A 5-Year Retrospective Analysis of Antibiotic Utilisation Pattern by AWaRe Classification in Qatar

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Abstract

Background: To analyse the trend and pattern of antibiotic consumption rates over a period of five years in a secondary care hospital in Qatar. Consumption of antibiotics is a crucial factor in the evaluation of antibiotic usage.

Methods: To measure and compare a five-year antibiotic consumption trend in inpatient department wards using Defined Daily Dose (DDD) per 100 bed days (DDD/100-BD). Antibiotics dispensed between January 2018 and December 2022 were evaluated. Data collection was done using Microsoft Excel. The analysis was done using the World Health Organization (WHO) AWaRe classification of antibiotics.

Results: The analysis showed that antibiotic consumption significantly increased from 2018 (4.11 DBD) to 2020 (15.55 DBD) and then sustained thereafter. Widely used antibiotic belongs to the third generation cephalosporins which is under Watch class of antibiotics. Ceftriaxone, cefuroxime, and amoxicillin clavulanate were the most consumed antibiotics in the hospital throughout the study period at 53.92 DBD, 32.22 DBD and 21.65 DBD respectively.

Conclusion: Establish benchmarking at the facility level. We observed the use of ceftriaxone is more as surgical prophylaxis, which is a Watch group of antibiotics, however there is zero use of restricted antimicrobials. Increase in parenteral fluroquinolone especially levofloxacin needs monitoring, which is not included in WHO essential list of medication. There is a scope to measure the appropriateness of antibiotics, as well as the duration of therapy. The goal of WHO Target $\geq 60\%$ of total antibiotic consumption being Access group antibiotics can be used as an index to analyse the comparative use Watch and Access group of antibiotics. J Pharm Care 2023; 11(2): 66-73.

Keywords: Antibiotic Consumption; Defined Daily Dose; World Health Organization

Introduction

The abuse and overuse of antibiotics is one of the primary causes of antibiotic resistance (AMR). Regardless of whether it is required, the widespread use of antibiotics exerts a selection pressure by limiting some microorganisms' capacity to reproduce, accelerating the emergence of AMR. Three significant parameters determining this selection pressure are the quantity of antibiotics prescribed, the number of patients treated with antibiotics, and the percentage of patients on antibiotics at a hospital. Unfortunately, Multi drug resistant organism (MDRO) infections are on the rise and AMR is becoming increasingly common in the Middle East. In many regions of the world, the threat of the emergence and spread of antimicrobial resistance (AMR) has grown due to the

abuse and inappropriate use of antibiotics (1-2). Countries of the Gulf Cooperation Council (GCC) are a political and economic union several factors have been linked to the emergence and spread of AMR in this region (3).

A continuous increase in AMR will increase drug-resistant illness fatalities from 700,000 to 10 million per year, with anticipated expenses of up to \$100 trillion globally by 2050. One of the major contributing factors of AMR is the overuse of antibiotics (4). In Qatar, it was estimated that around 45% of antibiotics prescribed for the treatment of upper respiratory tract infections in the private sector from May 2014 to December 2015 were for an inappropriate indication (5). In 30% to 50% of instances, the choice of antibiotic, indication, or duration is inappropriate according to studies (6). The irrational use of antibiotics includes prescribing antibiotics for viral infections, using

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the incorrect type of antibiotic, using the incorrect dose, duration, or route of administration, increasing the use of antibiotics in agriculture, and using broad-spectrum and last-resort antibiotics routinely. There is a significant correlation between antibiotic use and the growth of antibiotic-resistant bacteria (7). Unfortunately, AMR is becoming more prevalent in the Middle East and rates of infections with MDROs are on the rise (8).

Research conducted in Qatar in 2015 revealed a significant prevalence of Pseudomonas aeruginosa a multi-drug resistant organism in medical facilities (9). Thus, limiting the use of unnecessary antibiotics will reduce the antibiotic resistance rate and lessen the higher healthcare expenditures associated with drug-resistant diseases, which may be achieved by the implementation of an antibiotic stewardship program (ASP) (10-12).

