reflected the new policy that was implemented at the time for automatic i.v.-to-oral therapy conversion of antimicrobials by pharmacists (Table 2).

6 DISCUSSION

We describe an advanced ASP at a 360-bed quaternary care hospital in the UAE incorporating the use of real-time surveillance software and CDSS. Despite the significant increase in bed capacity, patient discharges, and increased complexity of patients seen, as evidenced
through our case-mix index (Table 1), the ASP continued to show a decrease in antimicrobial use and expenditure. Of note, our region observes high rates of resistance amongst Gram-negative organisms and approximately 30% of patients admitted to our facility are colonized with extended-spectrum beta-lactamase organisms. Despite these challenges, the ASP continued to demonstrate a reduction in the use of carbapenems over the reported period. We believe that the sustained reduction in antimicrobial consumption is linked to
the multi-strategy approach used by the ASP, the involvement of all hospital-based pharmacists in antimicrobial stewardship, and the high level of EMR and CDSS integration we achieved at our facility. Using this multi-pronged approach has led to antimicrobial consumption remaining within target despite a rapid and significant increase in both the number of prescribers and patient discharges during the reported period.

Although extensive IT support was needed for the development and implementation of CDSSs at our institution which is associated with significant implementation cost, CDSSs have clearly shown their role in optimizing antimicrobial utilization and have shown to be cost-effective. Some of the challenges of implementation of CDSS at our institution were the significant time required by the hospital IT department to implement those tools, the time required from the ASP team to validate the tools created, and the upfront cost of implementation. Of note, widespread implementation of the EMR system in the United States and publications on these experiences, provided the opportunity of the ease of sharing of best practices for ASP integration and allowed us to learn from the experiences of others of what to implement and what to avoid with widespread implementation of ASP strategies in the EMR. In the future, we plan on implementing additional CDSS tools in our EMR, particularly tools that provide real-time feedback to prescribers at the point of ordering to help with optimizing the choice of empiric antimicrobial therapy. In addition, we plan to continue to measure the outcomes of our program particularly clinical outcomes including length of stay, mortality, and readmission rates.

FIGURE 7  Hospital-onset *Clostridioides difficile* infection rates

FIGURE 8  Hospital-onset infection rates due to multidrug-resistant organisms
Our institution’s aggregate antimicrobial use of 561 DOT/1000 PDs is much lower as compared with US institutions, with estimates of 755 DOT/1000 PDs.23 This could be explained by our hospital’s size, the type of patients seen as a primarily quaternary institution, and the resistance patterns observed in the region. To date, there are no benchmarking data published from our region to allow for comparison in antimicrobial consumption.

One limitation of the study is the quasi-experimental design; consequently, the results can only suggest an association between ASP activities and the reported results. Randomization would not have been possible given the hospital-wide nature of the program and the involvement of every pharmacist. The impact observed on hospital-onset CDI rates and hospital-onset MDRO rates may be ascribed to both having an effective ASP program in addition to having a robust infection prevention program, a finding that has been previously described in the literature.24 Although no changes to infection prevention strategies have occurred during the study time period, it is noteworthy that hand hygiene compliance rates as measured by validated observers have improved during the time period 2015 to 2017 increasing from 91% in 2015 to 94% in 2017. During this time period, the hospital invested on various efforts such as such as hand hygiene awareness campaigns and performance improvement projects with timely feedback to the frontline caregivers. As described in the literature, hand hygiene is a cornerstone of all efforts to prevent hospital acquired infections.

7 | CONCLUSION

The implementation of an advanced ASP at a quaternary care hospital in the United Arab Emirates was associated with a decrease in antimicrobial utilization, antimicrobial expenditure, and a reduction in hospital-onset CDI and MDRO rates. To our knowledge, this is the first report describing the outcomes of an advanced ASP program at a quaternary care hospital utilizing real-time surveillance software and CDSS in the Middle East.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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