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Research Article

The Impact of the Antimicrobial Stewardship Program on Antibiotic Use, Resistance Patterns, and Cost in Madinat Zayed Hospital

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Article Info:

Abstract
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Antimicrobial resistance and excessive antibiotic usage are a growing public health concern. Antimicrobial Stewardship Programs (ASPs) aim to optimize antibiotic use and curb resistance. This retro-respective study evaluated the impact of an ASP at Madinat Zayed Hospital, Abu Dhabi (January 2021-December 2022). It analyzed electronic health records to assess the ASP's impact on antibiotic consumption, resistance patterns, and economic outcomes. Patients from intensive care units, medical wards, and outpatient settings were included, though patients admitted to obstetrics/gynaecology, paediatrics, neonatal intensive care, and surgical wards were excluded. The primary objective of this study was to report on the ASP experience and measure the prescribing appropriateness percentage of empirical antibiotic therapy along with the de-escalation of broad-spectrum antimicrobials, after ASP implementation at Madinat Zayed Hospital in Al Dhafra Region, United Arab Emirates. The secondary objectives were to reflect on the rate of Multidrug-Resistant Organisms (MDROs), total utilization using defined daily dose, and the total direct cost of antibiotics. Descriptive analysis, proportions, mean values, and percentage changes were employed for data analysis. The ASP achieved high compliance rates with restricted antibiotics (>90%) and approved guidelines (inpatient 97-100%, outpatient 93-98%). Antibiotic de-escalation rates were also high (>80%). Significant reductions in use were observed for cefixime (91.3%), levofloxacin (46.3%), and several others. Notably, cefepime use increased (1137.5%). Direct antibiotic expenditure decreased by 2% (saving Dhs2.6 million), and resistance decreased in some bacteria. However, a concerning rise in ceftazidime resistance against Pseudomonas aeruginosa was identified. This study concluded that the implementation of a new Antimicrobial Stewardship Program at Madinat Zayed Hospital demonstrated effectiveness in promoting responsible antibiotic use. The program achieved high compliance with restricted antibiotic use and approved guidelines, leading to significant reductions in overall antibiotic consumption.

Keywords: Antimicrobial, resistance, Multidrug-Resistant Organisms, de-escalation, consumption.

INTRODUCTION

Antimicrobial resistance (AMR) poses a significant global public health threat, resulting in over 700,000 deaths annually[1, 2]. By 2050, this number could surge to a staggering 10 million deaths per year [3], profoundly impacting countries' economies, particularly those of low- and middle-income nations (LMICs)[4]. The culprit are the alarming adaptability of microorganisms and antimicrobial misuse[5]. The need for responsible antibiotic use was recognized decades ago[5]. In 1996, McGowan and Gerding coined the term "antimicrobial-use stewardship", emphasizing the importance of optimizing antimicrobial selection, dosage, and treatment duration to fight the growing threat of AMR[6]. In 2015, this program was launched as part of a global action plan (GAP) by the World Health Organization (WHO) to preserve the current effectiveness of antibiotics and enhance their future efficacy[7].

Antimicrobial stewardship refers to a systematic approach that encourages the safe use of antimicrobial drugs[8, 9]. This term can be extended to encompass acts at national, individual, and even global levels, encompassing animal health, environment, and human health[9]. Antimicrobial stewardship programmes aim to improve patient outcomes, maximise the effectiveness of antimicrobials, decrease antimicrobial resistance and healthcare-associated infections, and reduce healthcare expenses, among other benefits[10]. The most commonly employed ASP interventions include prospective audits and feedback, preauthorization measures, and customized treatment recommendations, tailored to specific facilities[11].

Several nations worldwide have formulated and are executing national action plans (NAPs) on antimicrobial resistance (AMR), with antimicrobial stewardship (AMS) being a primary focus. In fact, numerous studies conducted in hospital settings, with a focus on inpatients, have shown that Antibiotic Stewardship Programs (ASPs) can enhance adherence to antimicrobial therapy guidelines and decrease the unnecessary use of antibiotics[12]. This leads to positive effects on rates of AMR, hospital-acquired infections, and patient outcomes[13-15]. Two studies have shown that AMS programmes lead to a substantial reduction in the use of antimicrobial drugs and the corresponding expenses, as well as improvements in infections caused by certain antibiotic-resistant organisms and the overall

duration of hospital stays [5, 6]. Subsequent research should prioritise the examination of the sustainability of these results and assess the possible advantageous long-term impacts of AMS programmes on mortality and infection rates [15].

