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EDITED BY
Gavin Barlow,
Hull York Medical School,
United Kingdom

REVIEWED BY
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University of Peradeniya, Sri Lanka
Linus Olson,
Karolinska Institutet (KI), Sweden

*CORRESPONDENCE
Jinan Shamseddine
jshamseddine@ssmc.ae

†These authors share first authorship

‡These authors share last authorship

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Impact of antimicrobial stewardship interventions on days of therapy and guideline adherence: A comparative point-prevalence survey assessment

Jinan Shamseddine[1*†], Ahmed Sadeq[1†], Khadija Yousuf[2], Rawan Abukhater[2], Lamia Omer Yahya[1], Maysaa Abdulatif Espil[1], Mohamed Elamin Hassan[1], Rayan Elamin Fadl[1], Rami Tag Elsir Ahmed[1], Islam Elkonaissi[1], Abeer Elmahi Abdelsalam[1], Aisha Al Naqbi[2], Nora Al Nuaimi[2], Maitha Al Hosani[2], Rowdha Al Marri[2], Asma Al Abdouli[2], Abdullah Mohamad Alakhras[3], Neamat Ibrahim Al Masri[4], Siobhan O'Sullivan[5], Dean Everett[6,7‡] and Zahir Osman Eltahir Babiker[3‡] on behalf of Antimicrobial Stewardship Study Group Sheikh Shakhbout Medical City in partnership with Mayo Clinic Abu Dhabi United Arab Emirates

[1]Department of Pharmacy, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates, [2]Division of Internal Medicine, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates, [3]Division of Tropical and Infectious Diseases, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates, [4]Division of General Paediatrics, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates, [5]Department of Molecular Biology and Genetics, Khalifa University, Abu Dhabi, United Arab Emirates, [6]Department of Pathology and Infectious Diseases, College of Medicine and Health Sciences, Khalifa University, Abu Dhabi, United Arab Emirates, [7]Biotechnology Center, Khalifa University, Abu Dhabi, United Arab Emirates

Background: Antimicrobial stewardship (AMS) is a crucial tool for rationalizing the use of antimicrobial agents and reducing the burden of antimicrobial resistance. We aimed to assess the impact of AMS interventions on antimicrobial utilization and adherence to antimicrobial guidelines.

Methods: We conducted a prospective quasi-experimental study at a major tertiary hospital in the United Arab Emirates. Using standardized World Health Organization's methodology, point-prevalence surveys (PPS) were performed in November 2019 and January 2022. Core AMS interventions consisted of proactive bloodstream infection service, proactive and reactive infectious diseases consult service, prospective audit and feedback by clinical pharmacists, development of antimicrobial guidelines based on cumulative antibiograms, and implementation of induction programs for new clinical staff.

Days of therapy (DOT) per 1000 patient days present and rate of compliance with antimicrobial guidelines were compared before and after the core interventions. Multiple logistic regression analysis was carried out to adjust for the potential confounding effects of age, gender, hospitalization within 90 days, central or peripheral line insertion, urinary catheterization, and mechanical ventilation. P-value<0.05 was considered statistically significant.

Results: Pre- and post-intervention PPSs included 292 and 370 patients, respectively. Both had similar age and gender distribution. Patients receiving antimicrobials were 51% (149/292) in 2019 and 45% (166/370) in 2022 (*p* 0.12). Univariate analysis showed a reduced post-intervention DOT per 1000 patients present (6.1 +/- 16.2 vs 2.4 +/-5.1, *p*<0.01) and an improved post-intervention guideline compliance (59% vs 67%, *p* 0.23). Following multiple logistic regression, the reduction in post-intervention DOT remained statistically significant (co-efficient -0.17 (95% CI -8.58 to -1.94, *p*<0.01), and the improvement in guideline adherence became statistically significant (adjusted odds ratio 1.91 (95% CI 1.05 to 3.45, *p* 0.03).

Conclusion: Coordinated and sustained AMS interventions have a significant impact on improving antimicrobial utilisation and adherence to guidelines.

KEYWORDS

antimicrobial stewardship, antimicrobial utilization, antimicrobial guidelines, days of therapy, antimicrobial stewardship (AMS)

1 Introduction

The advent of antimicrobial agents has drastically altered daily medical practice. Antimicrobials are advanced medical treatments; therefore, once fatal infections are now treatable and even preventable (1).