The usage of antimicrobials is usually linked to the emergence of resistant types of microorganisms (13). To encourage sensible usage, the consumption of antimicrobials must be quantified, and consumption patterns must be tracked. The optimal approach for quantifying antibiotic usage remains to be established. Calculating aggregated ratios on the amount of antibiotics used is the standard method for measuring antibiotic consumption with the objective of facilitating comparative assessments. These ratios typically consist of one of two reference units: the defined daily dosage (DDD) or the number of days of therapy (DOT) (14). ASPs are needed in all healthcare settings regardless of resources needed, size and location. Even small hospitals should have AMS (15).

According to a finding, antibiotic consumption rates were highest in North Africa and Middle East with a large increase in the consumption of fluoroquinolones and third generation cephalosporins in Middle East countries (16). In 2021 antibacterial for systemic use recorded consumption was 3.27 DDD/1000 bed days than any other category in Qatar (17). There is a National AMR committee, and one health framework is within the national action plan in Qatar to identify and mitigate the AMR. WHO's national workshops and a point prevalence survey were conducted at the end of 2022.

Antibiotic consumption patterns at Doha Clinic Hospital, a major private healthcare facility in Qatar, have not been previously reported, hence the amount and class of antibiotics consumed are unclear. Using the ATC/DDD technique and WHO AWaRE classification, this study aimed to quantify, track, and compare hospital antibiotic usage patterns over a five-year period. This methodology was created to improve the quality of patient treatment by conducting research and monitoring antibiotic consumption (5).

Methods

A five-year retrospective study from 2018-2022 which focused on the antibiotics consumed by the inpatient wards of the hospital was conducted. Doha Clinic Hospital, a 57 bedded acute private healthcare facility with medical, surgical, paediatric, intensive care unit (ICU), gynaecology, and obstetrics wards. The hospital's ethics committee waived the need for informed consent due to the observational nature of the study.

This study included antibiotics categorised as J01 category (drugs for systemic use) by the ATC classification system and antibiotics available at the Doha clinic Hospital and listed in the most recent edition of the Qatar National formulary. The amount of antibiotics dispensed for 60 consecutive months, i.e. January 2018 to December 2022, was reviewed and data was taken from pharmacy records. Antibiotics that met both requirements were included in the analysis. The World Health Organization (WHO) recommended in 2019 that antibiotics be divided into three groups: Access, Watch, and Reserve (AWaRe) groups. We utilized the 2019 database to categorize drugs appropriately (17). When an antimicrobial was available in both oral and parenteral forms, the total for both forms was documented. There were ten antibiotics in the Access group, eighteen in the Watch group, and none in the Reserve group (Table 1).

AntibiotiC	ATC Code	Route	WHO DDD18	AWaRe Group
Amikacin	J01GB06	Р	1	Access
Amoxicillin	J01CA04	0	1.5	Access
Amoxicillin + Clavulanate	J01CR02	0	1.5	Access
Amoxicillin + Clavulanate	J01CR02	Р	3	Access
Ampicillin	J01CA01	Р	6	Access
Azithromycin	J01FA10	0	0.3	Watch
Cefdinir	J01DD15	0	0.6	Watch
Cefixime	J01DD08	0	0.4	Watch
Cefotaxime	J01DD01	Р	4	Watch
Ceftazidime	J01DD02	Р	4	Watch
Ceftriaxone	J01DD04	Р	2	Watch
Cefuroxime	J01DC02	0	0.5	Watch
Cefuroxime	J01DC02	Р	3	Watch
Ciprofloxacin	J01MA02	0	0.5	Watch

Table 1. Antibiotics for systemic use included in this study.