Although the impact of ASPs has been well-documented in developed and some developing countries, there is a lack of literature examining ASP interventions in our country, suggesting a deficiency in implementation or possibly the unstructured execution of such programs [16]. The principal aim of this study was to provide a comprehensive overview of the ASP implementation experience to assess the appropriateness of empirical antibiotic therapy prescribing percentages and analyse the frequency of de-escalation of broad-spectrum antimicrobials following ASP implementation at Madinat Zayed Hospital in the Al Dhafra Region of the United Arab Emirates. Secondary objectives encompassed evaluating the prevalence of Multidrug-Resistant Organisms (MDROs), quantifying total antibiotic utilization using defined daily doses, and assessing the total direct cost of antibiotics. Through this study, we sought to gain insight into the impact of the ASP on antibiotic prescribing practices and antimicrobial resistance patterns, contributing to antimicrobial stewardship efforts in our healthcare setting.

2. METHODOLOGY

2.1 Study Design

A retrospective, single-centre study was conducted to assess the impact of the Antimicrobial Stewardship Program on the consumption, costs, and resistance patterns of various antibiotics, including Cefixime, Levofloxacin Hemihydrate, Moxifloxacin Hydrochloride, piperacillin/tazobactam, Meropenem 1000mg, Meropenem 500mg, Ceftriaxone, and Cefepime Hydrochloride.

This study used electronic health records from the Cerner© healthcare system at Madinat Zayed Hospital from January 1 2021 to December 31 2022, comparing various parameters following the implementation of the ASP.

The ASP at Madinat Zayed Hospital involved a multifaceted strategy designed to maximize the utilization of antibiotics. We developed a facility-specific Antibiogram to track resistance patterns and then used that data to develop evidence-based treatment guidelines for various infections. These guidelines were combined with the electronic health system to encourage adherence. Additionally, the ASP implemented interventions like pharmacist-led protocols, medication review, and nurse education to ensure appropriate antibiotic selection, dosage, and duration throughout a patient's journey.

2.2 Study Settings

This study was conducted at Madinat Zayed Hospital, located in Madinat Zayed City, Abu Dhabi. Madinat Zayed Hospital is a vital organization for the delivery of healthcare in the United Arab Emirates (UAE). Operating under the umbrella of SEHA (the largest healthcare provider in the UAE) and the Al Dhafra Hospitals network, this multi-specialty institution provides a broad spectrum of medical services to address a variety of requirements. Patients are granted access to emergency care as well as scheduled consultations in an extensive range of medical specialties, with a special focus on internal medicine, pediatrics, obstetrics & gynecology[16].

2.3 Inclusion and Exclusion Criteria

The inclusion criteria encompassed patients being treated in intensive care units, medical wards, and outpatient settings between 2021 and 2022. Patients admitted to obstetrics/gynecology (OB/GYN), pediatrics, and the neonatal intensive care unit (NICU) were excluded, as well as those undergoing surgical procedures.

2.4 The Primary and Secondary Endpoints

Primary Endpoint: The primary endpoints included compliance with the restricted antibiotic list and with approved antimicrobial guidelines both in inpatient and outpatient settings, and the conversion of antibiotic type.

Secondary Endpoints: The secondary endpoint included antibiotic usage trends, resistance patterns among microorganisms, and economic outcomes.

2.5 Data Analysis

A descriptive analysis was performed for each outcome including compliance with the restricted antibiotic list, compliance with approved antimicrobial guidelines (inpatient and outpatient settings), and conversion of antibiotic type. Proportions and mean values were used for descriptive statistics. We further explored trends in antibiotic utilization, cost, and resistance patterns by analysing percentage changes and creating data visualizations.

The following variables were used in the data presentation including antibiotic quantities, compliance with antimicrobial guidelines, conversion of antibiotic types, antibiotic expenditure, and antibiotic resistance patterns for various microorganisms.

2.6 Ethical Considerations:

The research was approved by AL Dhafra Hospitals Institutional Research Ethics Committee (ADHIREC) : Study No : ADH-IREC-339.

3. RESULTS

3.1 Antibiotic Stewardship Program Performance (2021-2022)

The Antimicrobial Stewardship program achieved exceptional results across key performance indicators (KPIs) from 2021 to 2022 (Table 1). Compliance with restricted antibiotics consistently met or exceeded the 90% target, achieving 98% in Q1/2021, 88% in Q2/2021, 91% in Q3/2021, 100% in Q4/2021, and 100% throughout 2022. Compliance with the guidelines was higher for inpatient (IP) settings compared to outpatient (OP) settings. The % of compliance with the Approved Guidelines for IP settings ranged from 97% to 100% across all quarters in both 2021 and 2022. In contrast, the % of compliance with the Approved Guidelines for OP settings ranged from 93% to 98% across the same periods. Additionally, the program effectively de-escalated antibiotic types, with rates above the 80% target in all quarters, ranging from 80% to 100%. These outcomes reflect the program's dedication to promoting responsible antimicrobial practices, ensuring favourable patient outcomes and combating antimicrobial resistance.

