Antimicrobial Consumption and Resistance of Restricted Antibiotics in a Level III Government Hospital

Abstract

Objectives. The Philippine General Hospital is known for providing antimicrobial stewardship (AMS) training to other private and government hospitals. However, there was an absence of monitoring antibiotic consumption data despite the implementation of the AMS program in the institution. The objectives of the study were to determine the antibiotic consumption of restricted antibiotics and to correlate this with resistance rate.

Methods. A retrospective review of pharmacy dispensing records was conducted in the adult internal medicine wards of a tertiary level teaching hospital in the Philippines between March 2019 to February 2020. Antibiotic consumption was determined using Defined Daily Dose (DDD) per 1000 patient-days (PD). Correlations between antibiotic consumption and antibiotic resistance of restricted antibiotics were done. Outcomes were compared between Ward 1 (with the presence of a unit-dose pharmacist) and Ward 3 (without a unit-dose pharmacist).

Results. Both wards showed decreasing trends of piperacillin-tazobactam consumption and increasing trends of ceftazidime consumption from quarter 1 to quarter 4. It was observed that levofloxacin was the most prescribed fluoroquinolone with the highest consumption recorded from March to May 2019 in Ward 3 of 350.2 DDD/1000 PD as compared with ciprofloxacin which has the highest consumption (23.3 DDD/1000 PD) during the period June to August 2019 in Ward 1. Antibiotic resistance of *A. baumannii* against ciprofloxacin, levofloxacin and piperacillin-tazobactam were statistically significantly different between the wards. In Ward 1, ciprofloxacin consumption was strongly positively correlated with *Escherichia coli* (r = 0.90). In Ward 3, a significantly moderately positive association was observed for ceftazidime consumption and *A. baumannii* resistance (r = 0.61), positive correlation in Ward 3 between piperacillin-tazobactam and *E. coli* resistance (r = 0.65) and a strong positive correlation in Ward 3 between levofloxacin and *P. aeruginosa* resistance (r = 0.71).

Conclusion. The decreasing trends in consumption of restricted antibiotics in both wards reflect that the AMS program of the hospital is serving its purpose in eliminating unnecessary use of restricted antibiotics. The success of the AMS program has been based on the collective efforts of the AMS team with the implementation of hospital policies, such as the AMS program, across the different sites in the hospital in order to achieve optimum patient health outcomes. For both wards, there was no significant difference in terms of resistance rates of the top 10 most commonly isolated bacteria. However, it was noted that the resistance rates of *A. baumannii* against ciprofloxacin, levofloxacin, and piperacillin-tazobactam were higher in Ward 3 compared to Ward 1 which makes infections very difficult to treat which may result to prolonged hospital stay, increased health-care costs and increased mortality rate. Pharmacists can contribute in the prevention of antibiotic resistance through reviewing antibiotic use of patients, monitoring trends of antibiotic use and ensuring compliance to the prescribed antibiotic regimen.

Keywords: Antibiotic consumption, antibiotic resistance, restricted antibiotics

INTRODUCTION

The rapid emergence of resistant bacterial infections is occurring worldwide, endangering the efficacy of antibiotics.[1] Antibiotic resistance happens when bacteria evolve and resist the effects of antibiotics which lead to higher medical costs, prolonged hospital stays, and increased mortality.[2] The emerging problem of antibiotic resistance not only interfere with the ability of antibiotics to treat infections but may also result to a broader societal and economic effects and may result to failure of achieving the Sustainable Development Goals.[3,4]

The acceleration of antimicrobial resistance (AMR) is caused by the misuse and overuse of antibiotics.[2] The WHO developed a Global Action Plan on AMR, including antibiotic resistance.[5,6] The WHO provided strategic and technical guidance on interventions to contain resistance which are directed towards providers and patients. One of the recommendations for intervention to prescribers and dispensers is to review both prescribing and dispensing practices to provide feedback on appropriate antibiotic prescribing. Researchers have recommended interventions to the hospital which includes monitoring antibiotics usage, quantity prescribed, and patterns of use and inform prescribers about the results. It was also part of their recommendations to designate an effective Pharmacy and Therapeutics Committee to oversee antibiotic use in hospitals.[7] According to the published manual entitled “Fighting Antimicrobial Resistance: The Contribution of Pharmacists”, pharmacists can play an active role in surveillance of antimicrobial consumption and resistance which are essential in determining the magnitude of AMR, help in establishing trends, and to further improve strategies to lessen the burden of antimicrobial resistance.[8]

Antimicrobial consumption data are collected using the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Dose (DDD) methodology developed by the WHO Collaborating Centre for Drug Statistics Methodology.[9] This study determined and compared the antimicrobial consumption of drugs for systemic use (ATC group J01) specifically restricted antibiotics of a Level III government hospital using the DDD per 1000 patient days between Ward 1 (with unit-dose pharmacist) and Ward 3 (without unit-dose pharmacist). The study also correlated antibiotic consumption of restricted antibiotics and antibiotic resistance rate of the top ten resistant microorganisms found in the Department of Medicine specifically Ward 1 and Ward 3.