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Table 1. Continued

Antibiotic	ATC Code	Route	WHO DDD18	AWaRe Group
Ciprofloxacin	J01MA02	Р	0.8	Watch
Clarithromycin	J01FA09	Ο	0.5	Watch
Clindamycin	J01FF01	0	1.2	Access
Clindamycin	J01FF01	Р	1.8	Access
Doxycycline	J01AA02	0	0.1	Access
Gentamycin	J01GB03	Р	0.24	Access
Levofloxacin	J01MA12	0	0.4	Watch
Levofloxacin	J01MA12	Р	0.4	Watch
Meropenem	J01DH02	Р	3	Watch
Metronidazole	J01XD01	Р	1.5	Access
Moxifloxacin	J01MA14	0	0.5	Watch
Moxifloxacin	J01MA14	0	0.5	Watch
Piperacillin + Tazobacum	J01CR05	Р	14	Watch
Vancomycin	J01XA01	Р	2	Watch

Calculation of antibiotic consumption rate

The DDD is a globally accepted unit of measuring drug consumption of different strengths,

Pack sizes or combinations. It can be used to compare rates between regions, countries, hospitals, and wards. Number of DDDs was calculated by first converting the total amount of antibiotic dispensed in a given year into grams; this was then divided by the standard WHO DDD value given in grams. All DDDs were based on the ATC/DDD index of 2022 version. Bed days is given by multiplying three variables the number of beds, the bed occupancy rate and the number of days in the study. When measuring antibiotic consumption in an inpatient setting DDD/100-BD is the recommended method(18-20). DDD/100-BD is given by dividing the number of DDDs by patient-days and multiplied by 100. To compare changes in consumption among the antibiotics we calculated the percent contribution of each antibiotic to the total antibiotic consumption of that year and scale it to 100, to enable us to see the "consumption percentage" of that antibiotic (Figure 1) (Table 2).

Table 2. Antibiotic consum	ption at ATC system and	AWaRe classification	DDD/100 Bed Days (DBD)

AWaRE Category	Item Description	DBD 2018	DBD 2019	DBD 2020	DBD 2021	DBD 2022
Watch	Ceftriaxone	13.77	12.31	80.06	83.96	79.49
Watch	Cefuroxime	88.15	27.38	34.88	53.86	46.99
Watch	Cefdinir	18.50	22.49	14.65	11.39	1.02
Access	Amoxicillin+Clavulanate	37.71	12.42	9.03	18.80	63.30
Watch	Cefixime	46.90	3.67	5.13	13.61	7.94
Watch	Ciprofloxacin	8.66	0.97	1.75	4.07	4.49
Access	Metronidazole	0.93	0.12	1.64	11.93	11.10
Watch	Azithromycin	2.09	0.40	1.11	1.91	0.52
Watch	Vancomycin	0.00	0.13	0.70	0.67	3.27
Watch	Moxifloxacin	4.63	0.28	0.88	0.82	2.26
Access	Gentamycin	0.65	0.57	0.50	1.62	3.99
Watch	Clarithromycin	2.59	0.33	0.37	1.14	0.14
Watch	Levofloxacin	1.13	0.42	0.35	2.13	2.45
Watch	Piperacillin + Tazobactum	0.00	0.00	0.16	1.26	0.92
Watch	Ceftazidime	0.00	0.00	0.16	0.00	0.00
Access	Clindamycin	0.00	0.25	0.12	0.28	0.24
Access	Amoxicillin	0.18	0.04	0.10	0.19	0.38
Access	Ampicillin	0.02	0.04	0.09	0.13	0.05
Access	Amikacin	1.34	0.04	0.07	0.60	0.25
Watch	Meropenam	0.00	0.00	0.04	0.23	0.15
Watch	Cefotaxime	0.00	0.00	0.02	0.28	0.01
Access	Doxycycline	0.00	0.02	0.00	0.00	0.00

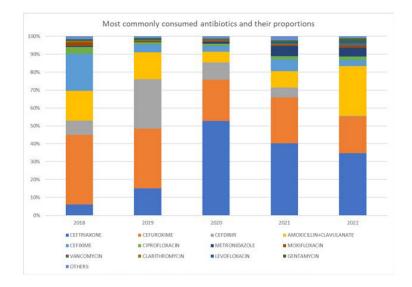


Figure 1. Most consumed antibiotics and their proportions from 2018 to 2022 given in percentage. Others: Azithromycin, Pipracillin+Tazobactum, Ceftazidime, Clindamycin, Amoxcillin, Ampicillin, Amikacin, Meropenam, Cefotaxime and Doxcycline.