**Table 1: Antibiotic Stewardship Program Performance Summary(2021-2022)**

Primary Outcomes	Target	Q1/ 2021	Q2/ 2021	Q3/ 2021	Q4/ 2021	Total 2021	Q1/ 2022	Q2/ 2022	Q3/ 2022	Q4/ 2022	Total 2022
% compliance with the restricted antibiotics list	≥ 90%	98%	88%	91%	100%	92%	100%	100%	100%	100%	100%
% compliance with the Approved Guidelines (IP)	≥ 90%	98%	93%	98%	100%	97%	100%	98%	97%	99%	98%
% compliance with the Approved Guidelines (OP)	≥ 85%	97%	96%	96%	100%	97%	96%	98%	96%	98%	97%
Conversion of antibiotic-type de-escalation	≥ 80%	100%	77%	89%	100%	88%	100%	100%	96%	100%	99%

Q1, Q2, Q3, and Q4 denote the four quarters of the year, with each quarter representing three consecutive months. Specifically, Q1 encompasses January, February, and March; Q2 April, May, and June; Q3 July, August, and September, and Q4 October, November, and December.

Figure A: Antibiotic Stewardship Program Performance
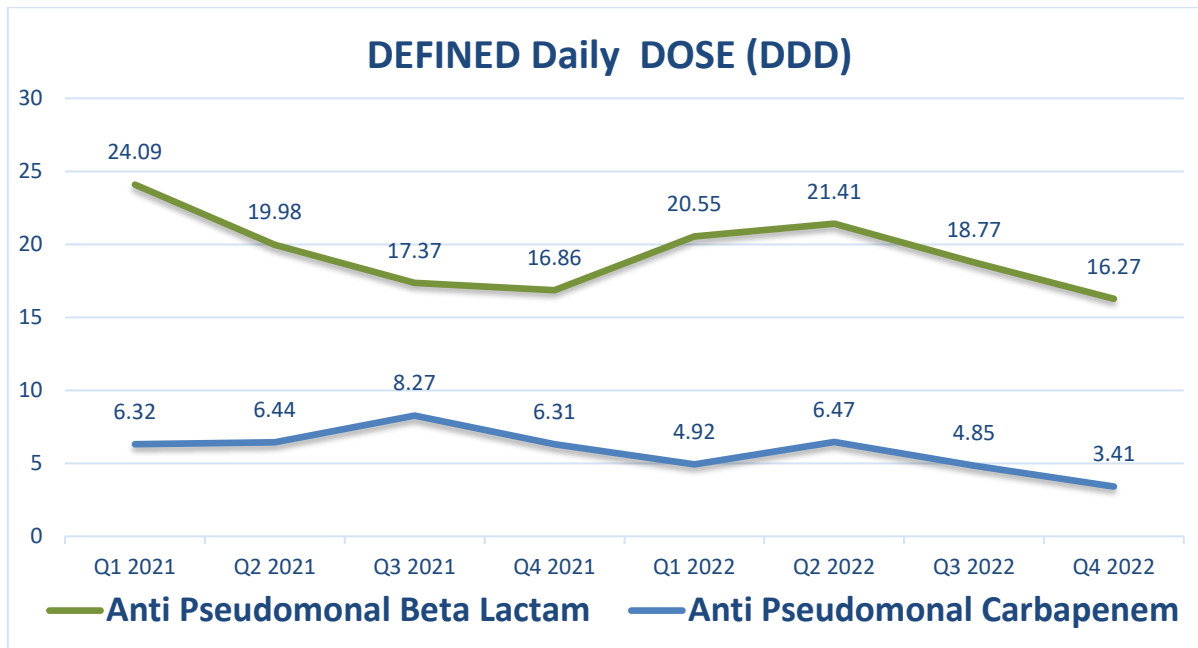
3.2 Defined Daily Dose
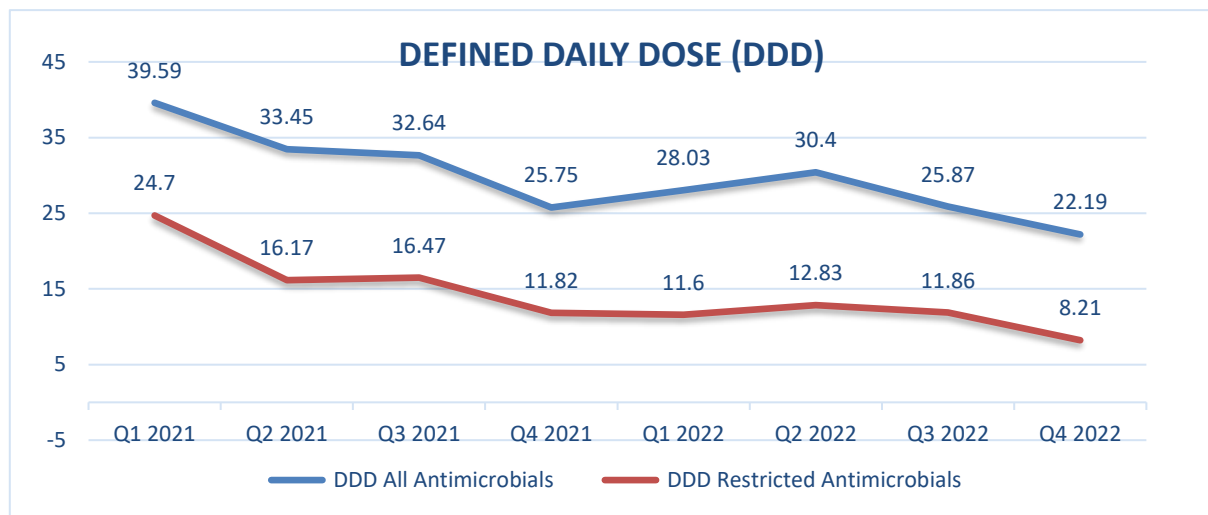
Figure B: Defined Daily Dosage: Consumption of all and of restricted anti-microbial per 100 patient days.

