Drug Utilization Review of Monitored Parenteral Antimicrobials in a Tertiary Care Private Hospital in Cebu City

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ABSTRACT

Background. Based on the 2017-2020 annual report of the Department of Health-Antimicrobial Resistance Surveillance Program, significant resistance patterns have been observed for common disease-causing pathogens. In the hospital setting, antimicrobial stewardship programs have been implemented to optimize the use of antimicrobials. Drug utilization review studies provide essential feedback to improve prescribing and use of medications.

Objectives. This study aimed to review drug utilization of monitored parenteral antimicrobials among patients admitted from January to December 2019.

Methods. The study employed a retrospective, cross-sectional, descriptive research design. A retrospective chart review of drugs administered to patients was conducted.

Results. A total of 821 patients charts met the inclusion criteria. The patients' ages ranged from 18 to 98 years old and 52% were females. General Internal Medicine practitioners (28%) were the top prescribers of monitored parenteral antimicrobials primarily for the management of moderate-risk community-acquired pneumonia (39%). They were mostly indicated for empirical treatment of infections (94%) and were given for an average of 5.73 days.

Only 58% of the total cases had orders for culture and sensitivity testing. Of which, principally 47% had colony cultures. Blood (29%) and sputum (27%) were the most common specimens taken for culture and sensitivity testing. The microorganisms often isolated were *Escherichia coli* (19%), *Klebsiella pneumoniae* (18%), and *Staphylococcus aureus* (9%). In addition, extended-spectrum beta lactamase-producing gram-negative pathogens (4%) and methicillin-resistant *S. aureus* (1%) were also isolated. All the microorganisms isolated showed most resistance to ampicillin (81%) and most susceptibility to colistin (100%).

There were drug therapy-related problems encountered. There was one case of an adverse drug reaction (0.1%) and two cases of contraindications (0.2%). Therapeutic duplication was also observed in 5% of the cases. Moreover, 39% had instances of drug-drug interactions.

Piperacillin-tazobactam had the highest consumption (79.50 defined daily doses/1,000-patient days) among the monitored parenteral antimicrobials.

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Some prescriptions were deemed inappropriate upon evaluation. 12% of cases were inappropriate based on the justification indicator. As for the critical indicators, duration of therapy (78%) was the main reason. Only four components of the DUE criteria indicators have met or exceeded the established threshold level.

The cost analysis indicated that the total actual cost of therapy with the monitored parenteral antimicrobials amounted to ₱17,645,601.73. Considering Department of Health National Antibiotic Guidelines recommendations, ideal total cost of treatment was ₱14,917,214.29. Potential cumulative cost savings of ₱2,728,387.44 could have been achieved for patients admitted last 2019.

Conclusion. Consumption of piperacillin-tazobactam was relatively high as compared to the other monitored parenteral antimicrobials covered in this study. Physicians at the study site seldom prescribe monitored parenteral antimicrobials as recommended by the National Antibiotic Guidelines. This is evidenced in the incidence of inappropriate therapy regimens, with inapt duration of therapy as the leading explanation.

From the patient's perspective, the main economic implication was on the direct medical costs, particularly the increased cost of the actual antimicrobial therapy prescribed to manage various infections. Adherence of physicians to the established guidelines and selection of the most cost-effective therapy could have resulted in considerable cost savings.

Keywords: drug utilization review, monitored antimicrobials, antimicrobial consumption, antimicrobial resistance, antimicrobial stewardship

INTRODUCTION

Infectious diseases are a public health concern. They are a heavy burden especially for developing countries.[1] In the Philippines, they remain as principal determinants of morbidity and mortality. Pneumonia and tuberculosis are among the top ten leading causes of mortality among Filipino adults.[2] A national survey of secondary and tertiary medical centers from different provinces in the country discovered that infectious diseases are a crucial reason for hospitalization. Some of the prevalent infections include pulmonary tuberculosis (PTB), diarrhea, pneumonia, urinary tract infection (UTI), and upper respiratory tract infection (URTI).[3]

Antimicrobial agents have revolutionized medical treatment since their discovery. Currently, medical practitioners rely heavily on these agents to combat various infectious diseases. Due to this, they are prone to misuse and overuse, which promotes the development of AMR.[4] Irrational use of medicines, especially antimicrobials, is a serious problem in the country. Both developed and developing countries share the same problem. Nevertheless, it is more critical in the latter with limited financial resources.[5]

Indiscriminate physician prescribing and patient consumption of antimicrobials are major drivers of antimicrobial resistance (AMR).[4] The multifaceted problem of inappropriate utilization of antimicrobials in the country is well documented. Multiple stakeholders are concerned – healthcare providers, consumers, as well as agriculture, aquaculture, and pharmaceutical industries[6]. Healthcare practitioners in low and middle-income countries (LMICs), including the Philippines, have high awareness on AMR.[7] However, this did not contribute to a reduction in antimicrobial dispensing and prescribing. Instead, it provided for an increase in available choices and selection of higher generation antimicrobials.[7]

The proliferation of AMR in the community jeopardizes the effective use of antimicrobials. In addition, the negative impact of AMR is apparent in clinical, economic, and societal aspects.[8] To mitigate its adverse consequences, the national government through the Department of Health (DOH) proposed an antimicrobial stewardship (AMS) program. AMS programs are a means for optimizing the use of antimicrobials. Its implementation in hospitals could lessen nosocomial infections, and eventually, curb AMR. It can help cut down healthcare-related expenditures, and more importantly, save precious lives.

The DOH AMS program has six core elements. The third core element focuses on the surveillance of antimicrobial use and AMR.[9] Drug utilization studies are important especially for antimicrobials as they are widely used in hospitals.[10] A drug utilization review (DUR) on antimicrobials is essential to describe patterns in prescribing and consumption. It can also be employed to evaluate and monitor AMS programs implemented. Ultimately, it is important to ensure constant provision of cost-effective and standardized medical care to patients.

Monitored parenteral antimicrobials have been observed to be frequently prescribed to patients with moderate to severe infections in the selected study site. Through the DUR, physician prescribing and patient consumption was evaluated. To assist in the provision of cost-effective treatment to patients, appropriateness of prescribing was checked with DOH NAG and a cost analysis was performed. The findings generated from this study served as basis for the creation of new policies and procedures to improve current clinical practices. Moreover, it served as a focal point for future AMS-related programs and activities of the infection control department. Through collective efforts of the hospital's healthcare team, AMR can continuously be mitigated.

