Assessment of drug utilization pattern of antimicrobial agents in hospitalized patients with Infectious Diseases: A cross-sectional study in the United Arab Emirates

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J. Adv. Pharm. Technol. Res.

Abstract

Efficacious use of antimicrobial agents (AMAs) is paramount to combat a wide range of infections, ensure patient safety, and reduce antimicrobial resistance. To assess the drug utilization patterns of AMAs in hospitalized patients with infectious diseases in a secondary care hospital. A prospective observational study was conducted for 6 months in the internal medicine department. Data were collected, antimicrobial prescription patterns were screened, and drug utilization was assessed using the anatomical therapeutic chemical/defined daily dose methodology. Furthermore, predictors of the prescription of multiple AMAs were also analyzed. A total of 146 patient case records were reviewed and 285 AMAs were prescribed during the study period with a mean patient age of 54.2 ± 24.4 years. The average number of antimicrobials administered per patient was 1.94 ± 0.94. Respiratory tract infection and urinary tract infection were the common indications, and penicillins were the most prescribed class of AMAs. Multivariate analysis showed that the presence of comorbidities ($P < 0.05$) and longer hospital stays ($P < 0.0001$) increased the likelihood of prescribing multiple AMAs. The study provides insight into the pattern of prescribing of AMAs which help to improve the quality of care. Prescribing AMAs by generics and from the hospital formulary list according to the recommendations of the World Health Organization is a good sign of clinical practice. The study signifies the need to continuously monitor AMAs to optimize drug therapy and enhance the quality of drug use in clinical practice.

Key words: Anti-infective agents, bacterial resistance, communicable diseases, drug utilization, health expenditure, World Health Organization

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Submitted: 05-Feb-2023 **Revised:** 01-May-2023
Accepted: 20-Jun-2023 **Published:** 30-Oct-2023

Access this article online	
Quick Response Code:	Website: www.japtr.org
	DOI: 10.4103/japtr.japtr_79_23

INTRODUCTION

Infectious diseases are an important global public health concern and a rapidly growing cause of morbidity and mortality among the population worldwide.[1] Pharmacotherapy with antimicrobial agents (AMAs) contributes significantly to disease management achieving better health outcomes. Irrational

How to cite this article: Nawa AI, Shareef J, Rao PG, Rashid AU. Assessment of drug utilization pattern of antimicrobial agents in hospitalized patients with Infectious Diseases: A cross-sectional study in the United Arab Emirates. J Adv Pharm Technol Res 2023;14:299-305.

use or inappropriate prescribing of antibiotics can lead to the development of drug resistance, adverse drug reactions, nonadherence to medications, and negative economic consequences.[2]

The Anatomical and Therapeutic Chemical Classification (ATC)/defined daily dose (DDD) methodology recommended by the World Health Organization (WHO) is an effective tool for monitoring drug utilization patterns and optimizing the use of AMAs.[3] Studies have documented variations in DDD and prescribed daily doses (PDD) between different classes of medications. These discrepancies may be caused by the severity of the disease, the dose of antibiotics, or different indications for a drug.[4]

WHO has established a global action plan with five objectives that must be addressed to combat antibiotic resistance.[5] Similarly, states of the Gulf Cooperation Council have developed a strategic plan to take action against antimicrobial resistance (AMR) by monitoring trends of antimicrobial consumption using different indicators.[6] A study carried out in the UAE estimating the occurrence of self-medication with antibiotics reported a high prevalence of self-medication behavior, increasing the risk of the emergence of antibiotic resistance.[7] Furthermore, studies evaluating the pattern of AMAs drug utilization pattern in hospitalized patients with infectious diseases remain limited in the northern emirate of UAE. Therefore, the consumption of AMAs should be monitored and measured in health-care settings to promote rational drug use and improve antimicrobial stewardship programs (ASPs). Taking into account these statements, the study was carried out to analyze the prescription trends and practices of AMAs and to compare the consumption of different AMAs with DDD and PDD in hospitalized patients with infectious diseases in a secondary care hospital.