Fig B: DDD: Defined daily dose. Consumption of all and of restricted anti-microbial per 100 patient days.

Figure B illustrates the changes in antimicrobial consumption relative to the ongoing ASP and some of the effect of the COVID-19 pandemic as well. There is a noticeable spike in DDD corresponding with surges in COVID-19 cases, particularly evident during the first quarter of 2021 and in the second quarter of 2022, with a DDD of 39.59 and 30.4 per 100 patient days consecutively. The increase in antimicrobial consumption is highly correlated with the percentage of hospitalized critically-ill patients due to surges in COVID-19 cases in the country. ASP interventions were initiated based on the evidence-based censuses guidelines for the use of selected antimicrobials for the treatment of COVID-9 infections. The impact of high-quality ASP interventions was seen to curb unnecessary antimicrobial consumptions. As the pandemic gradually waned by the third quarter of 2022, there was a subsequent reduction in antimicrobial consumption, with levels returning to baseline by the third quarter of 2022. This trend also held for restricted antibiotics, as depicted in Figure B.

Figure C: DDD per 100 patient days for specific antimicrobial classes.

Figure C: Defined daily dose (DDD) per 100 patient days for specific antimicrobial classes.

Figure C demonstrates the variations in DDD for specific antimicrobial classes. One of the ASP interventions is the de-escalation of broad-spectrum antimicrobials and carbapenem-sparing strategies. As carbapenem-sparing strategies control carbapenem us, the only major spike was seen in third quarter of 2021 when the DDD for antipseudomonal Carbapenems peaked at 8.27. The use of narrower-spectrum anti-pseudomonal agents affectively prevented the overuse of carbapenems, notably piperacillin tazobactam, tigecycline, colistin, ceftazidime-avibactam, ceftolozane-tazobactam, oral fluoroquinolones, and ertapenem. Culture-based de-escalation of broad-spectrum antimicrobials is a key contributing factor in reducing carbepenem use across the continuum of care

3.3 Antibiotic Utilization Trends at Madinat Zayed Hospital (2021-2022)

Our analysis of antibiotic utilization at Madinat Zayed Hospital between 2021 and 2022 revealed a promising trend towards reduced consumption overall. This trend was particularly noticeable across several antibiotic classes.

We observed significant decreases in the use of cefixime (PHX00223) by 91.3%, from 6.8 units in 2021 to 4.4 units in 2022, levofloxacin Hemihydrate (PHX00725) by 46.3%, from 112 units to 60.5 units, and moxifloxacin Hydrochloride (PHX01317) by 33.3%, from 13.2 units to 8.8 units.

Additionally, piperacillin/tazobactam (PHX02734) showed a significant decrease of 48.4%, from 24,017.25 units to 12,401.1 units, indicating a potential shift towards narrower-spectrum antibiotics. Moxifloxacin (PHX02859) and meropenem 1000mg (PHX02873) use also saw decreases of 43% and 43.7%, respectively. Moreover, Levofloxacin (PHX02888) had a significant decrease of 78,8% from 235.5 units to 50 units.