This study aimed to review drug utilization of monitored parenteral antimicrobials within the study period (January to December 2019) among patients admitted in a tertiary care

private hospital in Cebu City. Further, the study sought to determine the demographics and medical history of patients prescribed with monitored parenteral antimicrobials; describe the indication and dosage regimen of monitored parenteral antimicrobials as prescribed by the physician; categorize prescribed antimicrobial indication based on results taken from culture and sensitivity tests; examine appropriateness of actual prescriptions based on established criteria from the recommended national treatment guidelines (DOH NAG); describe the trends in the consumption of monitored parenteral antimicrobial agents through the calculated cumulative defined daily doses (DDDs) of each agent; identify the frequency of specific drug therapy problems associated with monitored parenteral antimicrobials; and, compare the total drug costs between the actual prescribing and prescribing patterns recommended in the national treatment guidelines (DOH NAG).

MATERIALS AND METHODS

Study Design and Setting

The study employed a retrospective, cross-sectional, descriptive research design. A retrospective chart review of patients admitted in a tertiary care private hospital in Cebu City was conducted. The medical records of the patients were accessed and obtained from the medical records department of the hospital.

The study site is a general tertiary care private hospital in Cebu City, Cebu, Philippines. As of January 2020, the hospital has a total authorized capacity of two hundred (200) beds. Currently, five (5) different medical departments are available to serve patients, which include: Family Medicine, Internal Medicine, Obstetrics-Gynecology, Pediatrics, and Surgery.

The study site was selected due to the hospital's AMS program. The program dissolved after its main proponent transferred to another hospital. Plans for reactivation were in place under a different specialist. There was a need to evaluate whether former objectives were met. Surveillance of trends in utilization of monitored parenteral antimicrobials was vital to measure effectiveness of existing policies and systems.

Inclusion and Exclusion Criteria

Charts that have met the following inclusion criteria were included in the study:

1. prescribed with at least one monitored parenteral antimicrobial agent (i.e., either ampicillin-sulbactam, ceftriaxone, ciprofloxacin, clindamycin, or piperacillin-tazobactam);
2. adult patients, aged 18 years old or older;
3. admitted at least once, within the period of January 1, 2019, to December 31, 2019; and
4. directly managed or co-managed by the Internal Medicine (IM) department, regardless of the availed service upon admission.

The following conditions served as the exclusion criteria:

1. patient medical records with incomplete variables regarding the prescribed monitored parenteral antimicrobial therapy;
2. patient medical records that could not be accessed or retrieved from the medical records department of the hospital;
3. patients who were diagnosed with two or more co-existing infections at the time of hospitalization; and
4. patients who underwent incomplete treatment (e.g., expired, left against medical advice of attending physician).

The following data were collected from the patient charts: prescriber background, patient demographics, antimicrobial therapy, culture and sensitivity (C/S) test results, and drug therapy-related problems (DTRPs). All information were gathered using an electronic standardized data collection form created using Epi Info™.

Data Processing and Analysis

Antimicrobial Consumption

Antimicrobial consumption in defined daily doses per 1,000 patient days (DDDs/1,000-PDs) for each monitored parenteral antimicrobial was calculated using the 2019 Antimicrobial Consumption (AMC) tool version 1.9.0.[11] The AMC tool is a downloadable software that allows for the calculation of antimicrobial consumption in DDDs. The assessment of the DDD values was reported on a per month basis.

Appropriateness in Prescribing

The appropriateness of actual prescribing was determined to assess the adherence to the DOH National Antibiotic Guidelines (NAG). All patient cases were then assessed using the established drug use evaluation (DUE) criteria indicators. The percentage of patient cases that have met or exceeded the established DUE criteria were compared with the threshold levels of each component as shown in Table 1. The DUE criteria indicators published in the guidelines by Moore et al., 1997[12] was modified for use in this study. As for the threshold levels, they were set by the researchers based on the target of the study site.

Each patient case was checked and validated using drug references to obtain data for the complication indicators (i.e., ADRs, contraindications, drug-drug interactions, and therapeutic duplication) especially when they were not stated explicitly in the patient's chart. The references used include MIMS Philippines, Medscape, and Micromedex. In this study, therapeutic duplication refers to the concomitant use of two (2) or more monitored parenteral antimicrobials simultaneously.

Table 1. DUE Criteria Indicators with their Corresponding Threshold Levels[12]

Indicators	Components	Threshold Level
Justification Indicators	• C/S of documented infection, susceptible to the prescribed monitored parenteral antimicrobial agent(s)	100%
Critical Indicators	• Prescribed monitored parenteral antimicrobial agent(s)	90%
	• Strength or dosage	95%
	• Frequency	95%
	• Route of administration	95%
	• Days of therapy	95%
Complication Indicators	• Adverse drug reactions	90%
	• Antimicrobial resistance	100%
	• Contraindications	100%
	• Drug-drug interactions	90%
	• Therapeutic duplication	90%

Cost Analysis

The cost analysis that was performed in the study mainly focused on cost savings. It involved the calculation of the actual drug costs (ADC) based on the actual prescriptions, and the ideal drug costs (IDC) based on the recommendations from the DOH NAG. The ADC and IDC for each case were compared. The cumulative differences in drug costs from all the patient cases were used to assess the economic impact on the patient's perspective. All prices that were used in the computation of drug costs were based on the price list obtained from the hospital's inpatient pharmacy. The following equations were used during calculation:

$$\text{ADC or IDC} = \text{unit cost price of drug} \times \text{frequency} \times \text{duration of treatment}$$

$$\text{Difference of drug cost per case} = \text{ADC} - \text{IDC}$$

Ethical Considerations

The study was duly approved by University of the Philippines Manila Research Ethics Board (UPM REB Code: 2020-645-1). Data collection through retrospective patient chart review commenced after due approval of the UPM REB was received.

RESULTS

Drug Utilization Review

For the entire study duration period from January 1, 2019, to December 31, 2019, there were a total of 6,154 in-patient admissions at the study site. The IM Department (33%) had the greatest number of admissions. This was followed by the Obstetrics-Gynecology (OB-GYN) Department (18%), and Pediatrics Department (14%).

Considering the total admissions for 2019, all 6,154 patient charts were examined for eligibility based on the inclusion criteria. Roughly 2,030 charts were considered potentially eligible as these were from the IM department. Overall, 821 patient charts were eligible, thus included in the study. These charts were individually reviewed and subsequently analyzed.