Philippine General Hospital (PGH) is a Level III government hospital administered and operated by the University of the Philippines Manila. It is the largest government hospital within Metro Manila with its 1,100 beds and 400 private beds. Since May 2016, the PGH Antimicrobial Stewardship (AMS) Program has been implemented within the hospital and has been organizing and providing training on AMS to other hospitals. The program is designed to enable antimicrobial prescriber (PGH physicians) as well as antimicrobial dispensers (PGH pharmacists) and practicing nurses, to use antimicrobial agents in the most rational, effective, efficient manner and eventually help curb antimicrobial resistance.

The WHO carried out a comprehensive review of antibiotics and classified AWaRe antibiotics into Access, Watch, and Reserve groups. The main goal is to reduce the use of Watch Group and Reserve Group antibiotics which are the most crucial antibiotics for human medicine and at higher risk of resistance and increase the use of Access Group.[10] In PGH, the available restricted antibiotics under the watch group includes cefepime, ceftazidime, ciprofloxacin, ertapenem, levofloxacin, meropenem, piperacillin - tazobactam, and vancomycin. The restricted antibiotics that are under the reserve group includes colistin (polymyxin E) and polymyxin B. These antibiotics require PGH restricted antibiotic request form (also known as PGH Form No. P-370066) which should be completely accomplished by the physician and will be subjected for approval of Infectious Disease Section (IDS) fellow/consultant.

METHODS

A retrospective cross-sectional design was conducted between two wards under the Department of Medicine from March 2019 to February 2020. Both wards have a 50-bed capacity in Philippine General Hospital, a level III government hospital. Ward 1 has a modified unit-dose drug distribution system (MUDDDS) with the participation of a unit-dose pharmacist. On the other hand, Ward 3 has an individual medication order system without a unit-dose pharmacist.

Participants and other data sources

The study included pharmacy dispensing records of charity in-patients who were admitted and transferred to the Department of Medicine specifically Ward 1 and Ward 3 from March 1, 2019, to February 29, 2020. Patients who were prescribed and dispensed with at least one dose of intravenous restricted antibiotics regardless of age, sex and co-morbidities were included in the study.

Instrumentation

The CVR (content validity ratio) or also known as Lawshe's method was used to quantify content validity of the antibiotic consumption form. Five infectious disease pharmacists, who have undergone training on infectious diseases at University of the Philippines, Manila, have been asked to evaluate the validity of the items in the data collection form using the evaluation sheet by indicating whether it is essential (item to be included in the form) or non-essential (item to be removed from the data collection form).

$$CVR = \frac{ne - \left(\frac{N}{2}\right)}{\frac{N}{2}}$$

The result was computed using the above formula. CVR stands for content validity ratio, *ne* pertains to the number of panel members indicating "essential," and *N* is the total number of panel members. The final evaluation to retain the item based on the CVR depends on the number of panels. In this study, for an item to be included, the CVR value per item should be 1.[11] Seven items had a CVR of less than 1 which are not included in the final data collection form.

Data collection

The Open ERP system was used to gather necessary data needed in the antibiotic consumption form. Data on antibiotic use were collected quarterly from March 2019 to February 2020 and antibiotic consumption data were expressed as DDD per 1000 patient-days. Data on the total number of units or vials were entered and analyzed using Antimicrobial Consumption Tool version 2019.

Resistance data were gathered from the antibiogram of the Department of Medicine specifically Ward 1 and Ward 3 provided by the Hospital Infection Control Unit of the hospital. Correlations between antibiotic consumption and antibiotic resistance in each ward were determined for those with at least six (6) observation months or complete information on resistance rates from March 2019 to February 2020.

Data processing and analysis

Trend analysis of quarterly consumption of restricted antibiotics was used to analyze pattern of use of antibiotic consumption of restricted antibiotics. Data on antibiotic consumption was converted to DDD per 1000 patient-days using the Antimicrobial Consumption Tool version 1.9. Independent t-test was used in the comparison of antibiotic consumption and comparison of resistance rates between Ward 1 and Ward 3. Pearson Correlation Coefficient was used to measure the strength of a correlation between antibiotic consumption and antibiotic resistance rates.

RESULTS

There were decreasing trends of piperacillin-tazobactam consumption on both wards (Figure 1A). Vancomycin consumption in Ward 1 showed a decreasing trend from March to February 2020 (Figure 1B). For cefepime, consumption spiked for both wards during December 2019 to February 2020 (Figure 1C). Ceftazidime consumption in both wards were observed to continuously increase from quarter 1 to quarter 4, with consumption slightly higher in Ward 3 compared to Ward 1 across all quarters (Figure 1D).