The antimicrobial stewardship program (ASP) consists of well-studied measurements and interventions to facilitate the optimal use of antimicrobial agents, aiming to help clinicians improve clinical outcomes and optimize the appropriate use of antimicrobials while minimizing the harm caused by unnecessary or suboptimal use of antimicrobial therapy. Consequently, reducing microbial resistance and decreasing the spread of infections caused by multidrug-resistant organisms (2).

Multiple interventions are being carried out worldwide to improve antimicrobial stewardship, increase compliance and adherence to antibiotics usage, and improve clinical/patient outcomes. Implementing frequent audits and feedback to the prescriber (either by the clinical pharmacist or by infectious disease specialist) has proven to reduce the usage and duration of antibiotics (3). In addition, adopting preauthorization systems for dispensing restricted broad-spectrum antibiotics may help reduce the burden of antimicrobial resistance (4). Furthermore, clinical education is considered a cornerstone for any successful antimicrobial stewardship, and it was found that it can lower the annual antimicrobial prescriptions rates through training sessions or telephone consultation (5, 6). The ASP implements institution-specific guidelines for common infectious diseases and effectively facilitates proper antimicrobial prescription. They can aid in significantly increasing the use of appropriate initial antimicrobial agents, de-escalation of treatment, and shorter duration of antimicrobial therapy (2).

One of the established methodologies within antimicrobial stewardship programs to evaluate antimicrobial use at an institutional level is point prevalence surveys. Point Prevalence survey is a practical, standardized tool to measure hospital antimicrobial prescribing. It collects antimicrobial prescription data, reflects on the population receiving the antimicrobials, and defines the most common infections while conducting the survey (7, 8). Therefore, the barriers to enhancing the appropriate use of antimicrobials and decreasing microbial resistance can be identified through PPS to optimize the clinical outcomes (7–9).

A point prevalence survey was conducted before and after implementing ASP interventions to compare the study outcomes. The goals are to assess the impact of ASP team interventions on antimicrobial days of therapy and compliance with local antimicrobial guidelines at the hospital.

2 Methods

2.1 Setting

This study was conducted at Sheikh Shakhbout Medical City (SSMC), a 750-bed governmental tertiary hospital providing medical, surgical and ICU services.

2.2 Study design

We conducted a prospective non-randomised quasi-experimental study assessing antimicrobial stewardship program (ASP) interventions and their impact on key performance indicators (e.g., days of therapy and compliance with hospital antimicrobial guidelines) through point-prevalence surveys.

WHO provides a standardised methodology for point prevalence surveys to support hospitals worldwide in collecting antimicrobial use data to evaluate the impact of the local antimicrobial stewardship programmes (ASP) and facilitates comparisons of antibiotic use over time and between hospitals (10).

The same methodology was adopted at SSMC, with a baseline survey conducted in September 2019 and a follow-up survey completed in February 2022. The survey was conducted for three weeks for both periods, considering a set of variables defined in WHO PPS guidelines.

2.3 Inclusion and exclusion criteria

Patients who were eligible for the PPS include adult and paediatric patients hospitalised on the day of the survey whether they are receiving antibiotics or not, patients admitted to the ward before or at 8 a.m., patients who are on antimicrobials at 8 a.m. on the day of the survey, and patients who have been prescribed surgical antimicrobials prophylaxis before 8 a.m. on the day of the study. In addition, the survey covered all antimicrobials administered through oral, parenteral, rectal or through inhalation.

On the other hand, patients attending outpatient clinics, renal dialysis units, day-surgery wards, and the Emergency Department are excluded. Furthermore, antimicrobial orders initiated after 8 a.m. on the day of the survey, antimicrobial orders stopped before 8 a.m. on the survey day, and dosage forms including topical antibiotics (i.e. ear drops, eye drops, or vaginal suppositories) were precluded from the analysis.

2.4 Interventions

After the PPS survey was conducted in 2019, the ASP team performed multiple interventions to improve clinical outcomes. The ASP team consisted of infectious disease (ID) physicians, clinical pharmacists, Infection prevention and control (IPC) nurses, and physicians from different specialities. ASP interventions included:

2.4.1 Bacteraemia services

ID physicians proactively reviewed cases identified with positive cultures collected from sterile samples (blood) and consequently defined a treatment plan.