The doctors that have prescribed monitored parenteral antimicrobials have varied IM specializations. General IM consultants (28%) were the top prescribers. The other top prescribers include pulmonologists (23%), cardiologists (13%), infectious disease specialists (8%), and gastroenterologists (6%) and neurologists (6%).

Majority of the patients availed of the medical service (90%) upon admission. For those patients that availed of the obstetrical or gynecological (2%) and surgical (8%) services, they have been co-managed by the medical service.

The patients' ages ranged from 18 to 98 years old. The mean age of the patients was 58.46 years old (SD = 19.41). There were slightly more females (52%) than males (48%) who were prescribed with monitored parenteral antimicrobials.

Table 2 summarizes the medical condition of the patients. Lower respiratory tract infections (LRTIs) accounted for the greatest number of cases (47%). Specifically, community acquired pneumonia – moderate risk (CAP-MR) (39%) was the most common infection. Complicated UTI (10%), sepsis (6%), cellulitis of the limbs (3%), typhoid fever (3%), and community acquired pneumonia – high risk (CAP-HR) (3%) were also among the usual conditions requiring treatment with monitored parenteral antimicrobials.

Most of the doctors had prescribed monotherapy (95%) as opposed to a combination therapy (5%). Piperacillin-tazobactam 4.5 g q8h (39%) was most frequently prescribed as monotherapy. For combination therapy, clindamycin 600 mg q6h + piperacillin-tazobactam 4.5 g q8h (1%) was the most common option among prescribers.

All the prescribed antimicrobial therapy were administered intravenously (100%). The average days of therapy (DOT) was 5.73 days. The prescribed antimicrobial therapy was mainly for empirical treatment (94%) of infections. Only a few were indicated for prophylaxis (5%) of surgical procedures or prescribed as definitive (1%) treatment after release of C/S test results.

Table 2. Summary of Infections by Organ System Grouping

Infections by Organ System	Frequency (%)
Lower Respiratory Tract Infections	384 (46.8)
Genitourinary Tract Infections	136 (16.6)
Skin and Soft Tissue Infections	89 (10.8)
Blood Infections	78 (9.5)
Gastrointestinal Infections	65 (7.9)
Surgical Procedures (Prophylaxis)	46 (5.6)
Upper Respiratory Tract Infections	13 (1.6)
Bone and Joint Infections	5 (0.6)
Other Conditions	3 (0.4)
Central Nervous System Infections	1 (0.1)
Dental and Oral Infections	1 (0.1)
Total	821 (100)

C/S testing was performed in 58% of the study population. There was a total of 618 samples taken for analysis. There were instances where more than one type of specimen was examined. Blood (29%) was the most common specimen sent for C/S testing. This was followed by sputum (27%), urine (24%), wound (8%), body fluids (5%), and tracheal aspirate (3%).

There were occurrences where more than one microorganism was isolated from cultures. Overall, 658 colonies were cultured. Only 47% had notable and sufficient colonies. Sensitivity testing was performed for these cases to determine their susceptibility profiles. Breakpoint value ranges established in the 2019 Clinical and Laboratory Standards Institute (CLSI) have been used for the interpretation of susceptibility profiles.

Only 300 out of 308 isolates were subjected to sensitivity testing. Testing was not performed on cultures due to several circumstances. The primary reason was attributed to insufficient number of culture colonies obtained.

Gram-negative organisms were identified in 232 (77%) isolates. *E. coli* (19%) was the most isolated pathogen. Other gram-negative organisms that were frequently isolated include *K. pneumoniae* (18%), *E. cloacae* (8%), *B. cepacia* (5%), and *P. mirabilis* (4%). Extended-spectrum beta lactamase (ESBL) – producing Gram-negative organisms were also isolated. *E. coli* (n=6, 55%) was the most common pathogen isolated that produced ESBL.

On the contrary, Gram-positive organisms were identified in 68 (23%) isolates. *S. aureus* (9%) was the most isolated pathogen. Other Gram-positive organisms that were commonly isolated include *S. epidermidis* (3%), *S. saprophyticus* (2%), *S. haemolyticus* (2%), and *S. salivarius* (2%). Four *S. aureus* isolates that were isolated were methicillin resistant.

The cumulative susceptibility profiles have revealed that the isolated microorganisms were most resistant to ampicillin (81%). Among the monitored antimicrobials, they were most resistant to ampicillin-sulbactam (30%) and were least resistant to piperacillin-tazobactam (9%). They were most susceptible to colistin, netilmicin, and ertapenem, at 100%, 95%, and 94%, respectively. Table 3 presents the complete rundown of the cumulative susceptibility profiles of the microorganisms to the antibiotics used during C/S testing.

The resistance rates of selected microorganisms (*E. coli*, *K. pneumoniae*, and *S. aureus*) to monitored antimicrobials are outlined in Table 4.

The patient cases with DTRPs are laid out in Table 5. There were ADRs, contraindications, therapeutic duplications, and drug-drug interactions, where monitored parenteral antimicrobials were involved.

A patient had experienced an ADR. It was a hypersensitivity reaction after seven days of therapy with clindamycin IV. There was the presence of maculopapular rash throughout his whole body. Prior to the report, the patient had already self-medicated with an anti-allergy medication. The patient described to have taken one tablet of betamethasone + dexchlorpheniramine maleate,

Table 3. Cumulative Susceptibility Profiles of all Microorganisms Isolated

Antibiotic	%R	%I	%S
Amikacin	2	8	90
Amoxicillin/Clavulanic acid	34	12	54
Ampicillin	81	3	17
Ampicillin/Sulbactam	30	13	58
Azithromycin	36	5	59
Aztreonam	8	4	88
Cefazolin	43	18	40
Cefepime	25	14	61
Cefixime	52	10	38
Cefoperazone	30	24	46
Cefotaxime	24	4	72
Cefoxitin	29	4	68
Ceftazidime	23	13	64
Ceftriaxone	26	18	56
Cefuroxime	37	39	24
Chloramphenicol	18	5	76
Ciprofloxacin	24	11	65
Clindamycin	17	11	72
Colistin	0	0	100
Ertapenem	6	0	94
Erythromycin	33	24	42
Gentamicin	13	8	79
Imipenem	14	9	76
Levofloxacin	23	2	75
Meropenem	7	6	87
Nalidixic acid	57	8	35
Netilmicin	2	3	95
Nitrofurantoin	21	3	76
Norfloxacin	47	0	53
Ofloxacin	67	0	33
Oxacillin	57	5	38
Penicillin G	68	2	31
Piperacillin/Tazobactam	9	24	68
Tetracycline	25	0	75
Trimethoprim/Sulfamethoxazole	45	1	54
Vancomycin	11	6	82