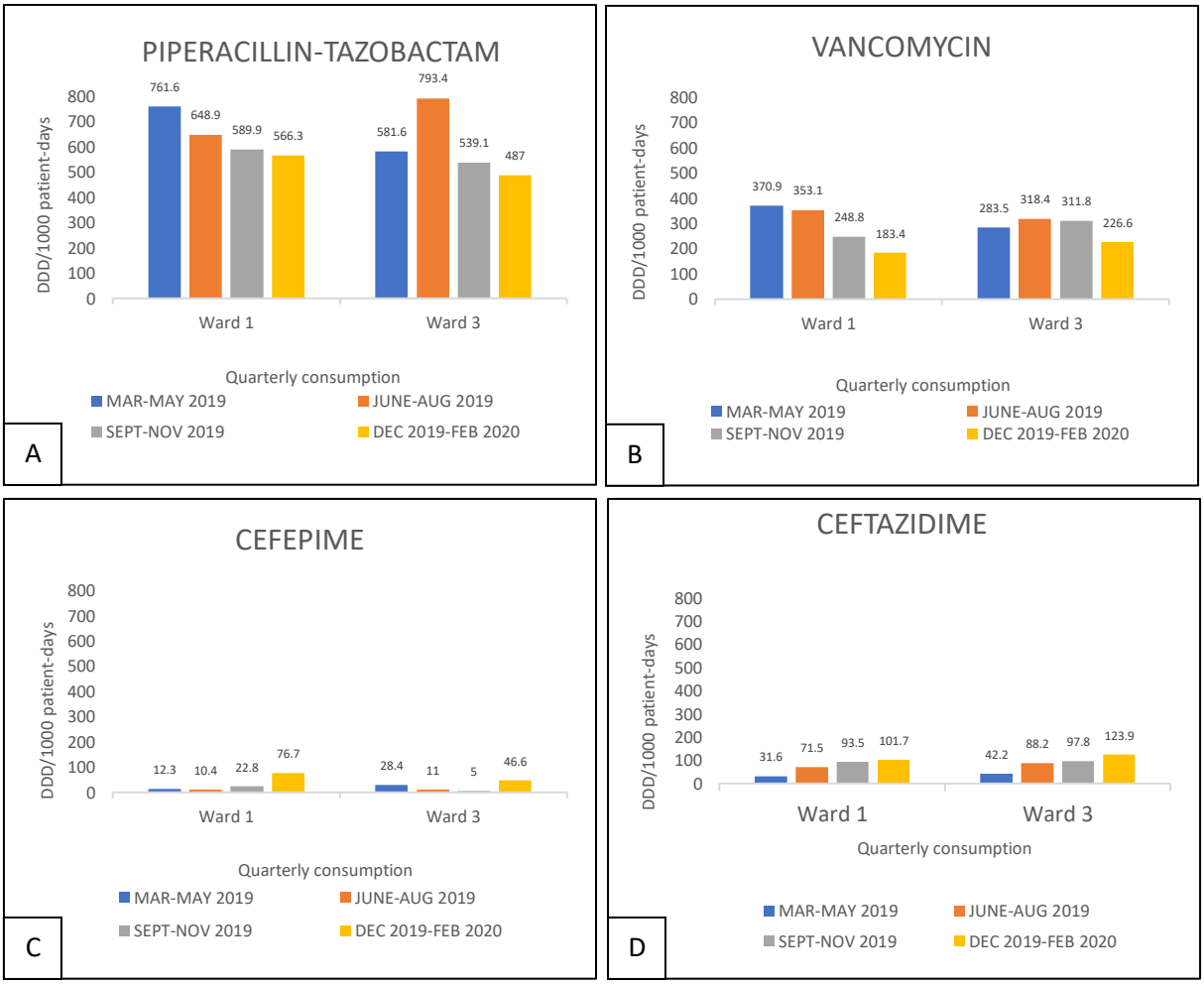

Figure 1. Quarterly consumption (DDD/1000 patient-days) of restricted antibiotics under watch group between Ward 1 and Ward 3 from March 2019 to February 2020. (A) Piperacillin-tazobactam, (B) Vancomycin, (C) Cefepime, (D) Ceftazidime.

There was a sudden increase in ciprofloxacin consumption in Ward 1 during June to August 2019 but was of relatively same levels in the remaining quarters of the observation period, while consumption in Ward 3 dropped in the second and fourth quarters (Figure 2A). In this study, it was observed that levofloxacin was more prescribed with the highest consumption recorded during the March to May 2019 in Ward 3 of 350.2 DDD/1000 PD as compared with ciprofloxacin which has the highest consumption during June to August 2019 in Ward 1 of 23.3 DDD/1000 PD (Figure 2B).

For ertapenem, consumption increased from March to November 2019 in both wards but shrank in December 2019 to February 2020 (Figure 2C). Ertapenem consumption was higher in Ward 1 in quarters 1, 2, and 4 than in Ward 3. High levels of consumption were recorded in Ward 1 and 3 for meropenem from March to November 2019 but declined in the fourth quarter of observation period (Figure 2D).