Notably, cefepime Hydrochloride (PHX03020) use saw a significant increase in its use in 2022, from 12 units to 149 units. Additionally, there was a modest rise in ceftriaxone (PHX03013) of 12.3%, from 3,326.38 units to 3,737 units, and meropenem 500mg (PHX02874) of 120.4%, from 103.5 units to 228 units.

Table 2: Antibiotic Utilization Trends (2021-2022)

ITEM_NAME	ITEM_NBR	TOTAL_QTY_2021	TOTAL_QTY_2022	Percentage Decline
Cefixime	PHX00223	6.8	4.4	91.3%
Levofloxacin Hemihydrate	PHX00725	112	60.5	46.3%
Moxifloxacin Hydrochloride	PHX01317	13.2	8.8	33.3%
piperacillin/tazobactam	PHX02734	24017.25	12401.1	48.4%
Moxifloxacin	PHX02859	47.6	27.2	43%
Meropenem 1000mg	PHX02873	3265.66	1850.5	43.7%
meropenem 500mg	PHX02874	103.5	228	120.4%
Levofloxacin	PHX02888	235.5	50	78.8%
Ceftriaxone	PHX03013	3326.38	3737	12.3%
Cefepime Hydrochloride	PHX03020	12	149	1137.5%
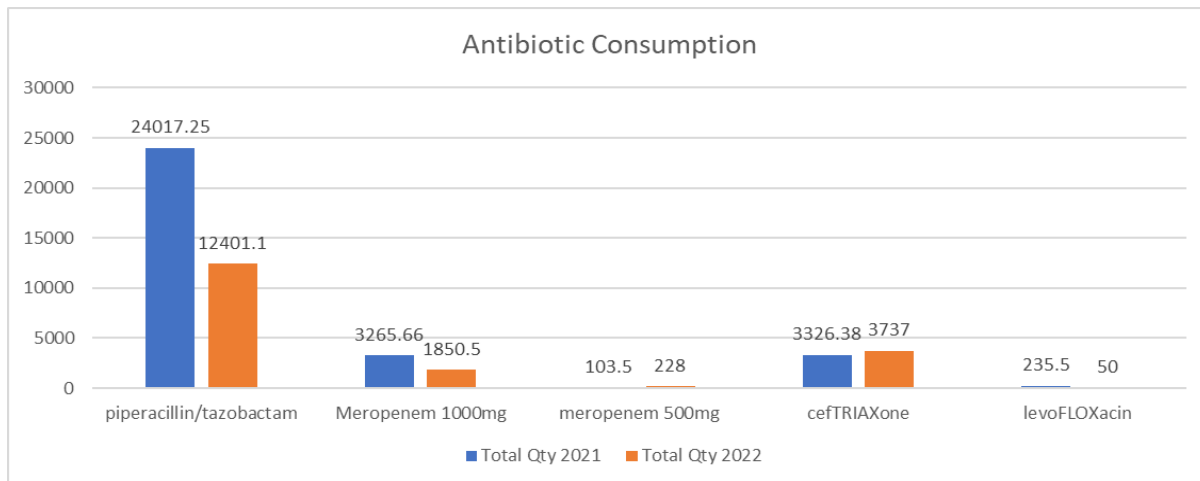
Figure D: Antibiotic Consumption Trends (2021-2022)

Figure D shows antibiotic consumption at Madinat Zayed Hospital in 2021 and 2022, for drugs including piperacillin/tazobactam, ceftriaxone, meropenem 500mg and 1000 mg, and levofloxacin.
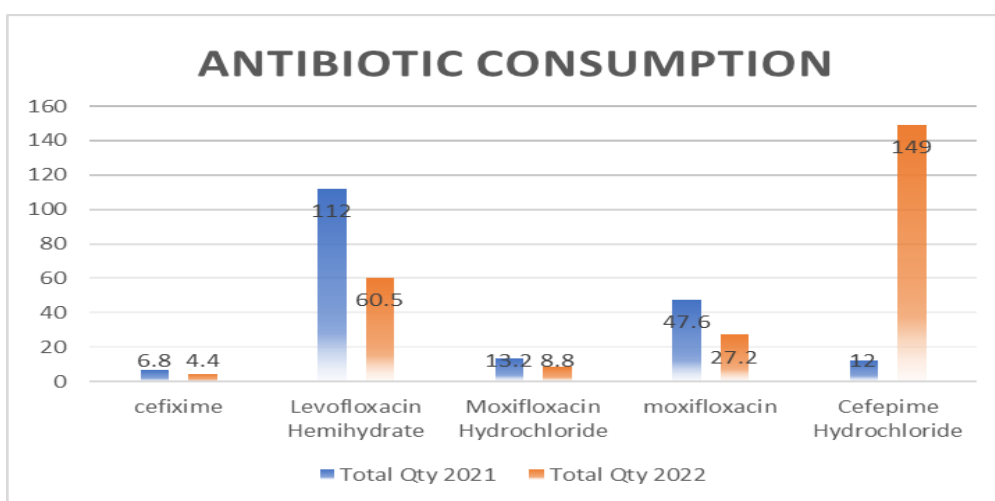