2.4.2 ASP stewardship queries

ID team initiated ID consult service where active on-call ID physicians received consultation over the phone for queries related to antimicrobials preauthorisation and consultation for complex cases.

2.4.3 Prospective audit and feedback by clinical pharmacists

Clinical pharmacists' teams perform prospective audits for antimicrobials prescribed for patients in the assigned wards, they review cases for antimicrobials appropriateness and intervene with the primary team physicians, and the feedback is delivered directly to them.

2.4.4 Guidelines development and implementation

Local antimicrobial guidelines were developed and shared with the hospital staff. Common indications for antibiotic use have been included, e.g. community-acquired pneumonia, urinary tract infection, intra-abdominal infection, skin and soft tissue infection and surgical prophylaxis.

The recommendations reflected in the local guidelines were based on hospital treatment preferences, susceptibilities, formulary options, and patient mix.

2.4.5 ASP induction program for new joiners (physicians, pharmacists, nurses)

Education is a crucial component of comprehensive efforts to improve hospital antibiotic use. The induction module is an effective tool to introduce and reinforce antimicrobial stewardship program objectives, highlight the key performance indicators, and emphasise the roles of clinicians, nurses, and pharmacists.

2.4.6 ID rounds in critical care units

ID physicians conduct regular reviews of antimicrobial therapy in critical care areas and provide patient-specific recommendations to optimise antimicrobial therapy during face-to-face meetings with physicians and pharmacists based in intensive care units (ICU).

2.5 Ethical statement

The study was approved by the antimicrobial stewardship subcommittee and was registered as a quality improvement project with the quality department at SSMC. (Registration no. SSMC/CA/2022/002). Data were anonymised and de-identified to preserve patient confidentiality.

2.6 Data collection

The KoBo toolbox® was used to design a password-protected and standardised data collection tool to gather de-identified and anonymised demographic, clinical and antimicrobial information. The database included demographic data (e.g. age, gender), clinical data (e.g. recent hospital admission in 90 days, length of hospitalisation, surgical intervention, and presence of vascular, urinary or tracheal lines) and antimicrobial data (e.g. receipt of antimicrobial agent, indication, empirical/directed, dose, route of administration, duration, antimicrobial-related interventions, agent review status within 48-72 hours of administration, and local guideline compliance). In addition, detailed microbiological information (e.g. culture collection, type of specimen, pathogen, and antimicrobial susceptibility) was also collected.

2.7 Study outcomes

The study outcomes comprise days of antimicrobial therapy (DOT) and local antimicrobial guidelines compliance rate. Since it is a point prevalence survey, we couldn't calculate the full antibiotic treatment days, however, DOT was calculated by counting the number of the days the patient had been on antimicrobial (s) until the date of the survey. If the patient was on more than one antimicrobial, the DOT for each antimicrobial will be summed to give one DOT product for all the antimicrobials that the patient had been on.:

The local antimicrobial guidelines compliance rate was calculated by dividing the number of patients whose antimicrobial therapy complied with hospital guidelines by the total number of patients on antibiotic therapy. The product was multiplied by 100 as per the following equation:

$$\text{Rate of guidelines compliance} = \frac{\text{No. of patients with antimicrobial therapy complying with the guidelines}}{\text{total number of patients on antibiotics}} \times 100$$

2.8 Statistical analysis

SPSS® version 26 has been used for data analysis. Patients' baseline characteristics and clinical outcomes were summarised by means and standard deviations for continuous data, while frequencies and percentages summarised categorical variables. Chi-squared ($\chi 2$) test was used for comparing categorical variables and independent Sample t-test for comparing continuous variables. A p-value of < 0.05 was considered statistically significant. Outcomes with a p-value<0.25 were chosen for a backward multiple regression analysis adjusted for multiple infection risk factors to remove the effect of the possible confounders on the study outcomes. The square roots of continuous variables that were not normally distributed were used to meet the independent t-test and regression analysis assumptions of normality for the continuous variables.

3 Results

Patient's baseline characteristics from pre- and post-intervention groups are shown in Table 1. The pre-intervention group (first group) had 292 patients, whereas the post-intervention group included 370 patients who were questioned following the intervention (second group). Both groups had a similar average age of 30.3 and male gender predominated.