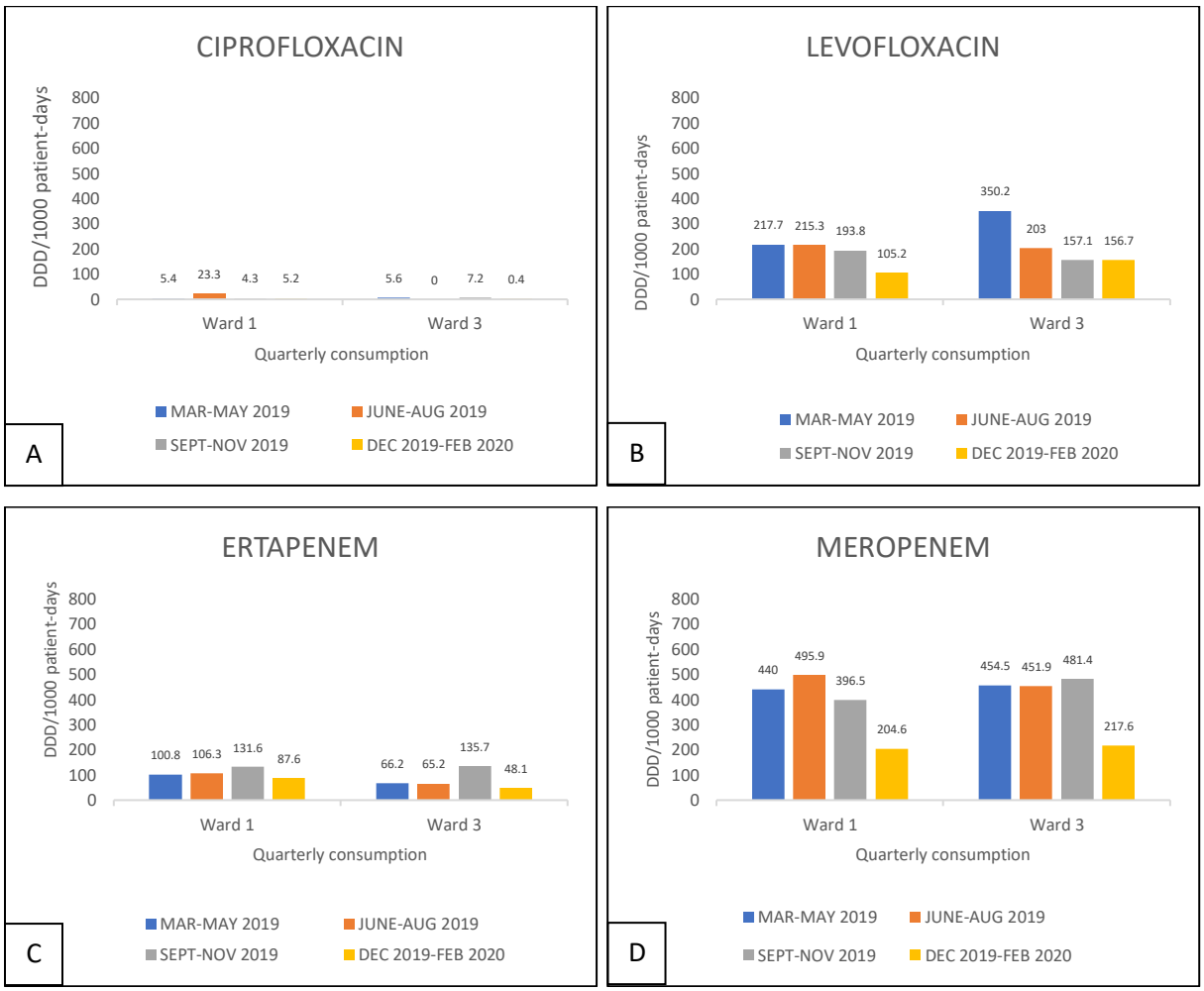

Figure 2. Quarterly consumption (DDD/1000 patient-days) of restricted antibiotics under watch group between Ward 1 and Ward 3 from March 2019 to February 2020. (A) Ciprofloxacin, (B) Levofloxacin, (C) Ertapenem, (D) Meropenem.

Colistin (also known as polymyxin E) consumption was observed to decrease from quarter 1 through 4 in both wards, with greater consumption levels in Ward 1 compared to Ward 3 except in September to November 2019 (Figure 3A). Polymyxin B has an increasing trend of consumption from first quarter to third quarter of the study, however, consumption declined on the fourth quarter of the study (Figure 3B).