Figure E: Antibiotic Consumption Trends (2021-2022)

Figure E shows antibiotic consumption at Madinat Zayed Hospital in 2021 and 2022 for drugs including cefixime, levofloxacin hemihydrate, moxifloxacin (both formulations), and cefepime hydrochloride.

3.4 Direct Antibiotic Expenditure

Direct antibiotic expenditure showed a 2% decrease from 2021 to 2022. In 2021, spending was at 26%, whereas in 2022, it declined to 24%. Total antibiotic expenditure decreased from Dhs4,265,923 in 2021 to Dhs1,594,401 in 2022, resulting in savings of Dhs2,671,522.
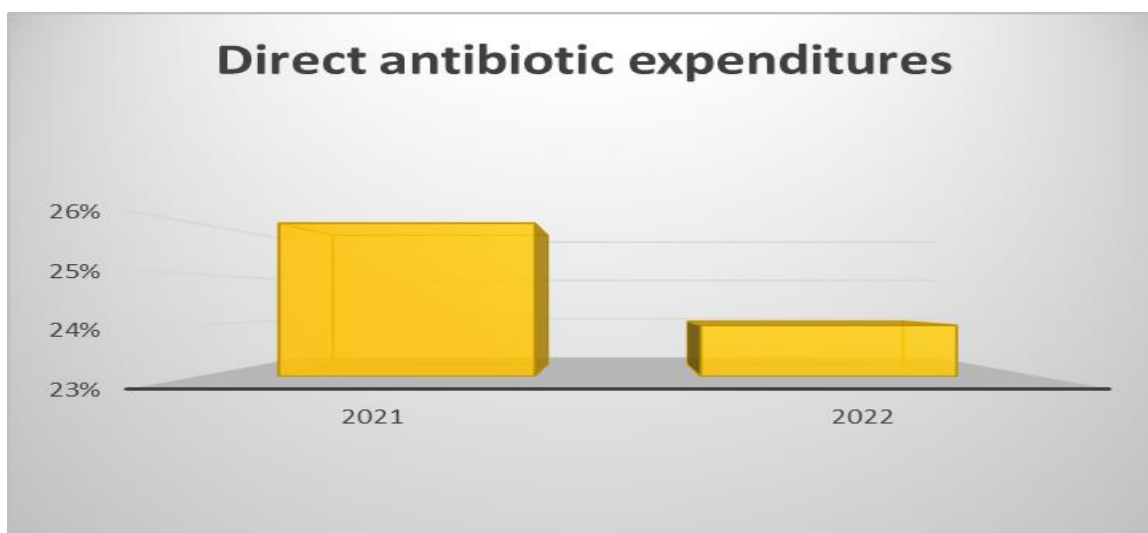
Figure F: Direct Antibiotic Expenditure (2021-2022)