Legend: %R: percent resistance, %I: percent intermediate, %S: percent susceptible

Table 4. Resistance Rates of Selected Microorganisms to Monitored Antimicrobials

Microorganisms	Monitored Antimicrobials	% Resistance
E. coli	Ciprofloxacin	53%
	Ampicillin-sulbactam	46%
	Ceftriaxone	43%
	Piperacillin-tazobactam	22%
K. pneumoniae	Piperacillin-tazobactam	48%
	Ciprofloxacin	41%
	Ceftriaxone	34%
S. aureus	Clindamycin	23%
	Ciprofloxacin	0%

Table 5. Summary of Drug Therapy-related Problems

DTRPs	Frequency (%)
ADRs	
Yes	1 (0.1)
No	820 (99.9)
Contraindications	
Yes	2 (0.2)
No	819 (99.8)
Therapeutic Duplications	
Yes	43 (5)
No	778 (95)
Drug-Drug Interactions	
Yes	322 (39)
No	499 (61)

Table 6. Frequency of Drug Interactions with Monitored Parenteral Antimicrobials

Monitored Antimicrobials	Frequency (%)
Piperacillin-tazobactam	281 (60.4)
Ciprofloxacin	126 (27.1)
Ceftriaxone	43 (9.2)
Ampicillin-sulbactam	15 (3.2)

250 mcg/2 mg. His attending physician ordered that the anti-allergy medication was to be continued for five days more. He also ordered the discontinuation of the IV clindamycin. After the discontinuation of IV clindamycin and completion of the anti-allergy treatment, the condition had subsided.

There were two cases (0.2%) where therapy with monitored parenteral antimicrobials were contraindicated. In both cases, the patients were prescribed with piperacillin-tazobactam IV even if there was documentation of allergy to penicillin. Despite the situation, the patients have completed the prescribed course of therapy and their condition improved.

Patients who were prescribed a combination therapy (5%) – were cases of therapeutic duplication. Drug-drug interactions were observed in 39% of cases. Drug interactions were documented with four monitored antimicrobials. Table 6 displays the summary of the frequency of these interactions.

The most frequently recorded drug-drug interaction was that of piperacillin-tazobactam and azithromycin (38%). Other frequent interactions that were observed include piperacillin-tazobactam and enoxaparin (11%), piperacillin-tazobactam and aspirin (8%), ciprofloxacin and metronidazole (5%), and ceftriaxone and furosemide (5%).

Upon thorough review, the interaction of ceftriaxone and piperacillin-tazobactam with enoxaparin were classified as serious in severity. If suitable based on the patient's case, an alternative medication could have been given to replace enoxaparin. Close monitoring was also warranted.

The monthly breakdown of the consumption (in DDDs/1,000-PDs) of each monitored parenteral antimicrobial agent is consolidated in Table 7. The combined consumption of the five monitored parenteral antimicrobials was 141.57 DDDs/1,000-PDs.

The outcome of the evaluation of appropriateness in prescribing are tabulated in Table 8. The criteria were met when the frequency of appropriate cases was equivalent or above the threshold values. Only four of the components have met the criteria.

From the cases where C/S results were obtained, the isolated microorganisms have demonstrated resistance to the antibiotics tested. Yet, it is significant to highlight that there were no cases (0%) where therapeutic failure of the prescribed antimicrobial therapy has occurred because the pathogen has acquired or developed resistance. After completing the prescribed antimicrobial therapy, patients have shown clinical improvement. Thus, the criterion was met for the AMR component under the complication indicator.

Cost Analysis

The summary of the actual costs, ideal costs, and cost differences by month is presented in Table 9. With the total actual cost of ₱17,645,601.73, roughly ₱48,344.11 was spent per day. The monthly average spending was around

Table 7. Summary of the Consumption of each Monitored Parenteral Antimicrobial Agent by Month

Month	Consumption in DDDs/1,000-PDs				
	Ampicillin-sulbactam	Ceftriaxone	Ciprofloxacin	Clindamycin	Piperacillin-tazobactam
January	7.93	29.48	4.42	19.71	89.64
February	2.58	29.92	2.77	18.10	93.89
March	2.50	53.07	1.86	4.81	81.48
April	6.56	19.16	5.77	8.22	89.43
May	1.07	39.52	11.43	17.94	99.57
June	5.17	31.41	8.23	24.51	82.44
July	3.17	69.58	4.58	26.48	80.09
August	4.02	31.75	2.30	15.59	81.43
September	4.02	14.20	1.57	5.99	29.94
October	5.27	23.81	2.40	2.23	45.31
November	6.35	48.09	4.72	12.25	96.25
December	4.20	49.16	15.63	31.26	84.48
Mean	4.41	36.60	5.47	15.59	79.50

Table 8. Evaluation of Appropriateness in Prescribing Monitored Parenteral Antimicrobials with the DUE Criteria Indicators

DUE Criteria Indicators	Frequency (%)	Threshold Level (%)	Interpretation
Justification Indicator			
Appropriate	214 (88)	100	did not meet criteria
Not appropriate	29 (12)		
Critical Indicators			
Prescribed agent			
Appropriate	366 (45)	90	did not meet criteria
Not appropriate	455 (55)		
Dosage			
Appropriate	278 (34)	95	did not meet criteria
Not appropriate	543 (66)		
Frequency			
Appropriate	246 (30)	95	did not meet criteria
Not appropriate	575 (70)		
Route			
Appropriate	786 (96)	95	met the criteria
Not appropriate	35 (4)		
Duration			
Appropriate	179 (22)	95	did not meet criteria
Not appropriate	642 (78)		
Complication Indicators			
ADRs			
Appropriate	820 (99.9)	90	met the criteria
Not appropriate	1 (0.1)		
Contraindication			
Appropriate	819 (99.8)	100	did not meet criteria
Not appropriate	2 (0.2)		
Therapeutic Duplication			
Appropriate	778 (95)	90	met the criteria
Not appropriate	43 (5)		
Drug-Drug Interactions			
Appropriate	499 (61)	90	did not meet criteria
Not appropriate	322 (39)		
AMR			
Appropriate	821 (100)	100	met the criteria
Not appropriate	0 (0)		

₱1,470,466.81. Per capita costs were approximately ₱21,492.82 for the entire therapy. Considering the average DOT, each patient spent ₱3,750.93 per day to complete the prescribed treatment. The recommended therapy from the DOH NAG would just cost ₱18,169.57 per patient. Per capita savings was calculated to be ₱579.97 per day or ₱3,323.25 for the entire therapy, if the most cost-effective NAG treatment option was selected by the prescriber.