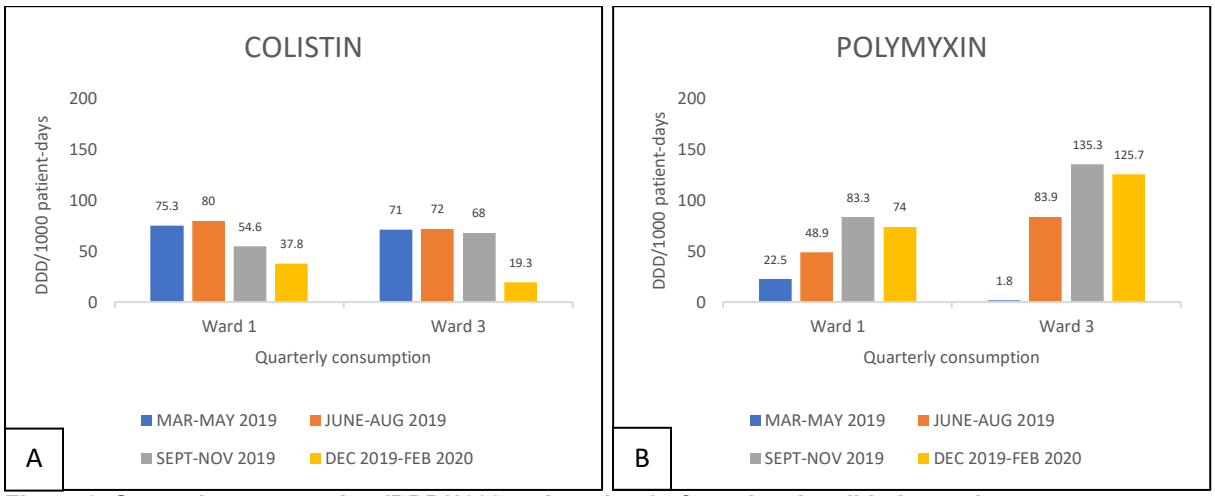

Figure 3. Quarterly consumption (DDD/1000 patient-days) of restricted antibiotics under reserve group between Ward 1 and Ward 3 from March 2019 to February 2020. (A) Colistin, (B) Polymyxin.

Antibiotic resistance of *K. pneumoniae* was highest against ceftazidime, with mean resistance of 67.2% in Ward 1 and 66.4% in Ward 3 (Table 1). However, antibiotic resistance was not statistically significantly different between the two wards.

Table 1. Antibiotic resistance of *K. pneumoniae* against selected restricted antibiotics in Ward 1 and Ward 3 from March 2019 to February 2020.

Restricted antibiotics	**Antibiotic resistance (%)⁺** *Klebsiella pneumoniae*		**p-value***
	Ward 1	Ward 3	
Cefepime	65.8 (60.4, 71.3)	65.8 (56.8, 74.8)	0.9909
Ceftazidime	67.2 (62.9, 71.5)	66.4 (56.6, 76.3)	0.8741
Ciprofloxacin	42.6 (32.9, 52.3)	47.4 (37.2, 57.6)	0.4594
Levofloxacin	41.3 (28.8, 53.9)	45.5 (33.8, 57.1)	0.5943
Meropenem	38 (26.7, 49.4)	42.1 (29.4, 54.7)	0.6045
Piperacillin-tazobactam	50.4 (39.3, 61.5)	55.9 (47.0, 65.0)	0.3980

⁺95% CI are in parentheses
*Significant at p-value <0.05

Average antibiotic resistance of *A. baumannii* was generally higher in Ward 3 than in Ward 1 across all restricted antibiotics (Table 2). *Acinetobacter baumannii* resistance to ciprofloxacin, levofloxacin, and piperacillin-tazobactam were statistically significantly different between two wards with Ward 3 having higher resistance compared to Ward 1.

Table 2. Antibiotic resistance of *A. baumannii* against selected restricted antibiotics in Ward 1 and Ward 3 from March 2019 to February 2020.

Restricted antibiotics	Antibiotic resistance (%)[+] *Acinetobacter baumannii*		p-value*
	Ward 1	Ward 3	
Cefepime	76.2 (62.2, 90.2)	90 (86.1, 93.9)	0.0572
Ceftazidime	71.1 (59.9, 82.3)	77 (67.8, 86.3)	0.3768
Ciprofloxacin*	69.6 (56.0, 83.3)	87.5 (82.3, 92.8)	0.0173
Levofloxacin*	66.2 (53.8, 78.6)	83.6 (76.0, 91.2)	0.0165
Meropenem	76.5 (63.2, 89.9)	88.6 (83.6, 93.6)	0.0820
Piperacillin-tazobactam*	78.1 (66.4, 89.8)	91.5 (87.3, 95.8)	0.0328

[+]95% CI are in parentheses
*Significant at p-value <0.05

Ciprofloxacin consumption in Ward 1 was significantly strongly positively correlated with *E. coli* resistance (Table 3). Meropenem consumption was weakly negatively associated with *E. coli* resistance.

Table 3. Pearson's correlation coefficient of antibiotic consumption (DDD) and antibiotic resistance (%RR) of *E. coli* in Ward 1 from March 2019 to February 2020.