3.5 Antibiotic Resistance (2021-2022)

Figure E shows the changes in antibiotic resistance trends among various microorganisms. In 2021, vancomycin exhibited 5% resistance against Enterococcus, which declined to 0% in 2022. Imipenem showed a reduction in resistance from 32% to 17% against Pseudomonas, while ceftazidime resistance against Pseudomonas aeruginosa increased from 8% to 17% from 2021 to 2022. Carbapenem resistance against Enterobacter decreased from 31% to 8%, and quinolone resistance against E. coli decreased from 40% to 34%.
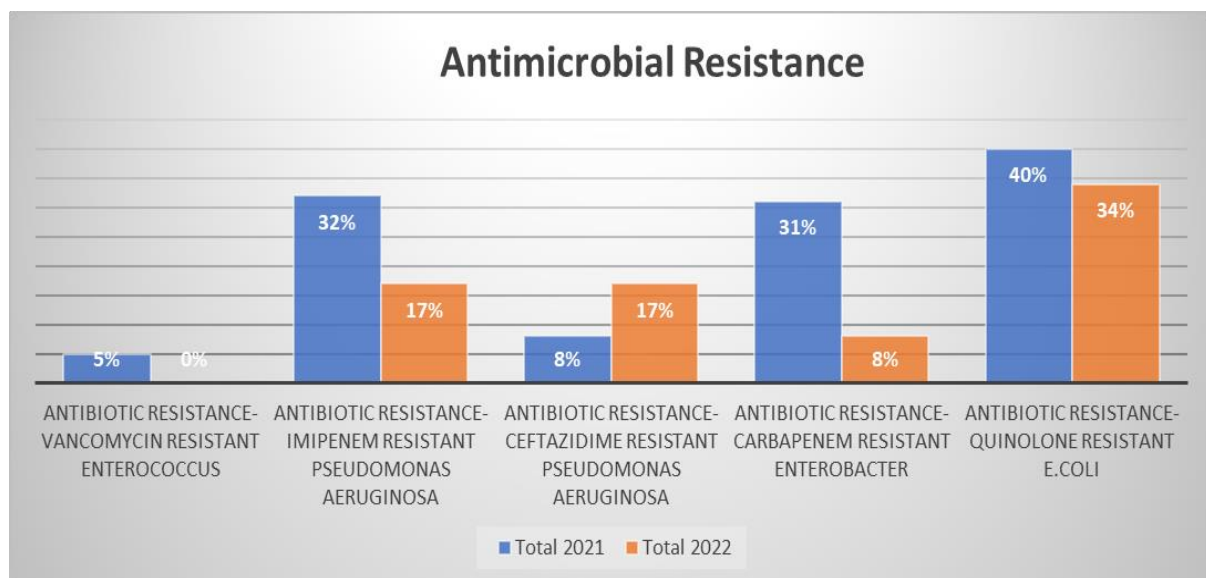

Figure G: Antibiotic Resistance Patterns

DISCUSSION

This study evaluated the effectiveness and impact of the Antimicrobial Stewardship Program (ASP) over a two-year period (2021-2022) by monitoring key performance indicators (KPIs). We assessed compliance with the restricted antibiotic list, adherence to approved antimicrobial guidelines for both inpatients and outpatients, and the rate of antibiotic de-escalation (conversion to narrower-spectrum options). By comparing data across these KPIs from 2021 to 2022, we aimed to determine the program's success in promoting responsible antibiotic use.

In our study, as per the ASP dashboard, all KPIs improved substantially from 2021 to 2022 in inpatient settings, in contrast to the outpatient setting where same rate of compliance was achieved for both years. A recent study examining antimicrobial stewardship program (ASP) performance between 2010 and 2014 had similar findings. This study, conducted in China, also showed notable improvement in compliance with antibiotics guidelines in inpatient settings, compared to outpatient settings[17]. Inpatient settings typically adhere to stricter protocols and benefit from closer supervision, facilitating faster and more consistent implementation of best practices. Outpatient settings often experience challenges in guaranteeing steady compliance due to the various patient populations they serve, which include individuals with different levels of healthcare literacy and adherence to prescribed medication plans.

Our research involved an in-depth review of antibiotic usage covering the years 2021 to 2022. The findings showed a substantial decline in most categories, with the exception of ceftriaxone and meropenem 500mg, which demonstrated slight increases. There was a more considerable increase in the consumption of cefepime, which can be attributed to physicians' increased familiarity with its prescription. These findings support the results of research conducted in a primary healthcare centre in Spain. This research aimed to investigate the impact of a comprehensive antimicrobial stewardship intervention on antibiotic consumption[18]. Notable decreases were detected in the use of amoxicillin/clavulanic acid and quinolones, with reductions of 21.88% and 25.06%, respectively. Furthermore, the percentage of patients prescribed antibiotics dropped from 26.41% to 26.70%. In addition, substantial cost savings of Dhs72,673 and Dhs2,671,522, respectively, were accomplished by both studies. In general, the findings of this study highlight the efficacy of antimicrobial stewardship initiatives in limiting antibiotic usage, improving the efficacy of antibiotics for prevalent infections observed in primary healthcare.

The emergence of bacterial resistance to antimicrobials as a global issue can be attributed to ineffective treatment durations and inappropriate antimicrobial selection[19, 20]. It is a challenging scenario characterized by higher levels of morbidity and mortality[21]. Furthermore, multidrug-resistant bacteria are making conventional antibiotics ineffective against infections[22]. Consequently, it is anticipated that antimicrobial resistance will contribute to 10 million fatalities per year by 2050, designating it a primary cause of death and inflicting a potential economic burden of $100 trillion[22]. The function of an ASP is therefore clear, as they have the ability to enhance patients' clinical outcomes by focusing on the underlying pathogen and its susceptibility profile, ensuring the most suitable medication is prescribed [23, 24]. Moreover, several studies have demonstrated that ASPs have numerous advantageous effects, including cost reduction and the promotion of rational antibiotic use [25-27].