METHODS

Study design, setting, and sampling

This prospective observational study was carried out for a period of 6 months from December 2021 to May 2022 in a secondary care hospital in Ras Al Khaimah. The Research and Ethics Committee approved the study (MOHAP/REC/2021/1-2021-PG-P). Raosoft calculator was used to calculate the sample size with a 5% margin of error, 95% confidence interval (CI), and a 50% response distribution.[8] The total sample size was 150 patients, assuming a dropout rate of 10%–15% in the study population. Patients of either sex, aged 18 years and older, hospitalized in the Department of Internal Medicine diagnosed with infectious diseases, and receiving a minimum of one AMA were included in the study. Patients who received AMAs for long-term therapy were referred from other departments, admitted to the intensive care unit (ICU), diagnosed with COVID-19, and receiving antibiotics, incomplete medical records, and pregnant/lactating were excluded from the study. The study investigator attended ward rounds daily, reviewed patient case records, and those who met the study criteria were included in this study after obtaining informed consent. Data relevant to the study including demographic details, microbiological data, and drug therapy were collected from electronic medical records. All the collected data were then reviewed to ensure completeness of the records.

Data analysis

All the antimicrobial drugs were coded using ATC Classification System derived from the WHO. The number of DDDs per 100 bed days was calculated by multiplying the amount of drug per item/WHO DDD measure. The PDD of the AMAs was calculated by multiplying the DDD by the ratio of the number of DDDs to the total number of treatment days. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 26 (IBM, SPSS Inc). Description statistics were used for sociodemographic details of the patients. Logistic regression analysis was used to examine the predictors between the number of AMAs and the different variables and to assess the association between the predictor variables and prescribing a specific class of AMAs in hospitalized patients. Results were expressed as odds ratio (OR) and (95% CIs). Statistical significance was considered at $P < 0.05$.

RESULTS

A total of 146 patients case records were reviewed, 75 (51.36%) were male and 71 (48.63%) were female. The mean age of the study population's was 54.30 ± 24.5 (mean ± standard deviation [SD]) years (range: 18–107 years). The majority (58 [39.72%]) of the study population belong to the age group 61–90 years (58 [39.72%]). Most of the study population (82 [56.16%]) had a hospital stay duration of 6–10 days and the mean hospital stay was 7.73 ± 2.76 (mean ± SD) days. Respiratory tract infections (54 [34.83%]) were the most common indication for prescribing AMAs in our study [Table 1].

Regarding the comorbidities, (80 [54.7%]) patients had a minimum of one or more comorbidities and (66 [45.2%]) of the patients did not have any comorbidities. Hypertension (43 [32.82%]), followed by diabetes mellitus (38 [29.0%]), was the most common comorbidity identified in our study [Figure 1].

A total of 1069 drugs were prescribed during the study period. Antibiotics were prescribed in 285 encounters and all drugs prescribed were from the hospital formulary by generic names. The mean number of antibiotics prescribed per patient was 1.94 ± 0.94 (mean ± SD). Majority (58.9% [n = 86]) of them received two or more antibiotics per prescription in our study [Table 2].

Penicillin (76 [26.6%]) was the most commonly prescribed AMA, followed by cephalosporin (63 [22.10%]). Among the class of drugs, the most frequently prescribed were tazobactam and piperacillin (62 [21.08%]), followed by levofloxacin (41 [14.96%]) [Table 3].

Prescribing AMAs according to indications, it was observed that the most commonly prescribed AMAs for respiratory tract infections were penicillin (38 [33.62%]) and fluoroquinolones (30 [26.54%]). For urinary tract infections, carbapenems (34 [35.78%]) and ceftriaxone (22 [23.15%]) and for sepsis, the most frequently prescribed were penicillin (18 [28.57%]) and fluoroquinolones (15 [23.80%]) [Figure 2].

In our study, β-lactams were the maximum number of daily defined doses consumed, followed by fluoroquinolones. The PDD/DDD ratios for the different classes of beta-lactam drugs ranged from 1.90 to 13.16. The most commonly prescribed penicillin-enzyme inhibitor was found to be piperacillin–tazobactam combination compared to other beta-lactam AMAs [Table 4].