Statistical analysis

Consumption data of the antibiotic were aggregated according to the ATC classification and expressed in DDD and DDD/100-BD (DBD). Microsoft Excel 365 Version 2302 was used to enter and analyze data, and after data cleansing, it was exported to IBM SPSS Version 26 for descriptive and analytical investigations. The nonparametric Friedman's Test was used to analyze the annual change in antibiotic usage. Wilcoxon test was used for pairwise test for the consumption over five years. All statistical tests were deemed significant when the p-value of < 0.01.

Results and Discussion

The inpatient days observed during the study period with

3630 admissions in 2018 and 7541, 6782, 3513 and 4422 in 2019, 2020, 2021 and 2022, accordingly. In 2018, the total consumption of antibiotics was 227.27 DBD (95% CI 220.23-234.31), decreasing to 81.9 (95% CI 79.4-84.42), 151.8 (95% CI 145.95-157.67), 208.87 (95% CI 202.22-215.52), and 228.9 (95% CI 221.96-235.94), in 2019, 2020, 2021 and 2022, respectively. A significant decrease in consumption was observed in 2019 compared to 2018 (63.9%), 2020 (46%), 2021 (60.7%) and with 2022 (64.2%). and that of 2020 compared to 2018 (33.2%), 2021 (27.3%) and with 2022 (33.7%).

Total antibiotic consumption trend over the year was analysed. The usage of antibiotics has steadily increased. Throughout the five-year period, consumption rates peaked in 2018 and 2022, declined in 2020, and reached their minimum in 2019. The rate of increase was higher in 2021, it was never as high as it was in 2018 or 2022. (Figure 2).

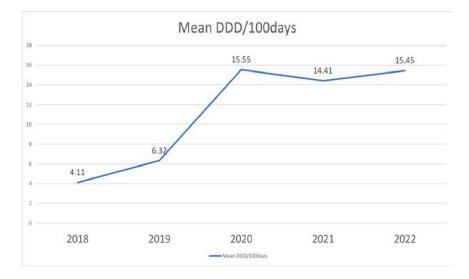


Figure 2. Antibiotic consumption rate from 2018 to 2022 in mean DDD per 100 bed-days.

The difference in the annual antibiotic consumption rates were significant for the five years under study χ^2 (4, N = 28) = 18.537, p<0.001; the mean antibiotic consumption difference between 2018 and 2021, 2022 were significant at p <0.002, the remaining eight comparisons were not statistically significant.

The use of cephalosporins reduced 16.9% from 163.1 DBD in 2021 to 135.44 DBD in 2022 while the

consumption of penicillin increased 68.5% during 2022 to 64.64 DBD from 20.4 DBD in 2021.

Antibiotic consumption trend analysis

In the hospital, both oral and parenteral routes of administration are often used. The usage of parenteral antibiotics increased over time and peaked in 2020, but the consumption of oral antibiotics fell after peaking in 2018 but began to rise from 2021 (Figure 3).

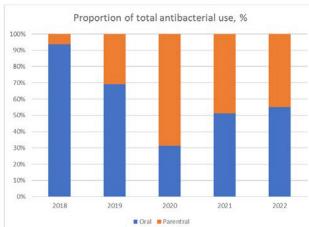
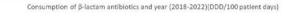


Figure 3. Route of administration of antibiotics consumed from 2018 to 2022-Proportion of antibiotic use in %

Ceftriaxone, amoxicillin clavulanate and metronidazole were the most consumed parenteral antibiotics, while cefuroxime, amoxicillin clavulanate, cefixime, and cefdinir were the top oral antibiotics consumed during the entire study period. Ceftriaxone's consumption percentage showed a steady increase from 2020 to 2022 as it is the mostly used as surgical prophylaxis. Cefuroxime consumption showed constant decrease while the consumption of amoxicillin clavulanate increased and peaked in 2022, due to the step-down therapy to oral. On the other hand, cefixime and cefdinir consumption decreased to its lowest in 2022 (Figure 1).