DISCUSSION

Drug Utilization Review

This study revealed the utilization of five different monitored parenteral antimicrobials in a tertiary care private hospital in Cebu City. Several studies have shown that majority of monitored parenteral antimicrobials were prescribed for patients admitted in the medical ward. This was observed for ceftriaxone[13], ciprofloxacin[14], clindamycin[15], and piperacillin-tazobactam[16]. Medical residents (65%)[17] and IM specialists (69%)[15] were the highest prescribers of piperacillin-tazobactam as reported from the studies of Alsaleh et al. and Ala et al., respectively.

Similarly, pneumonia was the main indication that involved treatment with monitored antimicrobials including piperacillin-tazobactam[18], clindamycin[15], ciprofloxacin[14], and ceftriaxone[19]. Next to pneumonia, piperacillin-tazobactam was also prescribed to manage sepsis (20%), skin and soft tissue infections (15%), and UTIs (14%).[17]

From the study, monotherapy with piperacillin-tazobactam 4.5 g q8h (39%) was regularly prescribed. Shiva et al. had observed the same therapy regimen (42%) prescribed for their patients.[18] Combination therapy with other antimicrobials was also seen and clindamycin 600 mg q6h (0.7%) was often given. Other concomitantly administered antimicrobials with piperacillin-tazobactam in literature was vancomycin[18,20] and clindamycin[21]. Clindamycin was often paired with third generation cephalosporins and carbapenems.[15] Better coverage of probable causative

Table 9. Summary of the Actual Costs, Ideal Costs, and Cost Difference by Month (in Philippine Peso, ₱)

Month	Actual Costs	Ideal Costs	Cost Difference
January	2,045,007.49	1,323,662.02	721,345.47
February	1,712,453.05	1,268,301.97	444,151.08
March	1,302,494.87	1,276,761.10	25,733.77
April	1,224,963.67	1,010,911.24	214,052.43
May	1,672,950.02	1,339,811.04	333,138.98
June	1,431,817.40	1,430,077.26	1,740.14
July	1,642,082.79	1,549,260.91	92,821.88
August	1,476,597.18	847,798.98	628,798.20
September	616,398.57	757,852.78	−141,454.21
October	875,108.11	1,018,706.50	−143,598.39
November	1,756,250.90	1,511,701.06	244,549.84
December	1,889,477.68	1,582,369.43	307,108.25
Total	17,645,601.73	14,917,214.29	2,728,387.44

pathogens is achieved when monitored antimicrobials are concurrently prescribed.

Combination therapy may be essential to broaden the antimicrobial spectrum. It decreases the risk of inappropriate selection in empiric treatment, thereby reducing mortality. The development of resistance among pathogens is also inhibited. Furthermore, certain combinations have additive or synergistic effects which potentiates the overall antimicrobial activity.

Overall, monitored parenteral antimicrobials were mainly indicated for empirical treatment (94%) of infections in this study, as it was in only 58% of the cases where C/S testing was performed. Numerous related studies including these agents in their analyses also emphasized empirical prescribing.[14,17-19,22] In addition, only 14% of cases had orders for C/S testing and 89% of patients had received piperacillin-tazobactam without prior C/S results in the investigation of Shiva and his colleagues.[18]

C/S testing is most important in diagnostics to identify the causative agent of the patient's infection and to determine their susceptibility to antimicrobials. Primarily, results from C/S testing may guide clinicians to prescribe a definitive antimicrobial therapy which is suitable and effective for patients. It also aids in the de-escalation of broad-spectrum empiric therapy that is commonly initiated prior to collection of specimens. Moreover, an antibiogram may be developed based on the cumulative C/S reports from different patients.

Variations in the average duration of treatment were encountered in literature. The following were the corresponding average DOT for each monitored antimicrobial agent: piperacillin-tazobactam (7 days[17] and 8.52 days[18]), ceftriaxone (7-14 days[19] and 5 days[22]), ciprofloxacin (4 days[14]), and clindamycin (7 days[15]). In comparison, these were the average DOT from this study: piperacillin-tazobactam (6.32 days), ceftriaxone (5.09 days), ciprofloxacin (3.73 days), and clindamycin (6.16 days). Differences in the average DOT are expected. These can be attributed to several factors which include the patient's co-morbidities, severity of infection, presence of resistant pathogens, and clinical response to prescribed therapy.

C/S Test Results

Study results were compared with data coming from the DOH Annual Report Summary from the Antimicrobial Resistance Surveillance Program (ARSP) of the Research Institute of Tropical Medicine (RITM).

Similarities of study findings with ARSP data may be attributed to the prevalence of significant pathogens of public health importance causing common infectious diseases in the locale. Several reasons may contribute for the differences as well. Predominantly, only charts of adult patients prescribed with monitored parenteral antimicrobials were reviewed. Thus, the C/S results gathered from this study only represents a part of the entire population of patients with available C/S results for 2019.

Second, prescribers might not routinely request for C/S unless infections are complex, life-threatening, or suspected to be caused by resistant pathogens.

Third, ARSP did not include and analyze data where there were less than 30 isolates obtained per species. In this study, however, all isolates from cultures with sufficient colonies that had results for susceptibility testing regardless of number were included.

Given all these factors, the rates of antimicrobial resistance could potentially be affected. Considering a lesser number of C/S tests were ordered and performed, the resistance rates reported could be greater as there would be a smaller overall population.

Blood (29%) was the most common specimen type taken for C/S testing in this study, followed by sputum (27%). A reverse trend was found in literature.[23-26] Table 10 outlines the details. Still, it is important to emphasize that regardless of the rate, either blood or respiratory samples (e.g., sputum) were often involved in C/S testing. In addition, other specimen types were also ordered for analysis.

Data coming from the ARSP 2017-2019 have revealed that *K. pneumoniae*, *E. coli*, and *P. aeruginosa* were the main isolates identified.[23-25] Findings from the study were consistent with ARSP data as *E. coli* (19%) and *K. pneumoniae* (18%) were often isolated from specimens tested.