Multivariate logistic regression analysis revealed that the presence of comorbidities (OR 0.32, 95% CI 0.11–0.90) and longer hospital stays (OR 1.37 95% CI 1.14–1.63) was associated with a higher chance of prescribing multiple AMAs [Table 5].

Patients diagnosed with sepsis received penicillin derivatives (OR: 4.42, 95% CI 1.074–18.18) and fluoroquinolones (OR: 5.42, 95% CI 1.35–21.76) compared to other AMAs. Similarly, carbapenems were prescribed in urinary tract infections (OR: 18.20, 95% CI 4.28–77.38) and fluoroquinolones (OR: 3.92, 95% CI 1.05–14.69) in respiratory tract infections. There was no association with gender or any age group with the prescription of AMAs except carbapenems (OR: 2.57, 95% CI 1.00–6.59) [Table 6].

DISCUSSION

The present study observed a male predominance with most

Table 1: Sociodemographic and clinical characteristics

Characteristics	*n*=146, *n* (%)
Gender	
Male	75 (51.36)
Female	71 (48.63)
Age wise distribution	
0–30	33 (22.60)
31–60	47 (32.19)
61–90	58 (39.72)
91 and above	8 (5.47)
Age (years), mean±SD	54.30±24.5
Co-morbidities	
Nil	66 (45.2)
1–2	50 (34.24)
3–4	29 (19.86)
≥5	1 (0.68)
Length of hospital stay	
1–5	38 (26.02)
6–10	82 (56.16)
11–15	21 (14.38)
≥16	5 (3.42)
Mean±SD (days)	7.73±2.76
Diagnosis	
Respiratory tract infections	54 (34.83)
Urinary tract infections	53 (34.19)
Sepsis	23 (14.83)
Gastroenteritis	11 (7.09)
Others*	14 (9.03)

*Pancreatitis (*n*=3), pyelonephritis (*n*=02), pelvic inflammatory disease (*n*=2), meningitis (*n*=1), enteric fever (*n*=1), diarrhea (*n*=2), food poisoning (*n*=2), ascites (*n*=1). SD: Standard deviation

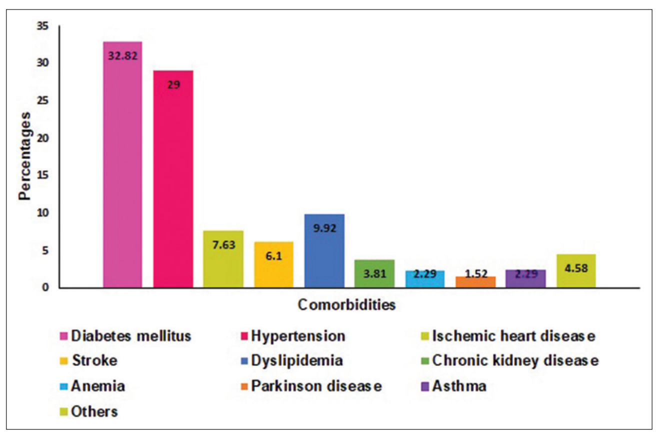

Figure 1: Associated co-morbidities ($n = 131$)

Table 2: World Health Organization drug prescribing indicators of antimicrobial agents

Prescribing indicators	*n*	Values (%)
Average number of drugs per encounter	1069/146	7.32
Percentage of drugs prescribed by generic	1069	100
Number of antibiotics prescribed per prescription	285/146	1.95
Percentage of encounters with injection antibiotics prescription	233/285	81.81
Percentage of drugs from formulary list of the study setting	1069/1069	100
Percentage of patient who received one antibiotic per prescription	60/146	41.09
Percentage of patients who received two or more antibiotics per prescription	86/146	58.9