During the pre-intervention stage of the research, the adult medical ward contributed the most (31%) patients to the study. While the adult surgical ward made the most contribution (35%) of patients to the research's post-intervention phase.

Antimicrobials were given to 149 patients in the first group, with 219 antimicrobials, and 166 patients in the second group, with 215 antimicrobials. Central lines, peripheral lines, hospitalisation within 90 days, urine catheters, and mechanical ventilation were all risk factors for infection in both groups of patients (11–14) (Table 1).

As indicated in Table 1, the proportion of patients who were on antibiotics was 51% (149/292) for the pre-intervention group and 45% (166/370) for the post-intervention group. The mean DOT measured in the pre-intervention group was 6.1 days (± SD 16.2) while 2.4 days in the post-intervention group (± SD 5.1), and the difference was statistically significant ($p< 0.01$). Compliance with the hospital's local antimicrobial guidelines was found to be 59% in the pre-intervention group compared to

TABLE 1 Patients' characteristics, risk factors for infection and antimicrobial stewardship outcomes at baseline in 2019 and post-antimicrobial stewardship interventions in 2022.

	Pre-intervention group (PPS[a] 2019) n = 292	Pre-intervention group (PPS[a] 2022) n = 370	p
Characteristics			
Age (mean ± standard deviation)	39.3 (±26.98)	39.5 (±27.06)	0.572
Gender			0.720
Male	168 (58%)	218 (59%)	
Female	124 (42%)	152 (41%)	
Ward type			< 0.1
adult medical	91 (31%)	53 (14%)	
adult surgical	81 (28%)	129 (35%)	
adult high Risk	10 (3%)	47 (15%)	
adult ICU	22 (8%)	55 (13%)	
paediatric medical	20 (7%)	18 (5%)	
paediatric surgical	16 (5%)	13 (4%)	
paediatric ICU	8 (3%)	8 (2%)	
neonatal medical	1 (0)	0	
neonatal ICU	6 (2%)	26 (7%)	
mixed	37 (13%)	21 (6%)	
Patient receiving an antibiotic			
Yes	149 (51%)	166 (45%)	0.115
No	143 (49%)	204 (55%)	
Number of prescribed antibiotics	219	215	
Risk factors for infection			
Central lines			0.015
Yes	31 (11%)	64 (17%)	
No	261 (89%)	306 (83%)	
Peripheral lines			0.911
Yes	204 (70%)	257 (69%)	
No	88 (30%)	113 (31%)	
Urinary catheter			0.912
Yes	61 (21%)	76 (21%)	
No	231 (79%)	294 (79%)	
Mechanical ventilation			<
Yes	47 (16%)	33 (9%)	0.01
No	245 (84%)	337 (91%)	
Surgery since admission			<
Yes, minimal invasive	42 (14%)	90 (24%)	0.01
Yes, invasive (as per NHSN[c])	66 (23%)	66 (18%)	
No	184 (63%)	214 (58%)	
Hospitalization within the past 90 days.			0.042
Yes	115 (39%)	116 (31%)	
No	165 (57%)	244 (66%)	
Unknown	12 (4%)	10 (3%)	
Hospitalised for at least 48 hours			0.188
Yes	235 (80%)	282 (76%)	
No	57 (20%)	88 (24%)	
Patient transferred from other hospital			0.633

(Continued)

TABLE 1 Continued

	Pre-intervention group (PPS[a] 2019) n = 292	Pre-intervention group (PPS[a] 2022) n = 370	p
Yes	29 (10%)	41 (11%)	
No	263 (90%)	329 (89%)	
Outcomes of antimicrobial stewardship			<
Days of therapy per 1000 patient days present	6.1 (±16.2)	2.4 (±5.1)	0.01
Compliance to antimicrobial guide			0.230
Yes	88 (59%)	111 (67%)	
No	38 (26%)	28 (17%)	
No policy	11 (7%)	22 (13%) 5 (3%). 0	
No indication documented	10 (7%)		
Not assessable	2 (1%)		

[a] point-prevalence survey.
[b] intensive care unit.
[c] National Health Care Safety Network, Centers for Disease Control, United States.

67% in the post-intervention group, which is considered statistically insignificant (P= 0.230) (Table 2).