Resistance against antimicrobials were obtained for *E. coli*, *K. pneumoniae*, and *S. aureus* in this study. Tables 11 and 12 describe the resistance rates against monitored and selected antimicrobials, respectively. ARSP resistance rates for 2018-2020 were much lower as compared to study findings (Table 11). *E. coli* and *K. pneumoniae* remain to have low rates of resistance with amikacin and meropenem. Although *S. aureus* appear to have high resistance against vancomycin (25%), this only reflects the resistance of a small number of isolates (n=26) (Table 12).

The specific in vivo mechanisms underlying the development of resistance to the monitored antimicrobials was no longer examined. This is beyond the scope of this study.

Additionally, there were no cases of treatment failure encountered due to infections caused by pathogens that developed resistance during the patient's course of therapy and hospital stay which could have warranted further investigation.

The isolation of ESBL-producing Gram-negative microorganisms and MRSA have implications in actual practice. First, this serves as concrete evidence of the prevalence of resistant strains most especially in the locale. Second, patients infected with these pathogens need to be managed by an infectious diseases specialist (IDS) as their infections are likely more complicated to manage. Third, C/S testing should be employed to identify these pathogens and their susceptibility patterns. Fourth, last line antimicrobials like colistin and linezolid could be prescribed. Lastly, pharmacists need to ensure availability of these antimicrobials, assist in the development and implementation of institution-specific

guidelines, and strongly advocate the rational use of these agents in the hospital.

Appropriateness in Prescribing

There were several cases where monitored parenteral antimicrobials were prescribed inappropriately. 12% of the cases were inappropriate based on the justification indicator. As for the critical indicators, therapy was unsuitable with duration of therapy (78%) as the leading reason. This was followed by the specified frequency (70%), strength or dosage (66%), choice of monitored antimicrobial agent (55%), and route of administration (4%) upon evaluation using the DOH NAG.

Several studies that assessed the prescribing of monitored antimicrobials were checked. Based on the justification indicators, Khan et al. discovered that in 1% of cases, isolated pathogens were resistant to piperacillin-tazobactam. However, therapy was not discontinued. Thus, use of piperacillin-tazobactam in these cases was deemed inappropriate.[16]

Other studies have revealed the cumulative rates of inappropriateness based on critical indicators of piperacillin-tazobactam (62%[18], 43%[16], and 39%[27]), ceftriaxone (56%[22] and 35%[13]), and ciprofloxacin (13%[28] and 4%[14]). Almost all were lower in contrast to the rates obtained from study findings. Several factors could account for the differences. The main factor is the difference in the standards, criteria, or basis used to establish appropriateness. Study population and duration should also be accounted for.

Drug therapy-related problems were also considered in the evaluation. No pathogens isolated developed resistance to the prescribed monitored antimicrobials during the entire duration of the patient's therapy. However, drug-drug interactions (39%) were frequently encountered. There were also cases where ADRs (0.1%) and contraindications (0.2%) were met. Furthermore, 5% had duplicated therapy.

Table 10. Summary of the most Common Specimen Taken for C/S testing in Comparison with ARSP

Rank	Study Findings	ARSP 2018[24]	ARSP 2019[25]	ARSP 2020[26]
1	blood (29%)	respiratory (31%)	respiratory (30%)	respiratory (32%)
2	sputum (27%)	blood (22%)	blood (24%)	blood (26%)
3	urine (24%)	urine (19%)	urine (19%)	wound (16%)
4	wound (8%)	wound (17%)	wound (16%)	urine (16%)
5	body fluids (5%)	tissue (5%)	tissue (4%)	tissue (3%)

Table 11. Summary of Resistance Rates of *E. coli*, *K. pneumoniae*, and *S. aureus* with Monitored Antimicrobials

Microorganisms	Monitored Antimicrobials	% Resistance			
		Study Findings	ARSP 2018[24]	ARSP 2019[25]	ARSP 2020[26]
E. coli	Ciprofloxacin	53%	40%	47%	47%
	Ampicillin-sulbactam	46%	35%	33%	*N/A
	Ceftriaxone	43%	38%	40%	40%
	Piperacillin-tazobactam	22%	11%	12%	13%
K. pneumoniae	Piperacillin-tazobactam	48%	22%	25%	24%
	Ciprofloxacin	41%	22%	45%	45%
	Ceftriaxone	34%	45%	47%	46%
S. aureus	Clindamycin	23%	12%	10%	11%
	Ciprofloxacin	0%	*N/A	4%	4%

**N/A: Data not available*

Table 12. Summary of Resistance Rates of *E. coli*, *K. pneumoniae*, and *S. aureus* with Selected Antimicrobials

Microorganisms	Selected Antimicrobials	% Resistance			
		Study Findings	ARSP 2018[24]	ARSP 2019[25]	ARSP 2020[26]
E. coli	Cefuroxime	79%	38%	42%	45%
	Amikacin	5%	4%	4%	4%
	Meropenem	5%	5%	6%	9%
K. pneumoniae	Cefepime	36%	34%	35%	31%
	Amikacin	13%	6%	5%	6%
	Meropenem	7%	12%	14%	14%
S. aureus	Erythromycin	48%	*N/A	12%	12%
	Vancomycin	25%	1%	1%	1%
	Tetracycline	8%	9%	7%	9%

**N/A: Data not available*

From all the patient cases, there was a single case (0.1%) where an adverse drug reaction occurred. It was a hypersensitivity reaction with clindamycin IV therapy. Naranjo's algorithm[29] was employed to determine the extent of the causality of the adverse drug reaction. The patient's score was 4, indicating that clindamycin was a possible cause. However, the researcher was limited to the information provided in the patient's chart.

There was no documentation available regarding the re-administration of clindamycin, presence of toxic concentrations of clindamycin in the blood and/or other body fluids, and confirmation from the patient of a previous similar encounter. The patient's response after the discontinuation of IV clindamycin coupled with the therapy to manage the allergic response may very well support the possibility of clindamycin triggering the said adverse drug reaction.

Rutkowski et al. had explained in their paper that hypersensitivity reactions with clindamycin are relatively unusual, although not totally impossible from happening. According to literature, the patient may have experienced a delayed maculopapular exanthem. This is a common type of hypersensitivity reaction from clindamycin and is observed to occur after 7-10 days of therapy.[30]

Almost all the cases (99.8%) did not have any contra-indications, except for two (0.2%). Despite the documented penicillin allergy for both cases, the attending physician prescribed piperacillin-tazobactam IV therapy. Three drug references were reviewed (Medscape, Micromedex, and MIMS) regarding this contraindication. All the three clearly stated that any allergic reaction to beta lactam antibiotics (e.g., penicillin, cephalosporins), and beta lactamase inhibitors is a contraindication to piperacillin-tazobactam therapy.