Table 3: Frequencies of the antimicrobial agents prescribed

Class of AMAs	*n*=285, *n* (%)
Penicillin's	76 (26.66)
Tazobactam + piperacillin	62
Amoxicillin + clavulanic acid	16
Cephalosporin's	63 (22.10)
Ceftriaxone	48
Ceftazidime	7
Cefuroxime	8
Fluoroquinolones	54 (18.94)
Levofloxacin	41
Ciprofloxacin	13
Carbapenems	45 (15.78)
Meropenem	42
Ertapenem	3
Tetracycline	17 (5.96)
Doxycycline	15
Tigecycline	2
Glycopeptides	11 (3.85)
Vancomycin	11
Nitroimidazoles	12 (4.21)
Metronidazole	12
Macrolides	4 (1.40)
Azithromycin	2
Clarithromycin	2
Aminoglycosides	1 (0.35)
Gentamicin	1
Others (clindamycin [*n*=1], linezolid [*n*=1])	2 (0.70)

AMAs: Antimicrobial agents

of the study participants were geriatrics (aged ≥60 years), in developing infectious diseases and, therefore, received more AMAs explaining the increased prevalence of comorbidities in the aging population. In advanced-age populations, the risk of developing chronic and infectious diseases increases due to age-related physiological changes, gradual deterioration of the immune system, and a decline in functional elements. The average duration of the prescribed antibiotic treatment in our study was longer compared to the study findings carried out by Abdalla and Yousef, Mugada *et al*., which reported an average duration of 4.9 and 5.24 days, respectively.[9,10] A possible reason could be that the patients might have a severe infectious etiology that required antibiotic therapy for a longer duration to control the infection.

The present study identified that the percentage of generic drugs prescribed according to the hospital formulary list was 100%, which is in line with WHO recommendations. However, reports from other studies indicated that the generic drugs prescribed ranged from 64.5% to 96.7%.[11-14] The WHO recommends that physicians prescribe medications in generic names, as they are cost-effective and provide flexibility in procuring drugs from the central

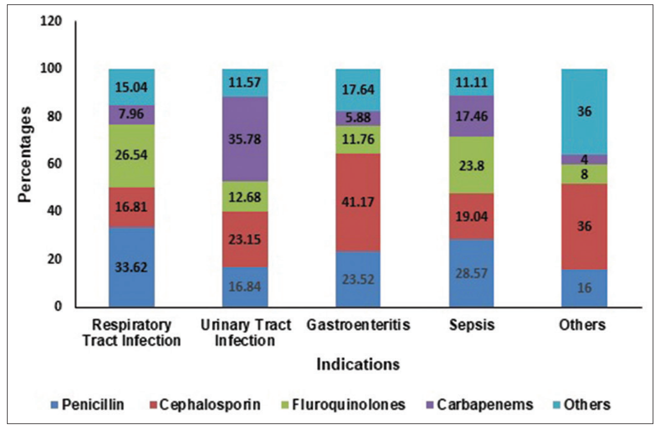

Figure 2: Most frequently prescribed class of antimicrobial agents according to the infectious diseases

medical store. This explains the fact that hospitals governed by the public sector in the UAE purchase drugs from the central government drug store based on the national formulary of the UAE.

In our study, the respiratory and urinary tract system was the predominant indication for the use of AMAs, echoing other studies.[15] However, studies conducted by Olayinka *et al*. and Khirasaria *et al*. reported that surgical prophylaxis and infections related to the central nervous system constituted the largest proportion of patients prescribed AMAs.[16,17] This disagreement in the research findings could be due to the difference in the study settings and methodology, as this analysis included all patients from the ICU and other specialty departments compared to our investigation, which focused only on the internal medicine department.

Penicillin was the most commonly prescribed class of AMAs in our study, followed by cephalosporins, fluoroquinolones, and carbapenems. These results are consistent with various other studies that reported similar findings.[13,18,19] However, few other studies highlighted cephalosporins and fluoroquinolones as the most commonly prescribed antibiotics.[12,16,20] The possible cause for the variability in the selection and prescription of AMAs for various infectious diseases could be the regional variation in susceptibility/resistance microorganisms, the prescribing pattern of physicians, differences in the prevalence of infectious diseases in various study settings, and lack or poor adherence to treatment guidelines. Among penicillins, piperacillin/tazobactam was the most commonly prescribed AMA in our study. The reason for the selection of this drug could be its broad-spectrum antimicrobial activity, covering both Gram-positive and Gram-negative microorganisms, better clinical efficacy, and favorable therapeutic profile. In addition, a narrative review reported that increased antimicrobial consumption and frequent use of AMAs with a broad spectrum of activities lead to the development of AMR.[21]