Restricted Antibiotics	Mar 2019		Apr 2019		May 2019		June 2019		July 2019		Aug 2019		Sept 2019		Oct 2019		Nov 2019		Dec 2019		Jan 2020		Feb 2020		Pearson's correlation (95% CI)	p-value*
	DDDs	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR		
Cefepime-	4.70	55.6	5.02	33.3	2.62	25	1.40	41.7	7.92	80	1.06	66.7	0.35	50	22.42	33.3		50	11.83	31.78	31.78	40	33.12	50	-0.16 (-0.72, 0.52)	0.6684
Ceftazidime-	16.95	55.6	14.70	33.3		25	9.60	41.7	46.69	80	15.25	100	33.51	62.5	41.10	33.3	18.85	62.5	9.57	65.38	65.33	40	26.83	50	-0.13 (-0.70, 0.54)	0.7146
Ciprofloxacin *++++		44.4	5.38	50		62.5	9.07	83.3	10.28	80	3.90	66.7		62.5	0.68	33.3	3.61	50	5.22			40			0.90 (0.34, 0.99)	0.0128
Levofloxacin +	104.03	55.6	75.27	60	38.44	62.5	41.17	75	103.17	60	70.92	66.7	95.74	62.5	67.93	33.3	30.16	50	43.15	17.66	17.66	40	44.41		0.21 (-0.49, 0.74)	0.5697
Meropenem--	139.04	22.2	138.11	16.7	162.83	25	226.80	25	130.59	20	138.53	66.7	141.13		153.53		101.85	25	58.22	118.53	118.53	20	27.88	50	-0.33 (-0.81, 0.43)	0.39
Piperacillin-tazobactam+	161.04	22.2	288.82	16.7	311.78	37.5	235.86	41.7	175.12	20	237.87	66.7	229.10	37.5	209.73		151.01	37.5	197.06	183.20	183.20	40	186.06	50	0.04 (-0.60, 0.65)	0.9077

*Significant at p-value <0.05
+ negligible positive; ++ weakly positive; +++ moderately positive; ++++ strongly positive
- negligible negative; - - weakly negative; - - - moderately negative; - - - - strongly negative

In ward 1 (Table 4), a negative correlation was observed for cefepime and *A. baumannii* resistance which indicates no linear relationship that, as consumption decreases, the resistance rate increases and vice versa. Moreover, contrary from what was observed in ward 3 (Table 5), a significantly moderately positive association was observed for ceftazidime consumption and *A. baumannii* resistance.

Table 4. Pearson's correlation coefficient of antibiotic consumption (DDD) and antibiotic resistance (%RR) of *A. baumannii* in Ward 1 from March 2019 to February 2020.

Restricted Antibiotics	Mar 2019		Apr 2019		May 2019		June 2019		July 2019		Aug 2019		Sept 2019		Oct 2019		Nov 2019		Dec 2019		Jan 2020		Feb 2020		Pearson's correlation (95% CI)	p-value*
	DDDs	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR		
Cefepime -	4.70	71.4	5.02	97.7	2.62	33.3	1.40	100	7.92	100	1.06	81.8	0.35	81.8	22.42	83.3		50	11.83		31.78	72.2	33.12	66.7	-0.16 (-0.72, 0.52)	0.6627
Ceftazidime +	16.95	71.4	14.70	73.7		33.3	9.60	93.3	46.69	81.8	15.25	75	33.51	81.8	41.10	83.3	18.85	50	9.57		65.33	72.2	26.83	66.7	0.07 (-0.59, 0.67)	0.8492
Ciprofloxacin +		71.4	5.38	97.7		33.3	9.07	78.6	10.28	81.8	3.90	91.7		72.7	0.68	83.3	3.61	50	5.22			61.1		44.4	0.08 (-0.78, 0.84)	0.8812
Levofloxacin+ ++	104.03	71.4	75.27	89.5	89.5	33.3	41.17	66.7	103.17	81.8	70.92	91.7	95.74	63.6	67.93	75	30.16	50	43.15		17.66	61.1	44.41	44.4	0.58 (-0.02, 0.88)	0.0597
Meropenem +	139.04	71.4	138.11	97.7	97.7	33.3	226.80	100	130.59	90.9	138.53	83.3	141.13	81.8	153.53	83.3	101.85	50	58.22		118.53	72.2	27.88	77.8	0.20 (-0.45, 0.72)	0.5456
Piperacillin-tazobactam +	161.04	71.4	288.82	97.7	97.7	50	235.86	100	175.12	100	237.87	83.3	229.10	81.8	209.73	75	151.01	50	197.06		183.20	72.2	186.06	77.8	0.10 (-0.54, 0.66)	0.7809

* Significant at p-value <0.05
+ negligible positive; ++ weakly positive; +++ moderately positive; ++++ strongly positive
- negligible negative; - - weakly negative; - - - moderately negative; - - - - strongly negative

Table 5. Pearson's correlation coefficient of antibiotic consumption (DDD) and antibiotic resistance (%RR) of *A. baumannii* in Ward 3 from March 2019 to February 2020.