Table 2 illustrates the compliance status to local hospital antimicrobial guidelines in each hospital unit. For adults, medical wards had the highest compliance rate compared to other wards. For paediatrics, there is a high percentages of "no policy" represented by 91% in the paediatric wards, Table 3.

The results of the multiple regression analysis (adjusted for age; gender; the presence of central line, peripheral line and urinary catheter; mechanical ventilation; and 90-day hospitalisation) are illustrated in Table 3. The difference in the DOT between the first and second groups remained statistically significant (p< 0.01) with a negative co-efficient value (-0.169), indicating less DOT in the post-intervention group. On the other hand, there is a statistically significant improvement in compliance with the guidelines found in the post-intervention group (p= 0.033).

4 Discussion

Our findings show that adherence to SSMC Clinical Guidelines was improved in the post-intervention group, along with many factors that contributed to such improvement. The presence of an effective hospital antimicrobial stewardship program could be attributed to the successful implementation of guidelines and antibiotics policies, in addition to the quality improvement initiative projects conducted by ASP core members. This is in line with multiple recent studies (15–19).

The implementation of a wide range of ASP interventions between the two surveys resulted in a statistically significant decrease in the number of days of therapy in the post-intervention group. The rapid expansion of ID and clinical pharmacy services played a pivotal role in driving the successful implementation of ASP interventions. Of importance, the role of the clinical pharmacist intervention is

TABLE 2 Antimicrobial guide compliance rate comparison between pre and post-intervention groups distributed as per ward type.

Type of Ward	Compliance		No Complinace		No Policy		No Documentation		Not assessable	
	Pre[a]	Post[b]	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Adult medical	40 (70%)	28 (93%)	14 (25%)	2 (7%)	2 (4%)	0	1 (1%)	0.	0	0
Adult surgical	23 (52%)	25 (48%)	12 (27%)	15 (29%)	2 (5%)	9 (17%)	6 (14%)	3 (6%)	1 (2%)	0
Adult high risk	10 (80%)	20 (87%)	0	3 (13%)	2 (20%)	0	0	0	0	0
Adult ICU[c]	10 (77%)	14 (56%)	1 (8%)	6 (24%)	2 (15%)	3 (12%)	0	2 (8%)	0	0
Paediatric medical	3 (38%)	1 (9%)	3 (38%)	0	2 (24%)	10 (91%)	0	0	0	0
Paediatric surgical	3 (38%)	5 (83%)	5 (62%)	1 (17%)	0	0	0	0	0	0
Paediatric ICU	3 (43%)	5 (100%)	0	0	1 (14%)	0	3 (43%)	0	0	0
Neonatal ICU	1 (100%)	8 (100%)	0	0	0	0	0	0	0	0
Mixed	2 (33%)	4 (67%)	3 (50%)	1 (17%)	1 (17%)	1 (17%)	0	0	0	0

[a] Pre, pre-intervention group (PPS 2019).
[b] Post, post-intervention group (PPS 2022).
[c] intensive care unit.

TABLE 3 Multiple regression analysis comparing Days of therapy and compliance with antimicrobial guidelines between the pre-intervention (PPS 2019) and post-intervention (PPS 2022) groups.

Characteristic	Days of therapy Co-efficient (95% CI[b])	P value	Guideline compliance Odds ratio (95% CI)	P value
Groups[a]		< 0.01		
	-0.169 (-8.575, -1.944)		1.905 (1.053, 3.446)	0.033
Gender	-0.013 (-3.843, 3.027)	0.8	0.897 (0.538, 1.494)	0.676
Age	0.138 (0.015, 0.144)	0.02	1.009 (0.999, 1.019)	0.073
Hospitalization within 90 days	-0.051 (-4.263, 1.594)	0.067	1.683 (0.964, 2.936)	0.849
Central line	-0.118 (-9.540, 0.212)	0.06	1.471 (0.674, 3.213)	0.333
Peripheral line	-0.293 (-16.763, -7.075)	< 0.01	0.243 (0.090, 0.651)	< 0.01
Mechanical ventilation	0.013 (-4.453, 5.546)	0.8	3.025 (1.118, 8.190)	0.029
Urinary catheter	-0.062 (-6.419, 2.034)	0.3	1.005 (0.535, 1.887)	0.987

[a] pre-intervention group (reference group) vs.
[b] post-intervention group; confidence interval.

always highlighted in improving compliance with hospital guidelines, improving antimicrobial stewardship outcomes, and reduction of days of therapy (20–22).