Beta-lactam are the most consumed antibiotic class like the national level consumption. Amongst which, Ceftriaxone was consistently the most consumed drug from 2020–2022 followed by cefuroxime and amoxicillin clavulanate. The DBD value of ceftriaxone was 53.9 DBD. Cefuroxime was the second highest consumed antibiotic 32.2 DBD. Amoxicillin clavulanate was the third highest consumed antibiotic 21.6 DBD over the five years.

Our study is primarily limited by its retrospective nature. The trends in consumption of cephalosporin may be due to the use of ceftriaxone as the major surgical antibiotic prophylaxis. The amoxicillin clavulanate, especially the oral form is the only antibiotic that increased in use during the study period, this is due to the broader coverage and switch from IV to oral therapy and the timely switch from IV to oral therapy to cefuroxime or amoxicillin clavulanate contributing to the high consumption. The use of ceftriaxone in parenteral and amoxicillin clavulanate in oral is similar to that reported by WHO(17). Fluoroquinolone consumption decreased in use during 2019, and then showing a considerable increase year on year from 2020-2022, however did not reach the maximum as 2018. Metronidazole use increased considerably due to its use in surgical prophylaxis of gastrointestinal procedures. The use of vancomycin is increased due to the increased number of neurosurgical procedures. (Figure 4 and Figure 5).



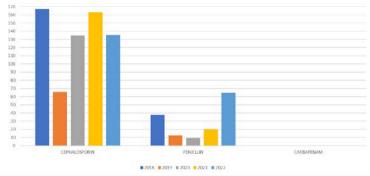


Figure 4. Consumption of β -lactam antibiotics and year (2018-2022) (DBD).

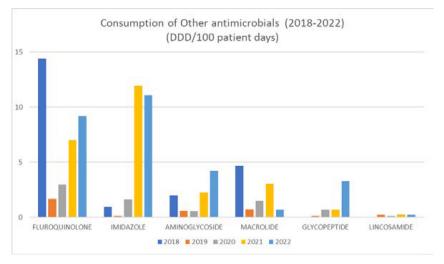


Figure 5. Other antibiotic consumption by year (2018-2022) (DBD).

As per the WHO 2019 AWaRe classification, we understand the consumption of Access group (34.64%) antibiotic significantly increased than the Watch group

(65.36%) in 2022, as compared to the previous years of this study, none of the Reserve class of antibiotic were used. (Figure 6).

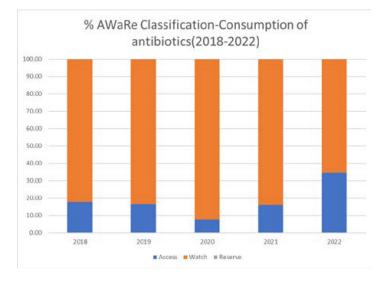


Figure 6. Percentage of AWaRe Classification consumption by year (2018-2022) (DBD).

During the study period, Drug utilisation (DU90%) list was prepared for J01 group. We compared the pattern of J01 consumption in 2018 and 2022 by DU90% methodology. By comparing DU90% at the beginning and end of the study, we found that most of the antibiotic remained unchanged. The limited number of substances of DU90% list during these years indicate the adherence of physicians to the first line treatment guideline and the availability in the country. From the study DU90%, the Access group of antibiotics consumption is (35.63%) and Watch group is (64.5%) in 2022 compared to the previous years the consumption of Access group increased (Table 3). Compared to the DU75% national report in 2021, oral agent (n=4) most used was Amoxicillin clavulanate 38%. Parenteral (n=9) ceftriaxone recorded the highest 21% than any other antibiotic.

Table 3. DU90%=Drug utilization 90% of systemic antibiotic J01					
(2018-2022).					