Restricted Antibiotics	Mar 2019		Apr 2019		May 2019		June 2019		July 2019		Aug 2019		Sept 2019		Oct 2019		Nov 2019		Dec 2019		Jan 2020		Feb 2020		Pearson's correlation (95% CI)	p-value*
	DDDs	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR		
Cefepime -	15.61	84.6	7.43	81.2	5.39	86.7	4.83	93.8	2.90	90.9	3.31	91.7	3.08	94.1	1.93	83.3		100	9.26	100	12.67	86.4	24.66	87.5	-0.19 (-0.80, 0.36)	0.57
Ceftazidime +++	28.42	84.6	12.73	68.8	1.01	53.3	26.57	64.7	23.36	66.7	38.27	69.2	34.24	94.1	22.86	83.3	40.67	81.8	30.42	100	32.67	81	60.76		0.61 (0.01, 0.86)	0.05
Levofloxacin -	148.76	84.6	157.00	73.3	44.48	73.3	53.14	81.2	68.32	83.3	81.51		84.92	100	34.13	75	38.03	100	33.73	100	59.34	73.9	63.62	75	-0.19 (-0.71, 0.46)	0.58
Meropenem -	163.50	84.6	173.26	75	117.70	86.7	151.60	94.1	116.44	91.7	183.80	84.6	217.54	100	165.48	83.3	98.36	100	87.86		58.22	87	71.48	87.5	-0.06 (-0.64, 0.56)	0.87
Piperacillin-tazobactam +	172.32	84.6	179.23		230.03	86.7	346.72	93.8	222.70	91.7	223.99	92.3	211.75	100	190.40	83.3	136.94	100	207.90	100	120.22	87	158.88	87.5	0.17 (-0.48, 0.70)	0.62

***** Significant at p-value <0.05
+ negligible positive; ++ weakly positive; +++ moderately positive; ++++ strongly positive
- negligible negative; - - weakly negative; - - - moderately negative; - - - - strongly negative

Ward 3 correlation between cefepime consumption and *P. aeruginosa* resistance was weakly negative (Table 6). Levofloxacin consumption was significantly moderately positively associated with *P. aeruginosa* resistance.

Table 6. Pearson's correlation coefficient of antibiotic consumption (DDD) and antibiotic resistance (%RR) of *P. aeruginosa* in Ward 3 from March 2019 to February 2020.

Restricted Antibiotics	Mar 2019		Apr 2019		May 2019		June 2019		July 2019		Aug 2019		Sept 2019		Oct 2019		Nov 2019		Dec 2019		Jan 2020		Feb 2020		Pearson's correlation (95% CI)	p-value*
	DDDs	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR		
Cefepime - -	15.61	17	7.43	50	5.39	17	4.83		2.90	25	3.31	50	3.08	43	1.93	17		100	9.26		12.67		24.66	11	-0.48 (-0.89, 0.34)	0.225
Ceftazidime +	28.42	33	12.73	50	1.01	17	26.57	33	23.36		38.27	63	34.24	57	22.86	17	40.67	100	30.42		32.67	22	60.76	11	0.17 (-0.52, 0.72)	0.647
Levofloxacin * +++	148.76		157.00	43	44.48	17	53.14	25	68.32		81.51	25	84.92	29	34.13	25	38.03		33.73		59.34	33	63.62	38	0.71 (0.01, 0.94)	0.049
Meropenem +	163.50	33	173.26	63	117.70	17	151.60	60	116.44	46	183.80	38	217.54	57	165.48	58	98.36	33	87.86		58.22	56	71.48	44	0.24 (-0.42, 0.74)	0.474

***** Significant at p-value <0.05
+ negligible positive; ++ weakly positive; +++ moderately positive; ++++ strongly positive
- negligible negative; - - weakly negative; - - - moderately negative; - - - - strongly negative

In Ward 3, there is moderately positive correlation between piperacillin-tazobactam consumption and *E. coli* resistance which is statistically significant (Table 7).

Table 7. Pearson's correlation coefficient of antibiotic consumption (DDD) and antibiotic resistance (%RR) of *E. coli* in Ward 3 from March 2019 to February 2020.

Restricted Antibiotics	Mar 2019		Apr 2019		May 2019		June 2019		July 2019		Aug 2019		Sept 2019		Oct 2019		Nov 2019		Dec 2019		Jan 2020		Feb 2020		Pearson's correlation (95% CI)	p-value
	DDDs	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR	DDS	%RR		
Cefepime - - -	15.61	25	7.43	33.3	5.39	83.3	4.83	40	2.90	37.5	3.31	40	3.08	75	1.93	75		33.3	9.26		12.67	44.4	24.66	33.3	-0.51 (-0.86, 0.18)	0.132
Ceftazidime - - -	28.42	25	12.73	50	1.01	83.3	26.57	40	23.36	50	38.27	40	34.24	75	22.86	75	40.67		30.42		32.67	44.4	60.76	37.5	-0.51 (-0.86, 0.17)	0.129
Levofloxacin - - -	148.76		157.00	50	44.48	100	53.14	80	68.32	75	81.51		84.92	50	34.13	100	38.03	100	33.73		59.34	44.4	63.62	55.6	-0.65 (-0.92, 0.02)	0.057
Meropenem + +	163.50		173.26	33.3	117.70	66.7	151.60	40	116.44	12.5	183.80	40	217.54	50	165.48	75	98.36	33.3	87.86		58.22	25	71.48		0.38 (-0.36, 0.84)	0.306
Piperacillin-tazobactam * +++	172.32		179.23	33.3	230.03	83.3	346.72	75	222.70	50	223.99	40	211.75	50	190.40	75	136.94	33.3	207.90		120.22	33.3	158.88	11.1	0.65 (0.04, 0.91)	0.042