The observed prevalence of antibiotic use in the pre and post-intervention groups were higher than the findings of global PPS studies in countries like Northern Ireland (23), were the prevalence was 45%.Compared with low and middle income countries, including Brazil, Ghana, Uganda, Zambia, and Tanzania, overall prevalence was found to be approximately 50% (24, 25).

Numerous metrics are used to track antimicrobial use and ASP efficacy, but there is no consensus on which metric is preferred. DOT/1000 patient day metric was chosen for this study because, compared to other metrics, it offers the best balance of feasibility and applicability. Furthermore, adding patient days to the denominator helps to compare the impact of the interventions within the same facility over time (26, 27).

The results of our study are aligned with other antimicrobial stewardship programmes that evaluated the impact of ASP and showed that the interventions were associated with a shorter duration of antibiotic therapy and less inappropriate antimicrobial use (19, 28).

The lack of guidance on using antibiotics in paediatric services needs to be addressed. Our results identified areas of potential improvement for appropriate prescribing of antibiotics for paediatric patients (Table 2), highlighting the need to implement more guidelines and policies in the paediatric wards. Repeated PPS needs to be part of the paediatric antibiotic stewardship strategy to identify prescribing trends over time and evaluate the efficacy of ASP initiatives in the paediatric department.

"Our second point prevalence survey was conducted during the coronavirus disease 2019 (COVID-19) pandemic, a time of profound hardship and stress on the healthcare system, promoting emergency measures such as early hospital discharge and community quarantine. Therefore, it is plausible that such interventions might have influenced the DOT estimate of the second survey. However, the formula we used to compute the DOT in this study utilized the number of days spent receiving antibiotics until the survey date rather than the discharge date. Therefore, we are confident that COVID-19 discharge interventions did not confound our DOT estimate."

This study has some limitations. First, the PPS study design is restricted to assessing only inpatient antibiotic use, though it is our targeted setting in this study; consequently, the antibiotics used in outpatient clinics were not reviewed. However, we plan to expand the audit to cover the outpatient setting using an appropriate auditing tool. Second, the point-in-time nature of the PPS design further limits insight into seasonal patterns in antibiotic use, but it still can give a clue about the practices and habits. Third, the two surveys occurred in two different seasons, which likely has the potential to skew antimicrobial use results. The survey conducted during the Post-intervention period included winter months when antimicrobial use would be expected to be higher than in the summer. Last, our study followed a non-randomised design and, as per WHO PPS methodology, all admitted patients should be surveyed.

In conclusion. Several areas of practice deserve specific attention to optimize the prudent use of antimicrobial in the hospital. Future Antimicrobial stewardship initiatives should be directed towards updating paediatric infectious disease guidelines and to follow any deviation of therapy particularly in the use of broad-spectrum, non–oral antimicrobials, and surgical prophylaxis practices. There is an opportunity to enhance quality in documenting indications and reporting a stop/review date.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Study group members

Marleine Pierre Bejjani Moukarze, Department of Pharmacy, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Rizwan Ali, Department of Pharmacy, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Prameela Maniamma, Infection Prevention and Control, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Fouzia Jabeen, Microbiology department, Union 71 laboratory, Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates; Ramesh Ganeshan, Division of Tropical and Infectious Diseases, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Ahmed Al Messabi, Division of Tropical and Infectious Diseases, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Robert Serafino Wani, Division of Tropical and Infectious Diseases, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates; Emmanuel Nsutebu, Division of Tropical and Infectious Diseases, Sheikh Shakhbout Medical City in partnership with Mayo Clinic, Abu Dhabi, United Arab Emirates.

Author contributions

JS, ZB contributed to the conception and design of the study. JS, AS, ME, KY, RAK, LY, ME, RE, RT, IE, AE, AA, NA, MA, RA, AA, NA, AA contributed to the data collection. AS, JS, ZB, ME performed data analysis JS, AS, ZB, SO'S, DE reviewed the drafts. MM, RA, PM, FJ, RG, AM, RW, EN Part of antimicrobial stewardship study group. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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