Cross-reactivity among beta lactam antibiotics is well recognized in literature. This is attributed to similarity of the R1 side chains. Nevertheless, the concept of allergy to "all" penicillins is false. A study conducted by Meng et al. elucidated that only 29% of the suspected patients were validated to have penicillin allergy. In addition, some patients in their study who were confirmed to have clavulanic acid and flucloxacillin allergy were able to tolerate the amoxicillin challenge.[31]

Each monitored parenteral antimicrobial investigated in this study were all broad-spectrum. Yet, clindamycin has better coverage against Gram-positive organisms. Meanwhile, ceftriaxone, ciprofloxacin, and piperacillin-tazobactam has greater coverage against Gram-negative organisms. Moreover, anaerobic organisms are targeted by ampicillin-sulbactam.[32]

Physicians often prescribe a combination therapy for the management of severe infections. These conditions potentially require good coverage for both Gram-positive and Gram-negative organisms. Some of these conditions include healthcare-associated pneumonia and sepsis. Clindamycin 600 mg q6h + piperacillin-tazobactam 4.5 g q8h (0.7%) was the most frequently prescribed combination therapy in the study. Other combinations were also prescribed like ceftriaxone + clindamycin, ciprofloxacin + clindamycin, and ampicillin-sulbactam + clindamycin.

The top drug-drug interaction was between piperacillin-tazobactam and azithromycin (38%). This interaction was usually drawn from patients diagnosed with CAP-MR. According to Medscape, this interaction is to be monitored closely. The bacteriostatic action of azithromycin may perhaps affect the bactericidal action of piperacillin causing pharmacodynamic antagonism. Prevalence of this antagonism is supported by literature. The investigation of Ocampo et al. has demonstrated that combination of bactericidal and bacteriostatic agents resulted in strong antagonism.[33] However, the benefit of azithromycin in the management of CAP-MR may be due to its immunomodulatory activity rather than its antimicrobial properties. Macrolides exert anti-inflammatory effect by reducing the release of interleukins and tumor necrosis alpha. Consequently, adherence of bacteria on respiratory epithelial cells is decreased.[34]

The other notable drug-drug interactions also involved piperacillin-tazobactam. These were with aspirin and enoxaparin. Through competition of attachment to protein binding sites, either aspirin or piperacillin could potentially enhance the action of the other. This interaction is considered minor in severity. On the contrary, a serious interaction is seen with piperacillin and enoxaparin. Platelet aggregation is inhibited by piperacillin which in turn potentiates the anticoagulation effect of enoxaparin. When prescribed with both agents, an alternative medication could be used if possible. If not, close monitoring is warranted.[35]

Antimicrobial Consumption

The researcher utilized the ATC tool to calculate the consumption of the five different monitored parenteral antimicrobials.

The total mean antimicrobial consumption was 141.57 DDD/1,000-PDs. This was lesser compared to the consumption (in DDDs/1,000-PDs) reported from hospitals in other countries like New Zealand[36] (1,176), Korea[37] (960), Ethiopia[38] (795), Belgium[39] (577.1), Mexico[40] (572), and Serbia[41] (419.5).

Several factors are responsible for the vast differences of the mean consumption. One of the main reasons was that this study focused solely on five monitored parenteral antimicrobials. Study population accrued, bed capacity and occupancy rate, as well as departments or wards included are also important factors to be considered.

The study nearly had similar outcomes with the analysis performed by Marasine and his colleagues. They were able to determine the mean consumption of several antimicrobials utilized in the medical ICU of a tertiary care hospital in Nepal. Consumption of the antimicrobials were as follows: piperacillin-tazobactam (77.9), ceftriaxone (61.4), clindamycin (9.1), ampicillin (5.1), and ciprofloxacin (1.8) Besides this, piperacillin-tazobactam was also most often prescribed to patients.[42]

Piperacillin-tazobactam was the monitored parenteral antimicrobial agent with the biggest consumption in the study site at 79.50 DDD/1,000-PDs. This is lower than the consumption as reported from other similar institutions involving those from Saudi Arabia[17] (152.4), ICU in South India[43] (192.2), and Australian and New Zealand ICUs[44] (124.7). However, it is more than two-fold higher in contrast to those coming from the United States[45] (30.3) and from an Indian hospital[46] (25.02).

Piperacillin-tazobactam had the biggest consumption as it was most frequently prescribed by IM consultants to manage moderate risk pneumonia and a variety of other infections. It has good coverage for Gram-negative and Gram-positive aerobic and anaerobic bacteria. Owing to its clinical efficacy, risk of complications or mortality from serious infections are minimized especially for empiric treatment.

Among cases of patients with CAP-MR, piperacillin-tazobactam could have been prescribed for numerous reasons. First, patients might have other underlying co-morbidities that predisposes them for multiple complications. For example, chronic lung problems (e.g., COPD) could cause structural changes which affects regular respiration especially with an ongoing infection. Second, during admission, the attending physician could have suspected the patient of having sepsis or septic shock. Pneumonia could cause hypoxemia and lowered respiratory rate. However, these could also be signs of a more critical condition such as sepsis.

Third, the patient might have been at risk of infection with *Pseudomonas*. Undernourishment, chronic steroid use, presence of severe underlying bronchopulmonary disease, and history of prolonged use of broad-spectrum antimicrobials puts patients at greater risk of a pseudomonal infection. Higher doses of piperacillin-tazobactam (e.g., 4.5 g q6h) are effective to combat *P. aeruginosa*. Lastly, prior antimicrobial use (e.g., macrolides) for the management of the similar conditions (i.e., respiratory tract infections) with no signs of improvement and relief from symptoms. This could suggest infection caused by a more virulent or resistant strain of bacteria.

Cost Analysis

All costs were converted into Philippine Peso to facilitate comparison. 2019 average exchange rates[47-50] were applied during conversion.

The total cost incurred by all patients prescribed with monitored parenteral antimicrobials for 2019 was ₱17,645,601.73. This would roughly translate to ₱48,344.11 per day, and the cost of the entire therapy for each patient was approximately ₱21,492.82. Studies conducted in other LMICs have revealed the total cost of antibiotics utilized in their respective institutions. The total cost of antibiotics for an entire year in an ICU department of an Indian hospital was ₱8,502,245.02. This was based on the cost of therapy per patient which was ₱23,293.82[51].