***** Significant at p-value < 0.05
+ negligible positive; ++ weakly positive; +++ moderately positive; ++++ strongly positive
- negligible negative; - - weakly negative; - - - moderately negative; - - - - strongly negative

DISCUSSION

The decreasing trends of piperacillin-tazobactam showed a decreased use of piperacillin-tazobactam among patients. Based on the antibiogram result, gram-negative bacteria were frequently isolated from patient's samples. Decreasing trend of vancomycin consumption may be associated with its inactivity against gram-negative bacteria, hence, the decreased in usage. The increase in the antibiotic consumption of ceftazidime must be monitored as it has the highest resistance recorded against *Klebsiella pneumoniae* in this study. In the study of Rice et al.,[12] the highest rates of resistance occurred in wards where ceftazidime was administered most frequently.

Although levofloxacin was the preferred fluoroquinolone compared with ciprofloxacin, its consumption fell in both wards from quarter 1 through quarter 4 due to decreased use in the wards which could mean that patient cases did not require its use. Levofloxacin and ciprofloxacin are both recommended for clinical application in UTIs and, though commonly prescribed, there's no conclusion on the comparative merit of the either one. Levofloxacin shows advantage over ciprofloxacin in terms of efficacy, disease reoccurrence and adverse event.[13] On the contrary, microbiology evidence shows that the uropathogen is more sensitive to ciprofloxacin. [14,15]

Ertapenem consumption was three times lower as compared with meropenem consumption because the spectrum of activity of ertapenem is more limited primarily because it lacks activity against *Pseudomonas aeruginosa* and *Acinetobacter spp*.[16] It was observed that meropenem was most consumed carbapenem antibiotic as compared with ertapenem. High consumption may be attributed to its activity against Gram-positive bacteria and Gram-negative bacteria, including extended-spectrum beta-lactamase-producing Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter spp*. [17]

Colistin consumption decreases as polymyxin consumption increases. Internal Medicine residents have opted to use polymyxin as polypeptide antibiotic than colistin. Polymyxin B is administered parenterally in its active form, while colistin is administered parenterally as an inactive pro-drug, colistimethate.[18] In addition, published clinical studies suggest that polymyxin B is less nephrotoxic than colistin. For these reasons, polymyxin B has become the predominant polymyxin used in many health centers and hospital.[19]

In the study of Yadav et al, [20] it was found that 99.4% of *A. baumannii* were resistant to ceftazidime and cefepime, 95% to piperacillin-tazobactam and ciprofloxacin, 89.4% resistant to meropenem. This is in contrast with the present study findings where in the recorded resistance rate to ceftazidime (71.1% in Ward 1 and 77% in Ward 3) and piperacillin-tazobactam (78.1% in Ward 1 and 91.5% in Ward 3) were lower. The result of the present study is similar with the study of Lai et al., [21] wherein the consumption of fluoroquinolones was positively correlated with the resistance rate of *P. aeruginosa*. This means that as the consumption of fluoroquinolones increases, the resistance to *P. aeruginosa* also increases. In the same study of Lai et al., [21] the use of piperacillin-tazobactam was positively correlated with the prevalence piperacillin-tazobactam-resistant *E. coli*. This is similar with the present study findings which shows that as piperacillin-tazobactam consumption increases, *E. coli* resistance also increases. The result of the present study is similar with the study of Lai et al., [21] wherein there was a positive correlation between increase of fluoroquinolones and emergence of ciprofloxacin-resistant *E. coli* based on 2007 to 2016 data. This means that ciprofloxacin consumption tends to be associated with *E. coli* resistance over the years.

CONCLUSION

Both wards showed decreasing trends in consumption of watch antibiotics except for ceftazidime which could mean that the antimicrobial stewardship program of the hospital is serving its purpose in eliminating unnecessary use of restricted antibiotics. The success of the AMS program has been based on the collective efforts of the AMS team with the implementation of hospital policies, such as the AMS program, across the different sites in the hospital in order to achieve optimum patient health outcomes.

There was no significant difference in terms of resistance rates of the top 10 most commonly isolated bacteria. However, it was noted that the resistance rates of *A. baumannii* against ciprofloxacin, levofloxacin, and piperacillin-tazobactam were higher in Ward 3 compared to Ward 1 which makes infections very difficult to treat which may result to prolonged hospital stay, increased health-care costs and increased mortality rate. There were significant positive correlations found between antibiotic consumption and antibiotic resistance which is why monitoring antibiotic consumption is important in controlling antibiotic resistance. Therefore, each hospital should monitor antibiotic consumption and further explore its relationship with resistance rate of each bacterium. Pharmacists can contribute in the prevention of antibiotic resistance through reviewing antibiotic use of patients, monitoring trends of antibiotic use and ensuring compliance to the prescribed antibiotic regimen.

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