Our findings provide a detailed understanding of the impact of ASPs on fighting resistance. They reveal a favorable trend with lessening resistance in vancomycin-resistant Enterococci (VRE), carbapenem-resistant Enterobacter, and quinolone-resistant Escherichia coli, aligning with the results of a study conducted by Abdallah et al. (2017) in Qatar[28]. However, a notable divergence from their results emerged: Abdallah's research reported a reduction in imipenem and meropenem resistance for Pseudomonas aeruginosa, but we found an

increase in strain resistance to ceftazidime. Additionally, our research indicated a substantial reduction in the susceptibility of E. coli and Klebsiella pneumoniae to carbapenems, further highlighting the complex nature of antimicrobial resistance patterns and the capricious effectiveness of stewardship interventions across different microbial strains. Additionally, in a study regarding P. aeruginosa sensitivity, the resistance of P. aeruginosa to imipenem and meropenem decreased substantially from 76.0 to 38.5% (p = 0.019) and from 74.1 to 30.0%[29]. This discrepancy in results may be attributable to the hospital's baseline resistance rates and local antibiotic prescribing practices.

Development and Implementation of the Specific Antibiogram at Madinat Zayed Hospital:

The Antimicrobial Stewardship Program at Madinat Zayed Hospital uses a complicated approach to optimize antibiotic usage and enhance patient care. An essential component of this initiative is the creation and application of an Antibiogram, which was carefully compiled using isolate data from multiple hospital facilities in 2019. By employing analytical surveillance software like WHONET®, our research team obtained important information for every culture specimen. This enabled us to calculate organism susceptibility percentages in accordance with the breakpoints suggested by the Clinical and Laboratory Standards Institute (CLSI). The Antibiogram is a vital instrument that provides guidance for formulary decisions, the development of treatment guidelines, and the monitoring of resistance trends within the corporation.

In order to enforce the strategies identified by the Antibiogram, the Madinat Zayed Hospital created treatment guidelines that are specific to their facility and address prevalent infectious diseases. These guidelines were carefully formulated for both inpatient and outpatient settings to address conditions such as urinary tract, respiratory tract, and intra-abdominal infections, and sepsis. By incorporating knowledge from local microbiology data and national guidelines, these standards were assembled in collaboration with multidisciplinary teams to ensure widespread acceptance and a range of perspectives. The effortless incorporation of the system into clinician workflows was enabled by the Health Information System, which enhanced both adherence and effectiveness.

Furthermore, the ASP employs proactive strategies that improve the usage of antibiotics and the quality of patient care, with a particular focus on managing allergies and high-risk cases. The program emphasizes interventions in accordance with critical microbiology findings via targeted audits. This enables a quick transition to oral antibiotics and addresses cases of unconfirmed antibiotic allergies. Pharmacists and infection preventionists serve as vital stakeholders in medication management and education, as they guarantee the appropriate and safe usage of antibiotics while also responding to new challenges, including that of the COVID-19 pandemic. By means of collaborative effort and evidence-based interventions, the Antimicrobial Resistance Programme (ASP) at Madinat Zayed Hospital persistently evolves, accomplishing attainable goals, nurturing favorable associations, and increasing its expertise to efficiently address antimicrobial resistance.

Our study is subject to several limitations. Firstly, this was a single-centre study and did not include demographic data for patients. Secondly, our study did not include pre- and post-intervention data, which could have provided valuable insights into the effectiveness of ASP initiatives over time. Lastly, we only monitored this program for two years; longer studies are required to fully understand the impact of ASPs on antibiotic usage.

CONCLUSION

The application of a new Antimicrobial Stewardship Program at Madinat Zayed Hospital proved its effectiveness in encouraging responsible antibiotic use. The program attained a high compliance rate with restricted antibiotics and antibiotics with approved guidelines, leading to substantial decreases in overall antibiotic use, particularly for cefixime, levofloxacin, and piperacillin/tazobactam. There was also a 2% decrease in direct antibiotic spending. While the program generated positive results in reducing resistance in several pathogens, a concerning increase in ceftazidime resistance against Pseudomonas aeruginosa highlights the necessity for constant monitoring and adaptation to address changing resistance patterns. These findings show that the ASP is a valuable tool for optimizing antibiotic use, reducing costs, and fighting antimicrobial resistance in a multi-specialty hospital setting. However, ongoing caution is vital to address developing resistance trends.

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