In addition, the following were the respective costs reported from hospitals in Ethiopia[52] (₱167,882.00), Bangladesh[53] (₱94,908.32), and Sri Lanka[54] (₱14,098.02). In contrast, two studies done from separate hospitals in upper-middle income countries have revealed that antibiotic therapy for a single day amounted to ₱173,452.19 in Istanbul[55], and ₱458,083.40 in Southeast Turkey[56]. Bozkurt et al. also found that unnecessary antimicrobial utilization in 2011 was as high as ₱69,802.74 per day (₱359.45 per patient).[56]

The total cost of antibiotics from other LMICs were much lower, and higher with upper-middle income countries when compared with the study findings. Various factors can account for the variations in costs. These include study population accrued, study duration set, antibiotics studied, wards or departments focused, and actual prescriptions encountered (i.e., generic versus brand prescribing).

Moreover, there were several limitations with the cost analysis performed. First, the prices used in the study were derived primarily from the main pharmacy of the study site. Second, there are huge differences in the pricing of drugs not only within different institutions locally but also in other countries. Third, the country's gross domestic product (GDP) and gross national income (GNI) could have an impact on the prices of medicines. Lastly, other costs, such as indirect and/or miscellaneous costs were no longer covered in this study.

Piperacillin-tazobactam was the most frequently prescribed monitored parenteral antimicrobial agent. Hence, it was also the greatest contributor to the actual costs overall. This is consistent with the results conducted involving ICU patients in an Indian hospital.[41]

From the patient's perspective, the main economic implication was on the direct medical costs, particularly the increased cost of the actual antimicrobial therapy prescribed to manage various infections. Based solely on the cumulative cost differences, each patient could have potentially saved ₱3,323.25. Although, there were numerous instances where potential savings was far greater considering the cases individually. The antimicrobial therapy that patients use is highly dependent on the prescribing patterns of physicians. Hence, if they have had followed NAG recommendations, and selected the most cost-effective option, patients could have had already saved some money from purchasing the antimicrobial therapy alone.

In addition, this study discovered that only 58% cases had performed C/S testing, and majority of the prescribed monitored parenteral antimicrobials were indicated for empiric therapy (94%). C/S testing is quite expensive. At the study site, it costs approximately ₱2,500.00. Prices may also vary depending on the type of specimen sent for analysis. Patients may opt not to have the C/S test performed because of financial constraints.

As a result, physicians would have to rely on broad-spectrum empiric therapy. Generally, these are much expensive compared to narrow-spectrum agents. In the long run, therapy with broad-spectrum agents covering the entire prescribed

treatment duration would be a more costly option, as opposed to the scenario where the broad-spectrum antimicrobial is shifted to a narrow-spectrum agent after results of C/S test are obtained. Without C/S results, escalation or de-escalation of therapy is difficult. Not to mention, undesirable complications may arise due to failure of escalation or de-escalation of therapy.

Finally, generic prescribing was often observed among IM consultants. Still, there were some cases where branded antimicrobials were preferred and subsequently prescribed. Generic medicines are usually cheaper compared to their branded counterparts. Prices of medicines are also typically higher inside the hospital pharmacy. At the study site, there were no existing policies that prohibits patients from buying medicines outside the hospital. Thus, for patients that are financially constrained, physicians should encourage them to buy generic medicines at other pharmacies where prices may be lower. In this manner, the burden of the cost of antimicrobial therapy would be lessened.

Study Strengths and Limitations

One of the major strengths of this study was the comprehensive review of the utilization of the monitored antimicrobials – encompassing the thorough evaluation of the appropriateness of prescribing, C/S test results, drug therapy-related problems, antimicrobial consumption, and cost analysis.

The findings of this study were a positive influence to the current practices in the hospital. For physicians, it was highly encouraged to prescribe cost-effective treatment options based on the DOH NAG. For hospital and clinical pharmacists, they constantly ensure and advocate rational use of antimicrobials.

There were also some limitations. A retrospective review was performed. Especially that there were inappropriate prescriptions, no changes or interventions were made at the time of actual prescribing. This could be accomplished in a prospective review. Accordingly, goals of therapy could be thoroughly communicated and understood by all the members of the health care team. Also, there could be the possibility of information bias. The investigators mainly relied on the data collected from the patient charts. Verification to the extent possible was done by the investigators to clarify vague details.

In this study, only those cases directly managed or co-managed by the IM department were included. Due to this, potentially there could be under selection bias. Without time and resource constraints, the scope of the utilization review could be broadened to include more antimicrobials and departments or wards of the hospital. Also, the time frame could be extended. The results and findings of the study could not be generalized for the entire study site, as only a specific group of patients and antimicrobials were considered.

Other local guidelines, such as those published by the Philippine Society for Microbiology and Infectious Diseases (PSMID) should also be considered in conjunction with the DOH NAG as these were also used by medical consultants and residents in the study site. Albeit similar, standards and guidelines may have slight variations in their recommendations. This could potentially have an impact specially in the assessment of appropriateness in prescribing. Furthermore, physicians provide recommendations depending on the severity of the case.

During the literature review, there were more international studies conducted compared to local ones. As a result, most of the discussion was focused on comparisons with institutions coming from other countries. Benchmarking would have been more relevant in our context if there were data coming from local hospitals in the Philippines. Likewise, other hospitals abroad might have more established antimicrobial stewardship programs.

With the focus on cost savings, the cheapest option among all the therapy recommended from the DOH NAG was selected by the researcher as the ideal cost for the case. In addition, some of the antimicrobials recommended in the DOH NAG was not available in the hospital formulary. There was an option to check the DOH Drug Price Reference Index (DPRI). As a private institution, the prices of medicines at the study site were considerably higher than the average prices in the DOH DPRI. If they were included, there would have been undue bias, as there would be a greater chance for the selection of that specific therapy being cheaper compared to the rest.

CONCLUSION

Overall, the prescribing pattern and consumption of ampicillin-sulbactam, ceftriaxone, ciprofloxacin, clindamycin, and piperacillin-tazobactam in 2019 were elucidated in this study. Consumption of piperacillin-tazobactam was relatively high as compared to the other monitored parenteral antimicrobials. Physicians at the study site seldom prescribe monitored antimicrobials as recommended by the DOH NAG. This is evidenced in the incidence of inappropriate therapy regimens, with inapt duration of therapy as the leading explanation.

From the patient's perspective, the main economic implication was on the direct medical costs, particularly the increased cost of the actual antimicrobial therapy prescribed to manage various infections. Adherence of physicians to the established guidelines and selection of the most cost-effective therapy could have resulted in considerable cost savings.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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