Table 4: Comparison of defined daily doses and prescribed daily doses of antimicrobial agents prescribed

Drug class	Route of administration	ATC code	Number of DDDs	Number of bed days	DDDs/100 bed days	WHO DDD	PDD
Beta lactams							
Piperacillin - tazobactam	Injection	J01CR05	615.6	656	94	14	13.16
Ceftriaxone	Injection	J01DD04	382	375	101	2	2.02
Cefuroxime	Injection	J01DC02	79	61	129	3	3.88
Ceftazidime	Injection	J01DD02	94.5	63	150	4	6.0
Amoxicillin - clavulanic acid	Injection	J01CR02	32.4	27	120	3	3.6
Amoxicillin - clavulanic acid	Oral		147.1	116	123	1.5	1.90
Carbapenems							
Meropenem	Injection	J01DH02	361.8	385	94	3	2.81
Ertapenem	Injection	J01DH03	22.5	25	90	1	0.90
Fluoroquinolones							
Levofloxacin	Injection	J01MA12	448.5	413	108	0.5	0.54
Ciprofloxacin	Oral	J01MA02	107	94	113	1	1.13
Tetracyclines							
Doxycycline	Oral	J01AA02	195	89	219	0.1	0.21
Tigecycline	Injection	J01AA12	2	12	16	0.1	0.016
Macrolides							
Azithromycin	Injection	J01FA10	1	5	20	0.5	0.1
Azithromycin	Oral		3.33	10	33	0.3	0.09
Clarithromycin	Oral	J01FA09	2	7	28	0.5	0.14
Aminoglycosides							
Gentamicin	Injection	J01GB03	1.33	7	19	0.24	0.04
Glycopeptide							
Vancomycin	Injection	J01XA01	21.5	86	25	2	0.5
Linezolid	Injection	J01XX08	1	14	7	1.2	0.08
Nitroimidazoles							
Metronidazole	Oral	P01AB01	63.75	85	75	2	1.5
Lincosamide derivatives							
Clindamycin	Injection	J01FF01	1.33	7	19	1.8	0.34

DDDs: Defined daily doses, PDDs: Prescribed daily doses, WHO: World Health Organization, ATC: Anatomical and therapeutic chemical

Table 5: Predictors associated with prescribing multiple antimicrobial agents

Variables	Number of patients		Multivariate analysis	
	1 AMA (*n*=110)	≥2 AMA (*n*=36)	OR (95% CI)	*P*
Gender				
Male	54 (48.6)	22 (61.1)	0.745 (0.327–1.698)	0.483
Female	56 (51.3)	14 (38.8)		
Age (years)				
≤50	53 (49.5)	16 (44.4)	0.942 (0.353–2.517)	0.905
>50	57 (50.4)	20 (55.5)		
Co-morbidity				
Absent	50 (53.1)	19 (52.7)	0.328 (0.119–0.908)	0.032*
Present	60 (46.8)	17 (47.2)		
Length of hospital stay				
≤6	59 (54.0)	9 (25.0)	1.370 (1.149–1.633)	0.0001**
>6	51 (45.9)	27 (75.0)		

*P<0.05, **P<0.001–statistically highly significant. OR: Odd's ratio, CI: Confidence interval, AMA: Antimicrobial agent

In our study, we calculated the PDD for various AMAs and compared them with the respective DDD defined by the WHO. For beta-lactams, PDD was lower or increased when compared to DDD, while for macrolides, aminoglycosides, and glycopeptides, PDD was lower than DDD. Overall, dissimilarity was observed between PDD and DDD for most

Table 6: Multiple logistic regression showing variables associated with prescribing of antimicrobial agents