	(2010 2022):				
Drug	2018	2019	2020	2021	2022
Cefuroxime	38.79	33.43	22.97	25.79	20.52
Cefixime	20.64	0.00	0.00	6.51	3.47
Amoxicillin clavulanate	16.59	15.17	5.95	9.00	27.65
Cefdinir	8.14	27.46	9.65	5.45	0.00
Ceftriaxone	6.06	15.03	52.74	40.20	34.72
Metronidazole	0.00	0.00	0.00	5.71	4.85

A 5-Year Retrospective Analysis of Antibiotic Utilisation Pattern

Monitoring consumption of the antibiotic is measured as an important part of our local program as it allows us to analyse the pattern and trends of consumption. Primarily, this measure does not identify deficiencies in the quality of prescriptions, but it provides information to conduct additional studies on this issue. Although evaluating the outcomes of the antimicrobial stewardship program was not the primary goal, during the study period none of the patients had healthcare associated C. difficile infection, or methicillin-resistant Staphylococcus Aureus infections (MRSA).

There is an alarming level of antimicrobial resistance to carbapenems according to a national surveillance of MDR in Qatar, however its use is limited in our facility (21).

As a single centre experience, our data may be used to analyse facility-level consumption and trends but cannot be compared to data from other facilities. The disparities in patient demographics, processes, and other elements that determine the complexity of the institutions were crucial in analysing antimicrobial usage. In addition, we have no statistics or information at the patient level consumption on the clinical use. This will limit the ability to identify targeted improvement methods. Nonetheless, ongoing monitoring of antibiotic prophylaxis in surgical procedures and focused audits have helped to mitigate this constraint.

Third generation cephalosporins are frequently consumed in hospitals (22-23) and are under Watch group of the AWaRe class used more due to lack of clinical practice guideline and the availability of the medications. The use of oral amoxicillin clavulanate as step-down therapy for intra-abdominal infections is a well-established practice both at our institution and elsewhere (24). It is the first choice of antibiotic for CAP, skin and softtissue infections, lower urinary tract infections, hospitalacquired pneumonia, and COPD. It is the second-choice antibiotic for bone and joint infections, otitis media, and surgical prophylaxis (25). Few fluctuations in antibiotic consumption seen over the five-year period could be due to the availability of the medicines in the country and may not accurately represent how the drugs would have been used if their supply had remained constant. The abuse of readily available broad-spectrum antibiotics may be traced back to a lack of consistency in medication supply, which is one reason why medicine consumption studies aim to show how medicine availability greatly affects medicine consumption.

Although Antimicrobial Stewardship Plans (ASPs) were implemented in all governmental hospitals in Qatar, national efforts and more resources are needed to further develop and improve these programs (26-27). This study's findings may be utilized to improve ASP and can motivate hospitals across the nation to assess their antibiotic consumption rates. Antimicrobial intake monitoring and reporting are essential components of ASP. As part of the multidisciplinary team, clinical pharmacists are crucial leaders of antimicrobial stewardship initiatives due to their knowledge of medication administration and ability to influence antibiotic overuse in hospital settings (28).

This study estimated antibiotic consumption rates based on the amount of antibiotics distributed to medical wards, which may not necessarily match the amount "consumed" by patients. Despite this intrinsic restriction of the study, we believe the proposed technique would be more than competent to provide an indication of the antibiotic consumption rate using a standard measure. Future research should concentrate on appropriate antibiotic use from all wards and utilize days-of-therapy to determine antibiotic usage.

Conclusion

This report provides a baseline consumption and pattern of antibiotic use in the facility. Also, link the antimicrobial exposure to the development of AMR. The consumption of national level antibiotics is in the Aware class (70%), this report can be used as a tool to enhance the access group use at the facility level to reach the WHO target 60%. Potential antimicrobial stewardship effects may be evaluated in the future. Focus on identifying the appropriateness of antibiotic prescribing, particularly for penicillin prescribing in adult and children, and on both reducing unwarranted antibiotic use and improving antibiotic selection when therapy is indicated.

Conflict of interest

The authors reported no conflict of interest, and no funding was received on the work.

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