Variables	Penicillins		Cephalosporins		Fluoroquinolones		Carbapenems	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Gender								
Male	2.154 (0.975–4.76)	0.058	1.532 (0.748–3.138)	0.243	1.068 (0.49–2.29)	0.867	0.462 (0.179–1.196)	0.112
Female								
Age (years)								
≤50	0.490 (0.221–1.087)	0.079	0.733 (0.354–1.519)	0.403	1.967 (0.904–4.279)	0.088	2.579 (1.00–6.59)	0.048*
>50								
Diagnosis								
Respiratory tract infection	3.039 (0.838–11.025)	0.091	0.485 (0.130–1.804)	0.280	3.92 (1.05–14.69)	0.042*	0.953 (0.22–4.00)	0.947
Urinary tract infection	0.318 (0.097–1.045)	0.059	0.483 (0.136–1.711)	0.259	0.892 (0.26–2.98)	0.852	18.20 (4.28–77.38)	0.0001**
Gastroenteritis	0.401 (0.074–2.190)	0.292	1.520 (0.272–8.494)	0.633	1.74 (0.283–10.82)	0.548	1.54 (0.12–18.66)	0.735
Sepsis	4.420 (1.074–18.18)	0.039*	0.852 (0.213–3.404)	0.821	5.42 (1.35–21.76)	0.017*	2.30 (0.45–11.74)	0.317
Others	0.702 (0.170–3.303)	0.702	2.101 (0.452–9.763)	0.344	2.71 (0.565–13.02)	0.212	0.476 (0.046–4.894)	0.533

*$P<0.05$, **$P<0.001$–statistically highly significant. OR: Odds ratio, CI: Confidence interval

AMAs. Other studies have also observed marked deviations between PDD and DDD for most antibiotics.[22,23] Evaluating the cause of these variations can lead to the formulation of guidelines or other appropriate interventions, such as strengthening ASPs to improve rational antimicrobial use.

The study observed a strong relationship between the number of AMAs prescribed and hospital stays and comorbidities. Patients hospitalized for longer periods (>6 days) received two or more AMAs compared to those who stayed for a short period. Furthermore, it should be noted that a longer hospital stay predisposes patients to hospital-acquired infections with resistant bacteria or presumably undergo invasive surgical procedures that will also increase the risk of infections. Patients with comorbidities such as diabetes and hypertension are more likely to be associated with an increased risk of infection that requires hospitalization and the prescribing of multiple AMAs. Our findings are comparable with the results of studies carried out by Abdalla and Yousef, Bansal *et al*., which reported similar observations.[9,24] However, patient characteristics, dosing schedule, common adverse effects, most likely pathogens, and cost-effectiveness are some of the factors to consider when selecting AMAs.

Limitations

Our study has a few limitations. The study was conducted in hospitalized patients from the internal medicine department and does not include other specialty and outpatient departments, and therefore may not accurately evaluate the entire antibiotic utilization pattern of the hospital. The data were collected through electronic access using the Wareed system and resource limitations. We were unable to conduct patient interviews or communicate with the prescriber to assess the factors contributing to current practice. The data were collected at a single point in time and we were unable to follow-up with the patients, and the outcome of antibiotic prescription could not be evaluated.

CONCLUSION

The present study analyzed the pattern of prescription of AMAs in various infections and serve as benchmark data for further studies in similar settings to identify trends in drug consumption over the years. ASPs such as antibiotic de-escalation and regular review of antimicrobial therapy with clinical progress and culture and sensitivity tests in hospitals will help to achieve rational and cost-effective health care. This is a long way to combat drug-resistant bacteria and minimize adverse events. The study signifies the need for continuous surveillance of AMAs is warranted to improve prescribing practices and to enhance the quality of care in clinical practice.

Acknowledgment

We would like to thank the administration of Ibrahim Bin

Hamad Obaidullah Hospital, Ras Al Khaimah, United Arab Emirates, for giving permission to conduct the study. The authors would like to thank the President of RAK Medical and Health Science University and the Dean of RAK College of Pharmacy and also Dr. Sathvik B. Sridhar, Chairperson In-charge, Department of Clinical Pharmacy and Pharmacology for their encouragement and support.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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